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Caroline Brand

PAPEL DA OBESIDADE E DA APTIDÃO FÍSICA NA RELAÇÃO ENTRE O EXERCÍCIO FÍSICO E OS FATORES DE RISCO CARDIOMETABÓLICOS EM CRIANÇAS

Porto Alegre
2019

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Papel da obesidade e da aptidão física na relação entre o exercício físico e os fatores de risco cardiometabólicos em crianças

Tese de Doutorado apresentada como requisito para obtenção do grau de doutor(a) no programa de Pós-Graduação em Ciências do Movimento Humano da Escola de Educação Física, Fisioterapia e Dança da Universidade Federal do Rio Grande do Sul.

Orientadora: Prof[a]. Dr[a] Anelise Reis Gaya

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Tese de Doutorado apresentada ao Programa de Pós-Graduação em Ciências do Movimento Humano da Escola de Educação Física da Universidade Federal do Rio Grande do Sul, como requisito parcial para obtenção do título de Doutor(a) em Ciências do Movimento Humano.

Conceito final: ....

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“...Pra não perder a magia de acreditar na felicidade real e entender que ela mora no caminho e não no final...”

(Keylla Cristina Dos Santos Batista)

RESUMO

O objetivo dessa tese foi verificar o papel da obesidade e da aptidão física na relação entre o exercício físico e fatores de risco cardiometabólicos em crianças. Nesse sentido, foram definidos cinco objetivos específicos: 1) Analisar as associações entre percentual de gordura e aptidão cardiorrespiratória com fatores de risco cardiovasculares em crianças e verificar se o percentual de gordura atua como mediador da associação entre aptidão cardiorrespiratória e fatores de risco cardiovasculares; 2)Verificar o papel mediador e moderador da adiposidade na relação entre aptidão física com os fatores de risco cardiometabólicos, adipocitocinas e inflamação em crianças; 3) Investigar os efeitos de uma intervenção multicomponente nos componentes da síndrome metabólica, incluindo marcadores da doença hepática gordurosa não alcoólica em crianças em idade escolar com sobrepeso/obesidade e de baixo nível socioeconômico; 4)Verificar o efeito de uma intervenção multicomponente nos fatores de risco cardiometabólicos e determinar a prevalência individual de responsivos nos fatores de risco cardiometabólicos em crianças com sobrepeso e obesidade; 5) Verificar se o percentual de gordura, aptidão física, atividade física e consumo total de calorias mediam o efeito de uma intervenção multicomponente nos fatores de risco cardiometabólicos em crianças com sobrepeso e obesidade; Para responder os dois primeiros objetivos específicos foram utilizados dados de corte transversal de uma amostra de crianças de Porto Alegre-RS, com idades entre 7 e 11 anos. Já para contemplar os demais objetivos específicos, foram utilizados dados longitudinais de crianças, na faixa etária entre 7 e 13 anos, com sobrepeso e obesidade de João Pessoa-Paraíba. Estas, foram submetidas à um programa de intervenção multicomponente, consistindo de exercício físico, orientação nutricional e intervenção parental, com a finalidade de melhorar os fatores de risco cardiometabólicos. A partir disso, os resultados demonstraram que a obesidade atua como mediadora da relação entre a aptidão física e os fatores de risco cardiometabólicos. Ainda, a força da relação entre a aptidão cardiorrespiratória e aptidão muscular com os fatores de risco metabólicos varia de acordo com o grau de adiposidade, ou seja, a obesidade é moderadora dessa relação. O programa de intervenção multicomponente foi efetivo, promovendo melhora dos fatores de risco cardiometabólicos em crianças com sobrepeso e obesidade, sendo que esse efeito foi mediado pelo aumento da aptidão muscular e atividade física, bem como diminuição da ingestão total de calorias e adiposidade. Portanto, os estudos apresentados nessa tese reforçam o papel determinante da obesidade nos fatores de risco cardiometabólicos e estabelecem que, para que se alcancem resultados benéficos nesses fatores de risco, é necessário que os programas de intervenção estejam voltados além da redução da adiposidade, para o aumento da aptidão muscular e atividade física vigorosa e diminuição da ingestão total de calorias.

Palavras-Chave: aptidão cardiorrespiratória, aptidão muscular, fatores de risco, saúde, crianças

ABSTRACT

The aim of this thesis was to verify the role of obesity and physical fitness in the relationship between physical exercise and cardiometabolic risk factors in children. In this sense, five specific aims were established: 1) To analyze the association between the percentage of body fat and cardiorespiratory fitness with cardiovascular risk factors in children and to examine whether percentage of body fat acts as a mediator on the association between cardiorespiratory fitness and cardiovascular risk factors; 2) To verify the mediator and moderator role of adiposity in the relationship between physical fitness with cardiometabolic risk factors, adipocytokines and inflammation in children; 3) To investigate the effects of a 12-week multicomponent intervention program in markers of metabolic syndrome and nonalcoholic fatty liver disease in Brazilian overweight/obese low-income school-aged children; 4) To verify the effect of a multicomponent intervention on cardiometabolic risk factors, and to determine the individual prevalence of responsiveness on cardiovascular risk factors among overweight/obese children; 5) To verify whether percentage of body fat, physical fitness, physical activity and total calorie intake mediate a multicomponent intervention effect on cardiometabolic risk factors in overweight/obese children. Cross-sectional data from a sample of children from Porto Alegre-RS were used to answer the first two specific aims. While to contemplate the other specific aims, it was used a data base with overweight/obese children from João Pessoa-Paraíba. These were included in a multicomponent intervention program, consisting of physical exercise, nutritional counseling and parental intervention, with the purpose of improving cardiometabolic risk factors. From this, the results showed that obesity is a mediator in the relationship between physical fitness with cardiometabolic risk factors. Besides, the strength of the relationship between cardiorespiratory fitness and muscular fitness with cardiometabolic risk factors varies according to the degree of adiposity, that is, obesity moderates this relationship. The multicomponent intervention program was effective, promoting improvement in cardiometabolic risk factors in overweight/obese children, and this effect was mediated by increasing muscular fitness and physical activity, as well as decreasing total calorie intake and adiposity. Therefore, the studies presented in this thesis reinforce the detrimental role of adiposity in cardiometabolic risk factors and establish that to achieve beneficial results in these risk factors it is necessary that intervention program be focus beyond the reduction of adiposity, for increasing muscular fitness and vigorous physical activity and decreasing total calorie intake.

Keywords: cardiorespiratory fitness, muscular fitness, risk factors, health, children

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LISTA DE ABREVIATURAS

%BF - Percentage of body fat

ALT - Alanina aminotransferase

AM - Aptidão muscular

AMP - Adenosina monofosfato

AMPK - Monofosfato adenosina quinase

ANOVA- Mixed analysis of variance

APCR - Aptidão cardiorrespiratória

AST - Aspartato aminotransferase

BMI - Body mass index

CG - Control group

CI - Confidence interval

CMRF - Cardiometabolic risk factors

CNPq – Conselho Nacional de Desenvolvimento Científico e Tecnológico

CRF - Cardiorespiratory fitness

CRP - C-reactive protein

CVD - Cardiovascular disease

DPB - Diastolic blood pressure

eNOS - Óxido nítrico-sintase endotelial

FRCM - Fatores de risco cardiometabólicos

HDL-C - Colesterol de lipoproteína de alta densidade

HOMA-IR - Homeostasis model assessment of insulin resistance

HOMA-IR - Modelo de homestase da resistência à insulina

HR - Heart rate

IE - Indirect effect

IG – Intervention group

IL-6 - Interleucina-6

IMC - Índice de massa corporal

IR - Insulin resistance

LDL-C - colesterol de lipoproteína de baixa densidade

LLS - Lower limb strength

MAP - Mean arterial pressure

MetS - Metabolic syndrome

MF - Muscular fitness

NAFLD - Nonalcoholic fatty liver disease

PA - Physical activity

PCR - Proteína C-reativa

PROESP-Br - Projeto Esporte Brasil

SBP - Systolic blood pressure

SD - Standard deviation

SPSS - Statistical Package for Social Sciences

TC - Total cholesterol

TG - Triglycerides

TNF-α - Fator de necrose tumoral

ULS - Upper limb strength

SUMÁRIO

INTRODUÇÃO

A saúde na infância e adolescência vêm sendo foco de inúmeras pesquisas recentes, que indicam um aumento na ocorrência de fatores de risco cardiometabólicos desenvolvidos precocemente (MOTLAGH et al., 2018; SAPUNAR et al., 2018). Além disso, observa-se hoje a agregação de fatores de risco, tais como resistência à insulina, concentrações elevadas de triglicerídeos e colesterol de lipoproteína de baixa densidade (LDL-C) e baixos níveis de colesterol de lipoproteína de alta densidade (HDL-C) em crianças e adolescentes (AHRENS et al., 2014). Cenário preocupante ao se considerar que estes aspectos estão relacionados ao aumento de doenças crônicas na idade adulta, dentre elas diabetes mellitus e hipertensão (WEIHRAUCH-BLÜHER; SCHWARZ; KLUSMANN, 2019). Nesse âmbito, ressalta-se a obesidade como elemento central, responsável pela origem de diversas desordens metabólicas, tais como dislipidemias, inflamação e esteatose hepática não alcoólica (GUILHERME et al., 2008; POLYZOS; KOUNTOURAS; MANTZOROS, 2017).

Ainda que o desenvolvimento dos fatores de risco cardiometabólicos esteja atrelado a predisposição genética em alguns indivíduos, grande parte é resultado de hábitos inadequados (SILVENTOINEN et al., 2016). Nesse contexto, a infância e adolescência são essenciais para o estabelecimento de um estilo de vida saudável, já que nesse período são determinadas diversas características que tendem a ser mantidas na fase adulta (ORTEGA et al., 2013; ROVIO et al., 2018). Em vista disso, comportamentos como prática de atividade física regular, bons hábitos alimentares, e uma rotina ativa devem ser incentivados e incorporados precocemente (LIPSKY et al., 2015; TRUDEAU; LAURENCELLE; SHEPHARD, 2009). Entretanto, o que vem sendo observado é que hábitos prejudiciais à saúde são cada vez mais recorrentes, estando estes atreladas ao alarmante aumento da prevalência de sobrepeso e obesidade e aos baixos níveis de aptidão física encontrados em crianças e adolescentes nos últimos anos (TOMKINSON, LANG, TREMBLAY, 2017; WHO, 2016).

O exercício físico é uma estratégia eficaz para reverter esse quadro, já que sua prática regular está atrelada a diminuição do excesso de peso e aumento da aptidão cardiorrespiratória (APCR) e muscular, considerados importantes indicadores de saúde (ORTEGA et al., 2008). Ademais, promove diversos benefícios à saúde, sendo amplamente recomendado como forma de tratamento e prevenção da obesidade e dos distúrbios metabólicos a ela relacionados (GARCÍA-HERMOSO; RAMÍREZ-VÉLEZ; SAAVEDRA, 2019; ORCI et al., 2016; SIRICO et al., 2018). É importante considerar também que o efeito do exercício físico nos fatores de risco cardiometabólicos pode ser causado por mecanismos indiretos (ÁLVAREZ et al., 2018; MORA-RODRIGUEZ et al., 2018). Nesse sentido, nossa hipótese centra-se na perspectiva de que a obesidade é mediadora e moderadora da relação entre a aptidão física e os fatores de risco cardiomatabólicos e que os efeitos benéficos do exercício físico ocorrem a partir da diminuição da adiposidade, bem como da melhora da aptidão física.

Neste contexto a presente tese, na forma de uma série de artigos, tem por objetivo geral:

- Verificar o papel da obesidade e da aptidão física na relação entre o exercício físico e fatores de risco cardiometabólicos em crianças.

O papel da obesidade e da aptidão física na relação do exercício físico e fatores de risco cardiometabólicos será verificado a partir dos seguintes objetivos específicos:

- Analisar as associações entre percentual de gordura e aptidão cardiorrespiratória com fatores de risco cardiovasculares em crianças e verificar se o percentual de gordura atual como mediador da associação entre aptidão cardiorrespiratória e fatores de risco cardiovasculares;
- Verificar o papel o papel mediador e moderador da adiposidade na relação entre aptidão física com os fatores de risco cardiometabólicos, adipocitocinas e inflamação em crianças;
- Investigar os efeitos de uma intervenção multicomponente nos componentes da síndrome metabólica, incluindo marcadores da esteatose hepática não alcoólica em crianças em idade escolar com sobrepeso/obesidade e de baixo nível socioeconômico;
- Verificar o efeito de uma intervenção multicomponente nos fatores de risco cardiometabólicos e determinar a prevalência individual de responsivos nos fatores de risco cardiometabólicos em crianças com sobrepeso e obesidade.
- Verificar se o percentual de gordura, aptidão física, atividade física e a ingestão total de calorias mediam o efeito de uma intervenção multicomponente nos fatores de risco cardiometabólicos em crianças com sobrepeso e obesidade;

A relevância do presente estudo justifica-se pela necessidade de preencher algumas inconsistências na literatura, principalmente no que se refere ao papel da obesidade e da aptidão física nos fatores de risco cardiometabólicos. Alguns dados indicam que a manutenção de um peso corporal adequado seria mais determinante para a saúde metabólica do que a aptidão física (DEMMER et al., 2017; PÉREZ-BEY et al., 2018), enquanto outros apontam que a aptidão física poderia combater os efeitos deletérios atribuídos a adiposidade (OKTAY et al., 2017; ORTEGA et al., 2018). No entanto, não existe um consenso a esse respeito, especialmente quando se trata da população infantil.

Além disso, a associação entre APCR e aptidão muscular com as adipocitocinas (leptina e adiponectina) já está descrita na literatura (AGOSTINIS-SOBRINHO et al., 2017a; STEENE-JOHANNESSEN et al., 2013), entretanto, de acordo com nosso conhecimento, pouco se sabe sobre o papel mediador e moderador da adiposidade nessa relação. Ou seja, pretende-se entender se a adiposidade explica as associações entre a aptidão física e os fatores de risco cardiometabólicos e se essas relações ocorrem de forma diferentes em crianças de peso normal e excesso de peso.

Cabe ressaltar ainda que os efeitos diretos do exercício físico na saúde cardiometabólica são conhecidos, porém poucos estudos foram desenvolvidos com a finalidade de determinar quais os potenciais mediadores envolvidos na sequência causal da relação entre o efeito da intervenção nos fatores de risco cardiometabólicos analisados. Nesse contexto, trata-se especificamente de compreender qual a contribuição da diminuição do percentual de gordura e do aumento da aptidão física na redução dos fatores de risco das doenças cardiometabólicas em crianças. Por fim, destaca-se que o conhecimento dos mecanismos mediadores permite determinar em quais aspectos devem ser focados as intervenções voltadas para a prevenção e promoção da saúde de crianças.

A partir disso, esta tese é constituída por sete capítulos:

- Capítulo I- Referencial teórico: cujo finalidade é demarcar o referencial teórico que sustenta o objetivo geral da tese;
- Capítulo II- Artigo 1: O papel da gordura corporal na relação entre a aptidão cardiorrespiratória com os fatores de risco cardiovasculares em crianças brasileiras. Publicado no periódico *Motriz*;
- Capítulo III- Artigo 2: Papel mediador e moderador da adiposidade na relação entre a aptidão física com fatores de risco cardiometabólicos, adipocitocinas e inflamação em crianças. Submetido no periódico *Pediatric Exercise Science*;
- Capítulo IV- Artigo 3: Efeito de uma intervenção multicomponente em componentes da síndrome metabólica: um estudo com crianças em idade escolar, com sobrepeso/obesidade e baixo nível socioeconômico. Submetido no periódico *Sports Science for Health*;

- Capítulo V- Artigo 4: Efeito de uma intervenção multicomponente em fatores de risco cardiometabólicos e prevalência individual de responsivos em crianças em idade escolar, com sobrepeso e obesidade. Submetido no periódico *Journal of Sports Science*;
- Capítulo VI- Artigo 5: Efeito de uma intervenção multicomponente em fatores de risco cardiometabólicos em crianças Brasileiras com sobrepeso e obesidade: uma análise de mediação. Submetido no periódico *Nutrition, Metabolism and Cardiovascular diseases;*
- Capítulo VII- Considerações finais e referências: Incluem aspectos conclusivos da tese analisada como um todo, bem como as referências utilizadas na introdução e referencial teórico.

As seções materiais e métodos, bem como resultados, discussão e referências encontram-se nos respectivos manuscritos científicos.

CAPÍTULO I

REFERENCIAL TEÓRICO

Obesidade e aptidão física

Fatores de risco cardiometabólicos em crianças

Efeitos de programas de intervenção nos fatores de risco cardiometabólicos

Papel mediador e moderador da adiposidade na relação entre aptidão física e fatores de risco cardiometabólicos, bem como no efeito do exercício nessas variáveis

REFERENCIAL TEÓRICO

Obesidade e aptidão física

A obesidade é um distúrbio metabólico caracterizado pelo acúmulo excessivo de gordura corporal, resultado de um balanço energético positivo crônico, com o consumo energético excedendo o gasto (LAVIE et al., 2016). Essa condição representa um importante risco para a saúde, contribuindo para o desenvolvimento de diversos fatores de risco cardiovasculares, como diabetes mellitus tipo 2, hipercolesterolemia, hipertensão arterial e inflamação, além de desempenhar efeitos adversos na estrutura e função cardíaca (BASTIEN et al., 2014; LAVIE et al., 2016).

O excesso de peso na infância e adolescência representa um grave problema de saúde pública. No mundo, a prevalência de sobrepeso e obesidade em crianças e adolescentes aumentou de 4% em 1975 para 18% em 2016 (WHO, 2016). Entretanto, depois de anos de um aumento consistente nesses dados, alguns estudos vêm apontando para uma manutenção ou até mesmo um declínio, observado principalmente em países desenvolvidos, como Estados Unidos e Austrália (HARDY et al., 2017; OGDEN et al., 2012). Além disso, a prevalência de obesidade está diminuindo em adolescentes de maior nível socioeconômico e aumentando naqueles de baixo nível socioeconômico (FREDERICK; SNELLMAN; PUTNAM, 2014).

No Brasil, um estudo de tendência desenvolvido entre os anos de 1975 e 1997 demonstrou um aumento na prevalência de sobrepeso e obesidade de 4,1% para 13,9% (WANG; MONTEIRO; POPKIN, 2018). Dados mais recentes indicam que 30% das crianças e adolescentes foram classificados com sobrepeso e obesidade no ano de 2011 (FLORES et al., 2013). Um fator extremamente preocupante, nesse contexto, é que a obesidade desenvolvida precocemente tem grandes chances de ser mantida na idade adulta (SIMMONDS et al., 2016). Ainda, pode impactar na incidência de fatores de risco cardiovasculares, bem como aumento na morbidade e mortalidade cardiovascular (SOMMER; TWIG, 2018).

Dentre as causas atribuídas a essa condição está a predisposição genética, que pode desempenhar importante papel na variação do índice de massa corporal (IMC) (SILVENTOINEN et al., 2016). Entretanto, essa suscetibilidade deve vir associada a contribuição de fatores ambientais e comportamentais, tais como hábitos alimentares, sedentarismo e nível socioeconômico. Fatores psicológicos, ambiente escolar e familiar também são determinantes (ALBUQUERQUE; NÓBREGA; MANCO, 2017; SAHOO et al., 2015).

Nesse contexto, a atividade física e a aptidão física são dois dos principais fatores associados ao sobrepeso e obesidade (CZYŻ et al., 2017). Entretanto, é elevado o número de crianças e adolescentes que não cumprem com a recomendação diária de 60 minutos de atividade física moderada a vigorosa (HALLAL et al., 2012; WORLD HEALTH ORGANIZATION, 2010). Ademais, crianças com sobrepeso e obesidade são menos fisicamente ativas e tem menores níveis de aptidão física, comparativamente aquelas de peso normal (RAISTENSKIS et al., 2016; SZMODIS et al., 2019).

Como consequência dos baixos níveis de atividade física nessa faixa etária, vem ocorrendo também declínio na aptidão física (TOMKINSON; LANG; TREMBLAY, 2017; VENCKUNAS et al., 2017). A aptidão física é uma medida integrada da maioria das funções corporais, incluindo, os sistemas musculoesquelético, cardiorrespiratório, hematocirculatório, psiconeurológico e endócrino-metabólico (ORTEGA et al., 2008). Em função disso, é considerada um importante indicador de saúde (ARTERO et al., 2011). A aptidão física relacionada a saúde consiste em diferentes componentes, como APCR, força e resistência muscular, composição corporal e flexibilidade (PESCATELLO, 2014).

Para o desenvolvimento desse trabalho, foram considerados especificamente a APCR e aptidão muscular. A APCR consiste na capacidade geral dos sistemas cardiovasculares e respiratórios e a habilidade de realizar exercício extenuante prolongando. Já a aptidão muscular consiste na capacidade de realizar trabalho contra uma resistência (ORTEGA et al., 2008). Dados de crianças e adolescentes brasileiros indicam que apenas 32% (27,7% meninos e 28,4% meninas) apresentam níveis de APCR adequados para saúde (GONÇALVES et al., 2018). Com relação a aptidão muscular os valores são um pouco mais elevados, com 40,2% de meninos com valores adequados e 31,9% das meninas (DAVOLI; LIMA; SILVA, 2018).

Estudos em crianças e adolescentes demonstram que bons níveis de aptidão física estão relacionados a efeitos benéficos na saúde metabólica (EKELUND et al., 2007; LANG; LAROUCHE; TREMBLAY, 2019). Nesse sentido, altos níveis de APCR e aptidão muscular são inversamente associados com diferentes fatores de risco metabólicos, como colesterol total, glicose, resistência à insulina, marcadores inflamatórios e obesidade (DRING et al., 2019; REUTER et al., 2019; RUIZ et al., 2016; SMITH et al., 2014). Além disso, a agregação desses fatores de risco está inversamente associada com esses componentes da aptidão física (ZAQOUT et al., 2016). Um perfil inflamatório mais saudável também é encontrado naquelas crianças e adolescentes com boa APCR e aptidão muscular (AGOSTINIS-SOBRINHO et al., 2017; STEENE-JOHANNESSEN et al., 2013). O mesmo é observado com relação as enzimas do fígado, com menores concentrações de alanina aminotransferase (ALT) encontradas em crianças com alta APCR (TRILK et al., 2014). Cabe destacar ainda que, bons níveis de aptidão cardiorrespiratória e muscular na infância e adolescência representam um papel protetor da saúde cardiometabólica na idade adulta (GARCÍA-HERMOSO; RAMÍREZ-CAMPILLO; IZQUIERDO, 2019; SCHMIDT et al., 2016).

No que se refere a relação entre a aptidão física e obesidade, cabe abordar os mecanismos pelos quais a APCR e aptidão muscular exercem seus efeitos na adiposidade. Entretanto, estes são complexos e não estão completamente entendidos. Especula-se que a influência da APCR na adiposidade está atrelada aos efeitos que o exercício aeróbico exerce na expressão e atividade da enzima cartinina palmitoil transferase, que controla o movimento dos ácidos graxos para a mitocôndria, assim como o aumento da atividade de enzimas β-hidroxiacil-CoA desidrogenase, que regulam a oxidação de gordura na mitocôndria (PURDOM et al., 2018). Além disso, o exercício aeróbico promove melhora da sensibilidade à insulina no tecido adiposo (OLIVEIRA et al., 2013). Com relação a aptidão muscular, seus efeitos na adiposidade estão atrelados ao aumento da eficiência metabólica do músculo, resultando em maior gasto energético diário (BOUCHARD; BLAIR; HASKELL, 2012).

Fatores de risco cardiometabólicos em crianças

Aspectos relacionados à saúde na infância e adolescência são considerados em diversas pesquisas que apontam para um cenário preocupante. Verifica-se um aumento na prevalência e severidade dos fatores de risco metabólicos (MOTLAGH et al., 2018; REUTER et al., 2016), que parecem se manifestar durante a infância, ocasionando maior risco de doenças cardiometabólicas na idade adulta (BUGGE et al., 2013). Além disso, observa-se hoje uma elevada ocorrência de agregação desses fatores (AHRENS et al., 2014), o que caracteriza a síndrome metabólica. Não existe um consenso para a definição dessa síndrome em crianças e adolescentes, entretanto os critérios diagnósticos concordam que alguns componentes essenciais devem estar presentes, como intolerância à glicose, obesidade central, hipertensão e dislipidemia (DE FERRANTI et al., 2004; GOODMAN et al., 2004; ZIMMET et al., 2007). Isso se reflete nos dados que apontam para uma prevalência de síndrome metabólica variando entre 6% a 39%, dependendo da definição do critério aplicado (REINEHR et al., 2007). Para superar essa barreira, vem sendo sugerido que os elementos da síndrome metabólica deveriam ser considerados como variáveis contínuas, através da soma dos z-escores de seus componentes, com a finalidade de quantificar o risco (ANDERSEN et al., 2015; EISENMANN, 2008).

A obesidade e a resistência à insulina são a origem fisiopatológica de diversos distúrbios metabólicos (RASK-MADSEN; KAHN, 2013). Nesse sentido, a insulina liga-se a receptores em múltiplos tecidos do corpo, incluindo fígado, gordura, músculo e vasos sanguíneos, causando diversos efeitos. Em condições normais, a insulina secretada pelas células β pancreáticas atua no fígado para suprimir a produção de glicose. Na condição de resistência a insulina, a supressão da produção de glicose hepática é prejudicada, ocorre capacidade reduzida da insulina em estimular a utilização da glicose. Então, as células β pancreáticas aumentam a produção e secreção de insulina como um mecanismo compensatório (RASK-MADSEN; KAHN, 2013). No entanto, mesmo em um estado resistente à insulina, nem todos os efeitos da insulina são prejudicados, a ação da insulina que estimula a lipogênese hepática não é prejudicada, causando a liberação de ácidos graxos livres e triglicerídeos na circulação, o que resulta em dislipidemia e deposição adiposa ectópica (BREMER; MIETUS-SNYDER; LUSTIG, 2012).

Uma das consequências do aumento da adiposidade é a resistência à insulina. A medida que esse tecido se expande, as células se tornam hipertróficas, sendo mais resistentes à ação da insulina para suprimir a lipólise (GUILHERME et al., 2008). A partir disso, quando a capacidade de armazenamento da gordura do tecido adiposo subcutâneo é excedida, resulta em aumento da gordura visceral (acúmulo de gordura em torno das vísceras e do peritônio, na borda dorsal do intestino e na superfície ventral do rim) (DESPRÉS, 2006) e ectópica (acúmulo de gordura em orgãos como fígado, músculo esquelético, pâncreas e coração) (SNEL et al., 2012).

Então, a gordura pode se acumular em diferentes tecidos, como é o caso da esteatose hepática não alcoólica. Essa doença é caracterizada pelo acúmulo de gordura patológica no fígado, que pode levar a danos hepáticos na forma de inflamação e fibrose (SIEGEL; ZHU, 2009). Estudos demonstram que elevadas concentrações séricas de aspartato aminotransferase (AST) e ALT, assim como ácido úrico, glicose de jejum e IMC são preditores da esteatose hepática não alcoólica em crianças e adolescentes (SARTORIO et al., 2007; VOS et al., 2017).

Além disso, o depósito de gordura ectópica resulta na liberação de adipocitocinas, causando um estado de inflamação de baixo grau, levando ao aumento de fatores inflamatórios como interleucina 6 (IL-6), fator de necrose tumoral (TNF-α) e proteína C-reativa (PCR) (YUDKIN, 2007). Portanto, o aumento da gordura corporal, o processo inflamatório de baixo grau e a resistência à insulina estão amplamente relacionados, sendo os principais agentes patológicos envolvidos no desenvolvimento dos fatores de risco cardiometabólicos (VOLP et al., 2008).

As inflamações crônicas de baixo grau são consequências do aumento da adiposidade e estão relacionadas ao aparecimento de outras doenças como, diabetes e lesões crônicas, provocando aumento na síntese de células, citocinas e proteínas pró-inflamatórias, tais como neutrófilos, monócitos, IL-6, PCR, dentre outras (VOLP et al., 2008). Essa resposta de aumento de neutrófilos e macrófagos está relacionada a maior síntese de IL-6 que aumenta a produção de PCR no fígado. Esta, por sua vez, diminui a atividade da óxido nítrico-sintase endotelial (eNOS), e a disponibilidade do vasodilatador óxido nítrico, além de aumentar a concentração do vasoconstritor endotelina; a partir disso, o processo de vasodilatação dependente do endotélio fica comprometido. Como efeito da diminuição da vasodilatação ocorre maior estresse de cisalhamento, provocando maiores danos ao vaso sanguíneo, o que favorece o processo de aterosclerose e formação de trombos. Cabe destacar que esse vaso em processo de aterosclerose também libera substâncias pró-inflamatórias, aumentando ainda o dano vascular e a inflamação (TEIXEIRA et al., 2014).

