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TESE

CONTROLE DO BIOFILME SUPRAGENGIVAL INTERPROXIMAL:

ESTUDOS SOBRE A POSSIBILIDADE DE COMPENSAÇÃO DO USO DO FIO DENTAL

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PORTO ALEGRE, NOVEMBRO DE 2020

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Tese apresentada ao Programa de Pós-Graduação em Odontologia da Faculdade de Odontologia da Universidade Federal do Rio Grande do Sul como requisito obrigatório para obtenção do título de Doutor em Odontologia, área de concentração Clínica Odontológica/Periodontia.

Orientador: Prof. Dr. Cassiano Kuchenbecker Rösing

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"*It's always me and you against the world... Love you 3000, Kiddo*"

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May God Bless Us All!

SUMÁRIO

RESUMO

O uso do fio dental é o meio mais difundido para a manutenção da saúde na região interproximal dos dentes onde mais se acumula biofilme. Em 2015, a US Dietary Guideline removeu do seu guia que é lançado a cada quinquênio o fio dental, o que levou a chamada polêmica do fio dental, na qual diversas revistas interpretaram como sendo demonstrativa da não necessidade do uso do fio dental na manutenção da saúde bucal. Os estudos que ~~sustentam~~ ~~suportam~~ estas conclusões apenas avaliam questionando ao indivíduo o uso ou não do fio dental levando, então, a resultados em revisões sistemáticas concluírem que o fio dental é ineficaz no controle das doenças bucais. No entanto, estes resultados mostram apenas haver dificuldades e não necessariamente que ele não é eficaz. Esta tese é composta por cinco artigos que sustentam os benefícios de dispositivos e métodos não interproximais com alguma possibilidade clinicamente relevante de remover biofilme interproximal. O primeiro artigo serve de sustentação da tese na qual a literatura foi buscada para se verificar as dificuldades no uso do fio dental e as possíveis formas de se compensar. Na sequência, dois artigos abordam o papel de escovas de dentes sobre a área interproximal (uma revisão sistemática da literatura e um ensaio clínico randomizado). Continuando, dois artigos abordam o uso de enxaguatório a base de cloreto de cetilpiridínio como possível compensador de efeito nas áreas interproximais. Os resultados apresentados na tese levam à conclusão de que são observados padrões adequados de higiene bucal na região interproximal em não usuários de dispositivos interproximais tanto quando se usam escovas de ponta cônica quanto com um enxaguatório a base de cloreto de cetilpiridinio. Estes resultados provêm possíveis alternativas para compensar as dificuldades com o uso do fio dental nas superfícies interproximais.

ABSTRACT

Flossing is the most widespread mean of maintaining health in the interproximal region of where biofilm accumulates the most. In 2015, the US Dietary Guideline removed dental floss from its guide, which is released every five years, which led to the so-called dental floss controversial, in which several magazines interpreted it as a demonstration of no necessity to use dental floss to maintain oral health. The studies that support these conclusions only evaluate by asking the individual whether or not to use dental floss, thus leading to results in systematic reviews concluding that dental floss is ineffective in the control of oral diseases. However, these results only show difficulties and not necessarily that it is not effective. This thesis consists of five articles that support the benefits of non-interproximal devices and methods with some clinically relevant possibility of removing interproximal biofilm. The first article supports the thesis in which the literature was sought to verify the difficulties in using dental floss and the possible ways to compensate. Following, two articles address the role of toothbrushes in the interproximal area (a systematic review of the literature and a randomized clinical trial). Continuing, two other articles address the use of a mouthwash based on cetylpyridinium chloride as a possible effect compensator in interproximal areas. The results presented in the thesis lead to the conclusion that good oral hygiene parameters are observed in the interproximal region in non-users of interproximal devices, both when using tapered-tip brushes and with a rinse based on cetylpyridinium chloride. These results provide possible alternatives to compensate for difficulties with flossing on interproximal surfaces.

APRESENTAÇÃO

A presente tese de doutorado intitulada "*Controle do biofilme supragengival inteproximal: estudos sobre a possibilidade de compensação do uso do fio dental*" está sendo apresentada ao programa de Pós-Graduação em Odontologia da Universidade Federal do Rio Grande do Sul como parte dos requisitos para obtenção do título de Doutor em Clínica Odontológica/Periodontia.

O financiamento dos estudos apresentados nesta tese esteve sob a responsabilidade da **Latin American Oral Health Association – LAOHA** assim como todo o financiamento do Doutorado do aluno em questão.

A temática apresentada nesta tese é de grande importância para a ciência e a prática clínica odontológica. A tese contém uma introdução geral, seguida de 5 artigos científicos e considerações finais. Nesse sentido, um estudo de revisão de literatura foi realizado sobre a polêmica do fio dental publicado em uma revista de circulação nacional com finalidade informativa a profissionais de todas as especialidades odontológicas na coluna Novas Tendências da Revista Clínica – International Journal of Brazilian Dentistry (ISSN – 1806-5015) como justificativa para realização desta tese. Adicionalmente, duas revisões sistemáticas da literatura, uma aceita para publicação numa revista internacional e a outra encontra-se submetida em um periódico internacional. Por fim, dois ensaios clínicos randomizados que foram aceitos para publicação em dois periódicos internacionais.

Artigo 1: A reflexão sobre a polêmica do fio dental: mitos e realidades.

Artigo 2: Antiplaque and antigingivitis efficacy of different bristles stiffness and end-shape on interproximal surfaces: A systematic review with meta-analysis.

Artigo 3: Efficacy of two soft-britles toothbrushes in plaque removal – A randomized controlled trial.

Artigo 4: Anti-plaque and anti-gingivitis efficacy of cetylpyridinium chloride with zinc lactate in comparison to essential oils mouthwashes: Randomized clinical trial.

Artigo 5: The effect of cetylpyridinium chloride mouthrinse as adjunct to toothbrushing compared to placebo on interproximal plaque and gingival inflammation - A systematic review with meta-analises

Esta tese é parte da trajetória acadêmica do candidato. Além dos artigos científicos aqui apresentados, outras produções foram realizadas durante o período do doutorado. A lista a seguir demonstra todas as produções realizadas pelo candidato durante esse período:

ARTIGOS:

1- Rosing CK, Langa, GPJ, Weidlich P. A nova classificação das doenças e condições do periodonto – Parte I: Saúde periodontal e condições gengivais. Clínica - International Journal of Brazilian Dentistry, Florianópolis, v. 15, n. 1, p. 104-106, jan./mar. 2019.

2- Muniz FWMG, Langa GPJ, Pimentel RP, Martins JR, Pereira DH, Rösing CK. Comparison Between Hand and Sonic/ Ultrasonic Instruments for Periodontal Treatment: Systematic Review with Meta-Analysis. J Int Acad Periodontol. 2020 Oct 1;22(4):187-204. PMID: 32980832.

3- Nicolini AC, Rotta IDS, Langa GPJ, et al. Efficacy of ozonated water mouthwash on early plaque formation and gingival inflammation: a randomized controlled crossover clinical trial. 2020. Clin Oral Investig. 2020;10.1007/s00784-020-03441-y. doi:10.1007/s00784-020-03441-y.

4- Rösing CK, Cavagni J, Langa GPJ, Mazzetti T, Muniz FWMG. Dental care and the COVID-19 pandemic: the precautionary principle and the best available evidence. Pesqui Bras Odontopediatria Clín Integr. 2020; 20(supp1):e 0115. https://doi.org/10.1590/pboci.2020.118.

CAPÍTULOS DE LIVROS:

1- Rosing CK, Langa GPJ, Arroyo D, Muniz FWMG. Condições de Risco (Fatores, Indicadores, Preditores/Marcadores) e sua relação com a Medicina Periodontal. In: Daiane Peruzzo. Medicina Periodontal. Página 1-6. ISBN: 9788578891787

2- Rosing CK, Muniz FWMG, Langa GPJ, Cavagni J. A importância do uso de enxaguatórios bucais no controle do biofilme supragengival. In: Giuseppe Romito, Patricia Bella Costa e Sergio Kahn. Perioline Clínico. Quintessence Editora Brasil e Sobrape.

INTRODUÇÃO

O biofilme dental é o principal fator etiológico das doenças cárie e doença periodontal, que são as principais doenças que afetam a cavidade bucal. A importância da remoção do biofilme supragengival está bem estabelecida na literatura com relação à manutenção da saúde bucal. Redução das taxas de cárie, doença periodontal e consequentemente, menores taxas de perda de dentes foi mostrado na literatura em populações com bons padrões de controle do biofilme, mais recentemente ainda, estudos mostraram melhores resultados na manutenção de implantes dentários são observados (1)(2-6). O método mais amplamente utilizado para manutenção da saúde bucal é a desrupção mecânica do biofilme supragengival (1).

A rotina de higiene bucal exige tempo, destreza e motivação o que muitas vezes torna difícil este procedimento. Portanto, são evidentes os limites da eficácia clínica da higiene bucal auto-realizada. Alguns estudos têm demonstrado a presença de biofilme remanescente apesar dos esforços na remoção do biofilme dentário (6, 7). A nova classificação das doenças e condições periodontais estabeleceu 10% como máximo de sítios com sangramento nos pacientes a serem classificados como saudáveis, o que se consegue com bons hábitos de higiene oral (8).

As escovas dentais são consideradas o padrão ouro para remoção do biofilme dentário. As cerdas das escovas dentais diferem na sua textura, ponta, dureza e até material, podendo ser naturais ou sintéticos. Estudos comparando a eficácia das escovas dentais disponíveis são escassos na literatura. O uso das escovas dentais de cerdas macias tem sido recomendado para melhorar a redução da placa e minimizar a lesão dos tecidos gengivais (9, 10). Portanto, estudos comparando a eficácia dos produtos disponíveis são importantes para melhor embasar a indicação de qualquer escova dental.

O uso da escova dental é naturalmente realizado em associação aos dentifrícios, que de certa forma auxiliam no efeito cosmético, a partir da limpeza pela remoção da gordura pelos detergentes, o combate a halitose e uma sensação de frescor que tanto agrada ao paciente. Os preventivos terapêuticos, prestam também um benefício extremamente importante para a saúde, tendo o exemplo dos fluoretos, que é considerada a principal razão do declínio da cárie em muitos países (11). O fluoreto estanoso apresentou também resultados significativamente melhores no controle de placa e gengivite quando comparado com um dentrifício comum (12), e, recentemente,

o uso dos sais de zinco, mostraram benefícios no controle de placa e gengivite significativamente melhores quando comparado a um dentifrício comum (13).

A região interproximal é frequentemente relatada como sendo a região de maior dificuldade de manutenção de níveis de saúde. As regiões interproximais dos dentes posteriores e anteriores são as áreas mais comuns onde a placa se acumula e afeta a prevalência de doenças bucais (14), estudos epidemiológicos mostram que as populações apresentam maiores índices de inflamação gengival na região interproximal quando comparado as faces livres (15, 16). Estes dados podem indicar uma maior prevalência de doença na região interproximal, dado ainda não abordado na literatura. O meio mais difundido para o controle de biofilme e gengivite na região interproximal é o fio dental. O uso do fio dental foi recentemente questionado quanto a efetividade na manutenção da saúde, e foi retirado da "Dietary guideline for Americans" (17). Este ato gerou a chamada polêmica do fio dental entre os anos 2015 e 2016, que teve como base, uma revisão sistemática publicada em 2011 por Sambunjak e colaboradores (18). Essa revisão apurou estudos publicados que compararam o uso da escovação com ou sem fio dental. A conclusão obtida é a de que a evidência existente era fraca e de baixa qualidade. Tendo em vista que uma informação como essa, apresenta alto impacto na população e nas políticas de saúde, é importante que se faça uma análise da literatura a respeito. Os estudos que suportam a não eficácia do fio dental, estão baseados apenas no questionamento do uso do fio dental pelo paciente, sendo que, o uso do fio dental auto-reportado não garante um correto uso do mesmo. Isso pode demonstrar as dificuldades que há na população em fazer o uso correto do fio dental. Desta forma, é importante então, que se destaquem possibilidades de compensação.

Um ensaio clínico randomizado reportou dados apresentando maior eficácia das escovas dentais de cerdas macias na redução dos escores de placa em toda a boca, bem como escores de placa interproximal com resultados promissores (19). A escova dental macia de ponta cônica demonstrou capacidade substancial na redução dos escores de placa interproximal mesmo na ausência de qualquer dispositivo de higiene interdental. Esse achado relatado no estudo é de importância clínica, visto que o uso do fio dental não é difundido, além do fato de que há dificuldades na sua utilização pela população tornando interessante o fato de uma escova dental poder atingir a região interproximal. Estes dados foram também achados de revisão sistemática

que mostrou uma redução significativamente maior de placa nas áreas interproximais pela escova dental de pontas cônicas (10).

Soluções químicas têm sido desenvolvidas como coadjuvante ao controle mecânico do biofilme na tentativa de auxiliar a dificuldade existente no controle do biofilme mecânico, pelo efeito anti-placa e anti-gengivite apresentado pela solução quando comparado ao efeito da escovação mecânica isolada (20)(21). Além disso, o uso de enxaguatórios bucais como coadjuvante a escovação dentária tem aumentado em todo o mundo (22).

As soluções químicas apresentam efeito antibacteriano e baixa ocorrência de eventos adversos mesmo após uso prolongado. Uma revisão sistemática demonstrou que o cloreto de cetilpiridinio (CPC) tem um efeito antiplaca e antigengivite pequeno, porém significativo quando usado como adjuvante a higiene mecânica (23). Além disso, um estudo clínico randomizado demonstrou que, a adição de lactato de zinco à formulação de CPC promove eficácia adicional na redução dos escores de placa e gengivite (24)(23).

O uso coadjuvante da solução química e da higiene mecânica além de trazer os benefícios já citados, também demonstrou capacidade de remoção de placa na região interproximal (19)(19). Esta é uma informação interessante, visto que a região interproximal se mostra não só como ja foi citado com maiores índices de placa e gengivite mas também, com maiores índices de cárie e doença periodontal mesmo em indivíduos que relatam fazer uso do fio dental (14, 18). Estudos que avaliam capacidade coadjuvada de uso de enxaguantes a base de óleos essenciais, mostram também resultados estatisticamente significativos para redução de placa e gengivite. Uma revisão sistemática publicada em 2016 (25) demonstrou resultados significativamente melhores que o placebo, cloreto de cetilpiridinio (isolado) e fio dental na região interproximal em pacientes incluídos em ensaios clínicos randomizados, o que demonstra, de uma forma geral, uma maior capacidade de redução de placa e gengivite na região interproximal.

Desta forma, a presente tese, tem como objetivo avaliar a eficácia de outros regimes de higiene bucal compensatórios ao uso do fio dental na capacidade de remoção do biofilme durante a realização da higiene bucal na região interproximal.

PROPOSIÇÃO

A presente tese tem por objetivo:

GERAL:

Avaliar a eficácia de outros regimes de higiene bucal compensatórios ao uso do fio dental na capacidade de remoção do biofilme durante a realização da higiene bucal na região interproximal.

ESPECÍFICOS:

- Verificar a capacidade da remoção do biofilme supragengival com o uso de um colutório a base de cetilpiridínio, lactato de zinco e flúor na sua composição.

- Avaliar a capacidade da remoção mecânica do biofilme interproximal de uma escova multicerdas.

ARTIGO 1 – UMA REFLEXÃO SOBRE A POLÊMICA DO FIO DENTAL: MITOS E REALIDADE

A DEEP THOUGHT ABOUT THE DENTAL FLOSS CONTROVERSY: MYTHS AND REALITY

Artigo publicado no periódico: “Clínica – International Journal of Brazilian Dentistry”

Novas Tendências

REFLEXÃO SOBRE A POLÊMICA DO FIO DENTAL: MITOS E REALIDADE

A deep thought on the dental floss controversy: Myths and reality

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RESUMO

A prevenção e o tratamento da cárie e das doenças periodontais baseiam-se, entre outras estratégias, no controle do biofilme dental supragengival. Para isso, instrumentos dedicados às faces livres e proximais foram desenvolvidos. Não há dúvida de que a utilização de escova de dentes e dentifrício constitui-se no método mais utilizado universalmente para o controle do biofilme supragengival. Entretanto, é importante ressaltar a limitação desses agentes nas áreas proximais, onde recursos adicionais são necessários. Em indivíduos que não apresentam perdas de inserção consideráveis, o uso do fio dental tem sido recomendado. Recentemente, publicações leigas têm veiculado informações advindas da interpretação de estudos científicos de que o uso do fio dental seria ineficiente e, portanto, desnecessário. Essa informação necessita ser profundamente estudada para que os benefícios do controle do biofilme não sejam negligenciados. Nesse sentido, o objetivo desta coluna é fazer uma reflexão sobre a efetividade do uso do fio dental como agente de prevenção e tratamento da cárie e das doenças periodontais.