A PCR é um fator independente de risco cardiovascular, sendo considerada melhor preditor, quando comparada a fatores de risco tradicionais como LDL-C e circunferência da cintura (SIGDEL, 2014). Nesse sentido, estudos com crianças e adolescentes demonstram que os concentrações de PCR estão associados positivamente com a adiposidade e com o risco cardiovascular (BO et al., 2010; BUGGE et al., 2012). Além disso, esse marcador está inversamente relacionado com a APCR e aptidão muscular (STEENE-JOHANNESSEN et al., 2013).

Além do tecido adiposo, o músculo esquelético também atua na secreção de citocinas, denominadas miocinas (PEDERSEN; FEBBRAIO, 2008). As miocinas produzidas pelo músculo esquelético em resposta à contração muscular medeiam alguns dos benefícios causados pelo exercício físico, inibindo o efeito nocivo das adipocitocinas. Portanto, o músculo esquelético é caracterizado como um órgão secretor capaz de comunicar-se com outros órgãos por meio de fatores humorais, liberados na corrente sanguínea, dentre os quais estão as miocinas IL-6, interleucina-8 e interleucina-15 (PEDERSEN, 2013; NIELSEN; PEDERSEN, 2007). A primeira identificada foi a IL-6, relacionada a alguns dos efeitos anti-inflamatórios do exercício, pois inibe a produção de TNF-α e estimula a liberação de outras citocinas anti-inflamatórias, como a interleucina-10 (PEDERSEN; FEBBRAIO, 2012).

Dadas as funções do tecido adiposo e sua relação com o processo inflamatório e a resistência à insulina, cabe agora considerar, de forma mais específica, as adipocitocinas (leptina e adiponectina) que foram investigadas no presente estudo.

A adiponectina é uma proteína, secretada pelo tecido adiposo e está envolvida na regulação do balanço energético, na inibição da inflamação vascular e no aumento da sensibilidade à insulina (GHADGE; KHAIRE; KUVALEKAR, 2018; PARKER-DUFFEN; WALSH, 2014). Está relacionada ainda com os metabolismos glicídico e lipídico, pois promove a fosforilação da adenosina monofosfato (AMP) através da monofosfato adenosina quinase (AMPK). Uma vez ativada, essa enzima atua no fígado diminuindo a síntese de lipídios e estimulando a queima de gordura, além de bloquear a produção de glicose. Já na musculatura esquelética, a AMPK atua principalmente estimulando a captação de glicose (YAMAUCHI et al., 2001; YAMAUCHI et al., 2002). Além disso, altas concentrações de adiponectina desempenham papel protetivo na síndrome metabólica, relacionando-se inversamente com a resistência à insulina, pressão arterial, triglicerídeos e glicose (CHOI et al., 2007; PANAGOPOULOU et al., 2008). Em crianças obesas, seus níveis encontram-se diminuídos, quando comparados a eutróficas (JAMURTAS et al., 2015). Entretanto, recentemente estudos demonstraram que altas concentrações de adiponectina são associadas com um risco aumentado de doenças cardiovasculares em adultos, indicando uma relação paradoxal da adiponectina com a saúde (CHOI et al., 2015; ESMAILI; XU; GEORGE, 2014). Ainda, contrariamente ao esperado, dados indicam relação inversa da adiponectina com APCR em adolescentes (AGOSTINIS-SOBRINHO et al., 2017a; MARTINEZ-GOMEZ et al., 2012). Em vista disso, mesmo que as concentrações de adiponectina sejam reduzidos em indivíduos obesos, o seu papel e sua relação com a saúde metabólica necessitam de maiores esclarecimentos, especialmente em crianças e adolescentes.

A leptina é um hormônio secretado pelos adipócitos, que inibe a ingestão de alimentos e estimula o gasto de energia (YADAV et al., 2013). Em situações normais, a leptina reduz a ânsia de comer quando a ingesta calórica mantém as reservas ideais de gordura, isso acontece mediante sua influência sobre certos neurônios na região hipotalâmica, os quais estimulam a produção de substâncias químicas que diminuem o apetite e/ou reduzem os níveis de substâncias neuroquímicas que estimulam o mesmo. Com um gene defeituoso para a produção de leptina pelo adipócito e/ou para a sensibilidade do hipotálamo à leptina (o que ocorre provavelmente nos seres humanos), o cérebro não consegue avaliar adequadamente o estado do tecido adiposo no corpo, o que poderia explicar a possível persistência da ânsia de comer (MCARDLE; KATCH; KATCH, 2013). A partir disso, surgiu o conceito de resistência à leptina, que é utilizado para definir estados de obesidade com hiperleptinemia e/ou uma resposta diminuída a administração de leptina (CRUJEIRAS et al., 2015). Então, a resistência à leptina está envolvida na patogênese da obesidade, já que uma dieta rica em gordura desencadeia resistência central e periférica à leptina e consequentemente hiperleptinemia devido a expansão do tecido adiposo (SCARPACE et al., 2005). Portanto, a falta de resposta à leptina afeta a regulação da ingestão alimentar, a absorção de nutrientes, o metabolismo e a sensibilidade a insulina, levando à desregulação do balanço energético (CRUJEIRAS et al., 2015).

Em crianças e adolescentes a leptina vem sendo considerada um marcador de síndrome metabólica e resistência à insulina (ANDERSEN et al., 2015; GONZAGA et al., 2014). Nappo et al. (2017) demonstraram que altas concentrações de leptina são associadas com a síndrome metabólica, mesmo após ajustes para o IMC e massa gorda em crianças. Além disso, quanto maiores os níveis de APCR e aptidão muscular, menores as concentrações dessa adipocitocina (DELGADO-ALFONSO et al., 2018).

Por fim, a escolha da utilização desses marcadores (leptina, adiponectina e PCR) em detrimento de outros, se deu em virtude de sua estreita relação com os fatores de risco metabólicos, incluindo a resistência à insulina. Ainda, essas relações podem servir como indicadores precoce de lesões em órgãos-alvo.

Efeitos de programas de intervenção nos fatores de risco cardiometabólicos

Os benefícios do exercício físico para a prevenção e promoção da saúde em crianças e adolescentes estão amplamente descritos na literatura (GARCÍA-HERMOSO; RAMÍREZ-VÉLEZ; SAAVEDRA, 2019; POZUELO-CARRASCOSA et al., 2018). Sua prática regular promove adaptações positivas em hormônios metabólicos, sendo também considerado uma importante ferramenta no tratamento da inflamação e das complicações relacionadas a obesidade (CAYRES et al., 2016). Entretanto, a magnitude dos benefícios pode variar de acordo com o tipo, a intensidade e a duração do exercício (PAES; MARINS; ANDREAZZI, 2015).

Nesse sentido, recentes revisões sistemáticas e metanálises vem abordando esses desfechos, tanto em crianças e adolescentes com sobrepeso e obesidade, quanto naquelas de peso normal. García-hermoso, Ramírez-vélez e Saavedra (2019) indicaram que intervenções baseadas em exercício físico promoveram melhoras em alguns parâmetros antropométricos, como massa corporal, IMC, obesidade central e massa gorda, bem como em parâmetros cardiovasculares (triglicerídeos, pressão arterial sistólica e diastólica, glicose e insulina de jejum), além da APCR, em crianças e adolescentes com sobrepeso e obesidade. Esse estudo demonstrou ainda que para o alcance de efeitos favoráveis nos parâmetros metabólicos é recomendável que a intervenção seja realizada de quatro a doze semanas, com uma frequência semanal de três vezes ou até menos e com duração da sessão de sessenta minutos cada.

De acordo com a revisão de Sirico et al. (2018) o treinamento com exercícios aumenta as concentrações de adiponectina e diminui as concentrações de leptina em crianças obesas. Além disso, para o alcance de resultados favoráveis na leptina é necessário que os programas sejam de longa duração e que promovam também redução da gordura corporal, já que ambas estão amplamente relacionadas (GARCÍA-HERMOSO et al., 2017). Com relação a esteatose hepática não alcoólica, exercícios aeróbicos e resistidos, com intensidades moderadas a vigorosas, volume maior ou igual a sessenta minutos a sessão e frequência maior ou igual a três vezes semanais, com o objetivo de melhorar a APCR e aptidão muscular, promoveram benefícios na gordura hepática, diminuição da concentração de AST e ALT em adolescentes (ORCI et al., 2016). Ainda, recente metanálise comparou o efeito do treinamento intervalado de alta intensidade e o treinamento contínuo de intensidade moderada e demonstrou que o primeiro é mais efetivo no aumento da APCR em crianças e adolescentes (CAO; QUAN; ZHUANG, 2019).

Além do importante papel do exercício físico na saúde metabólica, existem outras variáveis de extrema importância que influenciam nesses desfechos, dentre elas, a alimentação saudável e o suporte parental. Ademais, a prevenção e tratamento da obesidade, bem como de disfunções metabólicas, é complexa e necessita de uma abordagem multicomponente, que envolva a família e contemple aspectos sociais e individuais, para que de fato seja possível alcançar e manter um estilo de vida saudável (ELVSAAS et al., 2017; RANUCCI et al., 2017).

O foco não deve ser somente na atividade física, mas também nos hábitos alimentares saudáveis e na diminuição do comportamento sedentário. Nesse contexto, o papel dos pais é determinante uma vez que possibilita ações em múltiplos fatores que afetam a saúde, incentivando, por exemplo, o consumo de frutas e legumes e limitando o consumo de doces e alimentos industrializados, colocando regras que diminuam o tempo de tela e dando suporte constante para a prática de atividade física (PYPER; HARRINGTON; MANSON, 2016).

Em vista disso, algumas intervenções multicomponentes vêm sendo desenvolvidas com a finalidade de alterar o estilo de vida de crianças e adolescentes e consequentemente melhorar sua saúde cardiometabólica. Uma revisão sistemática com adolescentes latinos com sobrepeso indicou que exercícios de força, exercícios aeróbicos, intervenção nutricional e participação dos pais foram componentes de programas de intervenção efetivos na diminuição da obesidade e das complicações metabólicas relacionadas (DAVIS et al., 2010). Africa, Newton e Schwimmer (2016) analisaram diferentes estudos na literatura no que se refere a esteatose hepática não alcoólica em crianças e reportaram diminuição nas concentrações de ALT em nove estudos, sendo que a maioria das intervenções era baseada em exercício físico e nutrição. Além disso Labayen et al. (2019) demonstrou que o exercício físico, aliado a um programa de educação psicológica e estilo de vida promoveu redução da adiposidade, resistência à insulina e esteatose hepática em crianças com sobrepeso e obesidade. A efetividade de intervenções no estilo de vida na redução do diabetes e do risco de doenças cardiovasculares foi demonstrada ne revisão de Van Buren e Tibbs (2014), que recomenda a expanção do foco de intervenções tradicionais que incluem dieta e atividade física, para inclusão de outros fatores de risco, como uso de tabaco e depressão.

Intervenções multicomponentes também são voltadas especificamente para o tratamento e prevenção da obesidade e os resultados demonstram sua eficácia na diminuição do IMC, de seis até vinte e quatro meses de intervenção (ELVSAAS et al., 2017). Adicionalmente, programas desenvolvidos no ambiente escolar, que combinam dieta e exercício físico, bem como atividades realizadas em casa parecem ser efetivas para reduzir a obesidade em crianças (BLEICH et al., 2018). A importância de uma abordagem multicomponente para redução da obesidade se reforça, ao analisarmos, por exemplo, o estudo de Martínez-Vizcaíno et al. (2019), o qual interviu apenas no exercício físico, atraves de três sessões semanais, durante sete meses no ambiente escolar. Os resultados não demonstraram diminuição da obesidade, apesar de ter ocorrido melhora da APCR e aptidão muscular.

Contudo, é importante considerar que a maioria desses estudos vêm sendo realizados em países de alto nível socioeconômico. Nos estudos de revisões acima descritos, que abordaram intervenções multicomponentes, apenas três foram realizadas no Brasil. Leme et al. (2016) demonstraram diminuição da circunferência da cintura, tempo de tela e aumento no consumo de vegetais em meninas adolescentes, após seis meses de intervenção realizada no ambinete escolar, baseada em atividade atividade física e nutrição. Dois estudos abordaram o efeito de um ano de intervenção com dieta, exercício físico e suporte psicológico em fatores de risco metabólicos e adipocitocinas em adolescentes e encontraram melhoras em diversos parâmetros, como leptina, adiponectina, HDL-C, colesterol total e modelo de homestase da resistência à insulina (HOMA-IR), além de diminuição no IMC e gordura corporal (CAMPOS et al., 2012; SANCHES et al., 2014). Ressalta-se ainda que dentre esses, o estudo de

Bianchini et al. (2013) foi o único que aplicou intervenção voltada aos pais (uma vez ao mês), além do exercício físico (três vezes semanais) e da intervenção nutricional e psicológica (uma vez na semana). Os resultados demonstraram que houve melhora do colesterol total e pressão arterial sistólica e diastólica, assim como de parâmetros antropométricos, gordura corporal e APCR após dezesseis semanas, em crianças e adolescentes brasileiros com obesidade.

Portanto, faltam evidências acerca de estratégias eficazes para a promoção e prevenção da saúde em locais de predominância de baixo nível socioeconômico. Essa necessidade se justifica ao se considerar que crianças e adolescentes que vivem em zonas de vulnerabilidade têm menos acesso a alimentação saudável e atividade física, e ainda aquelas que vivem sem os pais têm menos oportunidades de um estilo de vida saudável, comparados aquelas que pertencem a famílias de alta renda (ROMERO, 2005).

Papel mediador e moderador da adiposidade na relação entre aptidão física e fatores de risco cardiometabólicos, bem como no efeito do exercício nessas variáveis

A relação entre aptidão física, obesidade e saúde cardiometabólica está amplamente descrita na literatura (DELGADO-ALFONSO et al., 2018; FRIEDEMANN et al., 2012). Porém, considerando que a aptidão física está inversamente associada a adiposidade (SANTOS et al., 2019), ambas podem estar relacionadas com a mesma via causal, dificultando estabelecer até que ponto cada variável afeta os diferentes indicadores de saúde. Nesse sentido, a análise de mediação permite determinar o percentual de efeito total (a influência de uma variável independente na variável dependente) que é exercido por uma terceira variável (mediadora) (BARON; KENNY, 1986).

A partir disso, estudos vêm analisando o papel mediador da adiposidade na relação entre a aptidão física e fatores de risco metabólicos. Dados recentes demonstraram que a adiposidade, avaliada através do IMC, medeia completamente a relação entre APCR e aptidão muscular com um escore de fatores de risco cardiovasculares em crianças e adolescentes (PÉREZ-BEY et al., 2019; PÉREZ-BEY et al., 2018). Já de acordo com Garcia-Hermoso et al. (2019), a relação entre a força de pressão manual com um escore de fatores de risco metabólicos foi atenuada pela inclusão da adiposidade no modelo. Ainda, Pozuelo-Carrascosa et al. (2017) encontraram que a obesidade explica a relação entre APCR e a média da pressão arterial, em aproximadamente 62% nos meninos (mediador completo) e 35% nas meninas (mediador parcial). No que se refere as adipocitocinas e marcadores inflamatórios as evidências disponíveis são limitadas. De acordo com Garcia-Hermoso et al. (2017) a relação entre APCR e PCR é completamente explicada pelo IMC.

Portanto, enquanto alguns resultados indicam que a adiposidade explica completamente a relação entre aptidão física e fatores de risco cardiometabólicos, outros encontraram que essa variável é um mediador parcial dessa associação. Então, o presente estudo pretende preencher algumas lacunas nesse sentido, partindo da hipótese que a adiposidade é um mediador parcial da relação entre a aptidão física e os fatores de risco cardiometabólicos em crianças.

A interação entre obesidade e aptidão física e seus desfechos na saúde metabólica também vem sendo investigada. Essa interação, também denominada moderação se refere a força da relação entre as variáveis independentes e dependentes que pode variar de acordo com uma terceira variável (BARON; KENNY, 1986). Nesse contexto, o conceito "Fat but Fit" sugere que moderados a altos níveis de APCR poderiam atenuar as consequências metabólicas deletérias atribuídas a um excesso de adiposidade central e total (Oktay et al., 2017; Ortega et al., 2018). Em crianças e adolescents algumas evidências confirmam esse paradoxo (DUBOSE; EISENMANN; DONNELLY, 2007; EISENMANN, 2007; MESA et al., 2006). Por outro lado, Demmer et al. (2017); Nyström et al. (2017) e Pérez-Bey et al. (2019) encontraram que o peso corporal adequado exerce maior proteção com relação aos fatores de risco cardiovasculares do que altos níveis de APCR.

De acordo com Silva et al. (2017) uma das causas para essas discrepâncias encontradas na literatura pode ser o uso da circunferência da cintura no escore de risco metabólico, o que poderia superestimar o papel da obesidade. Esse estudo comparou o uso de dois escores de risco metabólicos, um que incluiu a circunferência da cintura, pressão arterial sistólica e diastólica, glicose, HDL-C e triglicerídeos e o outro excluindo o indicador de obesidade central. Os resultados indicaram que a APCR teve relação mais forte e a obesidade mais fraca, com o escore de risco metabólico sem a circunferência da cintura, quando comparado ao outro escore. De fato, diversos estudos que abordam as relações entre APCR e obesidade em crianças e adolescentes utilizam a circunferência da cintura no escore de risco metabólico (DUBOSE; EISENMANN; DONNELLY, 2007; EISENMANN, 2007; PÉREZ-BEY et al., 2019).

No que se refere a interação entre aptidão muscular e adiposidade, foi encontrado que a força de preensão manual é associada com menor escore de fatores de risco metabólicos somente em crianças com sobrepeso, indicando um efeito protetor dessa variável apenas em indivíduos com esse fenótipo e não naqueles com maiores níveis de gordura corporal (GARCIA-HERMOSO et al., 2019). Resultados de um estudo recente demonstraram que o escore de fatores de risco cardiovasculares foi mais influenciado pela adiposidade do que pela aptidão muscular em crianças e adolescentes. Ainda, foi encontrado um papel protetor da aptidão muscular somente em indivíduos com sobrepeso e não nos obesos (PÉREZ-BEY et al., 2018). De acordo com outros estudos, a aptidão muscular exerceu um papel protetor nos fatores de risco cardiovasculares, tanto em crianças e adolescentes com sobrepeso e obesidade, o que significa que a aptidão muscular poderia combater, pelo menos em parte, os efeitos deletérios da obesidade em fatores de risco cardiovasculares (ARTERO et al., 2014; ARTERO et al., 2011).

Ademais, é importante considerar que o efeito nos fatores de risco cardiometabólicos, após um programa de intervenção pode ser parcialmente mediado por mecanismos indiretos (ÁLVAREZ et al., 2018; MORA-RODRIGUEZ et al., 2018). Ou seja, mudanças em variáveis como a aptidão física, atividade física, percentual de gordura e ingestão de alimentos podem interferir na sequência causal entre a intervenção e os fatores de risco cardiometabólicos. Nessa perspectiva, Mora-Rodriguez, Ortega, Morales-Palomo e Ramirez-Jimenez (2018) investigaram o efeito de dezesseis semanas de treinamento aeróbico em adultos com síndrome metabólica e encontraram uma redução média de 1,4% no peso corporal e um aumento médio de 16% na APCR. Os resultados indicaram que a perda de peso (ainda que em baixa proporção) e não o aumento da APCR promoveu diminuição do escore dos fatores de risco cardiometabólicos. Da mesma forma, dezesseis semanas de treinamento aeróbico intenso que promoveu aumento da APCR não foi capaz de reduzir os níveis de triglicerídeos, quando o peso corporal não foi reduzido (ORTEGA et al., 2014). O mesmo foi encontrado com relação a resistência à insulina após oito semanas de treinamento (STUART et al., 2013). Portanto, esses dados sugerem que a perda de peso durante um programa de exercícios tem mais influência na saúde metabólica do que o aumento da APCR.

Entretanto, os estudos apresentados acima foram realizados em adultos e os dados acerca de crianças são mais limitados. Álvarez, Martínez e Izquierdo (2017) encontraram que a diminuição da circunferência da cintura contribui diretamente para a explicar a diminuição do modelo de homeostase de resistência à insulina (HOMA-IR), enquanto que o aumento da força de membros inferiores pode contribuir diretamente para a diminuição da glicose, após seis meses de treinamento.

A partir disso, pretende-se determinar o efeito de uma intervenção nos fatores de risco cardiometabólicos em crianças e principalmente trazer novos conhecimentos acerca da influência de diferentes variáveis nessa relação. Nesse contexto, espera-se que a aptidão física e adiposidade atuem como mediadores do efeito da intervenção nos fatores de risco cardiometabólicos.

CAPÍTULO II

ARTIGO ORIGINAL- I

The role of body fat in the relationship of cardiorespiratory fitness with cardiovascular risk factors in Brazilian children

O papel da gordura corporal na relação entre aptidão cardiorrespiratória com fatores de risco cardiovasculares em crianças Brasileiras

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Abstract

Aims: To analyze the association between the percentage of body fat and cardiorespiratory fitness (CRF) with cardiovascular risk factors in children, and; to examine whether percentage of body fat acts as a mediator on the association between CRF and cardiovascular risk factor.

Methods: This cross-sectional study included 128 children aged 7-11 years (Mean 8.54, SD: 1.42). The following variables were evaluated: the percentage of body fat, CRF, diastolic and systolic blood pressure, glucose, triglycerides (TG) and total cholesterol. For statistical analysis were performed Partial correlation and mediation analysis. All analyzes were adjusted for sex, age and height.

Results: CRF, the percentage of body fat, mean arterial pressure (MAP) and TG showed a correlation between each other. Percentage of body fat mediated the association between CRF and MAP (Indirect Effect= -0.008; CI: -0.0159 -0.0030), explaining 29% of this association. However, it was found that the percentage of body fat was not a mediator of the association between CRF and TG.

Conclusion: The percentage of body fat mediates the association between CRF and MAP. Our findings show that the importance of a healthy body composition for the prevention of high blood pressure levels in childhood as well as the relevance of physical fitness on these parameters.

Keywords: schoolers, health, arterial pressure, triglycerides

Resumo

Objetivos: Analisar a associação entre percentual de gordura corporal e aptidão cardiorrespiratória (APCR) com fatores de risco cardiovasculares em crianças, e examinar se o percentual de gordura atua como mediador na associação entre APCR e fatores de risco cardiovasculares. Métodos: Esse estudo de corte transversal incluiu 128 crianças com idades entre 7 e 11 anos (Média 8,54; desvio padrão 1,42). As seguintes variáveis foram avaliadas: percentual de gordura corporal, APCR, pressão arterial sistólica e diastólica, glicose, triglicerídeos (TG) e colesterol total. Para análise estatística foram utilizadas correlações de Pearson e análises de mediação. Todas as análises foram ajustadas para sexo, idade e altura. Resultados: APCR, percentual de gordura, média da pressão arterial (MPA) e TG apresentam correlação entre si. O percentual de gordura mediou a associação entre APCR e MPA (efeito indireto= -0.008; IC: -0.0159 -0.0030), explicando 29% dessa associação. Entretanto, o percentual de gordura não foi um mediador da associação entre APCR e TG.

Conclusão: O percentual de gordura é um mediador da associação entre APCR e MPA. Nossos achados mostram a importância de uma composição corporal saudável para a prevenção de altos níveis de pressão arterial na infância, assim como a relevância da aptidão física nesses parâmetros.

Palavras-chave: escolares, saúde, pressão arterial, triglicerídeos

Introduction

The prevalence of cardiovascular disease (CVD) has been increasing all over the world[1]. Although, the presence of risk factors for CVD in children and adolescents has more clearly been identified over the last 20 years[2]. Initially, this kind of disease was considered a concern for the adult population, however studies have observed that many cardiometabolic abnormalities, including dyslipidemias, insulin resistance, and type 2 diabetes mellitus have its origin during childhood[3]. Thus, the early identification and intervention for children at risk of developing CVD would minimize the tracking of risk factors into adulthood[4].

Cardiorespiratory fitness (CRF) has been considered an important health indicator[5]. Studies have shown that there is an association between low levels of CRF and CVD risk factors in children and adolescent[6,7]. Furthermore, it has been suggested that moderate to high levels of CRF could attenuate some of the adverse metabolic consequences related to obesity[8]. Indeed, the general belief that normal weight is enough for being healthy could be wrong and it is now recognized that moderate to high levels of CRF plays an important role in health even for subject with body mass index (BMI) over 24.9 kg/m2.

Therefore, studies have shown that both fatness and fitness are independently associated with cardiometabolic risk factors among youth. It has been reported that when adiposity is included in the models the magnitude of the association between fitness and cardiometabolic risk appears to be small to moderate[9,10]. Furthermore, a mediation analysis revealed that BMI has a powerful influence on the relationship between CRF and metabolic syndrome in schoolchildren[11]. The same kind of analysis indicated that BMI mediates the relationship between CRF and mean arterial pressure in Spanish schoolchildren[12].

Although BMI, an anthropometric index, is widely used in epidemiological studies, it is unable to distinguish fat and lean mass[13]. Also, most studies have explored BMI as an intermediate and confounding variable in the relationship between CRF and cardiovascular risk factor[11,12]. Thus, considering percentage of body fat (%BF) could provide more precise information regarding adiposity influence on the association between CRF and CVD, the study aimed: 1) To analyze the association between percentage of body fat and CRF with cardiovascular risk factors in children; and 2) To examine whether percentage of body fat acts as a mediator on the association between CRF and cardiovascular risk factors.

Methods

Study design

This was a cross-sectional analysis using the baseline data from a longitudinal study that assessed the effects of a soccer intervention program on cognition-associated variables, metabolic syndrome and inflammatory markers in children. One hundred twenty-eight schoolchildren were included in this study (63 girls and 65 boys), aged 7-11 years, from a public school in the city of Porto Alegre-Brazil, selected by convenience. All children in the first to fifth grade were invited to participate in this project. The parents from those who agreed to participate signed the consent form as well as the children signed the assent form. The Ethics and Research Committee of Federal University of Rio Grande do Sul approved the study (2014997). The research received support from CNPq process number 401969/2016-9/ Universal Announcement.

The minimum number of subjects in the sample was calculated through the software G*Power version 3.1. For a sample calculation, an effect size F of 0.15 (medium effect, corresponding to 1.7 in prevalence ratio) was used, as well as the level of significance of 0.05 and a statistical power of 0.95. Linear regression models have used with approximately five predictors and a 20% increase to cover for possible losses and refusals. Based on these criteria, the minimum sample size was 107 children. The sample size was calculated for linear regression, considering that mediation analysis consists of different regressions. Thus, the sample size is sufficient for this analysis.

Measurements procedures

The variables were measured at school by trained researchers. Weight was measured using a digital anthropometric scale, graded from 0 to 150 kg, with a resolution of 0,05 kg. The children should be lightly dressed and without shoes. Height was measured using a metric tape fixed on the wall and extended from the bottom upwards, with the children kept in a vertical position, with feet and trunk leaning against the wall. The described procedures followed the PROESP-Br standard[14]. CRF was assessed by running and walking test in six minutes[14,15]. The evaluated ones should accomplish the greatest number of turns, running or walking, in a sports court with the perimeter marked with 6 cones and the ground with indications of meters traveled (from 4 in 4 to close 54 meters). The measurement of the test was noted from the number of laps traveled, plus the meters in the case of those who at the end of the time did not complete a lap, so after multiplying the number of laps by the perimeter of meters covered was obtained the estimate of CRF.

Diastolic and systolic blood pressure levels (DPB and SBP) were determined by an automatic blood pressure monitor (Omron Digital Hem-7130), using different sized cuffs according to the circumference of the right arm. The children must be sitting, at least 5 minutes rest, with the arm supported. Mean arterial pressure (MAP) was calculated using the following formula: DBP+[0.333 × (SBP-DBP)]. We emphasize that a large number of published studies used MAP as an independent predictor of cardiovascular event[12,16]. Besides, adiposity is similarly associated with SBP, DBP and MAP, indicating that independently of the blood pressure component, children with more adiposity are more likely to have a higher risk of hypertension[17,18].

After twelve hours of overnight fasting, capillary samples were collected. The fingertip was pierced using an automated lancet and the first drop of blood removed with a sterile cotton swab. This method was used because it allowed the dosage to be performed at school with fewer traumas and better acceptance between the children. Total cholesterol and triglycerides was determined by using Accutrend Plus, while glucose was evaluated by On Call Plus. Capillary samples was tested and authorized by Food and Drug Administration, and the coefficient of results variation (accuracy > 95% with an agreement of laboratory measures) are in according to the index established by National Cholesterol Education Program[19].

Percentage of body fat was assessed using dual-energy X-ray absorptiometry Lunar Prodigy Primo (General Electric Healthcare; Madison, WI), by the same well-trained professional. This measurement was taken at the physical activity laboratory of Federal University of Rio Grande do Sul (Brazil).

Statistical Analysis

Descriptive analysis was expressed considering the mean and standard deviations of all variables included in the study. All variables were checked for normality. Independent Two-tailed T-tests were used to examine the sex differences. Considering that the variables, triglycerides, mean arterial pressure glucose and cholesterol, did not show differences between sexes, all the statistical analysis were performed with both sexes together to increase statistical power. Pearson correlation was used to determine the relationship between %BF and CRF with cardiovascular risk factors.

To examine whether the association between CRF and TG and MAP was mediated by %BF, linear regression models were fitted using the PROCESS macro for the Statistical Package for Social Sciences (SPSS) version 24.0 (IBM Corp, Armonk, NY). The goal of this model was to investigate the total (c) and direct effects (a, b, c'), reflected by the unstandardized regression coefficient and significance between the independent and dependent variables in each model. The model also investigated the indirect effect obtained from the product of coefficients (a × b), which indicates the change in the TG or MAP for every unit change in the CRF that is mediated by the proposed mediator (i.e. %BF). The PROCESS macro used bootstrapping methods recommended by Preacher and Hayes (2008)[20] for testing mediation hypotheses, using a resampling procedure of 10.000 bootstrap samples. Point estimates and confidence intervals (95%) were estimated for the indirect effect. The point estimate was considered significant when the confidence interval did not contain zero. Thus, the following criteria were used to establish mediation: (1) the independent variable (CRF) is significantly related to the mediator (%BF); (2) the independent variable (CRF) is significantly related to the dependent variable (MAP and TG); (3) the mediator (%BF) is significantly related to the dependent variable (MAP and TG); and (4) the association between the independent and dependent variable is attenuated when the mediator is included in the regression model. The analyzes were adjusted for age, sex and height.

All the analyses was carried out using the IBM SPSS 21(SPSS, Inc., Chicago, Illinois, USA). The level of statistical significance was established at $p < 0.05$.

Results

Table 1 presents the descriptive characteristics of the sample. The results indicated that there were differences in mean values of CRF and %BF between girls and boys. Boys presented higher levels of CRF, while girls showed higher % in BF.

Table 1. Characteristics of the study sample by sex.

	Total	Boys	Girls	
	Mean (SD)	Mean (SD)	Mean (SD)	**p**
Age (years)	8.82 (7.89)	8.36 (1.51)	8.43 (1.44)	0.39
Weight (kg)	33.14 (10.59)	32.86 (9.30	33.45 (11.83)	0.74
Height (cm)	1.34 (0.10)	1.34 (0.09)	1.33 (1.11)	0.21
Cardiorespiratory fitness (m)	770.52 (136.82)	798.10 (146.36)	741.36 (119.45)	**<0.001**
Percentage body fatness (%)	32.73 (8.36)	30.34 (8.80)	35.15 (7.15)	**<0.001**
Systolic blood pressure (mmHg)	103.49 (11.56)	103.40 (11.35)	104 (11.82)	0.62
Diastolic blood pressure (mmHg)	60.75 (8.83)	60.78 (9.13)	69.28 (9.28)	0.29
Triglycerides (mg/dL)	116.69 (61.68)	108.83 (66.79)	125.49 (54.46)	0.07
Glucose (mg/dL)	86.01 (7.46)	86.19 (7.23)	85.78 (7.79)	0.69
Cholesterol (mg/dL)	177.01 (22.34)	175.72 (23.15)	178.43 (21.46)	0.42

SD: Standard deviation; p≤0.05

Partial correlations between %BF, CRF and cardiovascular risk factors are presented in Table 2. MAP and TG were the variables that showed an association with %BF and CRF. Also, there was an association between %BF and total cholesterol.

Table 2. Partial correlation between body fat percentage and cardiorespiratory fitness with cardiovascular risk factors

	Percentage of body fat		Cardiorespiratory fitness	
	r	p	r	p
MAP	0.38	**<0.001**	-0.45	**<0.001**
TG	0.31	**0.004**	-0.31	**0.005**
Glucose	0.06	0.56	-0.09	0.35
Total Cholesterol	0.27	**0.009**	-0.05	0.62

MAP: Mean arterial pressure; TG: Triglycerides; CRF: Cardiorespiratory fitness; All analyses were adjusted for age, sex and height.

When we tested the mediator role of %BF in the association between CRF and MAP (Fig.1A), in the first regression equation, the association between CRF and %BF was negative (p=0.01). In the second equation, CRF was also negatively associated with MAP (p=0.002). Finally, in the third equation, when %BF and CRF were included simultaneously in the model, %BF was positively associated with MAP (p<0.001) and associated negatively with CRF (p=0.01). Furthermore, the association between CRF and MAP was attenuated when %BF was included in the model, indicating that %BF a mediator of this association (Indirect Effect= -0.008; IC: -0.0159 -0.0030), explaining 29% of this association. However, the analysis of the mediator role of %BF in the association between CRF and TG (Fig. 1B), showed that %BF is not a mediator of this association since the above-mentioned criteria for the mediation analysis were not observed.

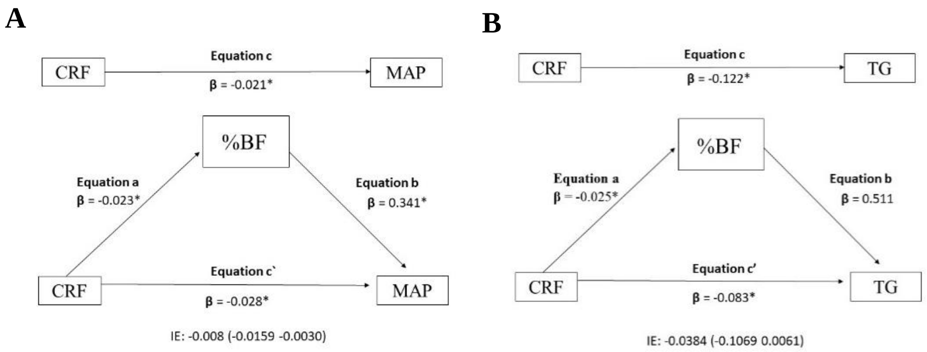

Figure 1. (A) Percentage of body fat mediation model of the relationship between cardiorespiratory fitness and mean arterial pressure; (B) Percentage of body fat mediation model of the relationship between cardiorespiratory fitness and triglycerides; CRF: Cardiorespiratory fitness; MAP: Mean arterial pressure; %BF: Percentage of body fat; TG: Triglycerides. *p<0.001. The analyzes were adjusted for age, sex and height.

DISCUSSION

Our study shows that %BF and CRF were associated with TG and MAP. Moreover, the mediation analyses disclosed that %BF was a mediator in the relationship between CRF and MAP and the estimated percentage of total effect mediated by %BF was 29%. Our findings also showed a negative association between CRF and TG, independent of %BF.

Our data agree with a study developed with 7.821 children and adolescents which indicated that %BF was associated with total cholesterol, HDL and LDL cholesterol and triglycerides[21]. Data from Brazil, showed that individual between the ages of 6 and 19 years with excess body weight, elevated %BF and waist circumference presented a positive correlation with alteration in the lipid profile[22]. Furthermore, Wheelock et al., (2016)[23] used BMI as an adiposity parameter and found that higher BMI was associated with blood pressure elevation and high TG levels in children and adolescents.

Likewise, our study found that CRF was associated with MAP and TG, which is in accordance, with previous study with Brazilian children showing that the prevalence of dyslipidemia is directly related to both obesity and lower levels of CRF[7]. CRF was also associated with blood pressure in children[24,25].

Therefore, CRF and adiposity are considered important health indicator in youth[26]. Studies have been demonstrated a relationship between CRF and adiposity with cardiovascular risk factor in children and adolescents[5,27]. However, it is not established which indicator, CRF or adiposity, is the most important for health and the link between both remain controversial, especially in the child population. Barry et al., (2014)[28] suggested that high levels of CRF could counteract the negative effects of obesity morbidity and mortality. Based on this assumption, obesity compared to CRF, would be less preponderant factor for health than is widely believed. On the other hand, Buchan et al., (2013)[29] found that adiposity, evaluated through BMI and non-CRF were independently associated with cardiometabolic risk factors.

Our mediation analysis offers new information into understanding the relationship between adiposity, CRF and MAP, suggesting that %BF parameter mediates the relationship between CRF and MAP. Thus, the effect of CRF on MAP seems to be minimized by the negative effect of body adiposity. These results were achieved after adjustment for sex, age and height and highlight that high CRF levels and a healthy body composition are important for maintaining adequate arterial blood pressure. Taking this aspect into consideration, physical activity program should be focused on reducing body fat and increasing CRF.

In accordance to our results, a study including 1.604 schoolchildren from Spain, indicated that adiposity assessed through BMI, mediates the relationship between CRF and MAP[12]. In the same line, Díez-Fernándes et al., (2014)[11] showed that BMI mediated the association between CRF and metabolic syndrome, including MAP, with a percentage of effect mediated by BMI of 16%. Similar results were found in young Spanish adults in which different body composition variables such as BMI, waist circumference, fat mass percentage acted as mediators between CRF and blood pressure[30]. Likewise, in 935 Colombian children and adolescents, García-Hermoso et al., (2017)[31] showed that high levels of CRF may not counteract the negative consequences ascribed to adiposity on inflammation.

Thus, high blood pressure levels are related with low levels of CRF and adiposity[12]. The mechanisms involved in increased blood pressure are associated with the adipokines secreted by visceral adipocytes, that have been linked to diminished insulin-mediated vasodilation[32]. Furthermore, the favorable impact of CRF on blood pressure is based on reduced sympathetic nervous system activity and decreased vascular peripheral resistance[33].

Conversely, %BF was not a mediator in the relationship between CRF and TG. Our finding indicates that there was a direct association between these variables, independent of %BF, suggesting the necessity of highlighted aerobic fitness as a health indicator. Indeed, studies have been shown that low CRF in children and adolescents is independently associated with cardiovascular risk factors, including TG[34].

A study developed with adults, indicated that changes over time in both adiposity and physical fitness predicted the development of cardiometabolic risk factors, such hypertension and dyslipidemia, but the impact of fitness appears somewhat better than did adiposity for future risk of this disorders[35]. In addition, increasing fitness was associated with reductions in all cause of cardiovascular mortality of about 15%, while regarding to BMI changes, no associations were found[36]. So, studies have indicated that being in a normal-height is not synonymous with being healthy[27].

Therefore, the relative and combined contribution of physical fitness and fatness to health are controversial, and studies developed with children are scarce. Considering that obesity is a major public health, and physical fitness is related to cardiometabolic risk, we highlight that lifestyle intervention programs should focus on reducing weight/fat, but also increasing CRF. Several studies suggest that intervention programs developed at school environment that address diverse components, such as physical activity and nutritional guidance, appear to be extremely effective for promoting an active and healthy lifestyle[37,38], even CRF[39]. Thus, effort should be concentrated to sustain an effective physical education curriculum, aimed to health promotion, during the key period of children and adolescents, considering that choices made in this period of life tend to remain in adulthood.

Our study has some limitations. The analysis had a cross-sectional design, so we cannot make cause-effect inferences, also the sample was selected by convenience. Furthermore, there are many factors that were not measured and influence cardiometabolic profile, especially in children, such as sexual maturity or diet. However, strengths of this study are the mediation analysis; one of the first studies that used this kind of analysis in Brazilian children; use of the gold standard to measure percentage of body fatness, while most studies considered BMI as an adiposity parameter. So, the data add to previous findings reported in the literature and give additional strength towards the influence of %BF in the association between CRF and cardiovascular risk factors in Brazilian children. Future studies should also considerate potential confounders, such as physical activity, sedentary habits and socioeconomic status to better explaining the role of %BF. In fact, cardiometabolic risk is a complex issue, related to lifestyle and genetic factors.

In conclusion, %BF mediates the association between CRF and MAP. So, our findings seems to emphasize that regardless CRF levels, it is important to maintain a healthy weight for the prevention of high blood pressure levels in childhood. However, our findings also showed a negative relationship between CRF and TG, suggesting the necessity of highlighted aerobic fitness as a health indicator among youth population.

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CAPÍTULO III

ARTIGO ORIGINAL- II

Mediator and moderator role of adiposity in the relationship between physical fitness with cardiometabolic risk factors, adipocytokines and inflammation in children

Papel mediador e moderador da adiposidade na relação entre aptidão física com fatores de risco cardiometabólicos, adipocitocinas e inflamação em crianças

Este artigo encontra-se sob revisão para possível publicação no periódico *Pediatric Exercise Science*.

ABSTRACT

Purpose: to verify the mediator and moderator role of adiposity in the relationship between physical fitness with cardiometabolic risk factors (CMRF), adipocytokines and inflammation in children.

Method: cross-sectional study with 150 children (80 boys), aged 6-11 years, from a school in the south of Brazil. Cardiorespiratory fitness (CRF) and muscular fitness (MF) were measured according PROESP-Br. Systolic and diastolic blood pressure were determined by an automatic monitor, while the percentage of body fat was assessed through dual-energy X-ray absorptiometry. Blood samples were collected to determine leptin, adiponectin and C-reactive protein (CRP) levels, high-density lipoprotein cholesterol, triglycerides, glucose and insulin to determine homeostasis model assessment of insulin resistance (HOMA-IR) and total cholesterol.

Results: Adiposity mediated the association between CRF with CMRF (Indirect effect (IE)=-0.0005; CI:-0.0010 -0.0002) and leptin (IE=-0.0116; CI-0.0185 -0.0062) explaining 25% and 67%, respectively. The association between MF and CMRF (IE:-0.0991; CI:-0.1971 -0.0217), leptin (IE:-3.0251; CI:-4.2660 -2.0956) and CRP (IE:-0.3590; CI:-0.6903 -0.0981) were also mediated by adiposity in 24%, 67% and 37%, respectively. Furthermore, adiposity is a moderator in the relationship between CRF and CMRF (β=0.0001; p=0.04) and leptin (β=0.0008; p=0.02), as well as between MF and CMRF (β=0.01; p=0.02).

Conclusion: this findings support the relevance of adiposity for cardiometabolic health, given its role as a mediator and moderator. Therefore, although CRF and MF are inversely associated with CMRF, leptin and CRP, the deleterious effect of adiposity is not completely ameliorated by physical fitness.

Keywords: cardiorespiratory fitness; muscular fitness; cardiometabolic health

RESUMO

Objetivo: verificar o papel mediador e moderador da adiposidade na relação entre aptidão física e fatores de risco cardiometabólicos (FRCM), adipocitocinas e inflamação em crianças.

Métodos: estudo de corte transversal com 150 crianças (80 meninos), com idades entre 6 e 11 anos, de uma escola do sul do Brasil. A aptidão cardiorrespiratória (APCR) e aptidão muscular (AM) foram mensuradas de acordo com o PROESP-Br. A pressão arterial sistólica e diastólica foram determinadas por um monitor automático, enquanto que o percentual de gordura foi avaliado através de absortometria de raio-X de dupla energia. Amostras sanguíneas foram coletadas para determinar as concentrações de leptina, adiponectina e proteína C-reativa (PCR), lipoproteína de alta densidade, triglicerídeos, glicose e insulina para determinar o do modelo de homeostase de resistência à insulina (HOMA-IR) e colesterol total

Resultados: A adiposidade mediou a associação entre APCR e FRCM (efeito indireto (EI)= -0,0005; IC:-0,0010 -0,0002) e leptina (EI=-0,0116; IC:-0,0185 -0,0062, explicando 25% e 67%, respectivamente. As associação entre AM e FRCM (EI:-0,0991; IC:-0,1971 -0,0217), leptina (EI:-3,0251; IC:-4,2660 -2,0956) e PCR (EI:-0,3590; IC:-0,6903 -0,0981) também foram mediadas pela adiposidade em 24%, 67% e 37%, respectivamente. Além disso, a adiposidade é um moderador da relação entre APCR e FRCM (β=0,0001; p=0,04) e leptina (β=0,0008; p=0,02), assim como entre a AM e CMRF (β=0,01; p=0,02).

Conclusão: esses achados demonstram a relevância da adiposidade para a saúde cardiometabólica, dado seu papel como mediador e moderador. Portanto, embora a APCR e AM são inversamente associadas com os FRCM, leptina e PCR, o efeito deletério da adiposidade não é completamente melhorado pela aptidão física.

Palavras-chave: aptidão cardiorrespiratória; aptidão muscular; saúde cardiometabólica

Introduction

Accumulated evidence showed that increase in the prevalence and severity of cardiometabolic risk factors seems to manifest already during childhood, which may lead to a higher risk for cardiometabolic disease later in life [1]. Also, it has been suggested that some adipocytokines, including leptin and adiponectin, as well as classic proinflammatory biomarkers, such as C-reactive protein (CRP), are involved in this process and may predict future cardiovascular events (2,3). The development of cardiometabolic risk factor is linked to genetic predisposition and unhealthy lifestyle choices, such as physical inactivity and sedentary behavior, which leads to low levels of physical fitness and excess adiposity (4,5).

Physical fitness, namely cardiorespiratory fitness (CRF) and muscular fitness (MF) are of paramount importance and powerful markers of health (6). It has been well documented that children with high levels of CRF present a healthier inflammatory and cardiometabolic profile (7,8). In addition, recent studies support that low MF is associated with high cardiometabolic risk and high levels of leptin and CRP in children and adolescents (8,9). Despite the recognized importance of maintaining high levels of physical fitness, a decline in fitness has been observed among young population (10).

Moreover, the cardiometabolic health is importantly affected by adiposity (11). Given that CRF and MF are inversely associated to adiposity, they may lay on the same causal pathway, making it difficult to determine the extent to which each variable affects cardiometabolic risk factors. In this sense, it has been suggested that adiposity, assessed by body mass index (BMI), is a mediator in the relationship of CRF (12) and MF (11) with cardiometabolic risk factors in children and adolescents. However, these studies have used BMI as a measure of adiposity, which is unable to distinguish fat and lean mass (13). Thus, considering the percentage of body fat measured by dual-energy X-ray absorptiometry might provide more accurate information. In addition, it is already established that MF, CRF and adiposity are independently associated with cardiometabolic risk factors, CRP and adipocytokines in youth (4,14,15). Going further, we intend to understand the interactions between CRF, MF and adiposity on cardiometabolic risk factors, adipocytokines and CRP, once we hypothesized that high levels of CRF and MF may play a protective role in the deleterious effect of adiposity in those variables.

In this context, the present study aimed to verify the mediator and moderator role of adiposity in the relationship between physical fitness with cardiometabolic risk factors, adipocytokines and inflammation in children.

Methods

Study design and sample

This was a cross-sectional analysis with a quantitative approach. This study was developed in a public school in the city of Porto Alegre/Brazil. The sample included 150 children (53.33% boys) from elementary school, aged from 6 to 11 years (mean age 8.53±1.38 years). Parents who allowed their sons and daughters to participate signed the consent form. The Ethics and Research Committee of Federal University of Rio Grande do Sul approved the study (2014997).

Measures

Physical fitness variables and sexual maturation were measured at school by trained researchers. Nursing and physical education professionals measured blood samples and percentage of body fat in the laboratory of exercise physiology of the Federal University of Rio Grande do Sul.

Physical Fitness

The described procedures of physical fitness evaluation followed the *"Projeto Esporte Brasil"* (PROESP-Br) standard (16). CRF was assessed by 6-minute walk/run test (17), which the participants should accomplish the greatest number of turns, running or walking, in a sports court with the perimeter marked with cones and the floor with indications of meters. The measurement of the test was registered from the number of laps performed, plus the meters in the case of those who at the end of the time did not complete a lap, so after multiplying the number of laps by the perimeter of meters covered was obtained the estimate of CRF.

Lower limb strength test was carried out with a measuring tape fixed to the floor. The starting line was signaled using a chalk and the zero point of the measuring tape was on the starting line. The student was positioned immediately behind the starting line, with feet parallel and knees semi-flexed. At the signal, the children should jump as far as possible with both feet at the same time (16).

Abdominal strength test was performed with the children in the supine position, with knee flexed, arms crossed over the thorax and ankles fixed to the floor by the evaluator. The children must flex the trunk until touching the thighs with the elbow, returning to the starting position, as many times as possible in one minute (16).

The results of the lower limb strength and abdominal strength test were transformed to standardized values (z-scores). Then the sum of Z-scores was performed to create the MF score.

CRF and abdominal strength were categorized in “risk” and “healthy” according to the cut-off points of PROESP-Br (16). Lower limb strength was classified in “low” until “excellent” according to the same protocol.

Blood sampling

Venous blood samples were drawn by a specialized professional using disposable materials and were performed at the early in the morning following 10-12 hours fasting. Blood samples were routinely centrifuged and then, plasma and serum were aliquoted and frozen at -80 °C until analysis. Total cholesterol, high-density lipoprotein cholesterol (HDL-C), triglycerides and glucose levels were analyzed using an automatic colorimetric method (Cobas C111, Roche, Basel, Switzerland). Low-density lipoprotein cholesterol (LDL-C) was calculated from the Friedewald equation (Friedewald 1972). Glucose levels were determined using an automated analyzer (Cobas C111, Roche Diagnostics, Basel, Switzerland). Insulin concentrations were determined by ELISA using commercial kits (DRG International, Springfield, USA). As an index of insulin resistance, homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as the product of fasting glucose (mmol/L) and insulin (µlU/mL) levels divided by 22.5 (18). Leptin, adiponectin (Abcam, Cambridge, UK) and CRP levels (BosterBio, Pleasanton, USA) were determined by enzyme-linked immunosorbent assay (ELISA), following the specifications of the manufacturer

Adiposity

Body fat was measured by dual-energy X-ray absorptiometry (Lunar Prodigy Primo, General Electric Healthcare; Madison, WI, USA), by the same well-trained professional. Children were positioned on the dual-energy X-ray absorptiometry table in the supine position with the members properly separated from the trunk and should remain in that position throughout the procedure. The children were lightly dressed during this test. Adiposity was classified as low=24%; middle=33% and 41%.

Sexual maturation

Sexual maturation was determined according to Mirwald et al., (2002) (19). Using this method it is possible to determine the distance, in years, that the children is from peak high velocity. For this method the following measures were used: chronological age, height, body mass, length of lower limb and height in the sitting position. These variables were used in a specific equation for each sex.

Blood pressure

Systolic and diastolic blood pressure were determined by an automatic blood pressure monitor (Omron Digital Hem-7130), using different sized cuffs according to the circumference of the right arm. The children must be sitting, at least 5 minutes rest, with the arm supported.

Statistical analyses

Descriptive data are presented as means and standard deviation. All variables were checked for normality. Independent Two-tailed T-tests were used to examine sex differences. All the statistical analyses were performed with both sexes together to increase statistical power. The probability value $p \leq 0.05$ was considered to be significant for all analyses.

We calculated a cardiometabolic risk factor score (composite z-score) for each participant using the following formula: cardiometabolic risk factors= z-HDL-C + z-triglycerides + z-HOMA-IR+ z-total cholesterol + z-systolic blood pressure+ z-diastolic blood pressure. The HDL-C value was multiplied by −1, as it is inversely associated to cardiovascular risk.

Linear regression models were fitted to examine whether the associations of CRF and MF with cardiometabolic risk factors, leptin, adiponectin and CRP were mediated by adiposity, using the PROCESS macro for the Statistical Package for Social Sciences (SPSS) version 22.0 (IBM Corp, Armonk NY, USA). The goal of this model was to investigate the total (c) and direct effects (a, b, c'), reflected by the unstandardized regression coefficient and significance between the independent and dependent variables in each model. The model also explored the indirect effect obtained from the product of coefficients (a x b), which indicates the change in the dependent variables (cardiometabolic risk factors, leptin, adiponectin and CRP) for every unit change in the CRF and MF that is mediated by the proposed mediator (adiposity). The PROCESS macro used bootstrapping methods recommended by Preacher and Hayes (2008) (20) for testing mediation hypotheses, using a resampling procedure of 10.000 bootstrap samples. Indirect effect was estimated through point estimates and 95% confidence intervals. When the confidence interval did not contain zero, the point estimate was considered significant. Thus, the following criteria were used to establish mediation: (a) the independent variables (CRF and MF) is significantly related to the mediator (adiposity); (b) the independent variables (CRF and MF) is significantly related to the dependent variables (cardiometabolic risk factors, leptin, adiponectin and CRP); (c) the mediator (adiposity) is significantly related to the dependent variable (cardiometabolic risk factors, leptin, adiponectin and CRP); and (d) the association between the independent and dependent variables is attenuated when the mediator is included in the regression model. The analyses were adjusted for age, sex and sexual maturation.

Different linear regression models were done to test interaction between CRF and MF x adiposity in dependent variables (cardiometabolic risk factors, leptin, adiponectin and CRP), also using PROCESS macro for SPSS. CRF, MF and adiposity were classified according to tertiles: CRF (low=628m; middle=758m and high=888m), z-score MF (low=-0.86; middle=0.02 and high=0.91) and adiposity (low=24%; middle=33% and 41%).

Results

Participant's characteristics are shown in Table 1. Boys presented higher levels of CRF, abdominal strength, lower limb strength and adiponectin than girls. While, girls showed higher levels of leptin, insulin, triglycerides, HOMA-IR and percentage of body fat. Additionally, 65.5% of the children were at risk for CRF and 35% at risk for abdominal strength, while 63.5% presented low levels of lower limb strength.

Table 1. Participant's characteristics

Variables	**n**	**All** Mean (SD)	**Boys** Mean (SD)	**Girls** Mean (SD)
Age (years)	150	8.46 (1.51)	8.55 (1.58)	8.40 (1.40)
Weight (kg)	143	33.64 (10.31)	32.39 (10.15)	35.14 (11.25)
Height (cm)	142	1.34 (0.10)	1.33 (0.10)	1.33 (0.10)
Sexual maturation	138	-2.77 (1.80)	-3.94 (1.03)	-1.54 (1.61)*
Cardiorespiratory fitness (m)	145	751.16 (130.27)	785.33 (136.21)	712.47 (112.10)*
Abdominal strength (rep)	145	25.57 (10.84)	27.45 (10.76)	23.44 (10.61)*
Lower limb strength (cm)	145	110.08 (23.74)	117.29 (23.59)	104.04 (22.04)*
Adiponectin (µg/mL)	150	10.92 (6.51)	12.07 (7.02)	9.51 (5.69)*
Leptin (ng/mL)	150	4.14 (6.23)	3.11 (4.93)	5.37 (7.31)*
C-Reactive protein (mg/L)	150	2.34 (1.68)	2.29 (1.69)	2.43 (1.70)
Total cholesterol (mg/dL)	150	149.28 (27.47)	151.19 (26.48)	147.70 (28.40)
Triglycerides (mg/dL)	148	72.45 (32.73)	66.98 (31.60)	79.14 (33.13)*
HDL-C (mg/dL)	150	44.48 (10.66)	44.88 (11.02)	43.53 (8.81)
LDL-C (mg/dL)	150	90.62 (27.00)	92.54 (24.78)	89.36 (29.26)
Insulin (uU/mL)	148	15.85 (11.98)	13.46 (10.57)	18.1 (12.81)*
Glucose (mg/dL)	149	89.35 (9.10)	88.33 (7.52)	90.43 (10.62)
Insulin resistance (HOMA-IR)	148	3.50 (2.10)	2.97 (2.37)	3.99 (2.71)*
Systolic blood pressure (mmHg)	150	103.39(12.79)	102.14(13.64)	104.81(11.68)
Diastolic blood pressure(mmHg)	150	60.85(10.79)	59.53(10.56)	62.37(10.92)
Percentage of body fat (%)	118	33.52 (8.55)	31.50 (8.54)	36.17 (7.72)*

HDL-C: High-density lipoprotein cholesterol; LDL-C: Low-density lipoprotein cholesterol; *independent t-test for differences between boys and girls (p≤0.05)

Table 2 displayed that adiposity is a mediator in the association between CRF and MF with cardiometabolic risk factors and leptin, and that a mediation was found for MF with CRP. In the first regression (equation a), the association between CRF and adiposity was negative (β=-0.034; CI95%: -0.034 -0.012; p<0.001). In the second regression (equation b), adiposity was positively associated with cardiometabolic risk factors and leptin. Equation "c" showed that CRF was negatively associated with cardiometabolic risk factors and leptin. Finally, in the fourth regression (equation c´), when adiposity and CRF were included simultaneously in the model, adiposity was negatively associated with cardiometabolic risk factors and leptin. Furthermore, the relationship between CRF with cardiometabolic risk factors and leptin, was attenuated when adiposity was included in the model, indicating that adiposity is a mediator (indirect effect), explaining 25% for cardiometabolic risk factors and 67% for leptin.

Regarding MF, equation "a" showed that MF was negatively associated with adiposity (β=-5,996; CI95%: -0.7413 -4.570; p<0.001). Equation "b" indicated that adiposity was positively associated with cardiometabolic risk factors, leptin and CRP. Equation "c" displaced that MF was negatively associated with the same variables. Lastly, when adiposity and MF were included simultaneously in the model, adiposity was negatively associated with cardiometabolic risk factors, leptin and CRP. Thus, adiposity is a mediator of this relationship and explains 24% for cardiometabolic risk factors, 67% for leptin and 27% for CRP.

Results also showed that adiposity is not a mediator in the relationship between CRF and MF with adiponectin, and between CRF with CRP, once the criteria for the mediation analysis were not observed.

Table 2. The mediator role of adiposity in the relationship between cardiorespiratory and muscular fitness with cardiometabolic risk factors, leptin, adiponectin and C-reactive protein.