ABSTRACT

Prevention and treatment of caries and periodontal diseases are based, among other strategies, on the control of supragingival dental biofilm. For this purpose, instruments dedicated for free and proximal surfaces have been developed. There is no doubt that the use of toothbrushes and toothpastes is the most universally used method for controlling the supragingival biofilm. However, it is important to highlight the limitation of these agents in the proximal areas, where additional resources may be required. Flossing has been recommended for individuals who do not present considerable loss of attachment. Recently, lay publications have provided information from the interpretation of scientific studies that flossing would be inefficient and therefore unnecessary. This information needs to be thoroughly studied so that the benefits of biofilm control are not neglected. In this sense, the purpose of this column is to reflect on the effectiveness of dental floss as an agent for prevention and treatment of caries and periodontal diseases.

O controle do biofilme supragengival é considerado um dos recursos mais importantes em termos de prevenção e tratamento da cárie e das doenças periodontais. Estudos têm demonstrado que programas de controle do biofilme supragengival resultam em menor incidência de cárie, doenças periodontais e, como resultado mais importante, redução de perdas dentárias.[1]

Classicamente, o controle do biofilme precisa ser realizado com instrumentos destinados às faces livres (tendo como exemplo os diferentes tipos de escova de dentes) e para as faces proximais (sendo o fio dental o meio mais conhecido). Além do uso da escova e do fio dental, a necessidade do dentifrício é amplamente considerada, o qual tem as funções de remoção de gordura, prevenção de manchamento e, principalmente, veículo de aplicação de flúor, de suma importância para o manejo da cárie.

O consumo de produtos de higiene bucal tem sido um indicador pelo menos da intenção das populações em realizar controle do biofilme. No Brasil, por exemplo, no início dos anos 2000, consumia-se menos de uma escova de dentes por habitante por ano, em torno de 600 g de dentifrício e somente 5 m de fio dental. Esse consumo refletia que o dentifrício tinha ampla penetração no Brasil, com consumo semelhante ao dos Estados Unidos e maior do que na maioria dos países da Europa. No que se refere às escovas, o consumo de menos de uma escova pode ser considerado baixo, especialmente levando-se em conta as disparidades sociais do país. Isso significa que muitas pessoas utilizam escovas por períodos muito longos. Entretanto, a situação mais impactante é que o consumo total de fio dental no início dos anos 2000 era de 5 m por habitante por ano. Esse consumo é irrisório e reflete que se dava muito pouca importância ao controle do biofilme interproximal.[2]

Com o passar dos anos, houve uma evolução do padrão de consumo de produtos de higiene bucal mundialmente, e isso não foi diferente no Brasil. Os dados obtidos referentes ao consumo de produtos de higiene bucal para o ano de 2010 demonstram que o consumo praticamente duplicou, com um consumo médio *per capita* de 1,9 escova de dente. O consumo de dentifrício apresentou-se estável ao longo desse período, o que era esperado tendo em vista que, desde o início dos anos 2000, já era comparável a sociedades mais desenvolvidas.[3] Entretanto, naquela publicação não foram apresentados dados a respeito do uso do fio dental.

Em um estudo que acompanhou 13 anos de amostras representativas de uma cidade brasileira, observou-se que houve um provável incremento do uso de fio dental de 48% para 59%. Esse incremento esteve associado a renda familiar, idade e nível educacional. Observou-se que os mais jovens tendem a utilizar o fio dental mais do que os mais velhos.[4]

Um fato importante em relação à questão do uso do fio dental é a problemática epidemiológica. Estudos são claros em demonstrar em diferentes populações que as cáries proximais são bastante prevalentes.[5,6] Entretanto, em relação à cárie, o consumo de fluoretos acaba por compensar, pelo menos em parte, as dificuldades com o uso ou a ausência de uso de fio dental. No que se refere às doenças periodontais, a literatura é uníssima em demonstrar maiores prevalências de gengivite e de diferentes estágios de periodontite nas áreas interproximais.[5]

Recentemente, uma publicação na imprensa laica, mais especificamente no The New York Times, questionou a importância do uso do fio dental, com suporte em uma revisão sistemática da literatura com metanálise.[7] Essa revisão apurou estudos publicados que compararam o uso da escovação com ou sem fio dental. A conclusão obtida é a de que a evidência existente era fraca e de baixa qualidade. Tendo em vista que uma informação como essa, dentro de políticas públicas de saúde, tem altíssimo impacto, é importante que se faça uma análise da literatura a respeito. Estudos realizados no Brasil também apontam para algumas das fragilidades do fio dental, entretanto não são capazes de dar suporte a uma informação talvez equivocada e perigosa de que não existe mais necessidade de usá-lo.

Para fins dessa publicação, gostaríamos de usar dois exemplos de estudos realizados no Brasil diretamente vinculados a essa temática que, em que se pese terem resultados parecidos com os que compuseram a metanálise, recebem interpretação distinta, não gerando suporte para a exclusão do fio dental do grupo de instrumentos para o controle do biofilme. Em uma escola do Rio Grande do Sul foram comparadas as condições de higiene bucal – placa e gengivite – em indivíduos que se declaram usuários ou não do fio dental.[8] Nessa amostra de indivíduos, escolares de ensino médio, não foram observadas diferenças estatisticamente significativas nos índices de placa e de gengivite. A interpretação dada para o estudo não foi a de que fio dental não funciona, mas que somente reportar o uso não significa adotá-lo, tampouco fazê-lo de forma eficiente. Concluíram os autores que o fio dental, da forma como é utilizado pela população, não traz benefícios, e sugerem atividades educativas que estimulem o uso correto do fio dental.

No mesmo grupo de estudantes do estudo supracitado, um programa de higiene bucal supervisionada foi realizado com orientações aos estudantes três vezes por semana.[9] Nesse estudo 30 estudantes que não se declaravam usuários de fio dental foram divididos para, em dois períodos de experimento, usarem ou não o fio dental. Os resultados demonstraram um excelente efeito de um programa de controle do biofilme supervisionado, entretanto sem demonstrar benefícios tangíveis da inclusão do fio dental no regime de higiene bucal. O estudo tem um baixo poder tendo em vista o número de indivíduos incluídos, o que talvez limite a demonstração do efeito do fio dental. Entretanto, mais importante do que isso é a demonstração de que, quando

indivíduos se dedicam a um programa de higiene bucal, apresentam melhoras em todas as faces dos dentes.

Sabendo-se que há claras dificuldades do uso correto do fio dental, é importante que se observe sua indicação. Por exemplo, indivíduos que somente com a escovação apresentam ausência de inflamação gengival talvez não necessitem da inclusão do fio dental. É importante ter clareza de que a ausência de inflamação gengival clinicamente detectável não seja resultado do mascaramento do sangramento gengival pelo hábito do fumo. Também é importante que se olhem questões anatômicas da área dentogengival. Por exemplo, indivíduos que já experienciaram perda de inserção proximal por doença periodontal beneficiam-se mais do uso de escovas interdentais do que do fio dental. Na verdade, interpretando os dados da literatura, a escova interdental é mais indicada do que o fio dental nesses pacientes.[10]

Considerando as dificuldades expostas até aqui a respeito do uso do fio dental, é importante que se destaquem possibilidades de compensação delas. Recentemente um estudo realizado com duas escovas dentais macias demonstrou que ambas têm potencial de, mesmo sem o uso do fio dental, diminuir a placa das regiões interproximais. Inclusive, no referido estudo uma das escovas teve mais capacidade do que a outra em atingir as áreas interproximais. A interpretação do resultado desse estudo é que existem diferentes agentes para controle de placa com diferentes capacidades de ação e que, diante das dificuldades de uso do fio dental, o uso de escovas com características morfológicas que facilitem a entrada nas ameias proximais é uma perspectiva interessante.[11]

Da mesma forma, o uso de agentes químicos para o controle do biofilme, seja sob a forma de dentifrícios ou de soluções colutórias, também merece destaque. Assim, agentes com triclosan, cloreto de cetilpiridínio, zinco e óleos essenciais também encontram espaço para compensar o fio dental. Também recentemente se estudou o efeito de uma solução para bochecho contendo cloreto de cetilpiridínio, lactato de zinco e fluoreto, e observou-se que há benefício nas áreas interproximais, independentemente do uso do fio dental.[12]

A reflexão apresentada nesta coluna tem por objetivo que a comunidade odontológica reflita sobre o controle do biofilme como estratégia preventiva e terapêutica para as doenças mais prevalentes da cavidade bucal – a cárie e as doenças periodontais. Da mesma forma, é estratégia fundamental para a manutenção de saúde ao redor de reabilitações protéticas sobre dentes e implantes, sendo considerado um dos pilares da profissão. Assim, a simples observação de que as evidências que suportam o uso do fio dental são fracas não dá suporte ao entendimento de que ele não é necessário. Em epidemiologia clínica há uma máxima que diz: "*The absence of evidence is not evidence of absence*". Isso quer dizer que, quando não se tem evidência sobre determinado assunto, não se pode negar terminantemente seu benefício. Assim, tanto o Ministério da Saúde do Brasil quanto as entidades de classe odontológica consideraram que as afirmações veiculadas referindo que o uso do fio dental seria dispensável são vazias e, de certa forma, irresponsáveis. Cabe ao profissional da odontologia continuar propagando a importância de um bom controle do biofilme supragengival mediante a utilização de todos os instrumentos disponíveis e a avaliação da necessidade de cada usuário.

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ARTIGO 2

ANTIPLAQUE AND ANTIGINGIVITIS EFFICACY OF DIFFERENT BRISTLES STIFFNESS AND END-SHAPE ON INTERPROXIMAL SURFACES: A SYSTEMATIC REVIEW WITH META-ANALYSIS

Short Title: Soft bristle toothbrush compared to other toothbrushes in interproximal plaque removal.

Artigo submetido no periódico: “Journal of the Evidence-Based Dental Practice” (Anexo 1)

Anti-plaque and anti-gingivitis efficacy of different bristle stiffness and end-shape on interproximal surfaces: a systematic review with meta-analysis

Short Title: Toothbrush efficacy in interproximal surfaces.

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ABSTRACT

Objective: This systematic review aimed to evaluate the efficacy of interproximal plaque scores and gingival inflammation reduction of different toothbrush bristle stiffness and end-shape. **Methods:** Randomized clinical trials evaluating the effect of different toothbrushes on interproximal plaque/gingivitis reduction, with a minimum follow-up of 1 week. MEDLINE-PubMed, Scopus and Embase were searched. Soft tapered-tip bristle toothbrushes were compared to soft end-rounded, medium (any end-shape), or hard (any end-shape) bristle toothbrushes. Two meta-analyses were performed for plaque and gingivitis reduction. For plaque index (PI) and gingival index (GI), a standard mean difference (SMD) and mean difference between baseline and 4 weeks were calculated. In all analyses, random effect models were used. **Results:** Nine studies were included. All included studies demonstrated statistically significant improvement, in at least one parameter, in favor of the tapered-tip bristle toothbrush compared to the end-rounded bristle toothbrush. When analyzing toothbrush stiffness, medium and hard toothbrushes presented significantly higher improvement when compared to soft toothbrushes in all parameters. In the meta-analyses, groups that used soft tapered-tip bristle toothbrushes demonstrated significant greater reductions in PI (SMD -2.64; 95% CI: -4.26 – -1.01) and in GI (MD -0.14; 95% CI: -0.18 – -0.10) when compared to soft end-rounded bristle toothbrushes. **Conclusion:** It is concluded that, when considering interproximal surfaces, better results may be expected for tapered-tip bristle toothbrushes when compared to end-rounded bristles toothbrush. Additionally, better results may be expected in medium or hard toothbrushes, regardless of the bristle end-shape, in non-interproximal cleaners.

Keywords: Dental Devices; Dental Plaque; Gingivitis; Oral Hygiene; Toothbrushing.

INTRODUCTION

Encouraging efficient plaque control through regular toothbrushing has always held a position of high importance within dental education and health promotion activities. Among all the educational and health promotion actions carried in Dentistry, encouraging efficient plaque control has always assumed major importance. For decades, the profession has provided sound literature that supports this approach [1]. There is no doubt that emphasizing regular toothbrushing has been responsible, at least in part, for the decline of caries (mainly due to the use of fluoride toothpaste) and periodontal diseases [2]. The control of supragingival biofilm by the patient is the most important measure to obtain and maintain oral health [1]. Other measures to reinforce good oral health care, such as professional biofilm removal during active treatment and maintenance appointments, also have an important role and are recommended according to individual needs [3,4].

Dental plaque accumulation occurs on tooth surfaces and can be clinically detected as early as within 24 hours following professional removal [5]. Interproximal regions of the posterior and anterior teeth are the most common areas where plaque accumulates and impacts prevalence of oral diseases [6]. Interdental cleaning is considered very important, since traditional toothbrushing methods supposedly do not reach such areas [7]. Also, studies have clearly reported higher occurrence of gingival inflammation in interproximal surfaces [8]. However, toothbrushes have evolved with respect to design and cleaning ability over the years, and a variety of clinical trials have been developed to compare different toothbrushes in terms of bristle stiffness concerning plaque removal, prevention of gingivitis and gingival abrasion [9, 10]. Therefore, more recent studies have tried to look at the effect of toothbrushing also in interproximal areas [11, 12].

One clinical trial has recently reported efficacy of soft bristle toothbrushes in reduction of whole-mouth plaque scores as well as interproximal plaque scores with promising results in the latter [11]. Toothbrushes with soft tapered-tip bristles demonstrated substantial capacity in reducing interproximal plaque scores even without the use of any interdental cleaning device. This finding is of clinical importance, as flossing is not widespread and often performed suboptimally, so the ability to reach interproximal areas using a toothbrush is highly desirable.

A review published in 2011 aimed to analyze clinical trials that evaluated the effectiveness of dental floss in removing interproximal plaque and, consequently, preventing caries and periodontal disease. Contradictory and impacting results not favorable to the use of dental floss in

preventing caries and periodontal disease were reported. In addition, dental floss did not demonstrate sufficient anti-plaque and anti-gingivitis effect in the interproximal region. This led to the precipitated conclusion that the adjunct use of dental floss in an oral hygiene routine is not proven in published studies in the literature [13]. Merging the results of studies assessing interproximal plaque removal from devices not developed for the interproximal area may encourage authors to report more of these results. Moreover, merging results makes it possible to indicate the best clinically proven devices to enhance oral hygiene quality for patients.

The aim of this study was to systematically review the literature that evaluates the efficacy of different toothbrush bristle stiffness and end-shape in reducing interproximal plaque scores and gingival inflammation. The null hypotheses underlying the present study is that there is no effect of toothbrushing in interproximal areas independently of bristle stiffness, as measured by plaque removal and gingival inflammatory signs.

MATERIALS AND METHODS

The present study followed the PRISMA guideline for systematic reviews [14]. The present study has two focused questions (one related to bristle end-shape and the other related to bristle stiffness) as follows: “In adult patients, are soft tapered-tip bristle toothbrushes as efficacious as soft end-rounded bristle toothbrushes in terms of plaque removal and gingival inflammation in interproximal areas? (PICO 1).” “In adult patients, are soft bristle toothbrushes as efficacious as medium or hard bristle toothbrushes in terms of plaque removal and gingival inflammation in interproximal areas? (PICO 2).”

Both PICO questions comprised adult individuals (Patients); soft tapered-tip bristle manual toothbrushes (Intervention); compared to soft end-rounded, medium (any end-shape) or hard (any end-shape) bristle manual toothbrushes (Comparison); and interproximal plaque and gingivitis score reduction (Outcome).

Search strategy

The search strategy was conducted in three electronic databases, MEDLINE-PubMed, Scopus and Embase. The literature search was performed up to June 3rd, 2020. In MEDLINE-PubMed, the search strategy is described below:

#1 - toothbrushing[MeSH Term] OR toothbrushing[Text Word] OR toothbrush[Text Word] OR toothbrushes[Text Word] OR oral hygiene[MeSH Term] OR oral hygiene[Text Word]

#2 - bristle[Text Word] OR bristles[Text Word] OR end-rounding[Text Word] OR filament[Text Word] OR soft[Text Word] OR medium[Text Word] OR hard[Text Word] OR end-form[Text Word] OR tapered[Text Word] OR conical[Text Word] OR “toothbrush filament”[Text Word] OR “toothbrush design”[Text Word] OR “toothbrush texture”[Text Word] OR “toothbrush bristle”[Text Word] OR manual[Text Word] OR commercially available[Text Word]

#3 - gingivitis[MeSH Term] OR “gingival inflammation”[Text Word] OR “gingival index”[Text Word] OR oral hygiene index[MeSH Term] OR oral hygiene index[Text Word] OR dental plaque[MeSH Term] OR dental plaque[Text Word] OR plaque[Text Word] OR biofilm[Text

Word] OR “antiplaque”[Text Word] OR “antigingivitis”[Text Word] OR “periodontal index”[MeSH Term] OR “periodontal index”[Text Word] OR bleed* [Title/Abstract] OR dental plaque index[MeSH Term] OR dental plaque index[Text Word] OR interproximal[Text Word]

#4 - #1 AND #2 AND #3

The Scopus and Embase databases had adapted search strategies.

Selection criteria

Studies were independently selected by two researchers (FWMGM and GPJL). First, title and abstract were screened for eligibility, and a third researcher (CKR) was involved only when discrepancies were observed. The full texts were then screened using the same process. Reproducibility was assessed with kappa statistics between researchers with values of 0.89 and 1.00 for screening of title/abstract and full text, respectively.

In order to be included, the studies had to present all the following criteria:

- Randomized clinical trials (RCTs);
- Adult participants of at least 18 years old;
- In the test group, soft tapered-tip bristle manual toothbrush;
- In the control group, end-rounded soft, medium (any end-shape) or hard (any end-shape) bristle manual toothbrush;
- Clear reporting that individuals should not use any interproximal plaque control devices during the experiment;
- Any type of plaque or gingival index in the interproximal region;
- A minimum of 7 days follow-up.

Studies that presented any of following characteristics were excluded:

- Letters to the editors, observational, *in vitro*, animal model, and review studies;
- Use of any type of adjunct substance;
- Use of toothbrushes with rubber bristles.

Data extraction

Two researchers independently performed the data extraction of all included studies (GPJL and TPW), using a spreadsheet specifically developed for this study. A third researcher (FWMGM) was involved if any discrepancy was detected. The spreadsheet contained the following variables: authors, year of publication, country, experimental design, follow-up, interventions made before the study, number of individuals in each group, number of smokers in each group, brushing time, brushing technique, mean age, plaque and gingival index, results for the plaque and gingival assessment of each experimental period that individuals were followed, and adverse events reported.

Risk of bias assessment

All articles were individually evaluated to assess the risk of bias using the RoB2 tool [15]. All six criteria were indepentently assessed by two reviewers (GPJL and FWMGM). A third researcher was involved only when a consensus was not possible (CKR).

Dealing with missing data

If any important information was not reported in the study, the corresponding author was contacted by e-mail in order to acquire the missing information. Authors of all studies that reported mean plaque or gingival scores for the whole mouth were contacted for interproximal scores for the present study. If this information was not provided by the authors, the study was excluded (n=27) (Table S1).

Statistical analysis

Two separate meta-analyses were performed, considering the anti-plaque effect with the Turesky modification of the Quigley-Hein plaque index and the Rustogi modification of the Navy plaque index and anti-gingivitis effect with the Löe & Silness gingival index. Data on mean difference and standard deviation were obtained or calculated from the selected studies. Standard mean

difference (SMD) and mean difference (MD) between baseline and 4 weeks after toothbrushing were calculated, respectively, to plaque and gingival indexes. In the plaque index meta-analysis, subgroups were created according to the different plaque indexes used.

All meta-analyses were performed in the Rev-Man software (version 5.3 for Windows). The Q test assessed the heterogeneity, which was qualified by the I^2 statistics. The overall quality of the evidence for each of the meta-analyses was rated using the GRADE approach [16].

RESULTS

Study selection

From the total of 1,780 studies initially screened, nine were included and analyzed in the present systematic review [10-12, 17-22]. Figure 1 shows the flowchart of study selection, retrieval and inclusion, with the main reasons for exclusion. Table 1 demonstrates the main descriptive characteristics and results of the included studies.

Characteristics of included studies

The nine included articles comprised ten RCTs with follow-up time ranging from 1 to 12 weeks [10-12, 17-22]. One article reported data from two RCTs [19]. All studies reported to have included systemically healthy patients. From all the included studies, one [20] reported including only non-smokers and the remaining studies reported including both smokers and non-smokers as participants.

From the nine analyzed studies, two [19, 22] reported performing professional oral prophylaxis before the study commencement. The remaining seven studies did not report any previous intervention. Regarding toothbrushing time, most of the studies reported establishing one minute as the required time to brush [10-12, 17, 19, 20], two studies [21, 22] reported two minutes, and one study [18] did not refer to the time of toothbrushing established as protocol.

Regarding brushing technique, two studies [21, 22] reported using the Bass toothbrushing technique, the remaining seven studies did not report any type of brushing technique, as the patient would brush conventionally.

Risk of bias assessment

Figure 2 shows the assessment of risk of bias. Overall, it was detected that almost all the included studies showed high or some concerns regarding risk of bias. The criteria randomization process demonstrated low risk of bias in only one study [11]. Additionally, one study showed high risk of bias in missing outcome data [17].

Qualitative results – Plaque scores

Regarding the PICO1 question, interproximal plaque scores were reported in all included studies. All of them reported that both test and control groups significantly reduced interproximal plaque scores when compared to baseline. The studies that reported plaque scores with the Quigley-Hein modified plaque index [12, 18, 21, 22] showed that toothbrushes with soft tapered-tip bristles [12, 18, 21] significantly reduced more interproximal plaque than soft end-rounded bristles. This was reported even in the study with longer experimental time [12].

The studies that reported results with the Rustogi modification of the Navy plaque index [10, 11, 17, 19, 20] presented similar results. They reported that reduction of interproximal plaque was significantly higher in soft tapered-tip bristles when compared to end-rounded bristles.

Regarding the PICO2 question, one study [22] was performed with three experimental groups in which non-labeled toothbrushes were assigned, with soft, medium and hard characteristics. The results demonstrated significantly more interproximal plaque reduction with the hard bristle toothbrush after 8 weeks of toothbrush usage, although with more adverse events reported concerning gingival lesions compared to the other assigned groups.

Qualitative results – Gingival scores

Regarding the results for the PICO1 question, two studies reported interproximal gingival inflammation [12, 18]. Both studies reported that test and control groups significantly reduced interproximal plaque scores when compared to baseline. The Löe & Silness gingival index was used in both studies and the results indicated that soft tapered-tip bristle toothbrushes were more capable of reducing interproximal gingival inflammation even after 12 weeks experimental time.

Regarding the PICO2 question, one study [22] reported better results for the group assigned to the soft toothbrushes when compared to medium and hard bristle toothbrushes. It is also important to mention that more gingival lesions were reported in the medium and hard bristle groups.

Meta-analyses for alterations in plaque scores

Figure 3 presents the meta-analysis for interproximal plaque score alteration between baseline and 4 weeks evaluation. Six studies were included in this analysis [10, 12, 17, 18, 20, 21], and a pooled SMD of -2.64 (95% CI: -4.26 – -1.01) was demonstrated, with a statistically significant difference between groups favoring the soft tapered-tip bristle toothbrush. This meta-analysis showed a high heterogeneity (I^2=97%, P<0.000001). Interestingly, when the Rustogi modification of the Navy plaque index was used, a similar trend of results was found (SMD: -4.31; 95% CI: -6.61 – -2.01). However, no significant difference between groups was found when the Turesky modification of the Quigley-Hein index was used (SMD: -0.99; 95% CI: -2.98 – 1.00).

Meta-analyses for alterations in gingival index

Figure 4 presents the meta-analysis for the interproximal anti-gingivitis effect between baseline and 4 weeks evaluation. Two studies were included in this analysis [12, 18], and a pooled MD of -0.14 (95% CI: -0.18 – -0.10) was demonstrated, with a statistically significant difference between groups favoring the soft tapered-tip bristle toothbrush. This meta-analysis showed a low heterogeneity (I^2=21% , P=0.26).

Quality of evidence at the review level

When considering both meta-analyses, very low quality of evidence was demonstrated by the GRADE criteria.

DISCUSSION

The present study aimed to systematically review the literature to address the interproximal anti-plaque and anti-gingivitis effects of different toothbrush bristle stiffness and end-shape in a minimum experimental time of 7 days. To our knowledge, no previous study has systematically reviewed the literature concerning the plaque and gingival inflammation reduction effects of toothbrushes in the interproximal area in participants who do not use interproximal cleaning devices. In the present study, regarding plaque and gingival scores, all included studies demonstrated significant reductions for soft tapered-tip bristle toothbrushes, compared to soft end-rounded bristle toothbrushes. Yet, when comparing toothbrush bristle stiffness, medium and hard bristle toothbrushes presented higher plaque reductions than soft bristle toothbrushes, regardless of end-shape. However, more adverse events were reported in hard bristle toothbrushes regarding gingival lesions. The meta-analyses demonstrated that the use of tapered bristle end-shape toothbrushes promoted significantly higher reduction in plaque and gingival indexes when compared to end-rounded bristles. The majority of the included studies presented either a high or some concerns regarding risk of bias. This is a demonstration of the quality of the literature surrounding the theme. Including studies with such risk of bias is important, however, caution should be taken in generalizing the results. In addition, the GRADE analysis showed that both analyses demonstrated a very low quality of evidence.

The meta-analysis for plaque scores, which included six studies, demonstrated a pooled SMD of -2.64 (95% CI: -4.26 – -1.01), with a statistically significant difference between groups favoring the soft tapered-tip bristle toothbrush. For the gingival scores meta-analysis, in which two studies were included, a pooled MD of -0.14 (95% CI: -0.18 – -0.10) was demonstrated, with a statistically significant difference between groups favoring the soft tapered-tip bristle toothbrush.

A subgroup analysis was performed for plaque, which could explain the high heterogeneity found in the plaque score meta-analysis. In studies that used the Rustogi plaque index, a significant result was found in favor of tapered-tip bristle toothbrushes over end-rounded. However, for studies that used the Quigley-Hein plaque index, no statistically significant difference was found in the result between both toothbrush bristles. Despite these contrasting results, heterogeneity could not be explained by the different plaque indexes used. In addition, analysis of publication bias was not performed since it is not recommended for systematic reviews that included less than 10 studies. However, this should not be ruled out.

A systematic review published in 2017 [23] concluded that when comparing whole-mouth plaque removal efficacy between tapered-tip bristle and end-rounded bristle toothbrushes, evidence supporting the recommendation of tapered-tip bristle toothbrushes over end-rounded is lacking. Regarding gingival index, a minimum of evidence favors tapered-tip bristle toothbrushes, although the authors declared that the clinical significance of the difference was likely negligible. It is important to note that, unlike the present study, the abovementioned review included studies in which interproximal cleaning devices were allowed. Thus, clinical trials have demonstrated better plaque and gingival score reduction from tapered-tip bristles in whole-mouth and interproximal plaque removal [11].

Clearly, toothbrushing with fluoride dentifrice is known to be the traditional method of maintaining oral hygiene regimens, with the eventual addition of dental floss. However, the efficacy of flossing has been questioned lately [13]. Also, it is noteworthy that the consumption of dental floss, despite an increase over time, is still low [24]. In an attempt to compensate for the lack of use or, at least, correct use of dental floss, the use of mouthwashes has been studied and some interproximal anti-plaque and anti-gingivitis effect was found [25]. To reduce improper brushing technique effect [26], manufacturers also established the goal of evolving toothbrushes to provide a better cleaning effect across the mouth, regardless of the type of movements or techniques used by the individual [27]. From studies comparing toothbrushes stiffness or comparing adverse events, it was demonstrated the tapered-tip bristle toothbrushes presented lower occurrence of gingival lesions [28-31]. Evolution in the design of toothbrushes has proven to increase their efficacy in the interproximal areas [11], although the focused capacity of toothbrush bristles to achieve interproximal plaque removal is not yet proven. In order not to add a source of confouding bias, in the present review, no studies with adjunct anti-plaque/anti-gingivitis chemical agent either in the dentifrice or mouthwashes were included.

Notably, it is clear that the majority of patients in the past were not capable of removing biofilm from interproximal sites [32], which usually led to development of gingivitis in this specific area. A more capable toothbrush, with better capacity to reach interproximal areas, would be beneficial to patients.

Regarding interdental cleaning devices and methods, interdental brushes and dental floss [33-36] are the most studied and the most used. Undoubtedly, interdental brushes are more efficacious when comparing all available literature on interdental cleaning devices [37-39]. Notwithstanding, a

sufficient gap between teeth is needed in order to allow the device to clean the interdental area. When this gap is not available, dental floss is the device, which the clinician can rely on. To evaluate the palpable capacity of dental floss in preventing caries and periodontal diseases, a Cochrane collaboration systematic review showed the limitations of dental floss in preventing the two most prevalent oral diseases, as the included studies proved to be weak and/or of low quality [13].

One study, which included teenage participants, demonstrated that a regimen of toothbrushing was efficient in terms of plaque and gingival bleeding reduction [40]. No additional efficacy, for the same outcomes, was demonstrated when dental floss was used by the sample participants. The inclusion of supervised flossing for a relatively short period also did not improve gingival inflammation. From this study, it may be hypothesized that toothbrushes may reach the interproximal areas. These results show that when individuals participate in an oral hygiene program, better clinical results are seen in all tooth faces. It is of utmost importance to study new possibilities to compensate for the limitation associated with dental floss usage.

Tapered-tip bristle toothbrushes have been tested and shown to be more effective in reaching not only interproximal areas of the teeth along the gingival margin and under the gum line where plaque accumulates the most, but also in reaching fissures when compared to end-rounded bristles [23, 41, 42]. This result was also positive in an *in vitro* study with artificial plaque, in which tapered-tip bristles demonstrated significantly better results in reducing plaque scores in the interproximal area [42]. Another *in vitro* study [43] evaluated the interproximal cleaning effect of commercially available manual toothbrushes when used alone. In addition, the authors attempted to identify the properties of manual toothbrushes that effect interproximal cleaning capacity. The results showed that none of the tested toothbrushes were able to reach interproximal areas. It is important to mention that toothbrush bristle end-shapes were not mentioned.

The higher efficacy of tapered-tip toothbrushes could be explained by the difference between the bristle filaments of both toothbrushes. The tapered filaments present endings in the shape of an extreme rotational ellipsoid while the tips of end-rounded filaments are shaped as hemispheres. This shape difference could help tapered bristle toothbrushes to more easily reach the interproximal space. Meanwhile, it is important to mention that tapered toothbrushes are chemically processed by agents, and not by a grinding machine as it is the end-rounded toothbrushes [44].

Regarding the PICO2 question of the present study, evaluating effects of toothbrushes stiffness, better interproximal scores were found concerning plaque levels in hard bristle toothbrushes as compared to soft and medium bristle toothbrushes. These results are in accordance with other published randomized clinical trials [28, 45]. Although the above-mentioned results for plaque are interesting, more gingival lesions are expected in patients using medium or hard bristle toothbrushes, regardless of the end-shape [46, 47]. However, only one of the included studies compared three different toothbrush stiffnesses [22], and another compared soft and medium toothbrushes [21]. In this sense, it was not possible to perform a meta-analysis for the comparison between toothbrush stiffnesses.

The authors are well aware of the strengths and intrinsic limitations of this review. The presented results could likely have more impact if studies including interdental hygiene devices were also allowed. On the other hand, including interdental hygiene devices could obscure the effect of the toothbrush in the interproximal area. Moreover, no systematic review has been published evaluating the actual efficacy of different toothbrushes alone in reaching the interdental space. It is important to note that no oral hygiene instruction was provided in the studies included in this review, which likely reflects on the patient oral hygiene daily habit.

The 2011 Cochrane collaboration systematic review [13] was updated and concluded that there is still weak evidence supporting the prevention of caries and periodontal diseases when flossing is used in adjunct to toothbrushing. The present study points to a different perspective to compensate flossing in adjunct to toothbrushing to prevent caries and periodontal diseases.

CONCLUSIONS

It is concluded that, when considering interproximal surfaces, better results may be expected for the soft tapered-tip bristle toothbrushes in individuals that do not use interproximal cleaning devices. Even though medium and hard bristle toothbrushes present better effect, more adverse events notably gingival lesions are expected.