	Equation b (95% CI)	p	Equation c (95% CI)	p	Equation c' (95% CI)	p	Indirect Effect (95% CI)	Proportion mediated (%)
Cardiorespiratory Fitness								
Adiposity								
CMRF (z-score)	0.020 (0.008 0.031)	<0.001	-0.001 (-0.002 -0.0007)	<0.001	-0.0009 (-0.0016 -0.0002)	0.010	-0.0005 (-0.0010 -0.0002)	25
Leptin (ng/mL)	0.499 (0.392 0.606)	<0.001	-0.013 (-0.021 -0.004)	0.002	-0.001 (-0.008 0.005)	0.679	-0.0116 (-0.0185 -0.0062)	67
Adiponectin (μg/mL)	-0.090 (-0.258 0.077)	0.289	-0.001 (-0.010 0.008)	0.832	-0.003 (-0.013 0.007)	0.556	0.0021 (-0.0016 0.0073)	-
CRP (mg/L)	0.099 (0.056 0.143)	<0.001	-0.002 (-0.005 0.0005)	0.106	0.0001 (-0.002 0.002)	0.969	-0.0023 (-0.0042 -0.0011)	-
Muscular Fitness								
Adiposity								
CMRF (z-score)	0.016 (0.002 0.030)	0.018	-0.237 (-0.339 -0.134)	<0.001	-0.137 (-0.267 -0.008)	0.036	-0.0991 (-0.1971 -0.0217)	24
Leptin (ng/mL)	0.500 (0.371 0.629)	<0.001	-3.132 (-4.305 -1.958)	<0.001	-0.107 (-1.329 1.115)	0.862	-3.0251 (-4.2660 -2.0956)	67
Adiponectin (μg/mL)	-0.074 (-0.277 0.128)	0.468	0.410 (-1.071 1.893)	0.584	-0.040 (-1.968 1.887)	0.966	0.4512 (-0.7463 1.5369)	-
CRP (mg/L)	0.059 (0.008 0.110)	0.022	-0.955 (-1.334 -0.576)	<0.001	-0.596 (-1.078 -0.115)	0.017	-0.3590 (-0.6903 -0.0981)	27

CMRF: Cardiometabolic risk factors; CRP: C-Reactive Protein. All models were adjusted for sex, age and sexual maturation.

Plots illustrating the moderations analysis are depicted in Figures 1 and 2. It was found a significant interaction term for CRF x adiposity with cardiometabolic risk factor and leptin. Data indicated that higher levels of CRF were associated with lower cardiometabolic risk factor score in low percentage of body fat. Furthermore, children with lower percentage of body fat and higher CRF were the ones who presented lower cardiometabolic risk factor score (Fig. 1A). Besides, it seems that CRF exert a protective effect, once it was found an association between CRF and leptin only in children with high percentage of body fat (Fig 1B). Concerning adiponectin and CRP it was not found interaction between CRF and adiposity.

The significant interaction term for MF x adiposity, showed that higher levels of MF were associated with lower cardiometabolic risk factors score, in medium and low percentage of body fat. Similarly to CRF, children with lower percentage of body fat and higher MF were the ones showing lower cardiometabolic risk factors score (Fig. 2A). For the other variables it was not observed interaction between MF and adiposity.

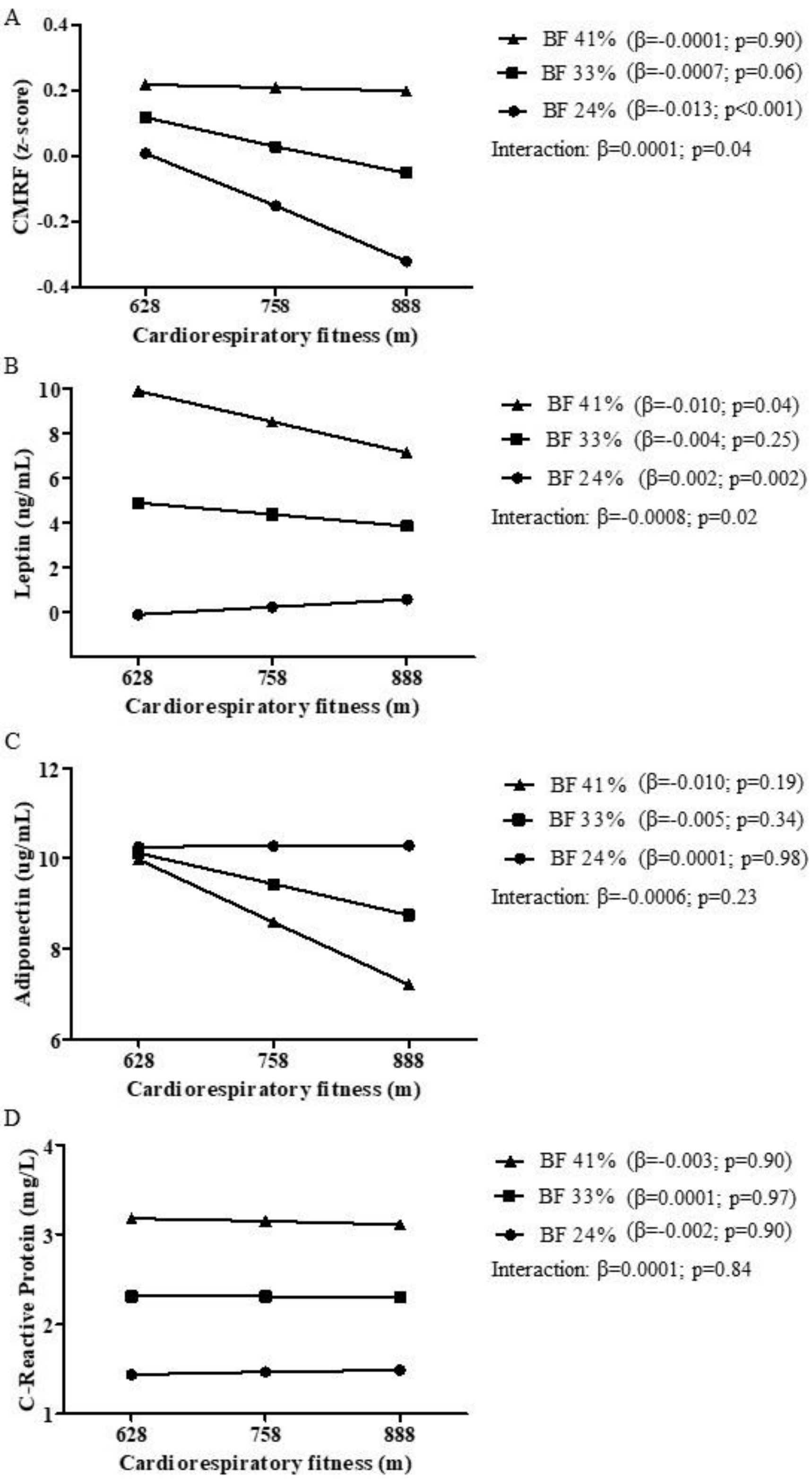

Figure 1. Moderation of adiposity on cardiorespiratory fitness and cardiometabolic risk factors (A), leptin (B), adiponectin (C) and C-reactive protein (D).

CMRF: Cardiometabolic risk factors; BF: Body fat. All analyses were adjusted for sex, age and sexual maturation.

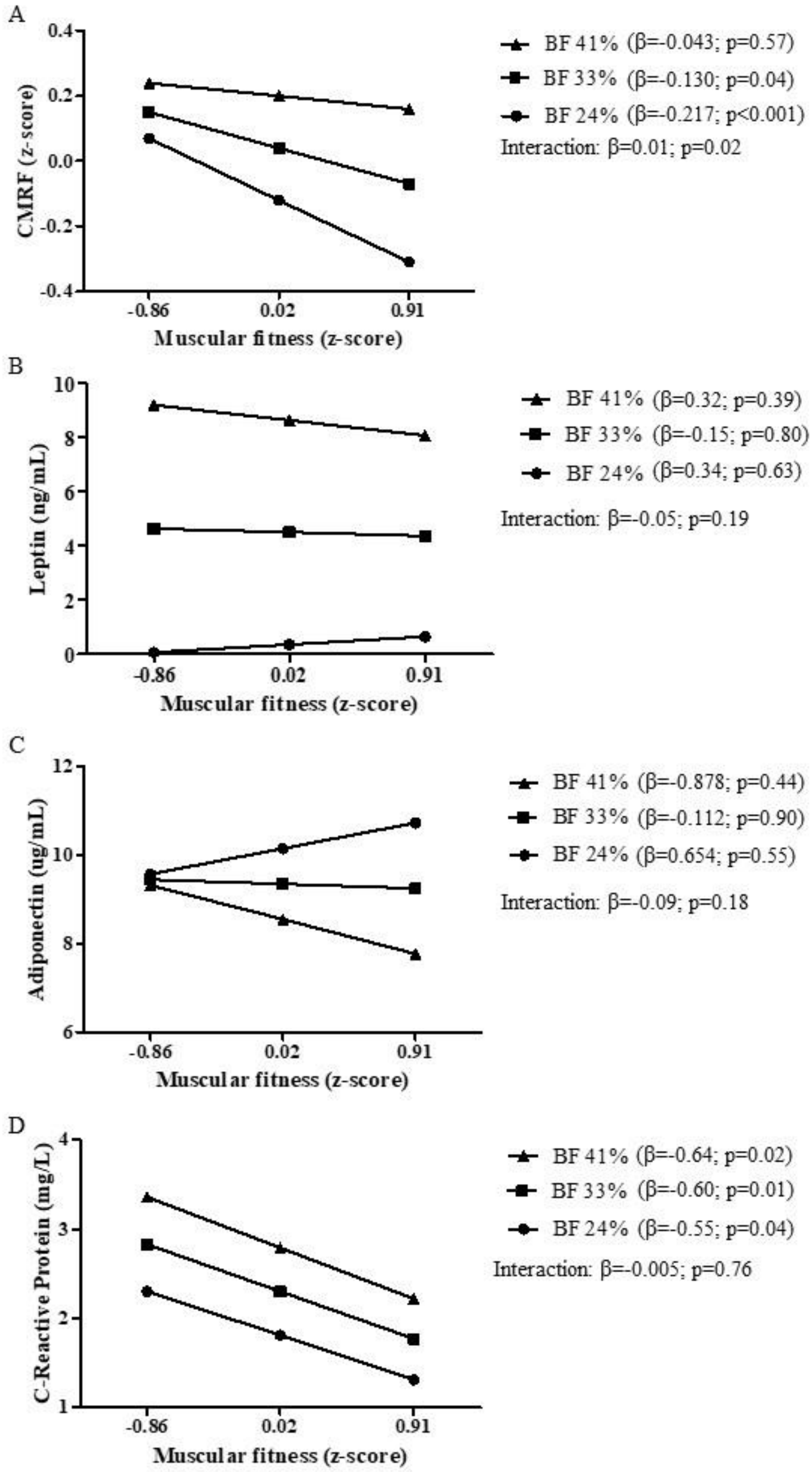

Figure 2. Moderation of adiposity on muscular fitness and cardiometabolic risk factors (A), leptin (B), adiponectin (C) and C-reactive protein (D).

CMRF: Cardiometabolic risk factors; BF: Body fat. All analyzes were adjusted for sex, age and sexual maturation.

DISCUSSION

The main findings of this study suggest that: 1) Adiposity is a mediator in the relationship between CRF with cardiometabolic risk factors and leptin, as well as in the relationship between MF with cardiometabolic risk factors, leptin and CRP; 2) Adiposity is a moderator in the relationship between CRF with cardiometabolic risk factors and leptin, as well as between MF and cardiometabolic risk factors.

Results of the present study contribute to the current knowledge indicating that MF and CRF may have a beneficial influence on cardiometabolic risk factors, as well as leptin and CRP levels in children. Some studies have described the independent association between CRF and MF with leptin, CRP and cardiometabolic risk factors, although most of them were carried-out in adolescents. Artero et al. (14) showed that MF was associated with CRP and leptin after adjustments for age, sex, pubertal stage, CRF and HOMA- IR. Agostinis-Sobrinho et al. (15) considered leptin and CRP in a continuous score of clustered inflammatory biomarkers and showed that MF was inversely associated with them. The same trend was observed for CRF, since lower levels of different cardiometabolic risk factors, leptin and CRP have been observed in children and adolescents (4,21).

The aforementioned relationships are widely described in the literature, but some recent studies have been developed in order to understand the percentage of the total effect (the influence of an independent variable on a dependent variable) that is carried by a mediator (22). Following this idea, our findings indicated that 25% and 67% of the total effect of CRF on cardiometabolic risk factors and leptin, respectively, were mediated by the percentage of body fat. Also, it was found that the percentage of body fat is a mediator in the relationship between MF and cardiometabolic risk factors (24%), leptin (67%) and CRP (27%). These results are in agreement with previous studies indicating that BMI plays a role as a mediator in the relationship between MF (23) and CRF (12) with cardiometabolic risk factors in children. Additionally, it was found that BMI is also a mediator in the relationship between CRF and CRP in children and adolescents (24). Thus, adiposity may be an intermediate step in the causal pathway between MF and CRF with cardiometabolic risk factors, leptin and CRP.

The specific mechanisms through which CRF and MF exerts its effect on adiposity are complex and not fully understood. CRF may affect adiposity for several pathways, including the increase of expression and activity of enzymes (e.g. β-Hydroxy acyl-CoA dehydrogenase) which regulates fat oxidation into the mitochondria (25) and marked increase of insulin sensitivity on adipose tissue afforded by aerobic exercise (26). Regarding MF, it may be related to increases in the metabolic efficiency of muscle, as well as skeletal muscle mass, resulting in greater overall daily energy expenditure (27). On the other hand, adipose tissue is responsible for producing many adipocytokines related to an inflammatory process (28). This may be the explanation for the high percentage of mediation that percentage of body fat exerts in the relationship between CRF and MF with leptin.

Given the mediator role of adiposity, we also intend to verify its role as a moderator, which refers to the strength of the relationship between independent and dependent variables that can vary according to a third variable (22). In this sense, we found that percentage of body fat modifies the association between the low, middle and high tertiles of CRF with cardiometabolic risk factors and leptin. In children with low percentage of body fat we observed a significant association between CRF and cardiometabolic risk factors. This means that in children classified as middle and high percentage of body fat, CRF may not counteract the negative effects of obesity on cardiometabolic risk factors. Thus, our results do not support the so call “Fat but Fit” paradox, although most of the knowledge available regarding this issue comes from studies developed with adults, and the information regarding children and adolescents are scarce (29,30). In this sense, we hypothesized that in our study, the lack of this protective effect of CRF could be due to the fact that 65% of the children analyzed presented low levels of CRF.

The crucial role of adiposity was evidenced by Pérex-Bay et al. (11), indicating that BMI and percentage of body fat were positively associated with a cluster of cardiometabolic risk factors, and these associations remained significant after the inclusion of CRF in the model. Likewise, Demmer et al. (31) pointed out in the same direction, indicating that fatness may be more determinant for cardiometabolic health than fitness. It is important to consider that we have found an inverse association between CRF with leptin only in children with high percentage of body fat. It thus appears that in this adipocytokine, CRF may play a protective role. In fact, some studies have reported the independent association between CRF and leptin (21,32), but we are not aware of studies addressing the moderator role of adiposity in this relationship in children.

To date, information about the interaction between adiposity and MF with cardiometabolic risk factors and mainly adipocytokines and inflammation is scarce (23), once most studies refers to the interaction between adiposity and CRF with cardiometabolic risk factors. Thus, our results bring new information, showing that the percentage of body fat is a moderator in the relationship between MF and cardiometabolic risk factors, since it was found association between these variables in low and middle percentage of body fat. Although MF was not associated to cardiometabolic risk factors in the highest tertile of percentage of body fat, the role of this variable as a protector for cardiometabolic risk factors it must be recognized, coinciding with those reported by other studies (33,34).

Indeed, MF and CRF are established as important indicators of health (35), and adiposity play a key role in this context (12). In order to improve physical fitness as well as decreasing adiposity, our results support current guidelines for physical activity which recommend participation in activities that maintain or increase endurance and muscular strength, more or equal to 3 days a week, in addition to aerobic moderate to vigorous physical activity (60 min/day) (36,37).

This study presents limitations including its cross-sectional design, which does not allow us to set conclusions about the direction of the association. The generalization of these results should be carefully considered due to the limited sample size. Further, we did not include any measure of diet, which may influence the analyzed variables. The strengths of our study include the assessment of both, mediator and moderator role of adiposity. Beyond cardiometabolic risk factors, we addressed also adipocytokines and inflammation parameter that have been less studies regarding this relationship in children. Also, we have utilized the gold standard to measure adiposity while most studies considered BMI.

In conclusion, adiposity is a mediator in the relationship between CRF with cardiometabolic risk factors and leptin, as well as MF with CRF, leptin and CRP. Additionally, it was found a moderator role of adiposity in the association between CRF with cardiometabolic risk factors and leptin, and MF with cardiometabolic risk factors. Therefore, although CRF and MF are inversely associated to cardiometabolic risk factors, leptin and CRP, the deleterious effect of adiposity is not completely ameliorated by physical fitness.

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CAPÍTULO IV

ARTIGO ORIGINAL- III

Effect of a multicomponent intervention in components of Metabolic Syndrome: a study with overweight/obese low-income school-aged children

Efeito de uma intervenção multicomponente em componentes da síndrome metabólica: um estudo com crianças em idade escolar, com sobrepeso/obesidade e baixo nível socioeconômico

Este artigo encontra-se sob revisão para possível publicação no periódico *Sports Science for Health*;

ABSTRACT

Purpose: to investigate the effects of a 12-week multicomponent intervention program in markers of metabolic syndrome and nonalcoholic fatty liver disease (NAFLD) in Brazilian overweight/obese low-income school-aged children.

Methods: This quasi-experimental study was developed with overweight/obese school-aged children, aged 7 to 13 years-old. The participants were assigned to intervention (n=17) or control group (n=18). The multicomponent intervention was developed during twelve weeks, consisting of exercise sessions (twice/week;1h), nutritional education sessions (once/month), and parental support (twice/week). The following variables were evaluated: anthropometric measures (height, body weight, waist circumference, percentage of body fat); biochemical assays (total cholesterol -TC, triglycerides-TG, high density lipoprotein cholesterol -HDL-C, glucose, aspartate aminotransferase-AST, alanine aminotransferase-ALT), cardiorespiratory fitness and maturational stage. A cardiovascular disease (CVD) composite z-scores (percentage of body fat, glucose, AST, ALT, TG, TC/HDL-C ratio) was also calculated. General linear models were used for data analysis.

Results: Compared to the control group, intervention group participants decreased percentage of body fat (Δ-0.97; $p<0.001$), glucose levels (Δ-0.15; $p=0.005$), ALT (Δ-2.84; $p=0.021$), TC/HDL-C ratio (Δ-0.93; $p<0.001$), CVD composite score (Δ-0.97; $p<0.001$) and total calorie intake (Δ -131.44;$p=0.03$), while there was no differences between groups on waist circumference, AST, TG and cardiorespiratory fitness.

Conclusion: A 12-week multicomponent intervention was effective on decreasing some metabolic syndrome parameters in overweight/obese school-aged children.

Keywords: metabolic risk factors, health, youth

RESUMO

Objetivo: Investigar os efeitos de uma intervenção multicomponente de 12 semanas nos componentes da síndrome metabólica, incluindo marcadores da doença hepática gordurosa não alcoólica em crianças em idade escolar com sobrepeso/obesidade e de baixo nível socioeconômico;

Métodos: esse estudo quase-experimental foi desenvolvido com crianças em idade escolar, com sobrepeso/obesidade e idades entre 7 e 13 anos. Os participantes foram designados para o grupo intervenção (n=17) e controle (n=18). A intervenção multicomponente foi desenvolvida durante 12 semanas, consistindo de sessões de exercício (duas vezes semanais; 1h), sessões de educação nutricional (uma vez ao mês), e suporte parental (duas vezes semanais). As seguintes variáveis foram avaliadas: medidas antropométricas (altura, peso corporal, circunferência da cintura e percentual de gordura corporal); avaliações bioquímicas (colesterol total -CT, triglicerídeos -TG, colesterol de lipoproteína de alta densidade -HDL-C, glicose, aspartato aminotransferase -AST, alanina aminotransferase -ALT), aptidão cardiorrespiratória e estágio maturacional. Também foi calculado um z-escore de fatores de risco cardiovasculares (FRCV) (percentual de gordura corporal, glicose, AST, ALT, TG, razão CT/HDL-C). Modelos de regressão linear foram utilizados para análise de dados.

Resultados: Comparado ao grupo controle, os participantes do grupo intervenção diminuíram o percentual de gordura (Δ-0,97; $p<0,001$), concentrações de glicose (Δ-0,15; $p=0,005$), ALT (Δ-2,84; $p=0,021$), razão CT/HDL-C (Δ-0,93; $p<0,001$), z-escore FRCV (Δ-0,97; $p<0,001$) e consumo total de calorias (Δ -131,44; $p=0,03$), enquanto que não houve diferenças entre os grupos na circunferência da cintura, AST, TG e aptidão cardiorrespiratória.

Conclusão: A intervenção multicomponente de doze semanas foi efetiva para diminuir alguns parâmetros da síndrome metabólica em crianças em idade escolar com sobrepeso/obesidade.

Palavras-chave: fatores de risco metabólicos, saúde, jovens

INTRODUCTION

Detrimental behavior to health, such as physical inactivity, sedentary habits and unhealthy eating, are increasingly recurrent in children and adolescent´s routine [1]. Apart from the genetic disposition, this lifestyle can be considered the main responsible for the alarming rise in the prevalence of overweight and obesity, as well as the physical fitness decrease observed in pediatric population [2,3].

Obesity is a multifactorial disease and is the central risk factor for metabolic syndrome (MetS) in youth characterized by a group of disorders that include, in addition to obesity, elevated levels of triglycerides (TG), low levels of high density lipoprotein cholesterol (HDL-C), insulin resistance and arterial hypertension [4] Although no global consensus has been reached regarding MetS definition in the pediatric population, studies have indicated that there is a high occurrence of cardiovascular disease (CVD) risk factors clustering even in early ages [5]. Moreover, Nonalcoholic Fatty Liver Disease (NAFLD) is another obesity-health problem [6] and has been identified as the leading cause of liver disease in pediatric populations worldwide [7]. It is characterized by pathological fat accumulation in the liver, which may lead to liver damage in the form of inflammation and fibrosis [8] placing NAFLD as the hepatic representation of MetS. Previous studies found that raised serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), uric acid, fasting glucose, and body mass index (BMI) are predictors of NAFLD among obese children and adolescents [9,10]. Although the MetS and the NAFLD prevalence are higher in adolescents, young children also exhibit MetS and NAFLD as obesity-related complications [11].

It is important to highlight that low-income children are the most affected by unhealthy behavior opportunities as well as having less access to health care, and therefore, being more likely to develop comorbidities associated with obesity [12]. Moreover, because of the multifactorial characteristic of obesity´s etiology, an effective behavioral change intervention should be considered, having a sustained commitment by children´s families [13].

In this context, a multicomponent approach [14], involving physical activity, nutritional education and family support, as well as working on individual and social aspects has been recommended [15]. Indeed, interventions including physical exercise and nutritional education were effective to decrease obesity and related metabolic diseases in Latino youth [16,17]. However, these studies were developed with adolescents and did not considered NAFLD markers in the analyses. Furthermore, the interventions were based on physical activity and/or nutrition, disregarding the essential role of parental support on these strategies. Thus, there is a lack of studies using a multicomponent intervention to improve cardiometabolic profile, especially regarding NAFLD parameters, in low-income Brazilian children. This seems to be worthy to consider because low cost preventive strategies should be adopted for the target population. Based on these aspects, we hypothesized that a 12-week multicomponent intervention program in overweight/obese low-income school-aged children is effective in improving markers of metabolic syndrome, and NAFLD.

Therefore, this study aimed to investigate the effects of a 12-week multicomponent intervention program in markers of metabolic syndrome and NAFLD in Brazilian overweight/obese low-income school-aged children.

METHODS

Study design and approach

This quasi-experimental study is part of the "ACTION FOR HEALTH" (Adolescents and Children in a Training Intervention for Health) project. This project was developed to target overweight/obese low-income school-aged children of both genders aged 7 to 13 years-old. It is a multicomponent intervention program aiming to promote physical activity after-school classes and included nutritional education as well as parental support sessions, based on the Behavior Change Ecological Model, which calls for the implementation of multidisciplinary actions [14]. Physical exercise sessions, nutritional education and parental support were offered to systematically target mechanisms of change at each level of influence (intrapersonal, interpersonal and environmental). More detailed information about study design and intervention process was published before [18].

All the Helsinki Declarations' ethical aspects were followed [19]. The evaluation methods and procedures were approved by the Scientific Board of the Research Unit that leads the project (excluded information for blind review) and is registered in www.clinicaltrials.gov (Number: NCT02929472).

The program was developed by four physical education teachers, one nutritionist, and one pediatrician who previously participated in weekly meetings (over six months), where methodologies and intervention sessions were prepared and tested. Seven graduate physical education students, and two graduate nutrition students collaborated in the program weekly sessions and were trained and supervised by the project coordinator.

The overall protocol was developed as follow: during the first day blood samples were collected, anthropometric variables were assessed, as well as the evaluation of maturational stages. On the second day, body scan was performed in the children, while parents were interviewed about children´s 3-Day food intake record. Lastly, during the third and fourth days, physical fitness tests were applied. Physical tests were carried out at the Physical Education Department of the Federal University of Paraiba. The blood analyses were carried out at a convened specialized laboratory in João Pessoa/Brazil. The same procedures were followed for post-intervention evaluation.

Participants and procedures

The project was publicized in 2 educational poles (6 public schools) from João Pessoa-PB (Brazil), which were located in regions nearby the intervention site. All schools were located in a deprived area, with low socioeconomic status: 62.5% of the mothers or fathers were unemployed and over 45% of the mothers and 64% of the fathers had concluded the 9th grade or less.

Parents of potential participants (n=276), according to school teacher´s or parent´s information) were invited to participate in early evening information meetings with the multidisciplinary staff. From those, ninety-six parents attended the meetings, where all the potential participants were screened for inclusion criteria, defined as being overweight or obese, according to Cole et al criteria [20], and being not involved in any other physical exercise or diet program. From those attending the first screening fifty-three were excluded and eight did not complete baseline evaluations. Thus, the final sample comprised thirty-five participants that were allocated either to control or intervention groups (Figure 1). Children and parents of the control group were advised to do not change their lifestyle during the period between the evaluations (12 weeks). They were advised that they could receive the same intervention of the intervention group after the 12-week period.

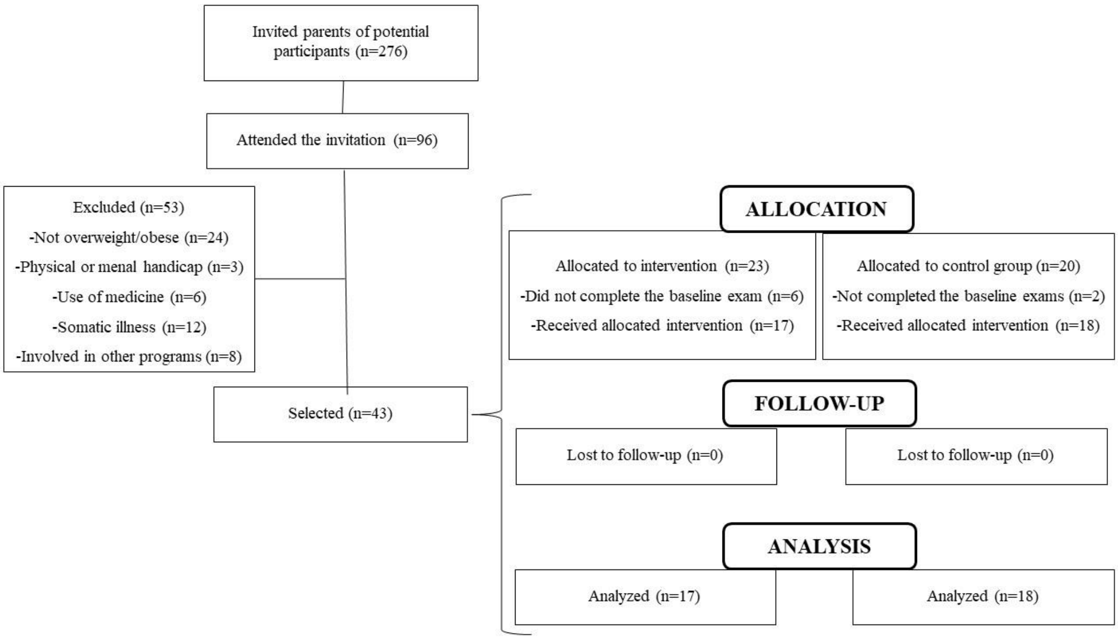

Figure 1. Sample´s flow diagram

Physical exercise intervention

The exercise sessions took sixty minutes, twice a week, for twelve weeks. The sessions were taught by the same physical education teachers. Each session included 4 phases; ten minutes of warm-up; thirty minutes of circuit training; fifteen minutes of pre-sports and recreational games; and five minutes of cool-down activities. Warm-up included aerobic/anaerobic and recreational activities. The circuit training phase, comprised six stations and included activities that prioritized physical fitness capacities [21]. Exercises were structured so that participants could maintain a high intensity throughout the circuit. This protocol has been used and tested in other intervention studies with a similar sample [22,23].