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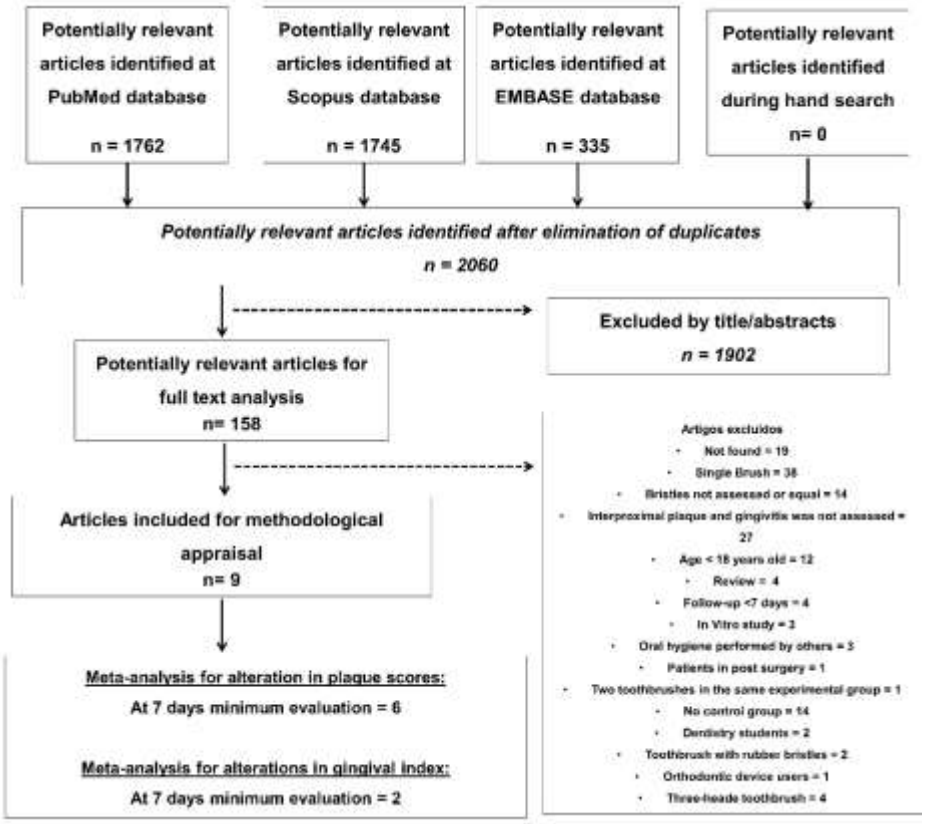
FIGURE LEGENDS

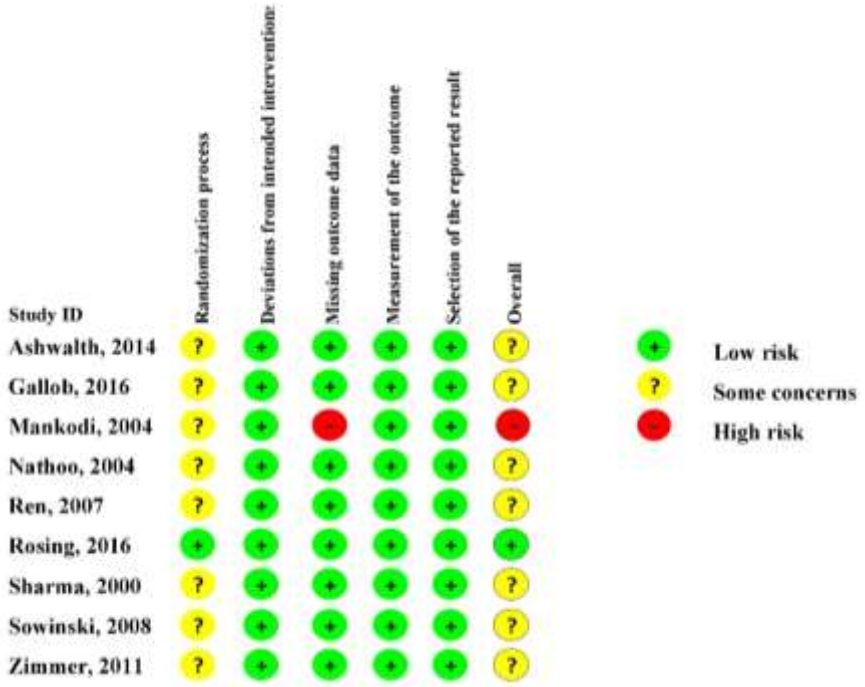
Figure 1. Flowchart of the systematic review.

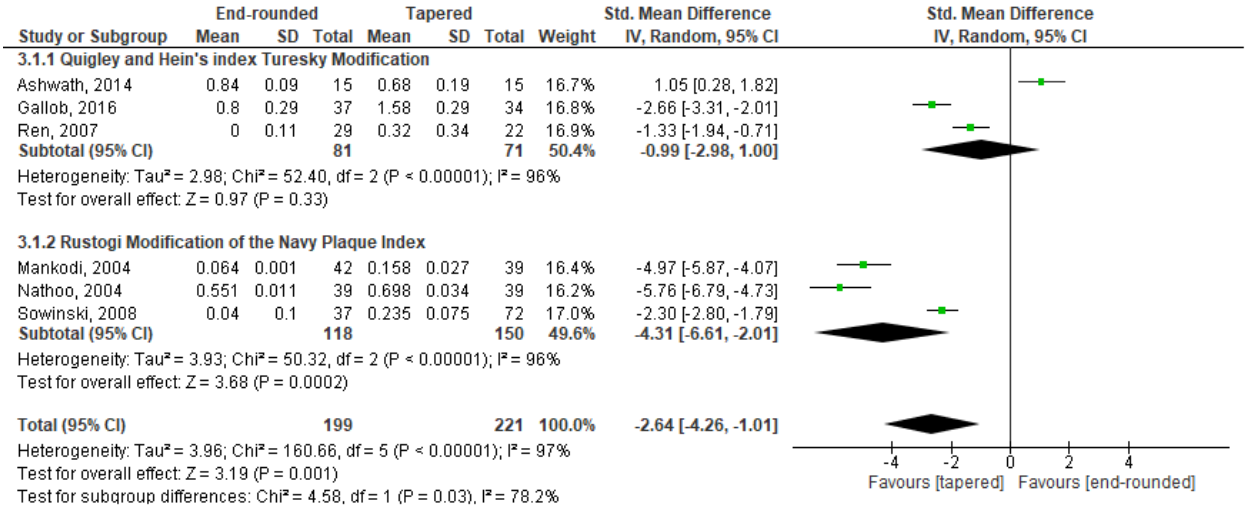
Figure 2. Risk of bias assessment of the included randomized clinical trials.

Figure 3. Forest plot for interproximal plaque score alteration, between baseline and 4 weeks of follow-up, considering different toothbrush end-shapes. Analysis is reported with subgroups according to the index used.

Figure 4. Forest plot for interproximal gingival index score alteration, between baseline and 4 weeks of follow-up, considering different toothbrush end-shapes.




Study ID
Randomization process
Deviations from intended interventions
Missing outcome data
Measurement of the outcome
Selection of the reported result
Overall
Ashwalth, 2014
Gallob, 2016
Mankodi, 2004
Nathoo, 2004
Ren, 2007
Rosing, 2016
Sharma, 2000
Sowinski, 2008
Zimmer, 2011
Low risk
Some concerns
High risk


End-rounded
Tapered
Std. Mean Difference
Std. Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
3.1.1 Quigley and Hein's index Turesky Modification
Ashwath, 2014 0.84 0.09 15 0.68 0.19 15 16.7% 1.05 [0.28, 1.82]
Gallob, 2016 0.8 0.29 37 1.58 0.29 34 16.8% -2.66 [-3.31, -2.01]
Ren, 2007 0 0.11 29 0.32 0.34 22 16.9% -1.33 [-1.94, -0.71]
Subtotal (95% CI) 81 71 50.4% -0.99 [-2.98, 1.00]
Heterogeneity: Tau² = 2.98; Chi² = 52.40, df = 2 (P < 0.00001); I² = 96%
Test for overall effect: Z = 0.97 (P = 0.33)
3.1.2 Rustogi Modification of the Navy Plaque Index
Mankodi, 2004 0.064 0.001 42 0.158 0.027 39 16.4% -4.97 [-5.87, -4.07]
Nathoo, 2004 0.551 0.011 39 0.698 0.034 39 16.2% -5.76 [-6.79, -4.73]
Sowinski, 2008 0.04 0.1 37 0.235 0.075 72 17.0% -2.30 [-2.80, -1.79]
Subtotal (95% CI) 118 150 49.6% -4.31 [-6.61, -2.01]
Heterogeneity: Tau² = 3.93; Chi² = 50.32, df = 2 (P < 0.00001); I² = 96%
Test for overall effect: Z = 3.68 (P = 0.0002)
Total (95% CI) 199 221 100.0% -2.64 [-4.26, -1.01]
Heterogeneity: Tau² = 3.96; Chi² = 160.66, df = 5 (P < 0.00001); I² = 97%
Test for overall effect: Z = 3.19 (P = 0.001)
Test for subgroup differences: Chi² = 4.58, df = 1 (P = 0.03), I² = 78.2%
-4
-2
0
2
4
Favours [tapered]
Favours [end-rounded]

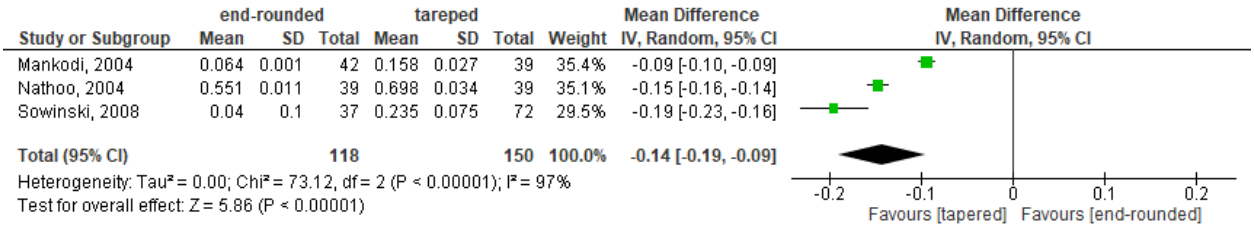

end-rounded
tareped
Mean Difference
Mean Difference
Study or Subgroup Mean SD Total Mean SD Total Weight IV, Random, 95% CI
IV, Random, 95% CI
Mankodi, 2004 0.064 0.001 42 0.158 0.027 39 35.4% -0.09 [-0.10, -0.09]
Nathoo, 2004 0.551 0.011 39 0.698 0.034 39 35.1% -0.15 [-0.16, -0.14]
Sowinski, 2008 0.04 0.1 37 0.235 0.075 72 29.5% -0.19 [-0.23, -0.16]
Total (95% CI) 118 150 100.0% -0.14 [-0.19, -0.09]
Heterogeneity: Tau² = 0.00; Chi² = 73.12, df = 2 (P < 0.00001); I² = 97%
Test for overall effect: Z = 5.86 (P < 0.00001)
-0.2
-0.1
0
0.1
0.2
Favours [tapered]
Favours [end-rounded]

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Table 1. Main characteristics and results of the included studies.

Name, Year **Study design**	**Experimental times**	**Systemic conditions**	**Smoking Status (n per group)**	**Test group** **Stiffness/End-shape** **(n male – n females;** **mean age)**	**Control group 1** **Stiffness/End-shape** **(n male – n females; mean age)**	**Control group 2** **Stiffness/End-shape** **(n male – n females; mean age)**	**Control group 3** **Stiffness/End-shape** **(n male – n females; mean age)**	**Brushing Time**	**Plaque index** **Gingival index**	**Main results**
SHARMA, 2000 **RCT – Parallel** **(Study I)**	Baseline, 6 and 12 weeks	Systemically Healthy	N/A	Oral B crossaction (Soft/End-round) 15 males – 33 females; 34.75±7.75	Dr best interdent (Soft/End-round) 22 males – 29 females; 35.31±10.66	N/A	N/A	1 minute	Rustogi Modification of the Navy Plaque Index Modified Gingival Index	**Plaque** Test (mean reduction): baseline 1.00±0.01; 6 weeks 0.46±0.26; 12 weeks 0.40±0.23 (P<0.05 from baseline) Control (mean reduction): baseline 1.00±0.00; 6 weeks 0.61±0.24; 12 weeks 0.63±0.23 (P<0.05 from baseline) The tested toothbrush had significantly reduced levels of interproximal plaque than the control groups.

									Gingival Information not available for interproximal sites.
SHARMA, 2000 **RCT – Parallel** **(Study II)**			Oral B crossaction (Soft/End-round) 17 males – 28 females; 36.31±9.54	Crest deep sweep (End-round) 13 males – 29 females; 33.90±8.69	N/A	N/A	1 minute	Rustogi Modification of the Navy Plaque Index Modified Gingival Index	Test (mean reduction): baseline 1.00±0.001; 6 weeks 0.55±0.26; 12 weeks 0.38±0.24 (P<0.05 from baseline) Control (mean reduction): baseline 1.00±0.00; 6 weeks 0.87±0.14; 12 weeks 0.65±0.22 (P<0.05 from baseline) The tested toothbrush had significantly reduced greater levels of interproximal plaque than control groups.
									Gingival Information not available for interproximal sites.
MANKODI, 2004	Baseline and 4 weeks	Systemically Healthy	N/A	Colgate 360 ° (Soft/Tapered)	Oral B indicator (Soft/End-round)	N/A	N/A	1 minute	Rustogi Modification of the Navy Plaque Index	**Plaque** Test (mean reduction): baseline 0.986±0.044; 4

RCT – Parallel			13 males – 26 females 48.5 (30-68)	5 males – 37 females; 48.2 (30-68)				Löe & Silness Gingival Index	weeks 0.828±0.190 (P<0.05 from baseline) Control (mean reduction): baseline 0.998±0.008; 4 weeks 0.934±0.096 (P<0.05 from baseline). The Colgate® 360 toothbrush removed significantly more interproximal plaque than the Oral-B® Indicator. **Gingival** Information not available for interproximal sites.
NATHOO, 2004 **RCT – Parallel**	Baseline and 4 weeks	Systemically Healthy	N/A	Colgate 360° (Soft/Tapered) 15 males – 24 females; 38.3 (20-67)	Oral-B cross-action (Soft/End-round) 16 males – 23 females; 33.7 (18-58)	N/A	N/A	1 minute	Rustogi Modification of the Navy Plaque Index Löe & Silness Gingival Index	**Plaque** Test (mean reduction): baseline 0.944±0.92; 4 weeks 0.246±0.165 (P<0.05 from baseline) Control (mean reduction): baseline 0.960±0.068; 4 weeks 0.409±0.0179 (P<0.05 from baseline) The Colgate® 360 toothbrush removed

									significantly more interproximal plaque than the Oral-B® CrossAction® toothbrush. **Gingival** Information not available for interproximal sites.
REN, 2007 **RCT – Parallel**	Baseline, 15 and 30 days	Systemically Healthy	N/A	Elmex sensitive (Extra-soft/Tapered) 13 males – 15 females; 32.6±9.7	Elmex sensitive (Soft/Tapered) 12 males – 15 females ; 33.4±8.1	ADA toothbrush (Soft/End-round) 13 males – 16 females 32.1±8.0	N/A	N/A	Quigley and Hein's index Turesky Modification Löe & Silness Gingival Index	**Plaque** Test (mean reduction): baseline 2.58±0.53; day15 2.31±0.49; day30 2.24± 0.45 (P<0.05 from baseline) Elmex sensitive (mean reduction): baseline 2.59±0.53; day15 2.32±0.41; day30 2.27±0.38 (P<0.05 from baseline) ADA (mean reduction): baseline 2.52±0.56; day15 2.49±0.59; day30 2.52±0.51 (P>0.05 from baseline)

										Gingival: Test: baseline 1.31±0.27; day15 1.20±0.19; day30 1.16±0.14 (P<0.05 from baseline) Elmex sensitive: baseline 1.32±0.28; day15 1.24±0.25; day30 1.14±0.15 (P<0.05 from baseline) ADA (mean reduction): baseline 1.35±0.30; day15 1.33±0.28; day30 1.29±0.22 (P<0.05 from baseline) The Elmex Sensitive Soft (Teste) and the Elmex Sensitive Extra Soft (Control) toothbrushes were significantly more effective in removing dental plaque and reducing gingival inflammation than the ADA standard toothbrush (Control).
SOWINSKI, 2008	Baseline and 4 weeks	Systemically Healthy	No smokers	Colgate 360° deep clean	Colgate 360° (Soft/Tapered)	Oral-B indicator	N/A	1 minute	Rustogi Modification	**Plaque**

RCT – Parallel	(Soft/Tapered) 12 males – 24 females 43 (18-67)	8 males – 28 females 39 (18-61)	(Soft/End-round) 11 males – 26 females 40 (18-68)	of the Navy Plaque Index Löe & Silness Gingival Index	Test: baseline 0.90±0.08 (post-B 0.61±0.18); 4 weeks 0.63±0.12 (post-B 0.27±0.10) Colgate 360° (tapered): baseline 0.89±0.08 (post-B 0.61±0.22); 4 weeks 0.70±0.12 (post-B 0.20±0.10) Oral-B indicator: baseline 0.92±0.07 (post-B 0.78±0.11); 4 weeks 0.86± 0.12 (post-B 0.04±0.10) The results indicate that Colgate 360º Deep Clean toothbrush in both models had significant reductions of interproximal plaque levels. **Gingival** Information not available for interproximal sites.

ZIMMER, 2011 **RCT – Parallel**	Baseline, 4 and 8 weeks	Systemically Healthy	N/A	Soft toothbrush N/A N/A	Medium toothbrush N/A N/A	Hard toothbrush N/A N/A	N/A	2 minutes	Quigley Hein index & Modified Approximal Plaque Index Papillary Bleeding index	**Plaque** Test: baseline 2.49±0.53; 4 weeks 2.29±0.47 (reduced 0.20±0.41); 8 weeks 2.42±0.40 (reduced 0.07±0.45) Medium: baseline 2.39±0.60; 4 weeks 2.22±0.50 (reduced 0.17±0.32); 8 weeks 2.23±0.45 (reduced 0.17±0.33) Hard: baseline 2.44±0.48; 4 weeks 2.32±0.53 (reduced 0.12±0.52); 8 weeks 2.09±0.50 (reduced 0.35±0.50) **Gingival:** Test: baseline 0.94±0.30; 4 weeks 0.58±0.25; 8 weeks 0.43±0.19 Medium: baseline 0.85±0.29; 4 weeks

									0.94±0.29; 8 weeks 0.60±0.20 Hard: baseline 0.73±0.16; 4 weeks 0.94±0.33; 8 weeks 0.83±0.28 Toothbrushes with hard bristles may remove better the interproximal plaque, but may also cause more soft tissue trauma compared to brushes with softer bristles.
ASHWALTH, 2014 **RCT - Parallel**	Baseline, 1, 2, 3 and 4 weeks	Systemically Healthy	N/A	Colgate Actiflex (Soft/Tapered) N/A; N/A	Colgate 360º (Soft/Tapered) N/A; N/A	Colgate zig-zag (Medium/End-round) N/A; N/A	Colgate navigator (Soft/End-round) N/A; N/A	2 minutes	Quigley Hein index Modified by Turesky-Gilmore-Glickman N/A	**Plaque** Test: baseline 0.90±0.18; 2 weeks 0.65±0.31; 28 days 0.26±0.14 Colgate 360° (tapered): baseline 1.02±0.20; 2 weeks 0.75±0.37; 28 days 0.34±0.08 Colgate zig-zag: baseline1.22±0.35; 2

										weeks 0.86±0.37; 28 days 0.38±0.07 Colgate Navigator: baseline 1.32±0.30; 2 weeks 1.02±0.41; 28 days 0.41±0.10 Plaque removal ability of the four toothbrushes tested at interdental sites failed to reveal any significant difference.
GALLOB, 2016 **RCT – Parallel**	Baseline, 6 and 12 weeks	Systemically Healthy	N/A	Colgate Slim soft (Soft/Tapered) 10 males – 24 female; N/A	ADA toothbrush (Soft/End-round) 7 males – 30 females; N/A	N/A	N/A	1 minute	Quigley and Hein's index Turesky Modification Löe & Silness Gingival Index	**Plaque** Test (mean reduction): baseline 1.58±0.29; 6 weeks 1.00±0.33 (P<0.05 from baseline); 12 weeks 1.08±0.34 (P<0.05 from baseline) Control (mean reduction): baseline 0.80±0.29; 6 weeks 0.33±0.27 (P<0.05 from baseline); 12 weeks 0.44±0.32 (P<0.05 from baseline)

										Gingival Test: baseline 1.49±0.18; 6 weeks 1.29±0.15; 12 weeks 1.21±0.15 (P<0.05 from baseline) Control: baseline 1.49±0.15; 6 weeks 1.45±0.18; 12 weeks 1.41±0.20 (P<0.05 from baseline) The tapered-tip bristles toothbrush provided significantly greater reductions in plaque and gingivitis after six and 12-weeks' use when compared to an ADA reference manual toothbrush.
RÖSING, 2016 **RCT – Parallel**	Baseline and 7 days	Systemically Healthy	N/A	Colgate Slim soft (Soft/Tapered) 13 males – 22 females; 31.89±10.21	Curaprox CS5460 (Soft/End-round) 19 males – 16 females;	N/A	N/A	1 minute	Rustogi Modification of the Navy Plaque Index N/A	**Plaque** Test (mean reduction): baseline 0.99±0.02 (Pre-B) 0.75±0.11 (Post-B); day7 0.99±0.01 (Pre-B) 0.76±0.09 (Post-B) Control (mean reduction): baseline 0.99±0.01 (Pre-B) 0.92±0.03 (Post-B); day7

		33.26±12.47	0.99±0.02 (Pre-B) 0.90±0.07 (Post-B)
			The use of the SlimSoft toothbrush (Test) resulted in greater interproximal plaque reduction than did the use of the Curaprox toothbrush (Control).

Legend: N/A: not applied. RCT: randomized controlled trial.

Table 2. Summary of the quality assessment to all outcomes included in the meta-analyses.

Certainty assessment							Summary of findings					
№ of studies	**Study design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Tapered**	**End-round**	**Relative (95% CI)**	**Absolute (95% CI)**	**Certainty**	**Importance**
Plaque index												
6	randomized trials	Very serious [a]	Very serious [b]	Not serious	Serious [c]	None	221	199	-	SMD **2.64 SD lower** (4.26 lower to 1.01 lower)	⨁◯◯◯ VERY LOW	CRITICAL
Gingival index												
2	randomized trials	Very serious [a]	Not serious	Not serious	Serious [c]	None	61	66	**-**	MD **0.14 SD lower** (0.18	⨁◯◯◯ VERY	CRITICAL

						lower to 0.1 lower)	LOW

Legend: CI: Confidence interval; MD: Mean difference; SMD: Standard mean difference. Explanations: a. Both studies presented a high risk of bias in several criteria. b. A high heterogeneity was detected. c. There is a moderate to high variability in the results found.

ARTIGO 3

EFFICACY OF TWO SOFT-BRISTLES TOOTHBRUSHES IN PLAQUE REMOVAL – A RANDOMIZED CONTROLLED TRIAL

RUNNING HEAD: **ANTI-PLAQUE EFFICACY OF SOFT-BRISTLES TOOTHBRUSHES**

Artigo aceito para publicação no periódico “AOL – Acta Odontológica Latinoamericana”(Anexo 2)

Efficacy of two soft-bristles toothbrushes in plaque removal – a randomized controlled trial

Running head: Anti-plaque efficacy of soft-bristles toothbrushes

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ABSTRACT

The aim of the present examiner-blind randomized controlled clinical study was to compare the efficacy two soft-bristles toothbrushes in terms of plaque removal. Seventy volunteers were randomly allocated to Group A (tapered-tip toothbrush) or Group B (end-rounded toothbrush). At baseline appointment (Day 0), volunteers underwent plaque examination using the Improved plaque identification index. Under supervision, they brushed their teeth for 1 minute with their assigned toothbrushes and the plaque examination was repeated. Volunteers continued the oral hygiene regimen (assigned toothbrush and a regular dentifrice provided by the researchers) for 7 days. The experimental procedures of Day 0 were then repeated. Separate statistical analyses were performed for mean percent reduction of plaque in the whole-mouth, interproximal and gumline scores in both moments, using Mann-Whitney test, $p<0.05$. After a single toothbrushing, at Day 0, the mean percent plaque reduction was significantly reduced in both groups ($p<0.05$), with statistically greater reductions of whole-mouth (21.39±12.44 vs. 11.40±11.17), gumline (6.32±7.37 vs. 2.89±4.57) and interproximal (10.82±10.49 vs. 5.21±7.68) for Group A as compared to Group B. However, at day 7, no significant difference was observed between groups for whole-mouth (29.94±20.91 vs. 26.58±18.64), gumline (14.04±18.82 vs. 13.78±17.63) and interproximal surfaces (26.41±22.77 vs. 23.12±20.98) ($p>0.05$). In conclusion, at Day 0, Group A presented higher efficacy in supragingival plaque removal than did the Group B, as reflected by whole-mouth, gumline and interproximal plaque scores.

Keywords: Toothbrush; Plaque Index; Treatment Outcomes.

EFICÁCIA DE DUAS ESCOVAS DE CERDAS MACIAS NA REMOÇÃO DE PLACA – UM ENSAIO CLÍNICO RANDOMIZADO

RESUMO

O objetivo desse ensaio clínico, examinador-cego, randomizado e controle foi de comparadas a eficácia de duas escovas de cerdas macias em relação ao controle de placa. Setenta voluntários foram randomicamente alocados para Grupo A (escova com ponta cônica) ou Grupo B (escova com ponta arredondada). Na consulta inicial (dia 0), voluntários receberam exame de placa utilizando o Índice de identificação de placa melhorado. Sob supervisão, eles escovaram seus dentes por 1 minuto com as escovas designadas e o exame de placa foi repetido. Voluntários continuaram seu regime de higiene oral (escova dental alocada e dentifrício comum fornecidos pelos pesquisadores) durante 7 dias. Os procedimentos da consulta inicial foram novamente repetidos. Análises estatísticas distintas foram realizadas para percentual de redução média de placa para os escores de boca toda, interproximal e linha gengival em ambos os momentos, utilizando teste de Mann-Whitney, $p<0,05$. Após único uso da escova, no dia 0, o percentual de redução média de placa foi significativamente reduzido em ambos os grupos ($p<0,05$), com reduções significativas para boca toda (21,39±12,44 vs. 11,40±11,17), linha gengival (6,32±7,37 vs. 2,89±4,57) e interproximal (10,82±10,49 vs. 5,21±7,68) no Grupo A quando comparada com o Grupo B. Entretanto, no dia 7, nenhuma diferença significativa foi observada entre os grupos para boca toda (29,94±20,91 vs. 26,58±18,64), linha gengival (14,04±18,82 vs. 13,78±17,63) e interproximal (26,41±22,77 vs. 23,12±20,98) ($p>0,05$). Em conclusão, no dia 0, a escova do Grupo A apresentou eficácia superior na remoção de placa supragengival quando comparada com a escova do Grupo B, como demonstrado nos escores de placa de boca toda, linha gengival e interproximal.

INTRODUCTION

Supragingival plaque removal is undeniably the best way to ensure better oral health in the population. It has proven to prevent caries and periodontal diseases, prevent tooth loss and, more recently, improve the outcome of dental implants[1-3].

Oral hygiene routine demands time, dexterity and motivation. Therefore, the limits of the clinical effectiveness of self-performed oral hygiene are evident. Some studies have demonstrated the presence of remaining biofilm despite efforts in removing dental plaque[2,4]. The new classification of periodontal diseases and conditions established 10% as maximum of bleeding sites in patients to be classified as healthy, which is achieved with good oral hygiene habits[3,5].

Some studies have investigated the consumption of oral hygiene products, showing that there has been an increase worldwide. For example, less than one toothbrush per capita was consumed in the 1990s in Brazil[4,6]. In 2010, this consumption virtually doubled[5,7]. However, the estimation of the consumption does not necessarily means there is better clinical results in effectiveness of plaque control.

Toothbrushes are the gold standard product to use to remove plaque from teeth. They differ in texture, tip, hardness, and even in their material, being natural or synthetic. Studies comparing the efficacy of available toothbrushes are scarce in the literature. The use of soft-bristles toothbrush has been recommended to improve plaque reduction while minimizing gingival tissues lesion[8,9]. Therefore, studies comparing the efficacy of available products are important to better support the indication of any given toothbrush.

The aim of the present examiner-blind randomized controlled clinical study was to compare the efficacy two soft-bristle toothbrushes in terms of plaque removal with regular fluoride toothpaste in controlling established dental plaque over a 7-day period.

MATERIAL AND METHODS

Study Design

This study was designed as a phase III randomized, single-center, two-cell, examiner-blind and parallel-group clinical study.

Ethical Considerations

The protocol was approved by the Institutional Review Board of the Federal University of Rio Grande do Sul, Brazil and all the volunteers signed an informed consent form. The study was conducted according to good clinical practice standards[10].

Sample Size Estimate

Sample size estimation was performed after a pilot study. Based on the standard deviation for the response measures of 0.58, a significance level of α=0.05 and 80% level of power, the present study was powered to detect a minimal statistically significant difference between study group means of 15% and 32 individuals per group were considered necessary. A 10% possible attrition rate was added. Therefore, 35 individuals per group were considered for participation.

Participants

Seventy healthy male and female individuals, aged 21-70 years, were enrolled. The recruitment was performed at the Federal University of Rio Grande do Sul, Brazil. The following inclusion criteria were used: good oral health; initial mean plaque index of at least 0.6, determined by the Improved plaque identification index[6,11]; and ≥20 natural uncrowned teeth, excluding third molars. Individuals were not included in the study if they had: orthodontic bands, removable partial dentures, tumor or significant pathology in the soft or hard tissues of the oral cavity, moderate or advanced periodontal disease (purulent exudate, tooth mobility, and/or extensive loss of periodontal attachment or alveolar bone), antibiotic use in the month prior to the study entry, participation in any other clinical study, pregnant or breast-feeding status, dental prophylaxis in the 2 weeks prior to the baseline examination, history of allergy to oral/personal care consumer products or their ingredients, use of any prescription medicine that might interfere with the study outcome, medical condition prohibiting abstinence form eating/drinking/chewing gum for 4 hours prior to the scheduled visit, and history of alcohol or drug abuse.

Experimental Procedures

Individuals had to refrain from any oral hygiene measurement 12 hours before reporting to the clinical site and from eating, drinking or smoking for 4 hours. The baseline examination comprised evaluation of the oral cavity soft tissue and perioral region followed by plaque disclosure with 10ml of 0.04% basic fuchsine solution (Replasul; Iodontosul, Porto Alegre – RS, Brazil). At Day 0, plaque examination was performed using the Improved plaque identification index before toothbrushing[11]. Supragingival plaque was assessed on the facial and lingual surfaces of each tooth. Scores of 0 to 4 were assigned to all disclosed surfaces of the maxillary and mandibular teeth using a dental light and dental mirror. Teeth were divided in nine units (A-I, Figure 1).

From these site-wise scores, a whole-mouth plaque score was determined for each participant by calculating the proportion of sites in the mouth at which plaque was present. Three areas are near the gingival margin, two are interproximal, and four are on the body of the tooth. This index allows for stratification of area(s) are of concern during the analysis.

Simple randomization was performed by a computer-generated list by an external researcher responsible for the allocation concealment. Toothbrushes were kept inside numbered opaque plastic bags. The experimental groups were:

1. Group A (Colgate Periogard, Colgate–Palmolive Co., New York, USA). This is a soft-bristle and tapered-tip toothbrush;
2. Group B (Oral-B Indicator, Oral-B Laboratories, Belmont, CA, USA). This is a soft-bristle and end-rounded toothbrush.

All participants were instructed to brush their teeth for one minute under supervision with the assigned toothbrush and a commercially available standard fluoride toothpaste (Colgate Cavity Protection; Colgate, São Paulo, Brazil). Plaque evaluation was then performed (Day 0 after toothbrushing). They were instructed to use the product at home twice daily (morning and evening) for the next 7 days and to refrain from any interproximal cleaning. At day 7, all participants returned to the clinical facility and the same procedures performed at Day 0 were repeated. The same examiner (CKR), who was unaware of group allocation, performed all plaque examinations.

Statistical Analysis

The main study outcome is plaque score reduction, determined by the Improved plaque identification index. Plaque Index was dichotomized into absence of dental plaque (scores 0 or 1) and presence of dental plaque (scores 2, 3 or 4). Therefore, the percent of sites with presence of dental plaque was calculated to each individual at all experimental periods (Day 0 and Day 7). The percent reductions of plaque before and after toothbrushing were then calculated to each experimental period as follows: percent of dental plaque after toothbrush x 100 / percent of dental plaque before toothbrushing.

Separate statistical analyses were performed for whole-mouth, interproximal, and gumline plaque scores. A per-protocol analytical approach was used. The statistician was blinded to product allocation of participants during the analyses. Percentage reductions between before toothbrushing and after toothbrushing were calculated to both Day 0 and 7-day for whole-mouth, interproximal and gumline regions. Comparisons between groups were performed using the Mann-Whitney test, as a non-parametrical data distribution was observed (Kolmogorov-Smirnov test showed a p-value <0.05).

Non-parametrical distribution was also identified to the number of present teeth. In this sense, Mann-Whitney test was used to compare the number of teeth between groups. Conversely, age between groups was compared by t-test for independent samples. Categorical data (sex and smoking exposure) between groups were analyzed by chi-square test. A significance level of $\alpha=0.05$ was established to all analysis. Data analysis was performed using the statistical package SPSS 21.0 (SPSS Inc., Chicago, United States).

RESULTS

One (1) individual of the 71 initially screened for the study was not included (Figure 2). From the 70 included participants, 67 completed the 7-day clinical trial. Three participants - 2 in Group A and 1 in Group B did not complete the study. Reasons for dropouts are mentioned in Figure 2. Groups did not differ in gender and mean age (Table 1).

With relation to scores of Day 0 before toothbrushing, a statistically significant difference between groups was detected ($P<0.001$) (Table 1). Therefore, the present study analyzes percent reductions and not means. Figure 3 demonstrates the mean percent reduction (from before

toothbrushing to after toothbrushing) at Day 0, considering the whole-mouth, interproximal and gumline and surfaces. Group A showed significantly greater reduction in mean whole-mouth (21.39±12.44%), interproximal (10.82±10.49%) and gumline (6.32±7.37%) plaque scores as compared to Group B that reduced 11.4±11.17%, 5.21±7.68% and 2.89±4.57%, respectively (Figure 3).

At the day-7 follow-up, a statistically significant difference was observed in the scores before toothbrushing ($P<0.007$) (Table 1) in whole-mouth surfaces. Individuals in Group A demonstrated no significantly difference in the whole-mouth (29.94±20.91%), interproximal (26.41±22.77%) and gumline (14.04±18.82) percent reduction of plaque scores when compared to Group B, which had 26.58±18.64%, 23.12±20.98% and 13.78±17.63, respectively. However, no statistically significant difference was observed in mean percent reduction of plaque (Figure 4).