Training intensity and compliance between individuals were defined to induce heart rate (HR) higher than 65% of HR_{max} of each participant. To monitor the activity, ten randomly selected participants wore a portable HR monitor (Polar Team^2 Pro, Polar, Finland) during sessions. Attendance average for intervention group was 85% (ranging between 73.6% and 88.9%).

Nutritional education intervention

The nutritional session was designed by the nutritionist staff, and consisted in two actions. The first one named dietary counseling. Each month, all participants and their parents were invited for a nutritional appointment in which was provided information about the food pyramid, weight loss importance, fat-free and low-energy foods, food calories, good nutritional choices on preparing low-coast meals, and decisions on food choices. The three sessions (1/month) were based on the information recorded through the participant´s 24h-recorded-dietary evaluation, which was done by the nutritional staff at baseline. The attendance to appointments was 100%. The second action consisted on the attempt to accomplishment of three daily dietary goals. These goals were focused on three main points: a) increase frequency and quantity intake of adequate food (fruit and vegetables); b) decrease of inadequate food intake (processed food and added sugar); and c) increase water consumption. Interventions focusing on these goals have been used in similar populations [16]. At the beginning of the intervention, participants received a worksheet to record day by day whether they met the daily goals. No significant inter subject variance was observed for the achievement of the proposed goals in the intervention group (data not shown).

Food intake was carried out by a 24-hour recall, which was applied three times (participants, along with their parents, informed food intake during the past two weekdays and one weekend day). Data from these three days were tabulated in the software “Virtual Nutri” to obtain the total energy intake values for each of the three days. The mean value of caloric intake among the three days was used and data were recorded in kcal.

Parental support intervention

Simultaneous to children’s program, exercise sessions were offered to all parents in order to encourage family support. Adults’ participation was voluntary and the parental support intervention was focused on improvement of three aspects: (a) encouragement through provision of transportation to PA facilities (100% attendance); (b) participation in PA with the children, when applicable (82% attendance); (c) watching the children during physical activities (95% attendance). The activities were carried out by a trained physical education teacher in the center of sports of Federal University of Paraíba, João Pessoa (Brazil) at the same time as their respective children.

Anthropometric measures

Height and body weight were assessed using a "Holtain" stadiometer, and percentage of body fat (%BF) was measured by a bioimpedance scale after 4-hour-fasting and low water intake (Inbody 720, Biospace Co. Ltd.), [24]. These measures were performed at a specialized laboratory in João Pessoa and followed standardized procedures (24). To measure waist circumference, NHANES protocol (US Department of Health and Human Services, 1996) [25] was followed.

Cardiorespiratory fitness (CRF)

CRF was measured using the 20m Shuttle-run Test [26]. Participants completed 20m shuttle runs keeping in time with an audible 'bleep' signal. The frequency of the sound signals was increased every minute by 0.5 km/h, increasing the intensity of the test, and youngsters were encouraged to run to exhaustion [26]. The number of completed laps was recorded for each participant and retained for analysis. This procedure has been used previously in studies with similar samples [27, 28]. Evidence for the acceptable reliability and validity of the 20m shuttle run test has been proven, with test-retest reliability coefficients ranging from $r = 0.78$ to $r = 0.93$ [29].

Biochemical assays

The circulating levels of plasma insulin, plasma glucose, plasma cholesterols (TC and LDL-C), plasma TG, ALT, AST, were measured through peripheral puncture in the cubital vein after a nocturnal twelve hour-fasting, by laboratory specialists, using standard techniques at an accredited partner laboratory. The analysis of TC, HDL-C, TG, and glucose was carried out by spectrophotometry (Cobas Integra 400 Plus) with Roche® kits. The LDL-C fraction was indirectly calculated using the Friedewald formula [30]. The AST and ALT levels were determined by enzyme kinetic assay for spectrophotometrically obtained after 10 minutes' centrifugation at 3500 rpm. All samples ran in duplicate and the mean was calculated. The intra-assay coefficient of variation was less than 20%, according to the manufacturer.

Confounder Variables

Maturational Stages

The breast stages (B1-B5) in girls and the genital stages (G1-G5) in boys, were assessed according to Tanner's criteria [31] by a pediatrician at the first day of measurements.

Statistical analyses

Stata for windows (version 13) was used for all the analyses. The composite CVD risk factor was calculated from the sum of z-scores of %BF, glucose, AST, ALT, TG, TC/HDL-C ratio, and CRF, by sex and age category (<9 years and 9+ years). This approach has been used before [5].

Means and standard deviations (SD) were calculated by group (intervention and control) to characterize the participants. Baseline differences between groups were calculated using general linear model adjusted for sex. Each of the dependent variables was standardized as follow at the given time point: standardized value = (value – mean)/ standard deviation. Change scores were calculated by subtracting post-intervention values from baseline values. General linear models were performed to analyze differences between intervention and control groups in change scores from baseline to post-intervention adjusted for sex, sexual maturation, age category and CRF baseline level. It was also presented the confidence interval (CI). The effect size (Cohen's d) of the intervention are also shown. The magnitude of effect size was classified according to Cohen [32] as: ≤0.20 (trivial), between 0.21 and 0.50 (small), between 0.51 and 0.80 (moderate), and >0.80 (large). We accepted 5% of error in our analyses.

The sample size was calculated a *posteriori* in the software G*power version 3.1, considering that participants were volunteered selected. Thus, for general linear model, a medium effect of the intervention on dependent variables (F^2= 0.15 to 0.35) was considered and the value of the statistical power was between 0.60 and 0.80, as well as the level of statistical significance was established as $p<0.05$.

RESULTS

Descriptive characteristics of the participants at baseline are shown in table 1. We only found statistically significant differences at baseline for CRF between intervention and control group.

Table 1. Descriptive characteristics of the participants at baseline.

	Intervention Group (n=17)	Control Group (n=18)	
	Mean (SD)	Mean (SD)	p
Age (years)	8.17±2.48	8.27±1.87	0.89
Weight (kg)	40.90±18.47	39.29±11.67	0.75
Height (m)	1.34±1.43	1.34±0.10	0.98
%BF	13.60 ± 10.09	14.13 ± 6.89	0.85
WC (cm)	71.26 ± 14.96	73.814± 11.37	0.57
CRF (number of laps)	10.82 ± 4.34	7.24 ± 2.42	0.005
Glucose (mg/dL)	83.12 ± 4.98	86.27 ± 7.34	0.15
AST (U/l)	28.65 ± 7.39	28.50 ± 13.32	0.96
ALT (U/l)	19.53 ± 2.93	18.95 ± 5.16	0.68
TG (mg/dL)	76.05 ± 28.12	80.63 ± 28.33	0.63
TC (mg/dL)	171.64±19.33	158.11±31.74	0.14
HDL-C (mg/dL)	46±7.95	50.61±12.59	0.20
Total calorie intake (kcal)	1807.62±1.17	1706.17±72.12	0.41

%BF. Percentage of body fat; WC. Waist circumference; CRF. Cardiorespiratory fitness; AST. Serum aspartate aminotransferase; ALT. Alanine aminotransferase; TG. Triglycerides; TC. Total cholesterol; HDL-C. High density lipoprotein cholesterol.

Table 2 presents physical characteristics, change scores (mean ± SD), adjusted differences by group (intervention and control group) and effect size at baseline and post-intervention. Compared to the control group, participants allocated to intervention group decreased %BF, with an adjusted difference of -1.747 (CI: -2.529 -0.964; p<0.001) and a trivial effect size (d=0.10). The same was observed for glucose levels (adjusted difference=-5.483; CI:-9.163 -1.803; p=0.005; d=0.03), TC/HDL-C ratio (adjusted difference=-1.478; CI=-1.917 -1.039; p=<0.001; d=1.28), CVD composite score (adjusted difference=-3.951; CI:-5.684: -2.218; p<0.001; d=0.87) and total calorie intake (adjusted difference=-134.28; CI: -258.53 -10.83; p=0.03; d=0.52), while there was no differences between groups on waist circumference, AST, triglycerides and CRF.

Table 2. Physical characteristics, change scores (mean ± SD), adjusted differences by group (IG and CG) and effect size at baseline and post-intervention.

Variables	Group	n	Baseline Mean ± SD	Post-intervention Mean ± SD	Change Scores ± SD	Adjusted difference (95% CI)	p	Effect size
%BF	IG	17	13.60 ± 10.09	12.62 ± 9.31	-0.97 ± 1.41	-1.747 (-2.529 -0.964)	<0.001	0.10
	CG	18	14.13 ± 6.89	14.98 ± 7.01	0.85 ± 0.77			
WC (cm)	IG	17	71.26 ± 14.96	69.26 ± 13.53	-2.00 ± 2.99	-1.528 (-3.710 0.655)	0.163	0.14
	CG	18	73.814± 11.37	73.45 ± 11.88	-0.36 ± 3.05			
Glucose (mg/dL)	IG	17	83.12 ± 4.98	82.96 ± 5.53	-0.15 ± 3.37	-5.483 (-9.163 -1.803)	0.005	0.03
	CG	18	86.27 ± 7.34	90.27 ± 6.18	4.00 ± 6.39			
AST (U/L)	IG	17	28.65 ± 7.39	26.19 ± 6.10	-2.46 ± 3.20	-1.305 (-4.236 1.626)	0.370	0.36
	CG	18	28.50 ± 13.32	27.93 ± 4.80	-0.56 ± 11.00			
ALT (U/L)	IG	17	19.53 ± 2.93	16.69 ± 3.29	-2.84 ± 4.48	-7.556 (-13.915 -1.198)	0.021	0.91
	CG	18	18.95 ± 5.16	23.77 ± 17.54	4.82 ± 13.32			
TG (mg/dL)	IG	17	76.05 ± 28.12	95.58 ± 24.02	19.52 ± 35.29	-1.178 (-22.660 20.305)	0.912	0.74
	CG	18	80.63 ± 28.33	100.83 ± 34.70	20.20 ± 29.93			
TC/HDL ratio	IG	17	3.84 ± 0.83	2.91 ± 0.60	-0.93 ± 0.80	-1.478 (-1.917 -1.039)	<0.001	1.28
	CG	18	3.26 ± 0.95	3.90 ± 0.92	0.63 ± 0.63			
CRF (number of laps)	IG	17	10.82 ± 4.34	13.41 ± 5.53	2.58 ± 4.57	0.712 (-2.091 3.514)	0.607	0.52
	CG	18	7.24 ± 2.42	9.23 ± 2.61	1.99 ± 2.26			
CVD composite scores	IG	17	-0.49 ± 2.73	-2.89 ± 2.74	-2.39 ± 2.69	-3.951 (-5.684 -2.218)	<0.001	0.87
	CG	18	0.47 ± 3.59	1.79 ± 3.16	1.32 ± 2.24			
Total calorie intake (kcal)*	IG	17	1870.62±306.01	1676.18±430.42	-131.44±209.90	-134.28 (-258.53 -10.03)	0.03	0.52
	CG	18	1706.17±413.01	1731.54±303.00	25.36±38.28			

IG. Intervention group; CG. Control group; SD. Standard deviation; %BF. Percentage of body fat; WC. Waist circumference; AST. Serum aspartate aminotransferase; ALT. Alanine aminotransferase; TG. Triglycerides; TC/HDL ratio: Total cholesterol, high density lipoprotein cholesterol ratio; CRF: cardiorespiratory fitness; Composite z-scores. Sum of (Body fatness, Glucose, AST, ALT, TG, TC/HDL-C ratio). Change scores from baseline to post-intervention by group (mean and SD). The adjusted difference between groups in change scores is the net effect of the intervention: IG change scores minus CG change scores adjusted for sex, sexual maturation, age category and CRF at baseline (mean and 95% confidence intervals (CI)); *Adjusted for sexual maturation.

DISCUSSION

We investigated the effects of a 12-week multicomponent intervention program in markers of metabolic syndrome and NAFLD in overweight/obese low-income school-aged children. However, it is not well-documented how such programs can be implemented. Indeed, only few investigations analyzed the implementation of a multicomponent approach [33–36], and at the best of our knowledge none in low-income children. The most important findings lie on the fact that the 12-week intervention had positive effect in decreasing %BF, glucose levels, ALT, TC/HDL-C ratio, the CVD composite score and total calorie intake of the intervention group.

Previous interventions highlighted similar results [37–41], especially those targeting youth metabolic syndrome [37,39–41]. Likewise, a systematic review and meta-analysis investigating the effectiveness of lifestyle interventions, based on nutrition and physical exercise, on cardiometabolic risk factors of obese children, showed positive effects in reducing body weight, as well as improvements in LDL-C, TG, fasting insulin and blood pressure [13]. Additionally, in accordance with our findings, Bianchini et al. [42] indicated that after a multidisciplinary intervention, including nutritional, parental and pediatrician intervention, developed during sixteen weeks with obese children and adolescents, there was a decrease in cardiometabolic risk factors and adiposity.

Regarding %BF, it was not found difference between groups in baseline and the large variability in the results was maintained in post-test, meaning that differences found at the end of the study were based on the intervention program and not really influenced by the procedure used to evaluate this variable. Thus, the observed decrease in body fat, associated to an improvement in some lipid profile indicators and glucose level, is an important indicator of the effectiveness of the proposed multicomponent intervention. Indeed, although Nascimento et al. (23), after an eight-month regular physical exercise program found similar results, our study promoted those improvements in a shorter period of time, which seems to hold promise for childhood obesity worldwide (43,44).

Moreover, the observed significant reduction in TC/HDL-C ratio (from 3.84 to 2.91) emphasize the multicomponent relevance, considering this ratio is an important marker of atherosclerotic risk [23]. Nybo et al. [45] reported that the TC/HDL-C ratio was the only component of the lipid profile that improved (decreasing from 3.41 to 2.92) after an exercise intervention for promoting health, however these study was conducted with untrained men. Those authors further suggest that could be a relationship between body fat and the alterations in lipid profile.

Despite the positive effects in general lipid profile, our study showed a negative and unexpected outcome regarding TG values, which increased from baseline to post-intervention in both groups. While the same trend of increasing TG values have been already shown after a multicomponent intervention in obese children of control and intervention group [46], literature suggests that programs focused on physical exercise is effective in reducing or even maintaining TG levels [47] as well as those using diet [13]. Thus, there are still some discrepancies regarding this issue. Moreover, the increasing of TG levels observed in the present study could also be associated with different factors besides diet or physical exercise, such as regional lipid concentration, genetics, or blood test technology [47].

Furthermore, its important to mention that control group showed worsening %BF, glucose, TC/HDL-C ratio and ALT after only 12 weeks. Thus, beyond the inherent damages and difficulties ascribed to both condition overweight/obese and low-income, if they are not under any kind of intervention program, the trend in this parameters is to worsen. Therefore, these negative changes indicate that children of the control group could be at higher risk of developing metabolic dysfunction, including type 2 diabetes and NAFLD.

Concerning CRF, intervention and control groups presented difference at baseline. Likewise, both groups showed improvements after 12 weeks. Nonetheless, it is important to highlight that intervention group presented higher difference from baseline to post-intervention, which could indicate a trend of improvement in this group, as seen in other studies applying longer periods of intervention with overweight children and adolescents [42,48].

While most of studies that implemented interventions targeting NAFLD in youth were based on exercise and nutrition intervention [38] our program highlighted the exercise, diet and parental support (twice a week). ALT has been considered one important marker of NAFLD. Indeed, it was shown that nine of eleven studies pointed out decreases in ALT levels as a result of intervention [38], that agrees with our findings and stressed the importance that multicomponent interventions might have on decreasing NAFLD markers in youth. Noteworthy to mention that our data were based on overweight/obese individuals belonging to a low socioeconomic level, which could lead to a potential extra value for the development of strategies for health prevention and promotion.

Therefore, a multicomponent intervention as developed in the present study seem to be an effective strategy to reduce %BF and improve several cardiometabolic risk factors in overweight/obese school-aged children. We also emphasize the relevance of implementing this intervention strategy in a low-income area, once children living in vulnerable zones have fewer physical activity facilities, low access to healthy nutrition, and some of them live without their parents that decrease their healthy opportunities compared to higher income families (49).

In summary, this study provides evidence of a successful multicomponent intervention among low socioeconomic status overweight/obese school-aged children. Given the positive effect, our approach could be used in further studies as well as to be considered by public health policy responsible for implementing this kind of intervention in a large scale action mainly when targeting overweight/obese children and low socioeconomic status population.

Limitations and strengths

The present study has some limitations that should be mentioned. The small sample size of intervention and control groups require caution regarding to generalization of these results to the wider population of Brazilian overweight/obese school-aged children. Nonetheless, the results were positive and added information to previous data. Besides, given the fact that we dealt with overweight/obese population our data might have would be of great clinical significance. Further, the intervention covered only limited period of time (12 weeks) and, it would be interesting to know whether a long-term program would result in continued improvement. Strengths of this study are the recruitment of low-income overweight/obese participants and the multicomponent design of intervention, that included besides physical exercise, nutritional education and intervention with the children's parents.

Conclusions

A 12-week multicomponent intervention was effective on decreasing some metabolic parameters in overweight/obese and low-income school-aged children. Therefore, this kind of intervention could be considered a tool for health promotion in this population.

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CAPÍTULO V

ARTIGO ORIGINAL- IV

Effect of a multicomponent intervention on cardiometabolic risk factors and prevalence of responsiveness in overweight/obese children

Efeito de uma intervenção multicomponente em fatores de risco cardiometabólicos e prevalência de responsivos em crianças com sobrepeso/obesidade

Este artigo encontra-se sob revisão para possível publicação no periódico *Journal of Sports Science*.

ABSTRACT

This study aimed to verify the effect of a multicomponent intervention on cardiometabolic risk factors, and to determine the individual prevalence of responsiveness on cardiometabolic risk factors among overweight/obese children and adolescents. This is a quasi-experimental study, developed with 35 overweight/obese children (control group=18; intervention group=17), aged between 7-13 years. Participants underwent a multicomponent intervention during 12 weeks, comprised of physical exercise, nutritional education and parental support. The following variables were measured: cardiorespiratory and muscular fitness, body fatness, food intake, phyisical activity and cardiometabolic risk factors. Mixed analysis of variance were used for statistical analysis. There was a significant time x group interaction on alanine aminotransferase (ALT), homeostasis model assessment of insulin resistance (HOMA-IR), total cholesterol (TC), high density and low density lipoprotein (HDL-C and LDL-C). Moreover, the prevalence of children that decreased values of cardiometabolic risk factors in intervention group was: aspartate aminotransferase (AST) (6.25%), triglycerides (18.75%), ALT (31.25%), LDL-C (37.5%), HOMA-IR (62.5%), TC (68.75%), while for HDL-C there was an increase of 75%. Prevalence between groups indicated differences in TC, HOMA-IR and HDL-C. The multicomponent intervention induced positive changes on cardiometabolic risk factors of overweight/obese children along with a high prevalence of positive adaptations in most of the cardiometabolic outcomes assessed.

Keywords: obesity; physical exercise; cardiometabolic health.

RESUMO

O objetivo desse estudo foi verificar o efeito de uma intervenção multicomponente em fatores de risco cardiometabólicos e determinar a prevalência individual de responsivos nos fatores de risco cardiometabólicos em crianças com sobrepeso/obesidade. Esse é um estudo quase experimental, desenvolvido com 35 crianças, com sobrepeso/obesidade (grupo controle=18; grupo intervenção=17), com idades entre 7 e 13 anos. Os participantes foram submetidos a uma intervenção multicomponente durante 12 semanas, consistindo de exercício físico, educação nutricional e suporte parental. As seguintes variáveis foram mensuradas: aptidão cardiorrespiratória e muscular, gordura corporal, consumo total de calorias, atividade física e fatores de risco cardiometabólicos. Houve uma interação tempo x grupo significativa na alanina aminotransferase (ALT), modelo de homeostase de resistência à insulina (HOMA-IR), colesterol total (CT), colesterol de lipoproteína de alta densidade e de baixa densidade (HDL-C e LDL-C). Além disso, a prevalência de crianças que diminuíram os valores dos fatores de risco cardiometabólicos no grupo intervenção foi: aspartato aminotransferase (AST) (6,25%), triglicerídeos (18,75%), ALT (31,25%), LDL-C (37,5%), HOMA-IR (62,5%), CT (68,75%), enquanto que para o HDL-C houve um aumento de 75%. A prevalência entre os grupos indicou diferenças no CT, HOMA-IR e HDL-C. A intervenção multicomponente induziu mudanças positivas nos fatores de risco cardiometabólicos de crianças com sobrepeso/obesidade, além de alta prevalência de adaptações positivas na maioria dos desfechos cardiometabólicos avaliados.

Palavras-chave: obesidade; exercício físico; saúde cardiometabólica.

Introduction

It has been widely described that high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) are strong and independent predictors of cardiovascular events (Toth et al., 2013). In addition, high triglycerides (TG) level is a marker for several types of atherogenic lipoproteins and a prevalent risk factor for cardiovascular disease (Talayero & Sacks, 2011). In this context, an alteration of the profile corresponding to abnormal blood levels of TG and/or cholesterol-carrying lipoproteins affecting one or all of the subfractions of blood lipids, is characterized as dyslipidemia. Insulin resistance (IR) is also an important metabolic disorder associated with obesity and diabetes mellitus (Yin et al., 2013). Moreover, Nonalcoholic Fatty Liver Disease (NAFLD) is another health problem related with all above-mentioned risk factors (Alkhater, 2015).

In this context, many systematic reviews and experimental studies have been describing the effect of physical activity intervention on cardiometabolic risk factors in youth. Escalante et al. (2012) and Fedewa et al. (2014) indicated that exercise training is effective on improving HDL-C, LDL-C and TG concentrations, as well as IR in children and adolescents. In addition, a lifestyle intervention of six months was effective in improving NAFLD markers and IR in severely obese children (Koot et al., 2011). Moreover, a recent evidence-based exercise recommendations to reduce hepatic fat content showed that exercise training is an important strategy to improve and prevent hepatic steatosis in the pediatric population (Medrano et al., 2018).

Findings regarding the benefits of physical activity on health in youth have been widely shown. However, studies on this issue are mainly focused in analyzing it in terms of “mean”. Notwithstanding, it has been shown that there is a wide interindividual variability in the effects of exercise interventions in health outcomes (Bonafiglia et al., 2016). It means that, under the same stimulus, while some individuals may achieve benefits after training, other can present an unchanged or worsened response (Bonafiglia et al., 2016). Those aspects have been investigated in adults, indicating that the cardiometabolic risk factors responses to exercise training, such as cardiorespiratory fitness, fasting insulin and glucose, have not been fully clarified (Álvarez, Ramírez-Campillo, Ramírez-Vélez, & Izquierdo, 2017a; Bouchard et al., 2012; Montero & Lundby, 2017). On the other hand, this interindividual variability has not been well explored in youth individuals.

Thus, the literature regarding interindividual variability in the adaptations to exercise in health outcomes is limited in children and adolescents (Alvarez, Ramírez-Campillo, Ramírez-Vélez, & Izquierdo, 2017b), especially considering a wide range of cardiometabolic risk factors and a multicomponent intervention. Therefore, the aim of the present study was (1) to verify the effect of a multicomponent intervention on cardiometabolic risk factors, and (2) to determine the individual prevalence of responsiveness on cardiometabolic risk factors among overweight/obese children. We hypothesized that this sample will present a high prevalence of positive response on cardiometabolic risk factors following a multicomponent intervention program.

Methods

Study design

This is a quasi-experimental study, part of the "ACTION FOR HEALTH" (Adolescents and Children in a Training Intervention for Health) project, developed with overweight/obese low-income youth of both genders, aged between 7 and 13 years. This multicomponent intervention program aims to promote physical activity after-school classes, nutritional education sessions, and parental support. All the procedures were approved by the Scientific Board of the Research Unit that leads the project *(excluded information for blind review)*, and is registered in www.clinicaltrials.gov (Number: NCT02929472). Also, all the Helsinki Declarations' ethical aspects were followed (World Medical Association, 2013). More detailed information about study design and intervention process was published before (Silveira et al., 2018).

Participants and procedures

This project was publicized in 2 educational poles (6 public schools) from João Pessoa-PB (Brazil), which were located in regions nearby the intervention site. All schools were located in a deprived area, with low socio-economic status: 62.5% of the mothers or fathers were unemployed and over 45% of the mothers and 64% of the fathers had concluded the 9th grade or less. Parents of potential participants (n = 276, according to school teacher´s or parent´s information) were invited to participate in early evening information meetings with the multidisciplinary staff. From those, ninety-six parents attended the meetings, where all the potential participants were screened for inclusion criteria, defined as being overweight or obese (Cole, Bellizzi, Flegal, & Dietz, 2000), and being not involved in any other physical exercise or diet program. From those, fifty-three were excluded, leaving 43 in the study, which were allocated in control group (CG, n= 20) and intervention group (IG, n=23). However, 2 participants did not complete baseline evaluation in CG, and 6 in IG, leaving a total of 17 participants in IG and 17 in IG.

Multicomponent intervention program

The program was developed by four physical education teachers, one nutritionist, and one pediatrician, who previously participated in weekly meetings (over six months), which methodologies and intervention sessions were prepared and tested. Seven graduate physical education students, and two graduate nutrition students collaborated in the program weekly sessions, and were trained and supervised by the project coordinator.

Physical exercise intervention

The exercise sessions took sixty minutes, twice a week, during twelve weeks, always taught by the same physical education teachers. Each session included ten minutes of warm-up; thirty minutes of circuit training; fifteen minutes of pre-sports and recreational games; and five minutes of resting activities. Warm-up included aerobic/anaerobic and recreational activities. The circuit, divided into six stations, included activities that prioritized physical fitness capacities (Weineck, 2005), for example rarely race, jump rope, throw different size balls training warm-up, High-knee skipping dribbling a ball, climb a rope, Jumping jacks in unstable platform. Exercises were structured so that participants could maintain a high intensity throughout the circuit. This protocol has been used in other intervention studies with a similar sample (Aires et al., 2016; Nascimento et al., 2014).

Training intensity and compliance between individuals were defined to induce heart rate (HR) higher than 65% of HR_{max} of each participant. To monitor the activity, ten randomly selected participants wore a portable HR monitor (Polar Team^2 Pro, Polar, Finland) during sessions. Attendance average for intervention group was 85% (minimum of 73.6% and maximum of 88.9%).

Nutritional education intervention

The dietary intervention, designed by the nutritionist staff, consisted of two actions: 1) three events (one per month) for dietary counseling with parents, based on the recorded-dietary evaluation of their children. The attendance to counseling appointments was 100%; 2) three daily dietary goals for participants. These goals were based on three main points: frequency and quantity of adequate and inadequate food, and water consumption. Participants received a worksheet to record whether they met the daily goals. No significant inter subject variance was observed for the achievement of the proposed goals in the intervention group (not presented).

Parental support intervention

Simultaneously, exercise sessions were offered to all parents in order to encourage family support. Adults' participation was voluntary and the parental support intervention was focused on improvement of three aspects: (a) encouragement through provision of transportation to PA facilities (100% attendance); (b) participation in PA with the children, when applicable (82% attendance); (c) watching the children during physical activities (95% attendance). The activities were carried out by a trained PE teacher in the center of sports of Federal University of Paraíba, João Pessoa (Brazil), during children's same schedule. Parent's attendance average for the three different actions was 88%.

Measurements

Baseline measurements were performed during a fourteen-days period, for CG and IG groups. On the first day, the blood collection was taken and anthropometric outcomes were assessed; on the second day, body scan was performed in the children participants, while parents were interviewed about children´s 3-Day food intake record. The third and fourth days were used to administer physical fitness tests. On the fourth day, participants received their accelerometer to be used during the last ten days of evaluation. All physical tests were carried out at the Physical Education Department of the Federal University of Paraiba. The blood analysis was carried out at a convened specialized laboratory in João Pessoa/Brazil. For post-intervention evaluation, the same procedures were followed.

Anthropometric measures and body composition

Height and weight were determined by a "Holtain" stadiometer, then body mass index was calculated, by dividing body mass (in kilograms) by height (in square meters). Body fatness was measured after 4-hour-fasting and low water intake with a bioimpedance scale (Inbody 720, Biospace Co. Ltd.). Those measures were taken following standardized procedures (Lohman, Roche, & Martorell, 1988).

Food intake

Food intake was carried out by a 24-hour recall. Participants, along with their parents, informed food intake during the past two weekdays and one weekend day before evaluation. Data from these three days were tabulated in the software “Virtual Nutri” to obtain the total energy intake values for each of the three days. For analytical procedures, the mean value of caloric intake among the three days was used and data were recorded in kcal.