Three possibly related adverse events were reported during the study. The individuals reported to the entire 7-day study. The reported adverse events were traumatic brushing, mouth ulcers and severe pain in teeth irradiated to ear and jaw as reported by the subjects. All three (3) adverse events were reported in the Group B and one individual preferred not to continue in the study due to the discomfort. All participants who reported adverse events were carefully followed until the issue was solved. As toothbrushing technique may explain these findings, all individuals received an individualized oral hygiene instruction after all experimental periods were completed.

DISCUSSION

The present study was designed as a phase III randomized, single-center, two-cell, examiner-blind and parallel-group clinical study, with the aim to compare the plaque removal efficacy of two soft-bristles toothbrushes in 70 healthy volunteers. Group A (tapered-tip toothbrush) resulted in greater reduction of plaque than did Group B (end-rounded toothbrush) in the first usage. This result was statistically significant in the percent reduction of Day 0 and was not significant at day-7.

Toothbrushing is known to be the most used method of oral hygiene. The contemporary paradigm of oral hygiene is based on the highest efficacy with the less harm. In order to increase effectiveness and reduce improper brushing technique effects, manufactures set the goal of

evolving their toothbrushes in terms of design and bristle characteristics. It is well known that soft-bristle toothbrushes are efficacious and have less harmful potential[8,9]. In order to provide better cleaning effect across mouth, regardless of the type of movements used by the user, different toothbrushes have been developed[12,13]. A variety of studies can be found in the literature regarding different design and morphologies of toothbrushes. Comparisons between the different studies are not easy, especially due to high heterogeneity in design, follow-up, brands used, etc. The findings of such studies are important as different types of toothbrushes are launched in the market and the need of support in sound studies in terms of efficacy and safety is constant.

Therefore, the present study was designed to compare the effect of a novel soft-bristles toothbrush (Group A) with a toothbrush well established in the market (Group B). It should be emphasized that even though both brushes are considered soft, the test study (Group A) has softer bristles. It is well known that softer bristles could be less efficacious[14]. However, the benefit of less harm is undoubtful[8]. This is not a double-blind study, since the participants received different toothbrushes. However, all additional procedures are identical for both groups. The study was designed as an efficacy study, which demonstrates the potential of a novel device. Even though numerically similar, initial plaque scores demonstrated a statistically significant difference between groups. Therefore, to normalize data, the present study analyzes percent reduction in plaque scores. The results demonstrated that Group A presented higher efficacy in reducing plaque in whole-mouth and interproximal at Day 0 (which was the first contact with the brushes), even having softer bristles. The results after 7 days did not display a statistically significant difference. The importance of the separate analyses performed herein relate to the capacity of the toothbrushes in achieving different special areas from the teeth. Of special interest is the plaque removal capacity in interproximal areas, since these are areas in which other devices (such as dental floss) present limitations. Also, these areas are special areas of interest in terms of occurrence of dental caries, gingivitis and periodontitis.

The study outcome was measured using the Improved plaque identification index[11]. Such index was designed to quantify the presence of dental plaque in each of the 9 divided zones of the teeth as the Navy plaque index. This method of evaluation could provide a more sensitive plaque reduction demonstrating more accurately differences of plaque levels. However, such kind of quantification tends to generate regression to the mean. In this sense, we dichotomized the index

to facilitate clinical interpretation. The results demonstrated that, in the first usage, Group A presented a higher efficacy. Moreover, Hawthorne effect may be one of the explanation the leveling of the results in the 7-day evaluation, since it may be expected that participants change the behavior in response to the awareness of being observed[15]. In addition, the effect of a learning curve should not be disregarded.

Tapered bristles toothbrushes have been tested and shown to be more effective in reaching not only interproximal areas of the teeth along the gingival margin and under gumline where plaque accumulates the most but also, to reach fissures when compared to end-rounded bristles. This result was also positive in an *in vitro* study with artificial plaque in which, tapered-tip bristles have demonstrated significantly better results in reducing plaque scores in the interproximal area[16]. These findings, could be of a great advantage when patients who do not include flossing as daily hygiene routine benefits from use of tapered-tip bristles toothbrushes, as it was shown in the updated review[17] that flossing did not prevent reduction of dental caries and periodontal disease.

As well as the study from Rösing et al. 2016[18], a 12-hour period established to refrain from any type of oral hygiene before both evaluations, showed that plaque accumulation resulted in an amount sufficient to test efficacy of the toothbrushes although this was significantly different before toothbrushing Day 0 period in Group A. Additionally, it is important to mention that, no brushing technique was imposed to the participants. This measure meant to exalt the perspective of a real daily brushing technique of the individuals.

Regarding adverse events, in the present study, three were reported. None of them were related to the study protocol. A majority of the reported adverse events could be explained by causes related to the brushing habits of the patients. One of the participants was excluded. It is also important to highlight that soft and extra-soft bristles toothbrushes, have been reported in a systematic review to be safer than other toothbrush stiffness when oral injuries are evaluated regardless of the end-shape[8]. Such review concluded that soft and extra-soft toothbrushes tend to be safe, regardless if tapered-tip or end-rounded bristles are being tested, presenting no clinical relevance concerning soft oral tissue damage.

Moreover, a one minute (1) brushing time was established to the individuals in this study. Many studies have used the same brushing time, and the main reason to it, is to avoid the patient

need to excessively brush[18-20]. Also, it has been demonstrated that patients do not invest more time in toothbrushing in general.

This study has strengths and limitations that should be noted. Among the strengths are the study design, with randomization of the participants, use of a standardized brushing time, examiner reproducibility, examiner and statistician blinding, and very high compliance rate. The limitation of the study is due to the efficacy design, in which a short time (7 days) was used. Neither effectiveness not effect on gingival inflammation can be depicted from our results.

Despite the abovementioned limitations of the study, a point that should be considered is the reflection of better interproximal results by the Group A, which can present some relevance considering that toothbrushes were not meant to reach this area. Studies have demonstrated similar results when tapered-tip toothbrushes are being studied [18-20]. It is important to remember that a systematic review published by the Cochrane collaboration and revisited in 2019 showed concerning results to the levels of periodontal disease and caries in dental floss users, being concluded that, the users of this device does not necessarily have less diseases [17]. In this sense, it is always important that newly designed toothbrushes are studied, especially as a possibility of compensating the limited effects of flossing in the way it is performed by individuals. Longer term randomized controlled trials are warranted, including the analysis of adverse events, in order to prevent gingival tissue harm.

The tapered-tip toothbrush performed better than the end-rounded toothbrush in terms of efficacy at the first evaluation.

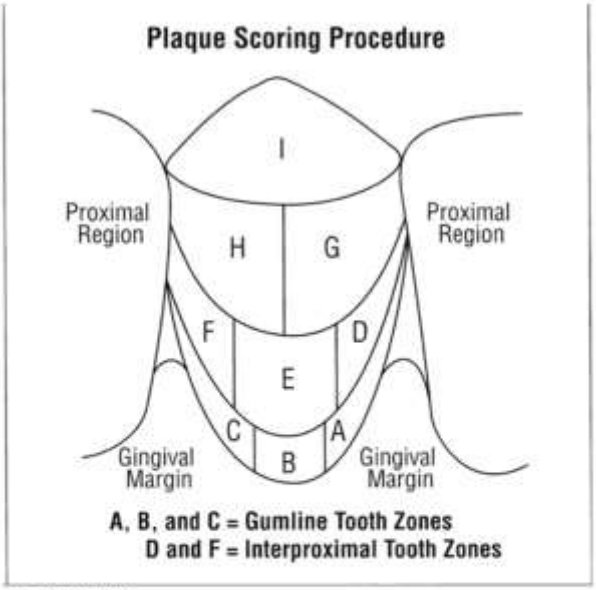
Figure legends

Figure 1. Improved plaque identification index (according to Ayad et al., 2016).

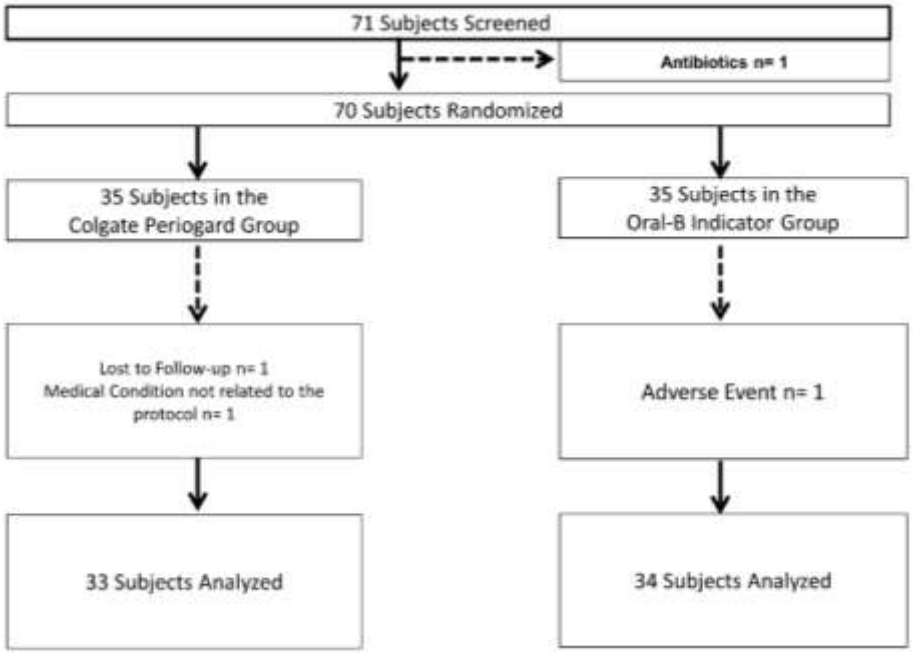
Figure 2. Study Flowchart.

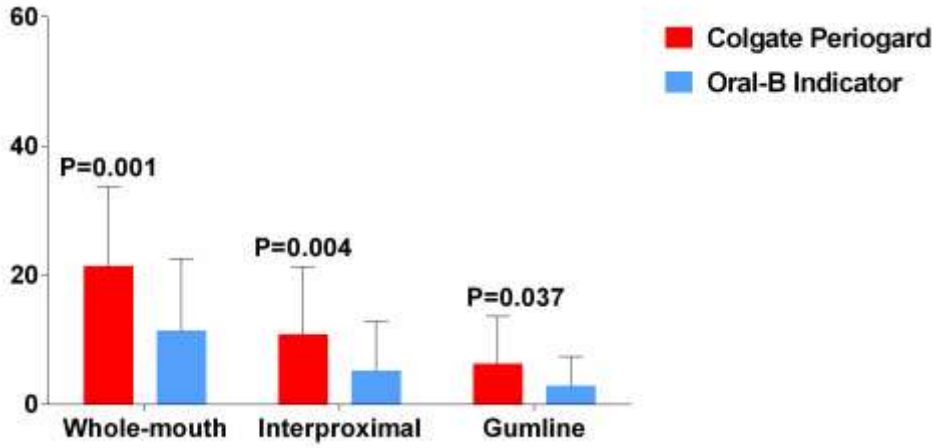
Figure 3. Mean percent reduction of plaque for Group A (tapered-tip toothbrush) and Group B (end-rounded toothbrush) at Day 0.

Figure 4. Mean percent reduction of plaque for Group A (tapered-tip toothbrush) and Group B (end-rounded toothbrush) at day-7.



0 = No plaque.
1 = Separate flecks of plaque covering less than one third of the unit surface.
2 = Continuous band of plaque covering less than one third of the unit surface.
3 = Plaque covering less than two thirds of the unit surface.
4= Plaque covering two-thirds or more of the unit surface.


71 Subjects Screened
Antibiotics n= 1
70 Subjects Randomized
35 Subjects in the Colgate Periogard Group
35 Subjects in the Oral-B Indicator Group
Lost to Follow-up n= 1
Medical Condition not related to the protocol n= 1
Adverse Event n= 1
33 Subjects Analyzed
34 Subjects Analyzed


60
40
20
0
P=0.001
P=0.004
P=0.037
Whole-mouth
Interproximal
Gumline
Colgate Periogard
Oral-B Indicator

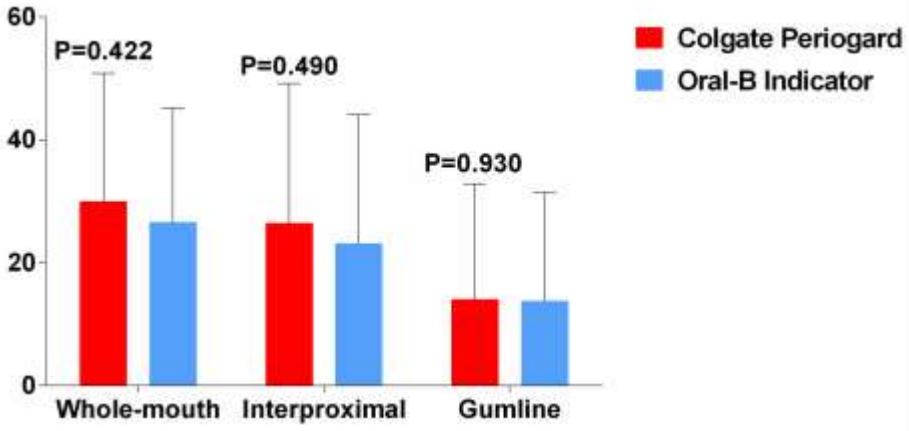

60
40
20
0
P=0.422
P=0.490
P=0.930
Whole-mouth
Interproximal
Gumline
Colgate Periogard
Oral-B Indicator

Table 1. Demographical and baseline characteristics of the study participants.

		Oral-B Indicator	**Colgate Periogard**	**P-value**
Sex	**Male – n (%)**	17 (48.6)	17 (48.6)	1.000*
	Female – n (%)	18 (51.4)	18 (51.4)	
Mean age±SD		35.89±10.80	32.29±9.86	0.150#
Mean number of teeth±SD	(median – min.; max.)	27.37±1.29 (28 – 23;28)	27.20±1.41 (28 – 23;28)	0.548µ
Mean percent of dental plaque(Whole-Mouth) at Day 0 before toothbrushing	Mean±SD	98.34±12.78	97.26±16.34	<0.001µ
Smoking exposure	**Non-smokers – n (%)**	29 (82.86)	35 (100.0)	0.025β
	Smokers – n (%)	6 (17.14)	0 (0.0)	

Legend: *Chi-square test; # t-test for independent samples; µ Mann Whitney test, β Fisher's exact test.

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ARTIGO 4

THE EFFECT OF CETYLPYRIDINIUM CHLORIDE MOUTHRINSE AS ADJUNCT TO TOOTHBRUSHING COMPARED TO PLACEBO ON INTERPROXIMAL PLAQUE AND GINGIVAL INFLAMMATION - A SYSTEMATIC REVIEW WITH META-ANALISES

Short Title: Cetylpyridinium chloride mouthrinse in plaque and gingival inflammation.

Artigo aceito para publicação no periódico “Clinical Oral Investigations” (Anexo 3)

Clinical Oral Investigations
https://doi.org/10.1007/s00784-020-03661-2

ORIGINAL ARTICLE

The effect of cetylpyridinium chloride mouthrinse as adjunct to toothbrushing compared to placebo on interproximal plaque and gingival inflammation—a systematic review with meta-analyses

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Abstract

Objectives The present study aimed to systematically review the literature about the interproximal anti-plaque and anti-gingivitis efficacy of cetylpyrydinium chloride (CPC) mouthrinse compared to placebo solution.

Materials and methods Three databases (PUBMED, SCOPUS, and EMBASE) were searched for randomized clinical trials that compared the interproximal anti-plaque and anti-gingivitis effect of CPC and placebo mouthrinses as an adjunct to toothbrushing, after a minimum of 6 weeks. Individuals with any periodontal diagnosis were considered. Two meta-analyses were performed for the Turesky modification of the Quigley-Hein plaque index and the Löe and Silness gingival index. For both analyses, the mean differences (MD) between baseline and 6-weeks were calculated using a random-effect model.

Results Eight studies were included. All included studies showed significant improvement in at least one of the parameters, favoring the CPC mouthrinse when compared to placebo. The meta-analysis demonstrated that groups that used CPC displayed a significantly greater reduction in the plaque index score (MD; 95% confidence interval [95%CI]: − 0.70; − 0.83 to − 0.57) and in the gingival index (MD; 95%CI: − 0.38; − 0.47 to − 0.28) when compared to placebo. However, high heterogeneity was observed in both analyses (I^2 = 89% and I^2 = 98%, respectively).

Conclusions When considering interproximal surfaces, CPC is efficacious both in plaque and gingival inflammatory parameters, demonstrating the potential to compensate for the limitations of interproximal plaque control.

Clinical relevance CPC may be a good alternative to compensate interproximal plaque removal, improving interproximal gingivitis

Keywords Cetylpyridinium · Dental plaque · Placebo · Gingivitis · Meta-analysis · Mouthwashes

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Introduction

Mechanical removal of supragingival plaque has a well-established role in oral health care. The most prevalent oral diseases—caries and periodontal disease—that may lead to tooth loss are, in some way or another, affected by good standards of plaque control. Adequate and frequent toothbrushing is the most common way to mechanically disrupt supragingival plaque and avoid inflammatory reactions caused by the biofilm [1].