Biochemical assays

The circulating levels of plasma insulin, plasma glucose, plasma cholesterols (TC and HDL-C), plasma TG, serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), were measured through peripheral puncture in the cubital vein after a nocturnal twelve hour-fasting, by laboratory specialists, using standard techniques at an accredited partner laboratory. The analyses of TC, HDL-C, TG, and glucose was carried out by spectrophotometry (Cobas Integra 400 Plus) with Roche® kits. The LDL-C fraction was indirectly calculated using the Friedewald formula (Friedewald, Levy, & Fredrickson, 1972). The AST and ALT levels were determined by enzyme kinetic assay for spectrophotometrically. Insulin was determined by Luminex-100 IS (Integrated System: Luminex Corporation, Austin, TX, USA), using the Linco Human Gut Hormone panel kit (Linco Research Inc., MO, USA). As a proxy measure of insulin resistance, homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as the product of basal glucose (mmol/L) and insulin (μlU/mL) levels divided by 22.5 (Matthews et al., 1985). All samples were run in duplicates and the means were calculated. The intra-assay coefficients of variation were less than 20%, according to the manufacturer.

Statistical Analysis

Descriptive procedures were performed for all independent and dependent variables, through means and confidence intervals. One-way ANOVA test was used to compare baseline variables, between control and intervention groups. The intervention effect on time, group and interaction (time x group), was verified through mixed analysis of variance (ANOVA), adjusted for age, sex and sexual maturation.

Prevalence of individual responsiveness in the outcome variables in control and intervention group were obtained according the theoretical model applied in previous studies with biochemical variables outcomes, considering the Δ% effect (Álvarez et al., 2018; Alvarez et al., 2017a; Álvarez, Ramírez-campillo, & Ramírez-vélez, 2017c). However, due to the impossibility of two basal measures in each outcome variable in the present study, we did not calculate the reliability intrasubject (typical error) as suggested to this kind of analysis (Alvarez et al., 2017b; Álvarez, Ramírez-Campillo, et al., 2017a; Hopkins, 2000). To minimize this limitation, we considered as acceptable clinical and individual effects, the least values of Δ% obtained from previous interventions with the same variables as parameters and cut-points to increased and decreased effects (Escalante et al., 2012; Hopkins, 2000; Koot et al., 2011). Thus, the cut-points values were defined as: HDL-C (effect of decrease or increase (E) >10%), LDL-C (E >10%), CT (E > 5%), AST (E > 26%), ALT (E > 20%), TG (E> 10%) and HOMA-IR (E > 30%).

Finally, to verify the difference in prevalence (increase and decrease) between IG and CG, Poisson regression was applied in generalized estimative equation. All the analyses were carried out using the IBM SPSS 21 (SPSS, Inc., Chicago, Illinois, USA). The level of statistical significance was established as $p < 0.05$.

Results

Characteristics for all variables in both groups at baseline are presented in table 1. There were no differences in the variance between groups in any of the variables analyzed at baseline.

Table 1. Sample characteristics and comparison between control and intervention group at baseline

	Control (n=18)		**Intervention** (n=17)		**Anova**	
	Mean	**95%CI**	**Mean**	**95%CI**	**F**	**p**
Age (years)	8.27	(7.42 9.12)	8.17	(7.06 9.41)	0.01	0.89
Weight (kg)	39.29	(34.16 44.75)	40.90	(32.62 50.21)	0.09	0.75
Height (m)	1.34	(1.29 1.38)	1.34	(1.27 1.41)	0.00	0.98
BMI (kg/m^2)	21.88	(20.28 23.52)	21.97	(19.57 24.54)	0.00	0.95
Body fatness	14.13	(11.04 17.38)	13.60	(8.97 18.67)	0.03	0.85
WC (cm)	73.81	(68.58 78.95)	71.26	(64.30 78.58)	0.32	0.57
Glucose (mg/dL)	86.27	(82.95 89.85)	83.12	(80.74 85.41)	2.17	0.15
HDL-C (mg/dL)	50.61	(44.98 56.52)	46.00	(42.15 49.75)	1.65	0.20
LDL-C (mg/dL)	94.49	(82.91 106.73)	97.93	(89.99 106.41)	0.20	0.65
TC (mg/dL)	158.11	(143.47 172.27)	171.64	(162.98 181.07)	2.28	0.14
AST (U/L)	28.50	(23.82 29.45)	28.65	(25.13 32.13)	0.98	0.32
ALT (U/L)	18.95	(16.85 21.54)	19.53	(18.20 20.94)	0.16	0.68
Insulin (UI/ml)	6.30	(5.24 7.61)	9.09	(6.85 11.67)	4.15	0.05
TG (mg/dL)	80.63	(68.53 94.19)	76.05	(63.31 89.72)	0.23	0.63
HOMA-IR	1.36	(1.09 1.68)	1.88	(1.41 2.41)	3.01	0.09

BMI: Body mass index; WC: Waist circumference; HDL-C: High-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; TC: Total cholesterol; AST: aspartate aminotransferase; ALT: alanine aminotransferase; TG: Triglycerides; HOMA: Homeostasis model assessment of insulin resistance.

Table 2 indicated the effect of time, group and interaction on cardiometabolic risk factors. It was found a significant interaction (time x group) on ALT, HOMA-IR, TC, HDL-C and LDL-C. Regarding AST and TG there was no significant effect of time, group and interaction.

Table 2. Intervention effect in time, group and interaction on cardiometabolic risk factors

					Mixed Anova*								
					Time			Group			Time x Group		
Variables	**Groups**		**Mean**	**SE**	**F**	**p**	**Eta**	**F**	**p**	**Eta**	**F**	**p**	**Eta**
AST (U/L)	CG	pre	28.50	3.05									
		post	27.93	1.13	0.01	0.92	0.00	0.09	0.77	0.00	2.21	0.15	0.08
	IG	pre	28.65	1.73									
		post	26.19	1.48									
ALT (U/L)	CG	pre	18.95	0.99									
		post	23.77	3.01	6.55	0.02	0.21	0.59	0.45	0.02	4.89	0.04	0.16
	IG	pre	19.53	1.02									
		post	16.69	3.10									
HOMA-IR	CG	pre	1.36	0.14									
		post	1.71	0.17	3.34	0.08	0.12	0.87	0.36	0.03	4.61	0.04	0.16
	IG	pre	1.88	0.25									
		post	1.46	0.20									
TC (mg/dL)	CG	pre	158.11	6.23									
		post	169.00	6.36	1.80	0.19	0.07	0.06	0.81	0.00	20.43	0.01	0.45
	IG	pre	171.64	6.41									
		post	156.22	6.55									
HDL-C (mg/dL)	CG	pre	50.61	2.49									
		post	44.87	2.37	0.60	0.44	0.02	1.51	0.23	0.06	29.70	0.01	0.54
	IG	pre	46.00	2.57									
		post	54.89	2.44									
LDL-C (mg/dL)	CG	pre	94.49	5.96									
		post	100.81	6.24	2.40	0.13	0.09	0.04	0.84	0.00	8.72	0.01	0.26
	IG	pre	97.93	4.14									
		post	94.79	4.62									
TG (mg/dL)	CG	pre	80.63	6.67									
		post	100.83	8.17	0.60	0.44	0.02	0.00	0.98	0.00	0.02	0.88	0.00
	IG	pre	76.05	6.82									
		post	95.58	5.82									

F: Mixed Anova; p: significance level <0.05; Eta: eta squared effect; CG: control group; IG: intervention group; SE: standard error; *adjusted for age, sex and sexual maturation.

AST. aspartate aminotransferase; ALT. alanine aminotransferase; HOMA-IR. Homeostasis model assessment of insulin resistance; TC. total cholesterol; HDL-C. High-density lipoprotein cholesterol; LDL-C. Low-density lipoprotein cholesterol; TG. Triglycerides

Figure 1 and 2 showed the individual prevalence of responsiveness on cardiometabolic risk factors, after the multicomponent intervention. In IG, 37.5% of individuals decreased levels of LDL-C, while CG increased 33.3% (Prevalence ratio (PR)=6.35; p=0.07). The same tendency was observed for ALT (IG=31.2%; CG=22.2%; PR=2.62; p=0.20), TC (IG=68.7%; CG=61.1; PR=11.64; p=0.01), TG (IG=18.7%; CG=72.2%; PR=3.17; p=0.29), HOMA-IR (IG=62.5%; CG= 38.8%; PR= 3.52; p=0.02), AST (IG=6.2%; CG=11.1%; PR= 3.58, p=0.30). Regarding HDL-C, IG increased 75% while CG decreased 61.1% (PR=13.76; p=0.008).

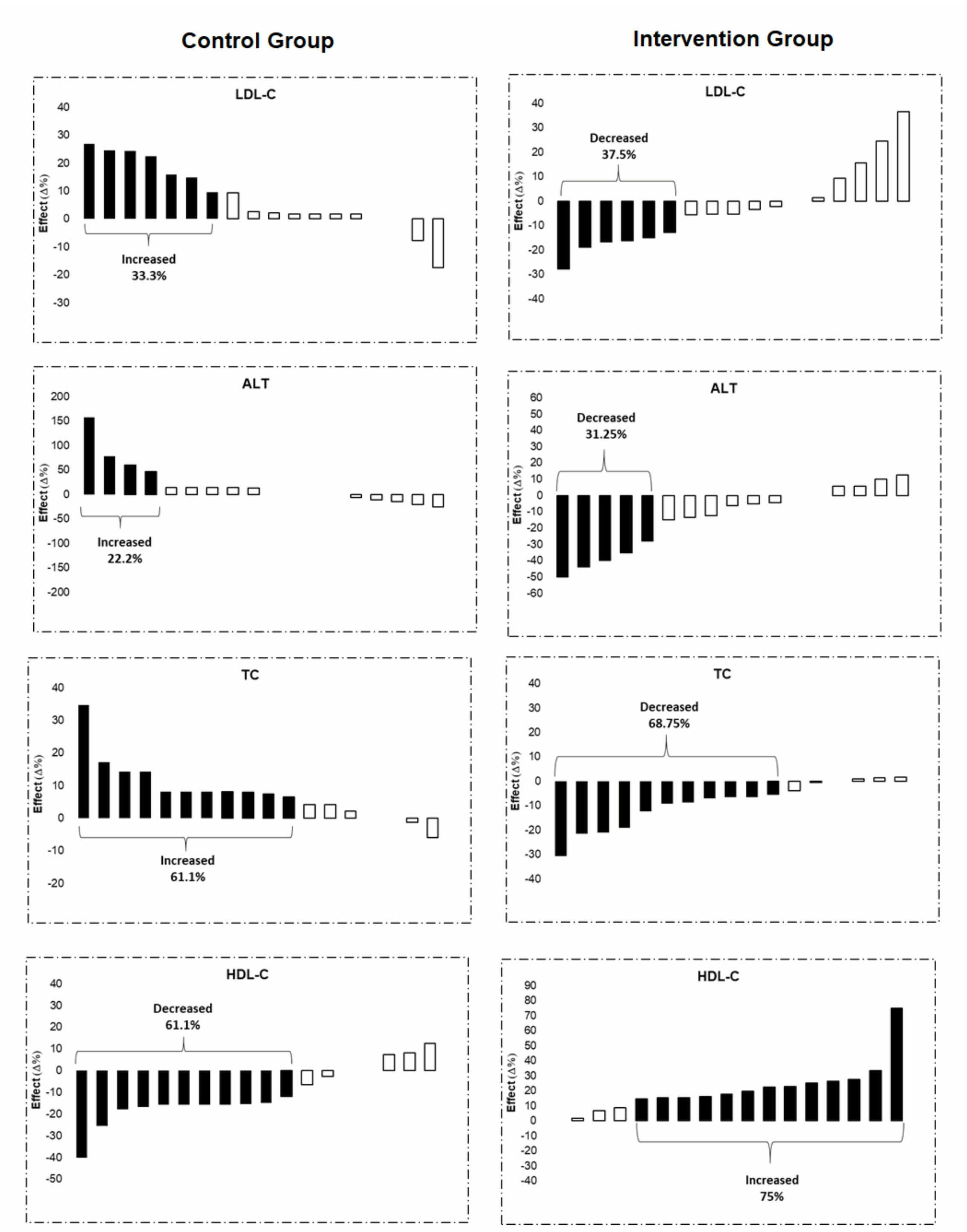

Figure 1. Individual responsiveness values of intervention and control group effects in delta percentual for LDL-C, ALT, TC and HDL-C.

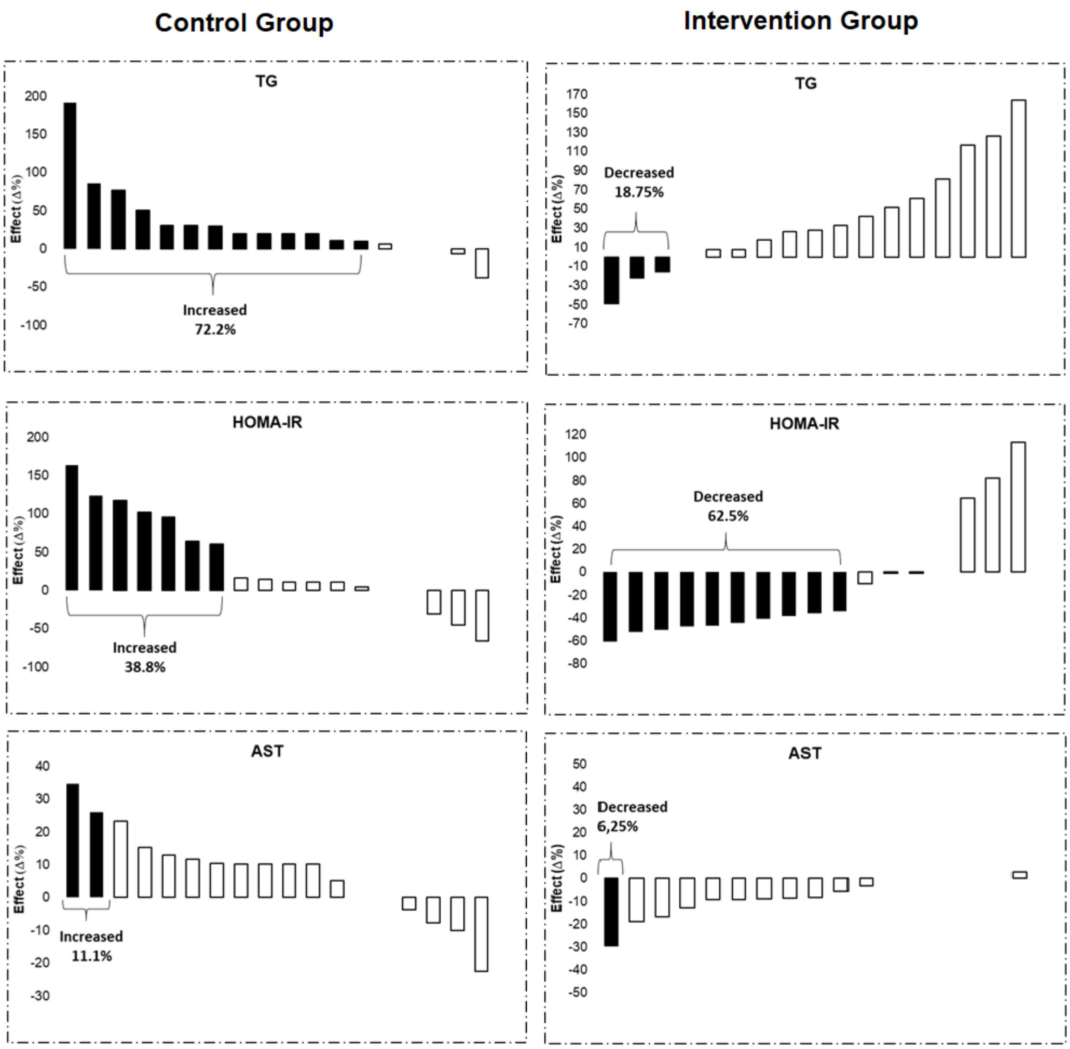

Figure 2. Individual responsiveness values of intervention and control group effects in delta percentual to TG, HOMA-IR and AST.

Discussion

The main findings of this study suggest that: 1) The multicomponent intervention group showed positive changes in several cardiometabolic risk factors such as HDL-C, LDL-C, TC, ALT and HOMA-IR, while no positive changes were observed in the CG; and 2) The prevalence of individuals that decreased values of cardiometabolic risk factors in IG was heterogeneous throughout the outcomes assessed: AST (6.25%), TG (18.75%), ALT (31.25%), LDL-C (37.5%), HOMA-IR (62.5%), TC (68.75%), while for HDL-C there was an increase of 75%, suggesting that individual responses to intervention in youth depends on the cardiometabolic outcome assessed, showing high level of intervariability. Regarding prevalence of responses between groups, it was found that 68.7% of individuals decreased TC in IG, while 61.1% of individuals increased this parameter in CG. This difference was also observed for HOMA-IR (IG=62.5% vs. CG= 38.8%), and HDL-C (IG=37.5; CG=33.3%). These findings suggest that youth in IG improved cardiometabolic risk factors after a multicomponent intervention, comparatively to those in CG, which worsened these parameters.

Regarding the effect of intervention considering mean values, previous studies have shown similar results. For instance, Nacimento et al. (2014) investigated the effect of a 8-month physical exercise program and found a reduction of TC, LDL-C, insulin, HOMA-IR, and an increase of HDL-C in obese children and adolescents. Similarly, Resaland et al. (2018) showed that a two-year school-based daily physical activity intervention was able to decrease TC to HDL-C ratio, TG and systolic blood pressure, as well as a clustered cardiovascular disease risk factors. However, although the results of the present study are in agreement to the above mentioned studies, the previous interventions were composed only by physical exercise. Therefore, studies aiming to determine the impact of multicomponent intervention are scarce, mainly regarding NAFLD parameters in Brazilian youth. In accordance with our findings, Africa, Newton, & Schwimmer, (2016). found a decrease of NAFDL markers in youths at risk profiles after lifestyle interventions; the studies included in this review had the durations ranging from 4 weeks to one year. The positive results regarding lipid profile were also observed in a systematic review and meta-analysis, indicating that lifestyle interventions are effective in decreasing levels of LDL-C, TG and fasting insulin in obese children after 4 weeks to 2 years of intervention (Ho et al., 2012).

Thus, our results add new findings on the effects of multicomponent intervention in the cardiometabolic risk outcomes in overweight/obese children and adolescents, showing that nutritional education and parental support may positively contribute along with exercise intervention in order to improve these outcomes in the participants. Also, our data reinforce that 12 weeks of intervention are enough to represents an improvement in overall cardiometabolic risk factors in overweight/obese, children and adolescents. This findings are especially relevant taken into consideration the high prevalence of obesity, as well as the increasing occurrence of risk to the cardiometabolic and musculoskeletal health in recent years in Brazilian children and adolescents (Flores, Gaya, Petersen, & Gaya, 2013; Gaya et al., 2017).

According to our knowledge, there is no evidence regarding the individual prevalence of responsiveness on cardiometabolic risk after a multicomponent intervention composed by exercise, nutritional education and family support in overweight/obese children. Some studies have described the effect of intervention in terms of "mean". Meyer et al. (2006) showed reductions of 5% in LDL-C, 26% in HOMA-IR and 23% in TG after a 6-month exercise program in obese children. In the same population, Karakabey et al, (2009) found improvements of 13% in HDL-C and reductions of 29% in LDL-C after 12 month of aerobic exercise program. Regarding NAFLD parameters, a 6-month lifestyle intervention for children presented reductions of 24% in ALT and 36% in AST (Koot et al., 2011). However, these authors did not report the individual prevalence of responsiveness among individuals. Considering that people exhibit a specificity of response, inducing a wide inter-individual variability in the adaptations to exercise training, we aimed to verify the individual prevalence of responsiveness on different cardiometabolic risk factors after a multicomponent intervention. Our findings indicated reductions of AST (6.25%), TG (18.75%), ALT (31.25%), LDL-C (37.5%), HOMA-IR (62.5%), TC (68.75%) and improvements in HDL-C (75%) in IG, and significant different prevalence between groups in TC, HOMA-IR, HDL-C. These findings indicate that the prevalence of individual increase or decrease depends on the cardiometabolic risk outcome assessed. Moreover, characteristics of training, such as volume, and exercise intensity (Kraus, 2002) have an effect on exercise-induced changes in blood lipids, and it seems that HDL-C is the most sensitive to exercise (Wang & Xu, 2017), which is in accordance with our findings.

In this line, a study developed with schoolchildren investigated the prevalence of non-responders, regarding different cardiometabolic and anthropometric indicators, after a high-intensity interval training and found that the prevalence of non-responders in a group of early maturation was 25% for HOMA-IR and 35% in normal maturation (Alvarez et al., 2017b). Although the multicomponent intervention developed in the present study had different methodological characteristics, the prevalence of individual that did not presented changes in HOMA-IR, was similar, i.e., approximately 38%. Alvarez et al., 2018 found lower prevalence of non-responders for HOMA-IR following a high-intensity interval training (17%), or a resistance training (18.5%); However, those children were diagnosed with insulin resistance (Álvarez et al., 2018), which was not the case in the present study. Some studies with adults, using different types of exercise, have reported the prevalence of non-responders. Álvarez et al., (2017c) showed that the prevalence of non-responders in woman with high HOMA-IR, was 25% and low HOMA-IR was 45% after a high-intensity interval training.

It is important to notice that the main responsible for inter-individual variability are genetic and environmental factors, such as different mode of exercise or health status (Bauman et al., 2012; Ridgers, Stratton, & Fairclough, 2011). Nevertheless, many of these factors have not been explored, in either adult and children (Mann, Lamberts, & Lambert, 2014). Also, some individuals experience adverse responses when exposed to regular exercise, but the causes of this phenomenon are still unknown (Bouchard et al., 2012). Thus, it is not known which mode of training may induce an increased or decreased amount of responders after interventions. Such information could be useful to develop physical activity programs taken into consideration the individual responsiveness, in order to be more effective promoting health among overweight/obese children.

The strengths of this study were that we included both the effect of a multicomponent intervention in a “mean term” as well as interindividual variability, which has been less investigated in relation to cardiometabolic risk factors among overweight/obese children. Otherwise, some limitation should me mentioned, such as the sample size that require caution regarding the extrapolation of these results, although we carried out the study with overweight/obese children and data regarding specific intervention among those population should be enhanced. Also, the intervention covered a limited time period (12 weeks) and, therefore, it would be interesting knowing whether a long-term program would result in continued improvement.

Conclusion

Our results suggest a positive, clinically relevant effect of a multicomponent intervention including exercise training, nutritional education and parental support on cardiometabolic risk factor of overweight/obese children. In addition, there was a high prevalence of positive responses in most of the cardiometabolic risk factors considered, which reinforce the program effectiveness. Thus, the implementation of this model of intervention might be considered by schools and policy makers, since its benefits seem to be established.

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CAPÍTULO VI

ARTIGO ORIGINAL- V

Multicomponent intervention effect on cardiometabolic risk factors among overweight/obese Brazilian children: a mediation analysis

Efeito de uma intervenção multicomponente em fatores de risco cardiometabólicos em crianças Brasileiras com sobrepeso e obesidade: uma análise de mediação

Este artigo encontra-se sob revisão para possível publicação no periódico *Nutririon, Metabolism and Cardiovascular Diesease*

ABSTRACT

Aim: To verify whether percentage of body fat, physical fitness, physical activity and total calorie intake mediate a multicomponent intervention effect on cardiometabolic risk factors in overweight/obese children.

Methods: This is a quasi-experimental study, developed with 35 overweight/obese school-aged children (control group=18 and intervention group=17), aged between 7 and 13 years (9.05±1.90). A 12-week multicomponent intervention was performed, consisting of physical exercise, nutritional education sessions and parental support. The following variables were evaluated at baseline and post-intervention: anthropometric measures and percentage of body fat, physical fitness, physical activity assessed by accelerometer, total calorie intake and biochemical assays. For statistical analysis generalized linear models were used.

Results: There was a significant intervention effect on changes in glucose, alanine aminotransferase (ALT), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), insulin and homeostasis model assessment of insulin resistance (HOMA-IR). In addition, the intervention effect on glucose was mediated by percentage of body fat (24%), muscular fitness (22%) and total calorie intake (40%). The same was observed for ALT, with a mediation proportion of 26%, 31% and 35%, respectively, as well as for HDL-C (percentage of body fat -30%, muscular fitness -30% and total calorie intake -33%); while vigorous physical activity mediated the intervention effect on glucose (40%), TC (37%), HDL-C (39%) and LDL-C (43%).

Conclusion: For an effective result on cardiometabolic risk factors among overweight/obese children, interventions strategies should focus on reducing percentage of body fat and calorie intake, and enhancing muscular fitness and vigorous physical activity.

Keywords: obesity; physical exercise; cardiometabolic health

RESUMO

Objetivo: Verificar se o percentual de gordura corporal, aptidão física, atividade física e ingestão total de calorias são mediadores do efeito de uma intervenção multicomponente em fatores de risco cardiometabólicos de crianças com sobrepeso/obesidade.

Métodos: esse é um estudo quase experimental, desenvolvido com 35 crianças com sobrepeso/obesidade (grupo controle=18 e grupo intervenção =17), com idades entre 7 e 13 anos (9,05±1,90). Foi realizada uma intervenção multicomponente, consistindo de exercício físico, sessões de educação nutricional e suporte parental. As seguintes variáveis foram avaliadas antes e após a intervenção: medidas antropométricas e percentual de gordura, aptidão física, atividade física avaliada por acelerômetro, consumo total de calorias e análises bioquímicas. Para análise estatística foram utilizados modelos lineares generalizados.

Resultados: Houve um efeito significativo da intervenção nas mudanças da glicose, alanina aminotransferase (ALT), colesterol total (CT), colesterol da lipoproteína de alta densidade e baixa densidade (HDL-C e LDL-C), insulina e modelo de homeostase de resistência à insulina (HOMA-IR). Além disso, o efeito da intervenção na glicose foi mediado pelo percentual de gordura corporal (24%), aptidão muscular (22%) and consumo total de calorias (40%). O mesmo foi observado para ALT, com uma proporção de mediação de 26%, 31% e 35%, respectivamente, assim como para o HDL-C (percentual de gordura corporal -30%, aptidão muscular -30% e consumo total de calorias -33%); enquanto que a atividade física vigorosa mediou o efeito da intervenção na glicose (40%), TC (37%), HDL-C (39%) e LDL-C (43%).

Conclusão: Para um resultado efetivo nos fatores de risco cardiometabólicos em crianças com sobrepeso e obesidade, as estratégias de intervenção devem ser focadas em reduzir o percentual de gordura e consumo de caloria, assim como aumentar a aptidão muscular e atividade física vigorosa.

Palavras-chave: obesidade; exercício físico; saúde cardiometabólica

INTRODUCTION

Cardiometabolic dysfunction and childhood obesity have been identified as important determinants of health, in early ages and adulthood. Research has made important contributions to understanding this scenario, indicating that there are many risk factors related to obesity and its cardiometabolic complications, such as dyslipidemia, insulin resistance and nonalcoholic fatty liver disease (NAFLD) [1–3]. Physical fitness and physical activity are considered health markers in children and adolescents, since studies have been shown that high levels of cardiorespiratory and muscular fitness, as well as physical activity may prevent the development of metabolic diseases and obesity [4,5]. Besides, dietary intake is also a predictor of cardiometabolic risk in youth [6].

However, children and adolescents do not meet the recommendation of physical activity and healthy eating [7,8]. Furthermore, a recent study with Brazilian children and adolescents indicated an increase in the occurrence of an aggregate risk to cardiometabolic risk (evaluated through body mass index and cardiorespiratory fitness) and musculoskeletal risk (flexibility and abdominal strength/resistance) over the years [9].

Based on these aspects, several physical activity intervention programs have been proposed for pediatric populations, indicating improvements in cardiorespiratory and muscular fitness, as well as in body composition [10,11]. Similarly, there is substantial evidence showing that exercise reduces cardiometabolic risk factors, such as insulin resistance, inflammatory biomarkers, dyslipidemia and hepatic lipid consumption in normal weight and obese, children and adolescents [11–14]. In addition to exercise, a multidisciplinary approach composed also by parental support and nutritional education interventions represent an appropriate strategy to promote health in this population[12,15].

However, it is important to consider that the relationship between the changes in cardiometabolic risk factors after an intervention program may be partly mediated by indirect mechanisms. Thus, we hypothesized that changes in physical fitness, physical activity, percentage of body fat and total calorie intake could intervene in the causal sequence between the intervention and cardiometabolic risk factors among overweight/obese youths. According to our knowledge, few studies were developed to understand the potential role of different mediators, which are related to modifiable risk factors, in the established effect of multicomponent intervention on cardiometabolic risk factors. Álvarez et al., (2018) recently suggested that the improvements in the lower body strength and the decreases in waist circumference could explain more the effects of the improvements in glucose control of insulin resistance schoolchildren after six weeks of resistance or high-intensity interval training. Also, we intend to present the relative contribution of each mediator. Finally, by knowing mediating mechanisms, what is relevant and what does not work, it allows researchers to determine in which aspects the intervention should be focused. Thus, the aim of the present study was to verify whether percentage of body fat, physical fitness, physical activity and calorie intake mediate the multicomponent intervention effect on cardiometabolic risk factors in overweight/obese children.

METHODS

This quasi-experimental study is part of the "Action for Health” (Adolescents and Children in a Training Intervention for Health) project, developed with overweight/obese low-income children of both genders, aged between 7 and 13 years. This multicomponent intervention program aims to promote physical activity after-school classes, nutritional education sessions, and parental support (Figure 1). It is based on the Behavior Change Ecological Model, which requires the implementation of multidisciplinary actions at different levels of intervention (intrapersonal, interpersonal and environmental) [17].

The evaluation methods and procedures were approved by the Scientific Board of the Research Unit that leads the project *(excluded information for blind review),* and is registered in www.clinicaltrials.gov (Number: NCT02929472). Also, all the Helsinki Declarations’ ethical aspects were followed [18]. More detailed information about study design and intervention process was published before [19].

Participants and procedures

The program was developed by four physical education teachers, one nutritionist, and one pediatrician who previously participated in weekly meetings (over six months), where methodologies and intervention sessions were prepared and tested. Seven graduate physical education students, and two graduate nutrition students collaborated in the program weekly sessions, and were trained and supervised by the project coordinator.

The project was publicized in two educational poles (six public schools) from João Pessoa-PB (Brazil), which were located in regions nearby the intervention site. All schools were located in a deprived area, with low socio-economic status: 62.5% of the mothers or fathers were unemployed and over 45% of the mothers and 64% of the fathers had concluded the 9th grade or less. Parents of potential participants (n = 276, according to school teacher´s or parent´s information) were invited to participate in early evening information meetings with the multidisciplinary staff. From those, ninety six parents attended the meetings, where all the potential participants were screened for inclusion criteria, defined as being overweight or obese, according to Cole et al criteria[20], and being not involved in any other physical exercise or diet program. From those attending the first screening fifty-three were excluded, leaving forty-three in the study, which were allocated in control group (CG, n=20) and intervention group (IG, n=23). However, two participants did not complete baseline evaluation in CG, and six in IG, leaving a total of 17 participants in CG and 18 in IG. Children and parents of the CG were advised to do not change their lifestyle during the period between the evaluations (12 weeks). They were advised that they could receive the same procedures of the IG after the 12-week period.

Multicomponent intervention program

Physical exercise intervention

The exercise sessions took sixty minutes, twice a week, during twelve weeks, always taught by the same physical education teachers. Each session included ten minutes of warm-up; thirty minutes of circuit training; fifteen minutes of pre-sports and recreational games; and five minutes of resting activities. Warm-up included aerobic/anaerobic and recreational activities. The circuit, divided into six stations, included activities that prioritized conditional and physical fitness components (muscular strength, CRF, balance, motor coordination and agility) [21]. Exercises were structured so that participants could maintain a high intensity throughout the circuit. This protocol has been used in other intervention studies with a similar sample [22,23].

Training intensity and compliance between individuals were defined to induce heart rate (HR) higher than 65% of HR_{max} of each participant. To monitor the activity, ten randomly selected participants wore a portable HR monitor (Polar Team^2 Pro, Polar, Finland) during sessions. Attendance average for IG was 85% (minimum of 73.6% and maximum of 88.9%).

Nutritional education intervention

The nutritional session was designed by the nutritionist staff, and consisted in two actions. The first one named dietary counseling. Each month, all participants and their parents were invited for a nutritional appointment in which was provided information about the food pyramid, weight loss importance, fat-free and low-energy foods, food calories, good nutritional choices on preparing low-coast meals, and decisions on food choices. The three sessions (1/month) were based on the information recorded through the participant´s 24h-recorded-dietary evaluation, which was done by the nutritional staff at baseline. The attendance to appointments was 100%. The second action consisted on the attempt to accomplishment of three daily dietary goals, during all the intervention development. These goals were focused on three main points: a) increase frequency and quantity intake of adequate food (fruit and vegetables); b) decrease of inadequate food intake (processed food and added sugar); and c) increase water consumption. Interventions focusing on these goals have been used in similar populations [24]. At the beginning of the intervention, participants received a worksheet to record day by day whether they met the daily goals. No significant inter subject variance was observed for the achievement of the proposed goals in the intervention group (data not shown).

Parental support intervention

Simultaneously, exercise sessions were offered to all parents in order to encourage family support. Adults' participation was voluntary and the parental support intervention was focused on improvement of three aspects: (a) encouragement through provision of transportation to physical activity facilities (100% attendance); (b) participation in physical activity with the children, when applicable (82% attendance); (c) watching the children during physical activities (95% attendance). The activities were carried out by a trained physical education teacher in the center of sports of Federal University of Paraíba, João Pessoa (Brazil), during children's same schedule. Parent's attendance average for the three different actions was 88%.

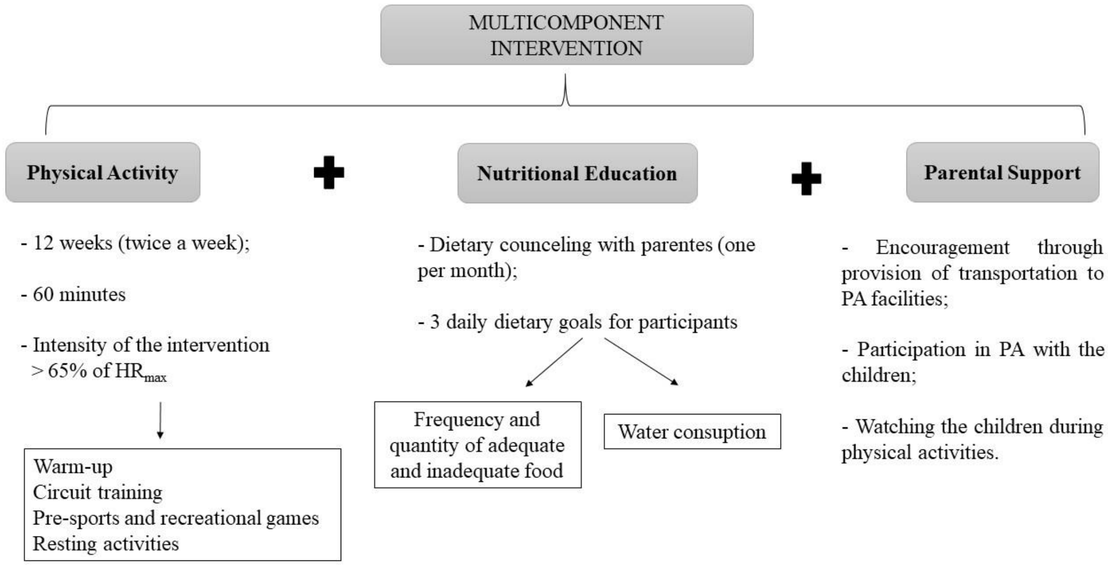

Figure 1. Organization of the multicomponent intervention.

Measures

Baseline measurements were conducted during a fourteen-day period, for CG and IG groups. On the first day, it was performed, the blood collection and anthropometric measures, on the second day, children did the body scan and participants and parents were interviewed about children´s 3-Day food intake record. The third and fourth days were used to administer physical fitness tests. On the fourth day participants received their accelerometer to be used during the last ten days of evaluation. All physical tests were carried out at the Physical Education Department of the Federal University of Paraiba. The blood analysis was carried out at a convened specialized laboratory in João Pessoa/Brazil. For post-intervention evaluation, the same procedures were followed.

Anthropometric measures and body composition

Height and weight were determined by a “Holtain” stadiometer, then body mass index was calculated, by dividing body mass (in kilograms) by height (in square meters). Percentage of body fat was measured after 4-hour-fasting and low water intake with a bioimpedance scale (Inbody 720, Biospace Co. Ltd.). Those measures were taken following standardized procedures [25].

Physical fitness

Cardiorespiratory fitness was measured using the 20m Shuttle-run Test. Participants completed 20m shuttle runs keeping in time with an audible "bleep" signal. The frequency of the sound signals were increased every minute, by 0.5 km/h, increasing the intensity of the test, and youth were encouraged to run to exhaustion (Léger, Mercier, Gadoury, & Lambert, 1988)[26]. The number of completed shuttles was recorded for each participant and retained for analysis. Evidence for the acceptable reliability and validity of the 20 m shuttle run test has been proven, with test-retest reliability coefficients ranging from r = 0.78 to r = 0.93 [27].

Upper-limb strength (ULS) was measured through a handgrip dynamometer (TKK 5101 Grip D; Takei, Tokyo Japan). The participant squeezed gradually and continuously for at least two seconds, performing the test with the right and left hands in turn, and with the elbow in full extension. The test was performed twice and the maximum score for each hand was recorded in kilograms. The sum of the scores achieved by left and right hands was used in the analysis. Lower-limb strength (LLS) test was carried out with was assessed by the standing-long jump. From a parallel standing position and with arms hanging loose to the side, participants were instructed to jump twice as far as possible in horizontal direction and to land on both feet. The test score (best of two trials) was the distance in centimeters, measured from the starting line to the point where the back of the heel landed on the floor. Abdominal strength was assessed by the cadence-based Curl Up Test (Cooper Institute for Aerobics Research, 1999)[28]. The results of the ULS, LLS and abdominal strength test were transformed to standardized values (Z-scores). Then the sum of Z-scores was performed to create a muscular fitness score.

Physical activity

Physical activity was measured by accelerometer (Actigraph, GT3X model, Florida). Participants used an accelerometer for ten consecutive days, and were provided with written instructions regarding care and placement of the accelerometers, along with a diary of activities in which they were required to record use and non-use time, and also habitual physical activities. Data reduction was performed by Actlife software, version6.11.7. Criteria for a successful recording were a minimum of four days of the week and one day of the weekend and more than 480 minutes per day [29], and the time of non-use was estimated based on periods of more than 20 consecutive minutes of zero [30]. Of these four days, two days should correspond to intervention days and two days without intervention (one weekend day). The epoch period was set at 15 seconds, based on recommendations to similar sample [31], and the output was expressed as counts per minute (counts/min). Activity counts were summed for each hour that the accelerometer was worn between 7:00 h and 24:00 h to provide a representative picture of daily activity. Specific cut points proposed by Evenson et al., (2008) were used to determine vigorous physical activity (≥ 4012) intensities.

Total calorie intake

Food intake was carried out by a 24-hour recall. Participants, along with their parents, informed food intake during the past two weekdays and one weekend day before evaluation. Data from these three days were tabulated in the software "Virtual Nutri" to obtain the total energy intake values for each of the three days. For analytical procedures, the mean value of caloric intake among the three days was used and data were recorded in kcal.

Biochemical assays

The circulating levels of plasma insulin, plasma glucose, plasma cholesterols (total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol (HDL-C)), plasma triglycerides (TG), alanine aminotransferase (ALT), aspartate aminotransferase (AST), were measured through peripheral puncture in the cubital vein after a nocturnal twelve hour-fasting, by laboratory specialists, using standard techniques at an accredited partner laboratory. The analysis of TC, HDL-C, TG, and glucose was carried out by spectrophotometry (Cobas Integra 400 Plus) with Roche® kits. The LDL-C fraction was indirectly calculated using the Friedewald formula [33]. The AST and ALT levels were determined by enzyme kinetic assay for spectrophotometrically obtained after 10 minutes centrifugation at 3500 rpm. Insulin was determined by Luminex-100 IS (Integrated System: Luminex Corporation, Austin, TX, USA), using the Linco Human Gut Hormone panel kit (Linco Research Inc., MO, USA). As a proxy measure of insulin resistance, Homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as the product of basal glucose (mmol/L) and insulin (μlU/mL) levels divided by 22.5 [34]. All samples were run in duplicates and the means were calculated. The intra-assay coefficients of variation were less than 20%, according to the manufacturer.

Statistical analyses

Descriptive data are presented as means and standard error. All variables were checked for normality. Independent t-tests was conducted to test for differences between the IG and CG in cardiometabolic risk factors at baseline.

Generalized linear models were used to analyze the mediated effect. To assess mediating effects, the product-of-coefficient test was used. This test consist of: (1) estimating the main effect of the intervention on changes in the dependent variables, where in the dependent variables (glucose, AST, ALT, HDL-C, LDL-C, total cholesterol, triglycerides, insulin and HOMA-IR) at post-intervention was regressed on the intervention condition and dependent variables at baseline (c-coefficient); (2) estimating the effect of the intervention on changes in the potential mediators by regressing the PI-values of the mediators (percentage of body fat, cardiorespiratory fitness, muscular fitness, vigorous physical activity and total calorie intake) onto the intervention condition, adjusted for baseline values of the mediators (a-coefficient); (3) estimating the independent effect of changes in the potential mediators on changes in the dependent variables, adjusted for the intervention condition, by regressing the post-intervention values of dependent variables onto the intervention condition, baseline values of dependent variables and the post-intervention and baseline values of the potential mediators (b-coefficient); and (4) computing the product of the two coefficients (a*b), representing the mediated effect. The statistical significance of the mediated effect was estimated by the Sobel test. All analyses were adjusted for sexual maturation. Whether there was no effect of the intervention on cardiometabolic risk factors mediation analyses was not conducted.

Furthermore, the proportion mediated was calculated by dividing the product-of-coefficient (a*b) by the total main effect of the intervention condition on the dependent variables (c-coefficient).

All the analyses were carried out using the IBM SPSS 21 (SPSS, Inc., Chicago, Illinois, USA). The sample size was calculated a *posteriori* in the software G*power version 3.1, considering that participants were volunteered selected. Thus, for linear multiple regression, a medium effect of the intervention and a medium effect of mediation on dependent variables (F^2= 0.15 to 0.35) were considered and the value of the statistical power was between 0.60 and 0.80, as well as the level of statistical significance was established as p<0.05.

RESULTS

Participated in the study 35 overweight/obese children (22 girls and 13 boys) mean 9.05±1.90 aged years old. There was no difference between CG and IG group at baseline, in the potential mediators: muscular fitness (CG: -0.01±0.23, IG: 0.01±0.12, p=0.91); percentage of body fat (CG: 14.13±1.62, IG: 13.60±2.44, p=0.85), vigorous physical activity (CG: 11.76±2.02, IG: 8.04±1.61, p=0.16) and total calorie intake (CG: 1706.17±72.12, IG: 1807.62±100.17, p=0.41). Cardiorespiratory fitness was the only potential mediator that showed difference at baseline (CG: 7.24±0.57, IG: 10.82±1.05, p=0.005).

Table 1 shows the cardiometabolic risk factors mean values of children in CG and IG, as well as the intervention effect. Insulin was the only variable that presented difference between groups at baseline (CG: 1706.17±72.12, IG: 1807.62±100.17, p=0.41). Furthermore, there was a significant intervention effect on changes in fasting glucose, ALT, TC, HDL-C, LDL-C, insulin and HOMA-IR.

Table 1. Cardiometabolic risk factors in control and intervention group at baseline and post-intervention and intervention effect on cardiometabolic risk factors.

	Baseline			Post-intervention		Intervention effect	
	Control (n=18)	Intervention (n=17)		Control (n=18)	Intervention (n=17)		
Cardiometabolic risk factors	Mean(SE)	Mean(SE)	p	Mean(SE)	Mean(SE)	c-coefficient (95%)	p
ALT (U/L)	18.95(0.99)	19.53(1.02)	0.68	23.77(3.01)	16.69(3.10)	-0.82 (-1.28 -0.35)	**<0.001**
AST (U/L)	28.50(3.05)	28.65(1.73)	0.96	27.93(1.13)	26.19 (1.48)	-0.02 (-0.51 0.46)	0.92
TC (mg/dL)	158.11(6.23)	171.64(6.41)	0.14	169.00(6.36)	156.22(6.55)	-0.88 (-1.28 -0.49)	**<0.001**
HDL-C (mg/dL)	50.61(2.49)	46.00(2.57)	0.20	44.87(2.37)	54.89(2.44)	1.20 (0.82 1.59)	**<0.001**
LDL-C (mg/dL)	94.49(5.96)	97.93(4.14)	0.65	100.81(6.24)	94.79(4.62)	-0.58 (-0.97 -0.20)	**0.003**
TG (mg/dL)	80.63(6.67)	76.05(6.82)	0.63	100.83(8.17)	95.58(5.82)	-0.10 (-0.80 0.59)	0.77
Glucose (mg/dL)	86.27(1.48)	83.12(1.53)	0.15	90.27(1.38)	82.96(1.42)	-0.91 (-0.42 0.73)	**<0.001**
Insulin (UI/ml)	6.30(0.95)	9.09(0.98)	**0.05**	7.66(0.90)	7.10(0.92)	-0.66 (-1.30 -0.03)	**0.04**
HOMA-IR	1.36(0.14)	1.88(0.25)	0.09	1.71(0.17)	1.46(0.20)	-0.79 (-1.38 -0.19)	**0.009**

AST. aspartate aminotransferase; ALT. alanine aminotransferase; TC. total cholesterol HDL-C. High-density lipoprotein cholesterol; LDL-C. Low-density lipoprotein cholesterol; HOMA-IR. Homeostasis model assessment of insulin resistance.

Table 2 shows the effect of the intervention on the mediator (2nd step on mediation analysis; a-coefficient), the effect of the mediator on dependent variables (3nd step on mediation analysis; b-coefficient) and the mediated effects for the intervention effect on the dependent variables (4nd step on mediation analysis; a*b). Percentage of body fat mediated the intervention effect on ALT (26%), total cholesterol (21%), HDL-C (30%) and glucose (24%). Cardiorespiratory fitness did not mediated the intervention effect on any of the cardiometabolic risk factors, while muscular fitness mediated the intervention effect on ALT (31%), total cholesterol (22%), HDL-C (30%) and glucose (22%). Regarding vigorous physical activity, it was observed a mediation effect on total cholesterol (37%), HDL-C (39%), LDL-C (43%) and glucose (40%). Finally, total calorie intake mediated the intervention effect on total cholesterol (32%), ALT (35%), HDL-C (33%) and glucose (36%).

Table 2. Potential mediators of the intervention effect on cardiometabolic risk factors

	Intervention effect on mediator a (95% IC)	p	Effect mediator on dependent variable b (95% IC)	p	Mediated effect a*b (95% IC)	p	Proportion mediated (%)
Percentage of body fat	-0.25(-0.35, -0.15)	<0.001					
ALT (U/L)	-	-	-0.88(-1.48, -0.27)	0.004	0.22(0.06, 0.37)	**0.007**	26.0
TC (mg/dL)	-	-	-0.76(-1.31, -0.20)	0.007	0.19(0.06, 0.32)	**0.01**	21.0
HDL-C (mg/dL)	-	-	1.50(0.98, 2.01)	<0.001	0.37 (0.22, 0.52)	**<0.001**	30.0
LDL-C (mg/dL)	-	-	-0.21(-0.72, 0.30)	0.42	0.05 (-0.06, 0.16)	0.42	-
Glucose (mg/dL)	-	-	-0.90 (-1.57, -0.23)	0.008	0.22(0.04, 0.39)	**0.01**	24.0
Insulin (UI/ml)	-	-	-0.21(-0.77, 0.53)	0.71	0.05 (-0.10, 0.20)	0.52	-
HOMA-IR	-	-	-0.29(-0.90, 0.32)	0.35	0.07(-0.06, 0.20)	0.35	-
Cardiorespiratory fitness	0.35(-0.25, 0.95)	0.25					
ALT (U/L)	-	-	-0.79(-1.31, -0.27)	0.003	0.27(-0.22, 0.76)	0.27	-
TC (mg/dL)	-	-	-0.84(-1.29, -0.38)	<0.001	0.29(-0.24, 0.76)	0.26	-
HDL-C (mg/dL)	-	-	1.14(0.70, 1.58)	<0.001	0.39(-0.79, 1.57)	0.25	-
LDL-C (mg/dL)	-	-	-0.57(-1.01, -0.12)	0.01	0.19 (-0.16, 0.54)	0.28	-
Glucose (mg/dL)	-	-	-0.82(-1.32, -0.32)	<0.001	0.28(-0.22, 0.78)	0.27	-
Insulin (UI/ml)	-	-	-0.41(-1.12, 0.29)	0.25	0.14(-0.19, 0.47)	0.41	-
HOMA-IR	-	-	-0.53(-1.18, 0.12)	0.11	0.18(-0.19, 0.55)	0.34	-
Muscular fitness	0.27(0.02, 1.52)	0.02					
ALT (U/L)	-	-	-1.06(-1.54, -0.58)	<0.001	0.28(0.01, 0.55)	**0.04**	31.0
TC (mg/dL)	-	-	-0.77(-1.18, -0.36)	<0.001	0.20(0.01, 0.39)	**0.05**	22.0
HDL-C (mg/dL)	-	-	1.03(0.62, 1.44)	<0.001	0.27(0.02, 0.25)	**0.03**	30.0
LDL-C (mg/dL)	-	-	-0.69(-1.10, -0.28)	<0.001	0.18(-0.01, 0.35)	0.06	-
Glucose (mg/dL)	-	-	-0.95(-1.48, -0.42)	<0.001	0.25(0.001, 0.50)	**0.05**	22.0
Insulin (UI/ml)	-	-	-0.94(-1.56, -0.32)	0.003	0.25(-0.02, 0.52)	0.07	-
HOMA-IR	-	-	1.05(-1.64, -0.46)	<0.001	0.28(-0.09, 0.45)	0.06	-

Vigorous physical activity	0.40 (0.10, 0.71)	0.009					
ALT (U/L)	-	-	-0.56(-1.02, -0.10)	0.01	0.22(-0.01, 0.45)	0.07	-
TC (mg/dL)	-	-	-0.84(-1.29, -0.38)	<0.001	0.33 (0.04, 0.62)	**0.03**	37.0
HDL-C (mg/dL)	-	-	1.17(0.74, 1.60)	<0.001	0.46(0.09, 0.83)	**0.01**	39.0
LDL-C (mg/dL)	-	-	-0.63(-1.06, -0.20)	0.004	0.25 (0.02, 0.48)	**0.04**	43.0
Glucose (mg/dL)	-	-	0.92(-1.46, -0.38)	<0.001	0.36(0.03, 0.69)	**0.03**	40.0
Insulin (UI/ml)	-	-	-0.54(-1.17, 0.09)	0.09	0.21(-0.08, 0.50)	0.15	-
HOMA-IR	-	-	-0.67(-1.26, -0.09)	0.02	0.26(-0.03, 0.55)	0.08	-
Total calorie intake	-0.34(-0.64, -0.04)	0.02					
ALT (U/L)	-	-	-0.87(-1.38, -0.36)	<0.001	0.29(0.001, 0.58)	**0.05**	35.0
TC (mg/dL)	-	-	-0.88(-1.31, -0.46)	<0.001	0.29(0.001, 0.58)	**0.04**	32.0
HDL-C (mg/dL)	-	-	1.20(0.78, 1.61)	<0.001	0.40(0.03, 0.77)	**0.03**	33.0
LDL-C (mg/dL)	-	-	-0.64(-1.02, -0.27)	<0.001	0.21(-0.001, 0.42)	0.06	-
Glucose (mg/dL)	-	-	0.92(-1.46, -0.38)	<0.001	0.36(0.03, 0.69)	**0.03**	40.0
Insulin (UI/ml)	-	-	-0.50(-1.15, 0.15)	0.13	0.17(-0.08, 0.42)	0.20	-
HOMA-IR	-	-	-0.62(-1.23, -0.01)	0.04	0.21(-0.06, 0.48)	0.13	-

ALT. alanine aminotransferase; TC: total cholesterol; HDL-C. High-density lipoprotein cholesterol; LDL-C. Low-density lipoprotein cholesterol; HOMA-IR. Homeostasis model assessment of insulin resistance

DISCUSSION

Considering that the direct effect of intervention on cardiometabolic risk factors is already known, our study aimed to add new information regarding the role of potential mediators in this relationship. Thus, our findings revealed that there was a significant intervention effect on changes in glucose, ALT, TC, HDL-C, LDL-C, insulin and HOMA-IR. Besides, percentage of body fat, muscular fitness, total calorie intake and vigorous physical activity mediated the intervention effect on above-mentioned cardiometabolic risk factors. We highlight that the present study is the first to investigate the role of different mediators in the intervention effect on cardiometabolic risk factors in overweight/obese children.

Our findings indicated that the multicomponent intervention was effective to reduce ALT levels, while for AST there was no changes. In line with the present results, a systematic review investigated the effect of lifestyle interventions on NAFLD and found a decrease in ALT levels in children[11]. More recently, Gonzales-Ruiz et al. (2017) indicated that exercise was associated with a reduction in visceral, subcutaneous and intrahepatic fat, but did not alter AST and ALT among overweight/obese youths. Given the direct effect of intervention on ALT, we also showed that decreases in percentage of body fat and total calorie intake, as well as increasing muscular fitness mediated this effect in 26%, 35% and 31%, respectively. We are not aware of studies investigating the role of potential mediators of the intervention effect on these variables. Thus, we hypothesized that these parameters mediated the intervention effect, considering that they are closely associated with changes in NAFLD parameters. Adiposity is a key factor for NAFLD [36], as well as dietary habits [37], thus reducing percentage of body fat and total calorie intake may mediate de effect of a multicomponent intervention on ALT. More recently, it has been suggested that increasing muscular fitness presented benefits on hepatic fat content reduction in youth [38]. The mechanisms through which muscular fitness might influences NAFLD have not been clarified, but it have been suggested that increased muscular fitness might improve lipid profile, glucose metabolism, as well as increased secretion of myokines, leading to the development of NAFLD at early ages [39].

The positive effect of the multicomponent intervention on lipid profile parameters is in accordance with previous studies developed with obese children and adolescents [14,23,40]. In addition, our findings indicated that change in percentage of body fat, muscular fitness and total calorie intake mediate the intervention effect on TC and

HDL-C. Moreover, vigorous physical activity mediates the intervention effect in the same variables, additionally LDL-C. This means that change in percentage of body fat, muscular fitness, total calorie intake and vigorous physical activity might be a biologically plausible mechanism explaining the intervention effects on lipid profile parameters. Some cross sectional studies have already explored the role of some of the potential mediators investigated in our study on different cardiometabolic risk factors in children [41,42]. For example, increased vigorous physical activity was associated with reduced cardiometabolic risk factors, including HDL-C and LDL-C in children (Vaisto, 2018). However, previous intervention research has not specifically examined the mediating role of change in lipid profile.

Regarding glucose metabolism, the intervention also showed positive effect, with reductions in fasting insulin, glucose and HOMA-IR. This findings are in agreement with previous systematic review and meta-analysis in young population with excess of adiposity [14,44]. Mediation analysis showed that percentage of body fat, muscular fitness, total calorie intake and vigorous physical activity mediated the intervention effect only for fasting glucose. Although the intervention was effective in reducing HOMA-IR and insulin, surprisingly none of the potential mediators mediate the intervention effect on these variables. Probably the amount of changes in the mediators was not enough to promote changes on the intervention effect of these variables. A recent study in Chilean children with insulin resistance showed that waist circumference changes directly contribute to explaining the variance in HOMA-IR changes (38%), whereas the lower body strength (leg press) might directly contribute to explaining the variance (27%) in glucose control and indirectly contribute to the improvement in body composition [16].

Some limitations of this study should be acknowledged. The intervention covered a limited time period (12 weeks) and, therefore, it would be interesting knowing whether a long-term program would result in continued improvement. Also, not randomization and the small sample size requires precautious generalization regarding to extrapolation of these results to the wider population of Brazilian overweight/obese children. The main strength is that as far as we know this is the first study using mediation analysis in the intervention effect on several cardiometabolic risk factors. Besides, we considered the role of different mediators. Finally, the multicomponent design of the intervention that included besides physical exercise, nutritional education and parents intervention is another important issue.

In conclusion, percentage of body fat, muscular fitness, vigorous physical activity and calorie intake mediate the multicomponent intervention effect on cardiometabolic risk factors in overweight/obese children. Thus, the results of this study provide new evidence, indicating that some intermediate variables should be considered when analyzing the relationship between the intervention effects on cardiometabolic risk factors. We also emphasize that to achieve this goal, clinical practice should recommend lifestyle changes, resulting in a combination of decreasing percentage of body fat and total calorie intake, but also increasing muscular fitness and vigorous physical activity, for a better cardiometabolic health profile among children.

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CAPÍTULO VII

CONSIDERAÇÕES FINAIS

REFERÊNCIAS

CONSIDERAÇÕES FINAIS

As principais conclusões da tese são as seguintes:

A obesidade atua como mediadora da associação entre a aptidão física e os fatores de risco cardiometabólicos. Além disso, a relação entre as variáveis APCR e aptidão muscular com os fatores de risco metabólicos varia de acordo com o grau de adiposidade, ou seja, a obesidade é moderadora dessa relação.

O programa de intervenção multicomponente foi efetivo, promovendo melhora dos fatores de risco cardiometabólicos em crianças com sobrepeso e obesidade. Sendo que esse efeito foi mediado pelo aumento da aptidão muscular e da atividade física vigorosa, bem como diminuição da ingestão total de calorias e adiposidade.