A larger accumulation of dental biofilm is detected in interproximal surfaces [2]. A systematic review, published in 2011, analyzed clinical trials that evaluated the effectiveness of dental floss in removing interproximal biofilm and, consequently, preventing caries and periodontal disease. This study highlighted the insufficient anti-plaque and anti-gingivitis

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effect of dental floss in this region. This information led to the conclusion that the adjunct use of dental floss in oral hygiene routine was considered not proven by randomized clinical trials [3].

Mechanical disruption of oral biofilms may be accompanied by other means that may help to control dental plaque and gingival inflammation, as self-performed plaque control can present some limitations, including motivation and dexterity [4]. Chemical solutions have been developed as adjuncts to mechanical plaque control, in an attempt to compensate for such difficulties with higher effectiveness, mainly by increasing the anti-plaque and anti-gingivitis effect in comparison to toothbrushing alone [5, 6]. Also, the use of mouthrinses as adjuncts to toothbrushing has increased worldwide [7].

These solutions present an antibacterial effect and a low occurrence of adverse events even after prolonged use. A systematic review demonstrated that cetylpyridynium chloride (CPC) has a small but statistically significant anti-plaque and anti-gingivitis effect when used as an adjunct to mechanical oral hygiene [8]. In addition, a randomized clinical study has demonstrated that adding zinc lactate to the CPC formulation promotes additional efficacy in the reduction of plaque and gingivitis scores [9].

The adjunct use of the chemical solution and mechanical hygiene has also demonstrated the capacity of removing plaque in the interproximal region [10]. The interproximal region of the posterior and anterior teeth is the most common areas where plaque accumulates and remains after standard oral hygiene regimens [11]. Toothbrushes that can penetrate these difficult areas and chemical solutions that can remove plaque in these locations may compensate for the use of interdental cleaning devices, such as dental floss and interdental brushes, where mechanical tools have been demonstrated to be inefficient.

This study aimed to systematically review the literature about the anti-plaque and anti-gingivitis efficacy of CPC mouthrinse when compared to a placebo solution in the interproximal surfaces when used as an adjunct to toothbrushing.

Materials and methods

This study followed the PRISMA guideline for systematic reviews [12]. The following focused question was used: "In adult patients, has cetylpyridinium chloride mouthrinse, as an adjunct to toothbrushing, an additional anti-plaque or anti-gingivitis effect compared to toothbrushing alone or in association with a placebo solution in the interproximal surfaces?".

The PICO question comprised adult individuals (patients), CPC with manual toothbrushing (intervention), compared to a placebo solution with toothbrushing or only toothbrushing (comparison) and interproximal plaque or gingivitis indexes reductions (outcome).

Search strategy

The search strategy was conducted in three databases, MEDLINE-Pubmed, Scopus, and EMBASE. The literature search was performed up to February 26, 2020. In MEDLINE-Pubmed, the search strategy is described below:

#1 — "antiplaque"[Title/Abstract]) OR "antigingivitis"[Title/Abstract]) OR "Gingivitis"[Mesh Term] OR gingivitis[Text word] OR "Periodontal Index"[Mesh Term] OR Periodontal index[Text word] OR "gingival inflammation"[Text word] OR Bleed*[Text word] OR "gingival index"[Text word] OR gingival bleeding[Text word] OR bleeding on probing[Text word] OR papillary bleeding[Text word] OR "Oral Hygiene Index"[Mesh Term] OR Oral hygiene index[Text word] OR "Dental Plaque Index"[Mesh Term] OR dental plaque index[Text word] OR dental plaque[Mesh Term] OR Dental plaque[Text word] OR "Oral Hygiene"[Mesh Term] OR Oral hygiene[Text word] OR plaque[Text word] OR biofilm[Text word] OR "Quigley-Hein Index"[Text word] OR "silness Loe index"[Text word] OR interdental plaque[Text word] OR interproximal plaque[Text word] OR dental deposit*[Text word]
#2 — Cetylpyridinium[Mesh Term] OR Cetylpyridinium[Text word] OR Cetylpyridinium chloride [Text word] OR CPC[Text word] OR 1-hexadecylpyridinium chloride[Text word] OR acetoquat[Text word] OR ammonyx CPC[Text word] OR ceepryn chloride[Text word] OR cepacol[Text word] OR plax[Text word] OR cetamium[Text word] OR dobendan[Text word] OR ipanol[Text word] OR merothol[Text word] OR pristacin[Text word] OR pyrisept[Text word] OR asept[Text word] OR mouthrinses[Text word] OR "mouthwash"[Text word] OR "mouthrinse"[Text word]
#3 — #1 AND #2

The SCOPUS and EMBASE databases were searched with adapted strategies.

Selection criteria and risk of bias assessment

Two researchers (FWMGM and GPJL) independently selected the studies. First, the title and abstract were screened for eligibility, and an additional researcher (CKR) was involved when discrepancies were observed. After that, full text eligibility was performed. The Kappa indices between researchers were 0.93 and 1.00 for the screening of title/abstract and full text, respectively.

The studies had to present all the following criteria to be included:

- Randomized clinical trials;
- Studies that involved adults at least 18 years old;
- Individuals with any periodontal diagnosis were considered (higher level of dental plaque only, gingivitis or patients with periodontitis after periodontal therapy);
- In the test group, mechanical hygiene in addition to CPC mouthwash;
- In the control group, mechanical hygiene with placebo solution or mechanical hygiene alone;
- The study had to evaluate any plaque or gingival index in the interproximal surfaces;
- A minimum of 6 weeks of follow-up. Mouthwash had to be used continuously during the follow-up period.

Studies that presented any of the following characteristics were excluded:

- Letters to the editors, observational, in vitro, animal model, and review studies;
- Studies that used any other type of adjunct substance;
- Studies that reported only microbiological outcomes.

Data extraction

Two researchers independently performed the data extraction of all included studies (GPJL and RSAC). A Microsoft Excel® spreadsheet was specifically developed for this study. A third researcher (FWMGM) was involved only if any discrepancy was detected. The spreadsheet contained the following variables: authors, year of publication, country, experimental design follow-up, intervention made before the study, number of individuals in each group, number of smokers in each group, brushing time, brushing technique, mean age, plaque and gingival index, results for the interproximal plaque, and gingival assessment of each experimental period that individuals were followed and adverse events reported.

Risk of bias assessment

In this systematic review, the risk of bias was assessed by the RoB2 tool, as recommended by Cochrane [13]. The following criteria were assessed: randomization process, deviations from the intended interventions, missing outcome data, measurements of the outcome, and selection of the reported result and overall. Two reviewers (GPJL and RSAC) independently assessed the risk of bias of each included study. A third reviewer was involved only when a consensus was not possible (FWMGM).

Dealing with missing data

If important information was not reported in the study, the corresponding authors were contacted by e-mail to provide it. All studies that reported mean plaque or gingival scores for the whole-mouth were contacted to provide raw data for the present study. If the authors did not provide this information, the study was excluded from the present study. Only two corresponding authors answered our request [14, 15], providing the raw data for interproximal plaque and gingival indexes.

Statistical analysis

Two meta-analyses were performed for the Turesky modification of the Quigley-Hein plaque index and the Löe and Silness gingival index. No meta-analysis could be performed for other indexes due to the low number of included studies for those other indexes. In both analyses, a mean difference between baseline and 6 weeks was calculated for each study and experimental group. When the 6-week follow-up was not available, the nearest follow-up period was evaluated. When a study presented two groups using different concentrations of CPC, each CPC group was included in the analysis separately. However, the number of individuals in the control group was divided by two.

Subgroup analyses were created for both meta-analyses, as different concentrations of CPC were used among the included studies. Subgroup analyses were also performed for the different follow-up periods using the same indexes. All meta-analyses were performed in the Rev-Man software (version 5.3 for MS Windows), using a random-effect model. The Q test assessed the heterogeneity, which was qualified by the I^2 statistics.

Results

Study selection

The initial screening reviewed 2,635 studies, of which 23 were fully read. Nine were included in the present systematic review. Figure 1 shows the flowchart of the review, including the main reasons for exclusion. Fifteen [16–30] studies were excluded as no information about the interproximal plaque or gingival scores was provided. Table 1 shows the main descriptive characteristics and results of the included studies.

Characteristics of the included studies

All the nine included studies were RCTs with follow-up from 6 weeks to 6 months [9, 14, 15, 31–36]. They reported to include only otherwise systemically healthy patients. From

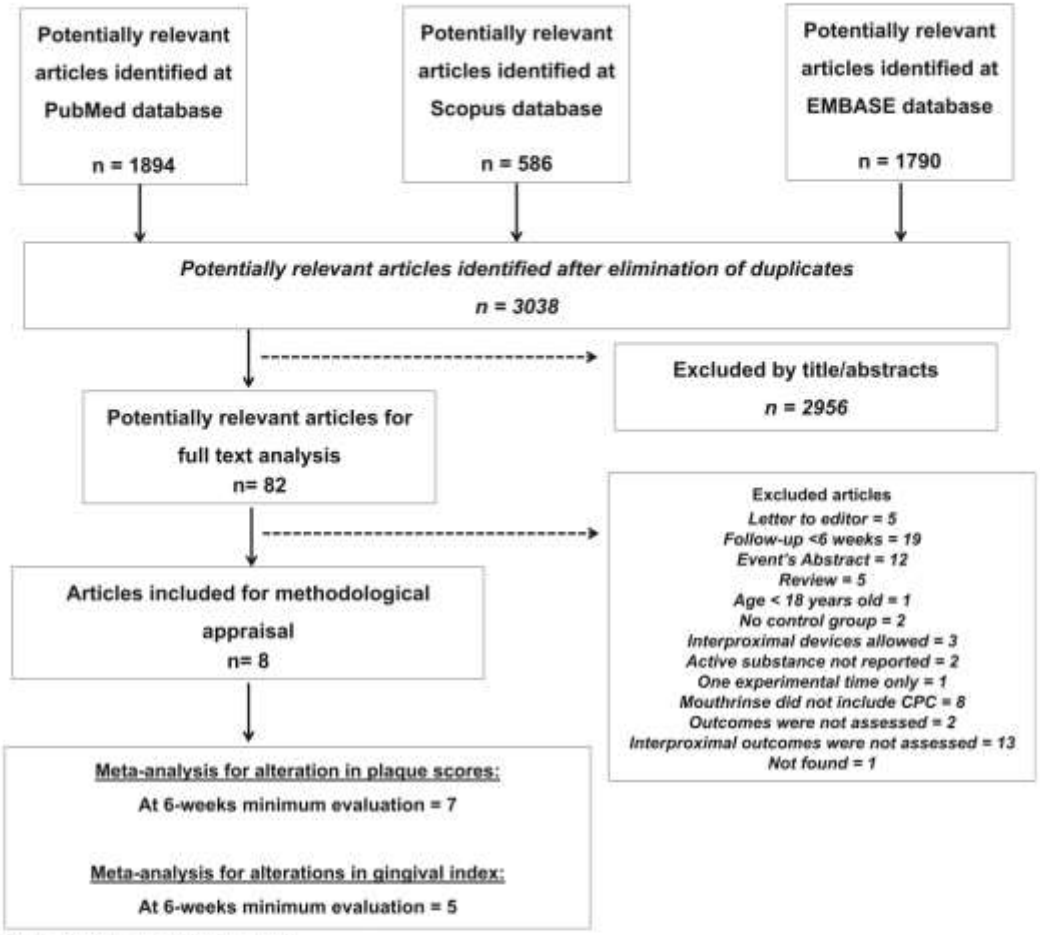

Fig. 1 Flowchart of the systematic review

the nine included studies, three studies [14, 35, 36] included smokers and non-smokers. Three studies [14, 15, 36] reported performing complete oral prophylaxis to have a standardized cutoff point. The remaining six [9, 31–34] did not report whether previous oral prophylaxis was performed. The included studies used different inclusion criteria, such as gingival index ≥ 1.0 [9, 31–34], a modified gingival index ≥ 1.75 [36], marginal probing ≥ 40% [14, 15], and papillary bleeding index per tooth > 0.5 [35].

Regarding the time of rinsing and amount of mouthwash, four studies [9, 31–33] specified 20 ml for 30 s as the pattern for all the patients, and two studies [14, 15] reported 15 ml for 30 s as the time needed. One study [34] referred to 15 ml for 1 min, another study [36] reported 20 ml for 1 min, while one last study [35] did not report any information regarding the time or amount of mouthwash used for each patient. Only one study explicitly allowed the use of interproximal cleaning devices [36]. Another study noted that no interproximal cleaning instructions were given to the individuals [14].

Different concentrations and formulations of the mouthrinse solution were used in the nine included studies. One study [31] used a solution composed of 0.075% CPC with fluoride in the test group and a solution of 0.05% fluoride as control, both in an alcohol-free base. One study [32] used a solution with 0.075% CPC in the test group, a 0.070% CPC solution as the positive control, both in an alcohol-free base, and a placebo free of fluoride and alcohol as the negative control. Another study [33] used a 0.075% CPC solution in the test group and a placebo solution free of

Table 1 Main characteristics and results of the included studies

Name, year (study design)	Follow-up period	Systemic conditions	Smoking status (*n* per group)	Cetylpiridinium chloride group (*n* male, *n* females; mean age), adverse events	Placebo group (*n* male – *n* females; mean age), adverse events	Negative control group, adverse events
AYAD, 2011 (RCT – parallel)	Baseline, 3 and 6 months	Systemically healthy	N/R	0.075% CPC and 0.05% NaF in alcohol-free base, (22 male, 32 female), age N/R	0.05% NaF in an alcohol-free base (23 male, 33 female)	N/A
BONETA, 2015 (RCT, parallel)	Baseline, 4 and 6 weeks	Systemically healthy	N/R	0.075% CPC fluoride-free, alcohol free (18 male, 19 female) N/R	0.07% CPC fluoride-free alcohol free (22 male, 18 female)	Fluoride-free alcohol-free (15 male, 24 female)
BONETA, 2015 (RCT, parallel)	Baseline, 4 and 6 weeks	Systemically healthy	N/R	0.075% CPC in fluoride-free, alcohol free N/R N/R	Commercially available mouthwash containing essential oil in fluoride-free, 21.6% alcohol free N/R	Fluoride-free alcohol-free non-bacterial mouthwash N/R
CORTELLI, 2012 (RCT, parallel)	Baseline, 3 and 6 months	Systemically healthy	Test = 10 Control = 8	0.05% CPC mounthrinse (52 male, 84 female)	5 % hydroalcohol mouthrinse (56 male, 80 female)	N/A
COSTA, 2013 (RCT, parallel)	Baseline, 3 and 6 months	Systemically healthy	Test = 11 Control = 6	0.07% CPC mouthrinse (20 male, 12 female) Mean age 24.6 ± 3.4	Placebo mouthrinse (22 male, 13 female) Mean age 26.4 ± 7.6	N/A
DE SILVA, 2009 (RCT, parallel)	Baseline and 6 weeks	Systemically healthy	N/R	0.05% CPC (18 male, 39 female) N/R	N/R (21 male, 32 female)	Negative control mouthrinse without 0.05% CPC N/A
LEEUWEN, 2015 (RCT, parallel)	Baseline, 3 and 6 months	Systemically healthy	N/R	0.07% CPC mouth rinse (5 male, 15 female) Mean age 22.5 ± 3.20	Placebo without CPC (7 male, 18 female) Mean age 21.1 ± 2.32	N/A
ROSING, 2017 (RCT, parallel)	Baseline, 4 and 6 weeks	Systemically healthy	N/R	0.075% CPC and 0.28% zinc lactate with 0.05% sodium fluoride in an alcohol-free base (15 male, 22 female) Mean age 31.86 ± 9.93	0.07% CPC with 0.05% sodium fluoride in an alcohol free base (14 male, 23 female) Mean age 30.73 ± 10.03	Mouthwash without CPC (14 male, 24 female) Mean age 31.26 ± 10.35
ZIMMER, 2006 (RCT, parallel)	Baseline, 4 and 8 weeks	Systemically healthy	Test = 12 Control = 6	0.1% CPC and 0.025% fluoride N/R N/R	Toothbrushing only N/R	N/A N/R