Portanto, os estudos apresentados nessa tese reforçam o papel determinante da obesidade nos fatores de risco cardiometabólicos e estabelecem que, para que se alcancem resultados benéficos nesses fatores de risco, é necessário que os programas de intervenção estejam voltados além da redução da adiposidade, para o aumento da aptidão muscular, atividade física vigorosa e diminuição da ingestão total de calorias. Ainda, cabe mencionar que o programa de intervenção aplicado não foi capaz de aumentar a APCR, nesse sentido chamamos a atenção para a dificuldade em melhorar esse componente da aptidão física, especificamente em crianças com sobrepeso e obesidade.

Por fim, destaca-se que a intervenção multicomponente utilizada foi bem sucedida promovendo melhora nos fatores de risco metabólicos em crianças, podendo então servir como base para o desenvolvimento de políticas públicas que visem a prevenção e promoção da saúde na população infantil.

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APÊNDICES

APÊNDICE A – Termo de consentimento livre e esclarecido (UFRGS)

APÊNDICE B – Termo de assentimento (UFRGS)

APÊNDICE C- Termo de consentimento livre e esclarecido (UFPB)

APÊNDICE D – Termo de assentimento (UFPB)

APÊNDICE A

Termo de Consentimento Livre e Esclarecido – Pais ou Responsáveis

Seu filho(a) está sendo convidado a participar de um estudo que visa avaliar alguns indicadores de saúde da criança. Este projeto está vinculado a Escola de Educação Física da Universidade Federal do Rio Grande do Sul (ESEFID-UFRGS). A participação do seu filho(a) nesse estudo é muito importante para podermos verificar o perfil de saúde dos escolares.

Caso você e seu filho(a) aceitem participar do estudo, o período de avaliação será de aproximadamente 2 meses, realizada na escola, sob responsabilidade dos pesquisadores. Serão avaliados peso corporal, estatura, composição corporal e massa muscular. Para estas avaliações, será necessário que ele use trajes esportivos (calção, bermuda, camiseta). Da mesma forma, será verificada a pressão arterial com uso de um aparelho específico que fará uma leve pressão no braço do participante. A capacidade física (velocidade, agilidade, resistência abdominal, flexibilidade e capacidade cardiorrespiratória). Além disso, serão aplicados entrevistas/questionários para avaliar o estilo de vida (tempo de sono, prática de atividade física). Da mesma forma, coletas de sangue serão necessárias para avaliar a quantidade de gordura e açúcar no sangue e substâncias inflamatórias. A coleta de sangue será realizada a partir do uso de uma seringa com uma picada em uma das veias perto da dobra do cotovelo. O procedimento será realizado por um profissional devidamente qualificado e certificado, com material descartável e esterilizado. Será coletada 8 ml de sangue para verificar os níveis de gordura e açúcar. Na segunda etapa, seu filho usará aparelho semelhante a um relógio que mede a quantidade de atividade física realizada fora das aulas de educação física durante cinco dias, esse relógio será usado durante todo o dia e somente será retirado para tomar banho ou durante atividades aquáticas.

Seu filho será avaliado por uma equipe de pesquisadores experientes, desta forma, os riscos serão mínimos. A participação neste estudo é absolutamente voluntária, sem qualquer tipo de gratificação. Entretanto, vocês terão direito a um laudo individual com os resultados, bem como, a todo e qualquer esclarecimento sobre o estudo. Vocês são livres para realizarem quaisquer perguntas antes, durante e após o estudo, estando livres para desistirem do mesmo em qualquer momento sem prejuízo ou penalidade alguma. Todas as informações referente ao estudo são totalmente confidenciais (dados de identificação, resultados, vídeos) tendo acesso somente os profissionais envolvidos no estudo e os responsáveis legais da criança. Todas as informações referente ao estudo ficarão armazenadas em local seguro na ESEFID-UFRGS por um prazo de cinco anos e após isso serão completamente destruídas/deletadas. Os dados serão submetidos em forma de artigos científicos em jornais especializados da área de forma a não identificar os voluntários. Todas as informações obtidas são absolutamente sigilosas e seu nome não será identificado em nenhum momento.

Qualquer dúvida ou dificuldade você pode entrar em contato com a Coordenadora do Projeto Anelise Reis Gaya pelo telefone (51) 99242909 ou se preferir tirar suas dúvidas diretamente no Comitê de Ética em Pesquisa da Universidade Federal do Rio Grande do Sul, o qual está localizado Av. Paulo Gama, 110 – 7° andar – Porto Alegre/RS ou pelo fone/fax 51 3308-4085 – email: pro-reitoria@propesq.ufrgs.br

Eu, ____ e meu dependente ____ fomos informados sobre os objetivos acima especificados e da justificativa desta pesquisa, de forma clara e detalhada aceitamos participar voluntariamente do estudo.

Este termo de consentimento livre e esclarecido deverá ser preenchido em duas vias, sendo uma mantida com o representante legal da criança, e outra mantida arquivada pelo pesquisador.

Porto Alegre, _________ de _________________________ de ____________.

____

Assinatura do responsável

____

Assinatura do participante da pesquisa

____

Assinatura do Pesquisador Responsável

APÊNDICE B

Termo de Assentimento

A pesquisa é uma maneira de aprender mais sobre as pessoas e o comportamento do exercício físico. Por isso, estamos fazendo uma pesquisa para entender como o exercício físico afeta a saúde das crianças. Então, você está sendo convidado a participar dessa pesquisa. Discutimos essa pesquisa com seus pais ou responsáveis e eles sabem que também estamos pedindo seu acordo. Mas se você não desejar fazer parte na pesquisa, não é obrigado, até mesmo se seus pais concordarem.

Estamos fazendo uma pesquisa para entender como o treinamento de futebol afeta a saúde das crianças. Além disso, queremos entender como as aulas de educação física podem trazer benefícios a sua saúde. Então precisaremos realizar alguns testes para ver o que mudou a partir da prática de exercício. Você precisará comparecer no Laboratório de Pesquisa e Exercício (LAPEX) na Escola de Educação Física, Fisioterapia e Dança da UFRGS para responder algumas perguntas sobre saúde e prática de atividade física, após iremos realizar avaliações físicas com medidas de peso, estatura, medidas de comprimento da cintura e quadril, e do percentual de gordura. Para realizar estas avaliações será necessário que você use trajes esportivos (calção, bermuda, camiseta). Além disso, será verificada a pressão arterial com uso de um aparelho que fará uma leve pressão no seu braço. Também mediremos sua resistência física durante o exercício com um teste de pedalada em bicicleta, para isso será colocada uma máscara que mede a quantidade de ar que você respira. Durante esse teste você poderá sentir-se cansado, como em uma aula de educação física. Também iremos tirar um pouco do seu sangue, porque só a partir desse teste que poderemos ver se o exercício físico é realmente bom, pois no momento que fazemos exercícios algumas substâncias no nosso sangue aumentam ou diminuem. Você sentirá uma picada em uma das veias perto da dobra do cotovelo, mas depois não deve sentir nada. O procedimento será feito por uma pessoa que faz isso muitas vezes em outras crianças como você.

Em um outro dia realizaremos alguns testes físicos com você que envolvem correr, medir a força dos braços e pernas e a sua flexibilidade. Para finalizar, você usará um aparelho similar a um relógio que mede a quantidade de atividade física realizada fora das aulas de educação física durante 5 dias. Nesses dias você não vai usar esse relógio somente durante o banho ou atividades aquáticas.

Você somente participará do estudo se quiser. Além disso, mesmo que você aceite participar do estudo assinando seu nome agora, você pode desistir de participar a qualquer momento e ninguém ficará chateado com você. Se qualquer coisa incomum acontecer a você, precisaremos saber e você deverá se sentir à vontade de nos chamar a qualquer momento. Quando acabar o estudo você terá direito a um laudo com todos os resultados das suas avaliações. Com os dados de todos os participantes nós escreveremos relatórios que não identificarão quem foram os participantes. Você pode fazer perguntas a qualquer membro da equipe de pesquisa e se você não compreender qualquer parte deste estudo, ou ainda se antes de participar você tiver alguma dúvida você pode ligar para o pesquisador responsável Caroline Brand ou Anelise Reis Gaya - (51) 99242909. Se você decidiu que você quer participar deste estudo, por favor escreva o seu nome abaixo. Todas as informações referentes ao estudo são totalmente confidenciais e ficarão armazenadas em local seguro na ESEFID-UFRGS por um prazo de cinco anos e após isso serão completamente destruídas/deletadas.

Porto Alegre, ________ de ________________________ de ___________.

Assinatura do responsável

Assinatura do participante da pesquisa

Assinatura do pesquisador responsável

APÊNDICE C

Termo de Consentimento Livre e Esclarecido

Prezado (a) Senhor (a) ,

Esta pesquisa, denominada Ação para a Saúde, trata de um PROGRAMA DE INTERVENÇÃO EM ATIVIDADE FÍSICA para crianças e adolescentes obesos e está sendo desenvolvida pela pesquisadora CLARICE MARTINS, do Programa Associado de Pós-Graduação UPE/UFPB. O objetivo do estudo é determinar os padrões, relações e impacto da atividade física, dos comportamentos sedentários e da aptidão física relacionada à saúde em indicadores de saúde / doença de crianças e adolescentes obesos. Já a finalidade deste trabalho reside em contribuir para que o seu filho / educando possa participar em um programa de promoção da saúde de qualidade e gratuito. Além disso, o (a) senhor (a) receberão informações relevantes em relação a parâmetros de saúde dos seus educandos, permitindo um maior esclarecimento em relação à importância dos temas abordados no projeto.

Solicitamos a sua colaboração para autorizar a participação do seu filho / educando no projeto, como também sua autorização para apresentar os resultados deste estudo em eventos e revistas científicas da área de saúde, mantendo o total anonimato dos participantes envolvidos. Informamos ainda que essa pesquisa não oferece riscos previsíveis para a saúde do seu filho / educando. Esclarecemos que a participação do seu filho / educando no estudo é voluntária e, portanto não é obrigado(a) a fornecer as informações e/ou colaborar com as atividades solicitadas pela Pesquisadora. Caso decida não participar do estudo, ou participando, resolva desistir do mesmo, não sofrerá nenhum dano.

Diante do exposto, declaro que fui devidamente esclarecido(a) e dou o meu consentimento para participar da pesquisa e para publicação dos resultados nela obtidos. Estou ciente que receberei uma cópia desse documento.

____
Assinatura do Responsável Legal

____
Assinatura da Testemunha

Caso necessite de maiores informações, favor contactar:
Profª Dra. Carice Martins (83) 99930116 / (81) 97782686
E-mail: clarice.br@fade.up.pt
OU Comitê de Ética em Pesquisa do Centro de Ciências da Saúde da Universidade Federal da Paraíba Campus I - Cidade Universitária - 1º Andar – CEP 58051-900 – João Pessoa/PB (83) 3216-7791 – E-mail: eticaccsufpb@hotmail.com

Atenciosamente,

____
Assinatura do Pesquisador Responsável

APÊNDICE D

Termo de Assentimento

Título do Projeto: AÇÃO PARA A SAÚDE
Investigador: Clarice Maria de Lucena Martins
Local da Pesquisa: Universidade Federal da Paraíba - UFPB
Endereço: Cidade Universitária – João pessoa / PB – cep:58051-900

O que significa assentimento?

O assentimento significa que você concorda em fazer parte de um grupo de adolescentes, da sua faixa de idade, para participar de uma pesquisa. Serão respeitados seus direitos e você receberá todas as informações por mais simples que possam parecer.

Pode ser que este documento denominado TERMO DE ASSENTIMENTO LIVRE E ESCLARECIDO contenha palavras que você não entenda. Por favor, peça ao responsável pela pesquisa ou à equipe do estudo para explicar qualquer palavra ou informação que você não entenda claramente.

Informações ao Paciente:

Você está sendo convidado a participar de uma pesquisa. As pesquisas têm como objetivo desenvolver novos conhecimentos sobre algo que a ciência ainda não tem resposta, ou não tem certezas. Esta pesquisa, que você está sendo convidado a participar é denominada Ação para a Saúde. Trata de um PROGRAMA DE ATIVIDADE FÍSICA para crianças e adolescentes obesos e está sendo desenvolvida pela pesquisadora CLARICE MARTINS, da Universidade Federal da Paraíba. O objetivo do estudo é entender o comportamento e o efeito do programa de atividades sobre a sua saúde. O programa é gratuito e você participará de diferentes atividades físicas com professores e uma equipe bem qualificada. Além disso, o (a) seu (sua) pai (mãe) receberá informações relevantes em relação à sua saúde.

Informamos ainda que essa pesquisa não oferece riscos previsíveis para a sua saúde que sua participação é voluntária. Portanto, você não é obrigado(a) a fornecer as informações e/ou colaborar com as atividades solicitadas pela Pesquisadora. Caso decida não participar do estudo, ou participando, resolva desistir do mesmo, não sofrerá nenhum dano.

Diante do exposto, declaro que fui devidamente esclarecido(a) e dou o meu consentimento para participar da pesquisa e para publicação dos resultados nela obtidos. Estou ciente que receberei uma cópia desse documento.

Contato para dúvidas

Se você ou os responsáveis por você tiver(em) dúvidas com relação ao estudo, direitos do participante, ou no caso de riscos relacionados ao estudo, você deve contatar a Investigadora Responsável pela pesquisa, professora Clarice Martins**,** telefone fixo 32456236 e celular 99930116**.** Se você tiver dúvidas sobre seus direitos como um participante da pesquisa, você pode contatar o Comitê de Ética em Pesquisa em Seres Humanos (CEP) do Centro de Ciências da Saúde da Universidade Federal da Paraíba.

O CEP é constituído por um grupo de profissionais de diversas áreas, com conhecimentos científicos e não científicos que realizam a revisão ética inicial e continuada da pesquisa para mantê-lo seguro e proteger seus direitos.

DECLARAÇÃO DE ASSENTIMENTO DO PACIENTE:

Eu li e discuti com o investigador responsável pelo presente estudo os detalhes descritos neste documento. Entendo que eu sou livre para aceitar ou recusar, e que posso interromper a minha participação a qualquer momento sem dar uma razão. Eu concordo que os dados coletados para o estudo sejam usados para o propósito acima descrito.

Eu entendi a informação apresentada neste TERMO DE ASSENTIMENTO.

Eu tive a oportunidade para fazer perguntas e todas as minhas perguntas foram respondidas.

Eu receberei uma cópia assinada e datada deste Documento DE ASSENTIMENTO INFORMADO.

NOME DO ADOLESCENTE - DATA

NOME DO INVESTIGADOR - DATA

ANEXOS

ANEXO A

UNIVERSIDADE FEDERAL DO RIO GRANDE DO SUL / PRÓ-REITORIA DE PESQUISA -

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: EFEITOS DE UM PROGRAMA DE INTERVENÇÃO COM FUTEBOL SOBRE AS VARIÁVEIS ASSOCIADAS À COGNIÇÃO, À SÍNDROME METABÓLICA E A MARCADORES INFLAMATÓRIOS EM CRIANÇAS

Pesquisador: Anelise Reis Gaya
Área Temática:
Versão: 3
CAAE: 58108916.0.0000.5347
Instituição Proponente: Escola de Educação Física da Universidade do Rio Grande do Sul
Patrocinador Principal: Financiamento Próprio
DADOS DO PARECER
Número do Parecer: 1.814.830
Apresentação do Projeto:
Trata-se de projeto de pesquisa associado a uma tese de doutorado apresentada ao PPG em Ciência do Movimento Humano da ESEF que retorna para uma terceira rodada de avaliação.

Objetivo da Pesquisa:
Objetivo Geral
Avaliar os efeitos de um programa de intervenção com futebol nas aulas de educação física e orientação nutricional sobre as variáveis associadas à cognição, à síndrome metabólica e a marcadores inflamatórios em crianças eutróficas e com excesso de peso corporal.

Objetivos Específicos
Avaliar os efeitos de um programa de futebol nas aulas de educação física e orientação nutricional sobre as seguintes variáveis nos momentos pré e pós intervenção:
- Níveis de aptidão cardiorrespiratória;
- Níveis de atividade física diário;
- Variáveis antropométricas e composição corporal;
- Pressão arterial sistólica e diastólica;
- Colesterol total, triglicerídeos, LDL e HDL;

- Níveis de PCR, adiponectina e leptina;
- Glicose e resistência à Insulina;
- Desempenho acadêmico e cognitivo;
- Verificar se as alterações nas categorias de risco dos componentes da síndrome metabólica e nos níveis dos marcadores inflamatórios, serão associados às alterações na aptidão cardiorrespiratória, independente das modificações na composição corporal.

Avaliação dos Riscos e Benefícios:
Os riscos e benefícios estão adequadamente apresentados, bem como estão apontadas as formas empregadas para minimizá-los.

Comentários e Considerações sobre a Pesquisa:
Trata-se de um projeto que busca avaliar os efeitos de um programa de intervenção com futebol nas aulas de educação física e orientação nutricional sobre as variáveis associadas à cognição, à síndrome metabólica e a marcadores inflamatórios em crianças eutróficas e com excesso de peso corporal. Considerando que os padrões de comportamentos prejudiciais à saúde, como sedentarismo, má alimentação e inatividade física são cada vez mais recorrentes na rotina de crianças e adolescentes; que estes fatores como os principais responsáveis pela ocorrência precoce da síndrome metabólica; que os programas de intervenção com futebol são referidos por promoverem aumento da aptidão cardiorrespiratória, diminuição da gordura corporal e consequentemente melhora dos fatores de risco cardiometabólicos das crianças; e considerando ainda o ambiente escolar para o seu desenvolvimento deste programa, não há dúvidas que se trata de um projeto meritório.

Farão parte do estudo100 alunos selecionados entre os 10 turmas do 1° ao 5° ano da Escola Estadual de Primeiro e Segundo Grau Presidente Roosevel, de Porto Alegre. Os participantes, divididos em dois grupos, controle e experimental, serão avaliados antes e após um programa sistematizado de futebol três vezes por semana com duração de 45-60 minutos, por 12 semanas.

Serão avaliadas variáveis antropométricas pela medida da estatura e massa corporal; percentual de gordura pela medição de dobras cutâneas; composição corporal pela técnica de absorciometria com raios X de dupla energia (DEXA); marcadores bioquímicos (perfil lipídico, glicose, insulina, etc) através da coleta de 8 ml de sangue; pressão arterial e frequência cardíaca; aptidão cardiorrespiratória por teste máximo em ciclo ergômetro juntamente com ergoespirométrica; nível de atividade física com acelerômetro (5 dias consecutivos); inquérito alimentar, preenchido pelos pais; desempenho acadêmico e cognitivo, pelas notas das crianças e pelo "Teste das Matrizes Progressivas Coloridas de Raven", respectivamente.
Os objetivos estão claros, a revisão de literatura é pertinente e atualizada e a metodologia está adequada aos objetivos do projeto.

Considerações sobre os Termos de apresentação obrigatória:
Folha de rosto, adequada.
Orçamento, adequado.
Cronograma, adequado.
Projeto completo, adequado
Termo de consentimento, adequado.
Termo de assentimento, adequado
Autorização de instituições participantes, adequado

Recomendações:
Não há recomendações.

Conclusões ou Pendências e Lista de Inadequações:

Na segunda rodada de avaliação, havia sido solicitado:
- esclarecimentos sobre a responsabilidade do projeto
- registro de todos os participantes na Plataforma Brasil
- esclarecimentos sobre o contato/convite com os participantes
- adequação do TCLE
- adequação do texto do projeto

Todos as solicitações foram adequadamente atendidas, estando o projeto em condições de ser aprovado.

Considerações Finais a critério do CEP:
Aprovado.
Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_P ROJETO_753574.pdf	13/10/2016 08:36:00		Aceito
Outros	CARTA_RESPOSTA.docx	13/10/2016 08:34:11	Anelise Reis Gaya	Aceito
Projeto Detalhado / Brochura Investigador	Projeto.pdf	13/10/2016 08:32:37	Anelise Reis Gaya	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE.pdf	13/10/2016 08:31:43	Anelise Reis Gaya	Aceito
Declaração de Instituição e Infraestrutura	DeclaracaoLapex1.pdf	17/08/2016 10:55:56	Anelise Reis Gaya	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Termo_Assentimento1.pdf	17/08/2016 10:55:10	Anelise Reis Gaya	Aceito
Folha de Rosto	folha_de_rosto.pdf	26/07/2016 10:59:23	Anelise Reis Gaya	Aceito
Outros	Parecer_compesq.pdf	11/07/2016 14:02:19	Anelise Reis Gaya	Aceito
Outros	Parecer_2.pdf	05/07/2016 12:19:47	Anelise Reis Gaya	Aceito
Outros	Parecer_1.pdf	05/07/2016 12:19:27	Anelise Reis Gaya	Aceito
Orçamento	Orcamento.pdf	05/07/2016 12:04:29	Anelise Reis Gaya	Aceito
Declaração de	TemoEscola.pdf	05/07/2016	Anelise Reis Gaya	Aceito

Instituição e Infraestrutura		12:01:10		
Cronograma	Cronograma.pdf	05/07/2016 11:56:11	Anelise Reis Gaya	Aceito

Situação do Parecer:
Aprovado

Necessita Apreciação da CONEP:
Não

PORTO ALEGRE, 10 de Novembro de 2016

Assinado por:
MARIA DA GRAÇA CORSO DA MOTTA
(Coordenador)

ANEXO B

UNIVERSIDADE FEDERAL DAPARAÍBA

CENTRO DE CIÊNCIAS DA SAÜDE

COMITÊ DE ÉTICA EM PESQUISA

C E R T I D Ã O

Certifico que o Comitê de Ética em Pesquisa do Centro de Ciências da Saúde da Universidade Federal da Paraíba — CEP/CCS aprovou por unanimidade na 9ª Reunião realizada no dia 18/09/2014, o Projeto de pesquisa intitulado: **“AÇÃO PARA A SAÚDE — ACTION FOR HEALTH — ADOLESCENTE AND CHILDREN IN A TRAINING INTERVENTION FOR HEALTH”** da Pesquisadora Clarice Maria de Lucena Martins. Protocolo 0390/14. CAAE: 33353414.1.0000.5188.

Outrossim, informo que a autorização para posterior publicação fica condicionada à apresentação do resumo do estudo proposto à apreciação do Comitê.

Andrea Márcia da C. Lima
Mat. SIAPE 1117510

ANEXO C

UFPB

DECLARAÇÃO

Eu, Clarice Maria de Lucena Martins, docente permanente do Programa Associado de Pós-Graduação em Educação Física da Universidade Federal da Paraíba e coordenadora do projeto de pesquisa intitulado “Ação para a Saúde — Action for Health — adolescent and children in a training intervention for health” (aprovado no comitê de ética e pesquisa, Protocolo 0390/14, CAAE: 33353414.1.0000.5188), autorizo a utilização dos dados do referido projeto, à professora Anelise Reis Gaya do Programa de Pós-Graduação em Ciências do Movimento Humano da Universidade Federal do Rio Grande do Sul, bem como da sua orientanda Caroline Brand.

Paraíba, fevereiro de 2018

Clarice Martins

Prof. Dra. Clarice Maria de Lucena Martins

DIVULGAÇÃO DO ESTUDO

DIVULGAÇÃO A – Modelo de relatório entregue aos alunos (UFRGS)

DIVULGAÇÃO B – Modelo de relatório entregue aos alunos (UFPB)

DIVULGAÇÃO A

Para cada aluno que participou do projeto realizado na escola de Porto Alegre foi entregue um relatório com os resultados dos testes físicos, avaliação nutricional e exames sanguíneos. Além disso foi realizada uma reunião com os pais e/ou responsáveis para apresentar os resultados encontrados, assim como sanar possíveis dúvidas.

Responsável: | **Aluno**

E.E.E.B PRESIDENTE ROOSEVELT

AVALIAÇÃO

IDADE

SÉRIE/TURMA

APTIDÃO FÍSICA RELACIONADA À SAÚDE E PERFIL NUTRICIONAL

TESTES	MEDIDA	CLASSIFICAÇÃO
PESO (Kg)	30	
ALTURA (m)	1,27	
IMC	18,6	Sobrepeso
PERÍMETRO DA CINTURA (cm)	62,5	
PRESSÃO ARTERIAL (mmHg)	108/64	
FLEXIBILIDADE (cm)	40	Saudável
ABDOMINAIS (rep)	24	Saudável
APTIDÃO CARDIORRESPIRATÓRIA (m)	616	Risco

A flexibilidade, abdominais e aptidão cardiorrespiratória referem-se às capacidades que estão profundamente relacionadas com a saúde e à qualidade de vida!

Quanto maior a aptidão física, mais energia para a realização das atividades do dia-a-dia e menor o risco de doenças crônico-degenerativas

APTIDÃO FÍSICA RELACIONADA AO DESEMPENHO ESPORTIVO

TESTES	MEDIDA	CLASSIFICAÇÃO
FORÇA MUSCULAR DE MEMBROS SUPERIORES (cm)	173	Razoável
FORÇA MUSCULAR DE MEMBROS INFERIORES (cm)	87	Fraco
AGILIDADE (seg)	9,46	Fraco
VELOCIDADE (seg)	5,59	Fraco

A força de membro superios e inferior, agilidade e velocidade compreendem os componentes necessários para a prática e o sucesso em vários esportes!

AVALIAÇÃO SANGUÍNEA

TESTES	MEDIDA	CLASSIFICAÇÃO
GLICOSE (mg/dL)	79	Desejável
TRIGLICERÍDEOS (mg/dL)	119	Elevado
COLESTEROL (mg/dL)	212	Elevado

Lembramos que esses são exames diagnósticos, caso detectado alguma alteração recomenda-se que procurem um médico!

RELATÓRIO SOBRE HÁBITOS ALIMENTARES

ASPECTO AVALIADO	PARECER
CAFÉ DA MANHÃ	Atingiu
INGESTÃO DE FRUTAS	Atingiu
INGESTÃO DE VERDURAS E SALADAS	Não atingiu
DOCES, REFRIS E INDUSTRIALIZADOS	Não atingiu
INGESTÃO DE ÁGUA	Não atingiu

Uma criança tem necessidades nutricionais específicas, comer carnes, arroz e feijão, ao menos duas frutas diariamente, leite e derivados vão contribuir com seu crescimento e desenvolvimento!

PROJETO ESPORTE E SAÚDE NA ESCOLA

Educação física e promoção da saúde a favor da comunidade escolar

Telefone: 33085883

DIVULGAÇÃO B

Para cada aluno que participou do programa de intervenção multicomponente foi entregue um relatório com os resultados da primeira e segunda avaliação, referente às variáveis antropométricas, físicas e bioquímicas.

UNIVERSIDADE FEDERAL DA PARAÍBA
CENTRO DE CIÊNCIAS DA SAÚDE
DEPARTAMENTO DE EDUCAÇÃO FÍSICA
PROJETO "ESCOLHINHA DO MOVIMENTO"

RELATÓRIO DE DADOS ANTROPOMÉTRICOS, BIOQUÍMICOS E FÍSICOS

VARIÁVEIS ANTROPOMÉTRICAS			
Variáveis	**T0 Maio/2015**	**T1 Setembro/2015**	**Referência**
Peso	34,90	28,40	
Altura	1,29	1,30	
IMC	21,10	21,20	
% GC	34,00	34,80	
TMB	867	874	
Água Corporal	16,90	17,10	
Proteínas	4,60	4,60	
Minerais	1,48	1,58	
Gordura Corporal	11,90	12,50	
Circunf. Cintura	72,00	68,00	
Circunf. Quadril	77,00	78,00	
VARIÁVEIS FÍSICAS			
Atividade Física Sedentária	383,8	381,9	
Atividade Física Leve	345,1	313,9	
Atividade Física Moderada	10,6	12,0	
Atividade Física Vigorosa	3,6	2,1	
Atividade Física Total	359,3	328,0	
Sentar e Alcançar Esq	30,50	30,50	≥23
Sentar e Alcançar Dir	29,00	29,75	≥23
Extensão de tronco	18,50	34,00	≥15
Abdominais	0	0	≥4

Flexões	0	0	≥3
Vai e Vem	10	13	-
Equilíbrio	25,00	38,00	
Saltos laterais	37	50	
Saltar com uma perna	25	24	
Transposição lateral	16	21	
Saltos pés juntos	94,00	110,50	
Dinamometria Esq	12,25	10,25	
Dinamometria Dir	11,00	11,00	
Resist. Respiratória	-	-	
VO² Máx.	-	-	
FC Máx.	-	-	
VE Máx.	-	-	
PAS Máx.	-	-	
PAD Máx.	-	-	
VARÁVEIS BIOQUÍMICAS			
Glicose	76,00	77,00	
HDL	51,00	60,00	
LDL	76,00	77,00	
Colesterol Total	140,00	154,00	
AST	30,00	33,00	
ALT	22,00	21,00	
Insulina	6,70	10,20	
HOMA	1,27	1,94	
Triglicerídeo	64,00	85,00	
CT/HDL	2,70	2,60	

Obrigada pela participação!