Name, year (study design)	Amount, time of rinse	Plaque index	Gingival index	Main results
AYAD, 2011 (RCT – parallel)	20 ml, 15 s	Turesky Modification of Quigley-Hein index	Loe-Silness index	Plaque: Test: baseline 2.70 ± 0.32 ($P < 0.05$); 3 months 2.11 ± 0.30 ($P < 0.05$ between baseline) Control: baseline 2.64 ± 0.38 ($P < 0.05$); 3 months 2.72 ± 0.39 ($P > 0.05$ from baseline) Test reduction ($P < 0.05$) between treatment Gingival: Test: baseline 2.23 ± 0.24 ($P < 0.05$); 3 months 1.78 ± 0.36 ($P < 0.05$ between baseline) Control: 2.24 ± 0.23 ($P < 0.05$); 3 months 2.29 ± 0.29 ($P > 0.05$ between baseline) Test reduction ($P < 0.05$) between treatment
BONETA, 2015 (RCT, parallel)	20 ml, 30 s	Turesky Modification of Quigley-Hein index	Loe-Silness index	Plaque: Test: baseline 3.87 ± 0.70; 4 weeks 3.54 ± 0.83; 6 weeks 2.95 ± 0.80. Control+: baseline 4.07 ± 0.47; 4 weeks 3.83 ± 0.54; 6 weeks 3.24 ± 0.52. Control-: baseline 3.79 ± 0.69; 4 weeks 3.79 ± 0.63; 6 weeks 3.69 ± 0.61 Gingival: Test: baseline 1.78 ± 0.52; 4 weeks 1.63 ± 0.48; 6 weeks 1.35 ± 0.43. Control +: baseline 1.68 ± 0.47; 4 weeks 1.59 ± 0.46; 6 weeks 1.34 ± 0.39. Control −: baseline 1.83 ± 0.47; 4 weeks 1.81 ± 0.46; 6 weeks 1.80 ± 0.44
	20 ml, 30 s			Plaque:

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Table 1 (continued)

BONETA, 2015 (RCT, parallel)		Turesky modification of Quigley-Hein index	Loe-Silness index	Test: baseline 4.03 ± 0.62; 4 weeks 3.43 ± 0.72; 6 weeks 2.92 ± 0.72 Control +: baseline 4.00 ± 0.55; 4 weeks 3.50 ± 0.71; 6 weeks 3.03 ± 0.59 Control −: baseline 3.88 ± 0.61; 4 weeks 3.73 ± 0.69; 6 weeks 3.87 ± 0.67 Gingival: Test: baseline 1.89 ± 0.56; 4 weeks 1.67 ± 0.57; 6 weeks 1.37 ± 0.43 Control +: baseline 1.85 ± 0.48; 4 weeks 1.64 ± 0.46; 6 weeks 1.45 ± 0.39. Control −: baseline 1.89 ± 0.41; 4 weeks 1.82 ± 0.43; 6 weeks 1.80 ± 0.36.
CORTELLI, 2012 (RCT, parallel)	20 ml, 60 s	Mean plaque index	Modified gingival index	Plaque: Test: baseline 3.21 ± 0.36; 3 months 2.64 ± 0.02; 6 months 2.67 ± 0.03 Control: baseline 3.21 ± 0.3; 3 months 2.86 ± 0.02; 6 months 2.77 ± 0.03 Gingival: Test: baseline 2.36 ± 0.15; 3 months 2.11 ± 0.01; 6 months 2.29 ± 0.0 Control: baseline 2.35 ± 0.17; 3 months 2.16 ± 0.01; 6 months 2.33 ± 0.02
COSTA, 2013 (RCT, parallel)	15 ml, 30 s	Turesky modification of Quigley-Hein index	BOMP index	Plaque: Test: baseline 2.57 ± 0.64; 3 months 1.67 ± 0.74; 6 months 1.84 ± 0.80 Control: baseline 2.35 ± 0.44; 3 months 2.06 ± 0.47; 6 months 2.16 ± 0.41. Gingival: Test: baseline 1.15 ± 0.29; 3 months 0.71 ± 0.29; 6 months 0.71 ± 0.27 Control: baseline 1.03 ± 0.38; 3 months 0.76 ± 0.29; 6 months 0.82 ± 0.27
DE SILVA, 2009 (RCT, parallel)	15 ml, 1 min	Turesky Modification of Quigley-Hein index	Loe-Silness index	Plaque: Test: baseline 2.59 ± 0.25; 6 weeks 1.78 ± 0.43 Control: baseline 2.64 ± 0.25; 6 weeks 2.47 ± 0.35 Gingival: Test: baseline 2.21 ± 0.27; 6 weeks 1.65 ± 0.32 Control: baseline 2.20 ± 0.24; 6 weeks 2.08 ± 0.27
LEEUWEN, 2015 (RCT, parallel)	15 ml, 30 s	Turesky modification of the Quigley-Hein Plaque index.	BOMB index	Plaque: Test: baseline 1.84 ± 0.39; 3 months 1.32 ± 0.19; 6 months 1.94 ± 0.36 Control: baseline 2.05 ± 0.37; 3 months 1.27 ± 0.27; 6 months 1.94 ± 0.36 Gingival: Test: baseline 1.24 ± 0.35; 3 months 1.32 ± 0.19; 6 months 1.16 ± 0.32 Control: baseline 1.26 ± 0.33; 3 months 1.27 ± 0.27; 6 months 1.28 ± 0.30
ROSING, 2017 (RCT, parallel)	20 ml, 30 s	Turesky modification of Quigley-Hein index	Loe-Silness index	Plaque: Test: baseline 3.54 ± 0.43; 4 weeks 1.50 ± 0.29; 6 weeks 1.48 ± 0.28 Control +: baseline 3.52 ± 0.47; 4 weeks 1.87 ± 0.44; 6 weeks 1.79 ± 0.33 Control −: baseline 3.53 ± 0.43; 4 weeks 2.31 ± 0.58; 6 weeks 2.42 ± 0.48 Gingival: Test: baseline 1.71 ± 0.17; 4 weeks 1.31 ± 0.20; 6 weeks 1.21 ± 0.12 Control +: baseline 1.67 ± 0.20; 4 weeks 1.46 ± 0.19; 6 weeks 1.44 ± 0.14 Control −: baseline 1.72 ± 0.18; 4 weeks 1.60 ± 0.21; 6 weeks 1.63 ± 0.15
ZIMMER, 2006 (RCT, parallel)	N/R	Modified proximal index	Papillary bleeding index	Plaque: Test: baseline 2.22 ± 0.30; 4 weeks 1.70 ± 0.49; 8 weeks 1.40 ± 0.49 Control: baseline 2.20 ± 0.33; 4 weeks 2.05 ± 0.45; 8 weeks 1.88 ± 0.50 Gingival: Test: baseline 1.25 ± 0.45; 4 weeks 0.86 ± 0.45; 8 weeks 0.75 ± 0.49 Control: baseline 1.27 ± 0.45; 4 weeks 0.98 ± 0.43; 8 weeks 0.89 ± 0.46

RCT randomized clinical trial, *N/R* not reported, *N/A* not available

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fluoride and alcohol in the negative control group. Two studies [14, 15] reported the use of a 0.07% CPC solution in the test group, and one [34] used a 0.05% CPC solution in the test group. Both studies used a placebo solution with the same formulation without CPC in the control group. One study used a 0.05% CPC mouthrinse in the test group and a 5% hydroalcohol solution as the control [36]. One study [9] used two alcohol-free base CPC solutions, a 0.075% CPC, 0.28% zinc lactate with 0.05% fluoride solution in the test group, a 0.07% CPC with 0.05% fluoride solution in the positive control group and a placebo solution with the same formulation without the CPC as the negative control. Finally, one study [35] used a 0.1% CPC solution with 0.025% fluoride in the test group and toothbrushing only in the control group.

Risk of bias assessment

Figure 2 shows the risk of bias assessment of the included studies using the Rob2 tool. Five studies [9, 14, 15, 33, 36] did not present any concern, showing a low risk of bias to all evaluated criteria. Three studies [31, 32, 34] showed some concerns regarding the randomization process and overall risk of bias. A high risk of bias was found regarding deviations from intended interventions and overall risk of bias in one study [35].

Qualitative results—plaque scores

Interproximal plaque scores were reported in all nine studies. The Turesky modification of the Quigley-Hein plaque index was used in seven studies [9, 14, 15, 31–34], one [35] reported to using the modified proximal plaque index, and another used a mean plaque index [36]. All studies reported no statistically significant difference between groups for plaque scores in the baseline evaluation. For the comparison within groups, reduction of plaque scores in all experimental times was reported in the test group when compared to baseline. Four studies [9, 14, 34, 36] reported that the placebo group presented statistically significant different plaque scores compared to baseline, although one study [35] did not report the *P* values showing if the reductions were statistically significant. In all nine studies, CPC-based solutions were reported to have reduced interproximal plaque scores significantly more than the groups using fluoride solutions or placebo.

Qualitative results—gingival scores

Interproximal gingival scores were reported in all included studies. Five studies [9, 31–34] used the Löe and Silness gingival index. These five studies reported no statistically significant differences at baseline between the test and control groups. At the final examinations, the CPC groups

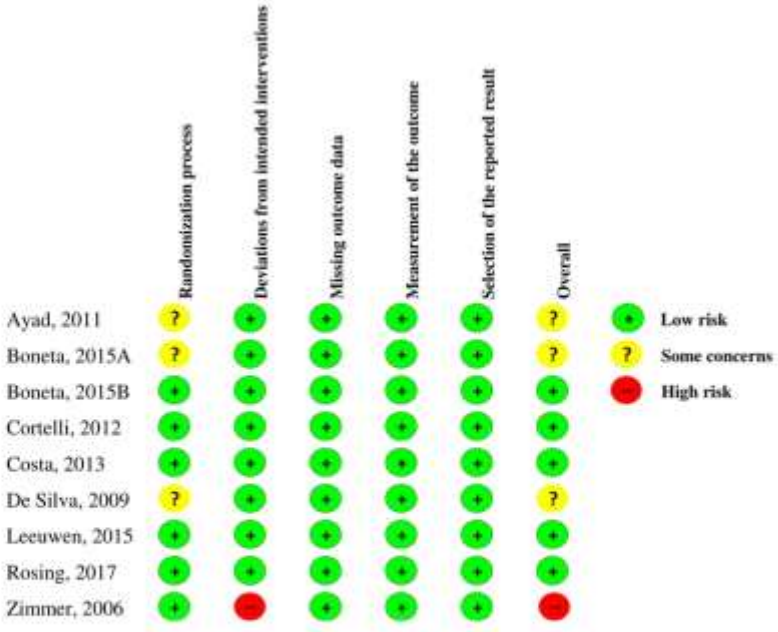

Fig. 2 Risk of bias assessment of the included studies

demonstrated statistically significant higher reductions when compared to fluoride or placebo solutions.

Two studies [14, 15] used marginal bleeding (MB) within 30 s to evaluate gingival inflammation. One of them [14] demonstrated significant reduction levels both in test and control groups. The group that used CPC presented significantly lower MB when compared to the control group. Another study [15] demonstrated no significant reduction levels in all experimental times.

One study [35] used papillary bleeding index, and no *P* values were available. Baseline, test, and control groups reduced interproximal gingival scores. The test group presented a higher reduction of gingival inflammation than control groups, but *P* values were not reported in the study.

The last study [36], in which interproximal cleaning devices were permitted, used a modified gingival index. No statistically significant differences in baseline between test and control groups were observed. At final examinations, CPC groups demonstrated statistically significant higher reduction when compared to the control group.

Side effects

Only three studies [9, 35, 36] reported adverse events on the oral hard or soft tissues, of which one [9] reported 22 adverse events throughout the study. From these, 20 participants completed the study [9]. Fifteen of these events were reported in the positive control group (0.07% CPC solution), all of which were tongue numbness, decrease or loss of taste, gingival bleeding, tooth statin, and sublingual swelling. In the test group (0.075% CPC + 0.28% zinc lactate), three adverse events, bitter taste and dentin hypersensitivity, were reported. In the negative control group, four individuals reported having tooth sensitivity, dentin hypersensitivity, and nausea. One study [35] reported 25 non-serious adverse events in the test group (0.1% CPC). Most of the events were staining of the teeth or tongue, and this staining was solved after the study finished. In the control groups, two non-serious adverse events were reported. The last study [36] reported 14 side effects, 7 in each group (test and control). A low percentage of the reported effects was related to the mouthrinses. The effects were sensitivity of the teeth (control = 1; test = 2), mouth ulceration (control = 2), glossodynia (control = 4; test = 3), dysgeusia (test = 2), and oral discomfort (test = 1).

Meta-analysis for alterations in plaque scores

Figure 3 presents the forest plot of the meta-analysis for the MD of interproximal plaque scores between baseline and 6-week evaluation. When the 6-week evaluation was not available, the closest follow-up period was used: in three studies [14, 15, 31], the 3-months data were used. Data from the 6 weeks of follow-up were used in the other studies. Seven studies [9, 14, 15, 31–34] were included in the analysis. Two studies were not included in this analysis, as a different plaque index was used [35], or the study allowed the use of interproximal cleaning device [36]. In the CPC groups, a statistically significant reduction of 0.70 scores (95%CI: − 0.83 to − 0.57) in plaque index was observed when compared to the control group. However, high heterogeneity was detected in this analysis (I^2: 98%, $P < 0.001$). The same trend of results was observed for all subgroup analyses, and no significant differences among the subgroups were detected ($P = 0.08$). Within the subgroups analyses, high heterogeneity was still observed.

When the different follow-up periods were considered a subgroup analysis, no statistically significant difference between groups was detected (6 weeks [MD; 95%CI]: − 0.81; − 0.98 to − 0.64 and 3 months [MD; 95%CI]: − 0.48; − 0.80 to − 0.16. Test for subgroup differences: $P = 0.07$).

Meta-analysis for alterations in gingival index

Figure 4 presents the forest plot of the meta-analysis for the MD of the interproximal gingival index between baseline and 6-week evaluation. In this analysis, only one study included data from the 3-month follow-up [31]. Five [9, 31–34] studies were included in this analysis. The other four studies were not included, as they used different gingival indexes [14, 15, 35, 36]. In the CPC group, a significant reduction of 0.38 score (95%CI: − 0.47 to − 0.28) in the gingival index was observed when compared to the control group. High heterogeneity was also detected (I^2: 99%, $P < 0.001$). Regardless of the concentration of the CPC solution, the same trend of results was detected.

For the subgroup analysis of the different follow-up periods, a statistically significant difference between groups was detected (6 weeks [MD; 95%CI]: − 0.35; − 0.47 to − 0.24 and 3 months [MD; 95%CI]: − 0.50; − 0.52 to − 0.48. Test for subgroup differences: $P = 0.01$).

Discussion

The present study aimed to systematically review the literature for studies reporting interproximal anti-plaque and anti-gingivitis effect of mouthrinses containing CPC compared to a negative control in a minimum experimental time of 6 weeks. To our knowledge, no previous study has systematically reviewed the anti-plaque and anti-gingivitis efficacy of mouthwashes containing CPC in the interproximal area. The present study demonstrated that adjuvant use of CPC along with toothbrushing promotes a significant reduction in plaque and gingival indexes when compared to toothbrush alone or in association with a placebo. It is important to highlight that, in the present study, patients with any periodontal diagnosis

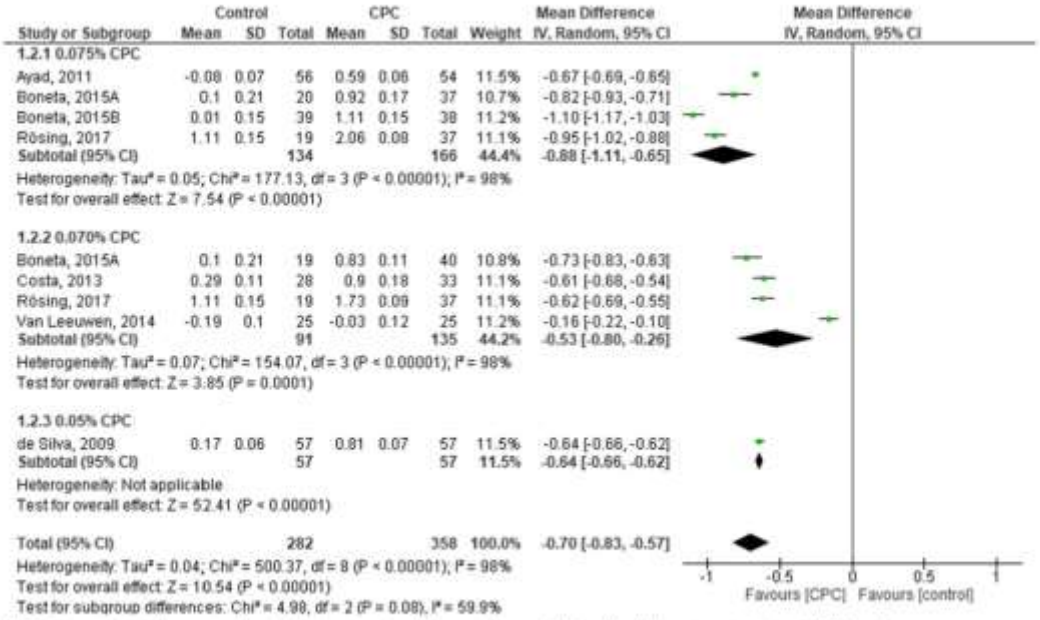

Fig. 3 Forest plot for the meta-analysis of the interproximal plaque index, considering the different concentrations of CPC as subgroups

were involved, including individuals without a precise periodontal diagnosis. A previous systematic review published in 2016 by Haas et al. [37] evaluated the efficacy of essential oils when compared to placebo or CPC, and some results

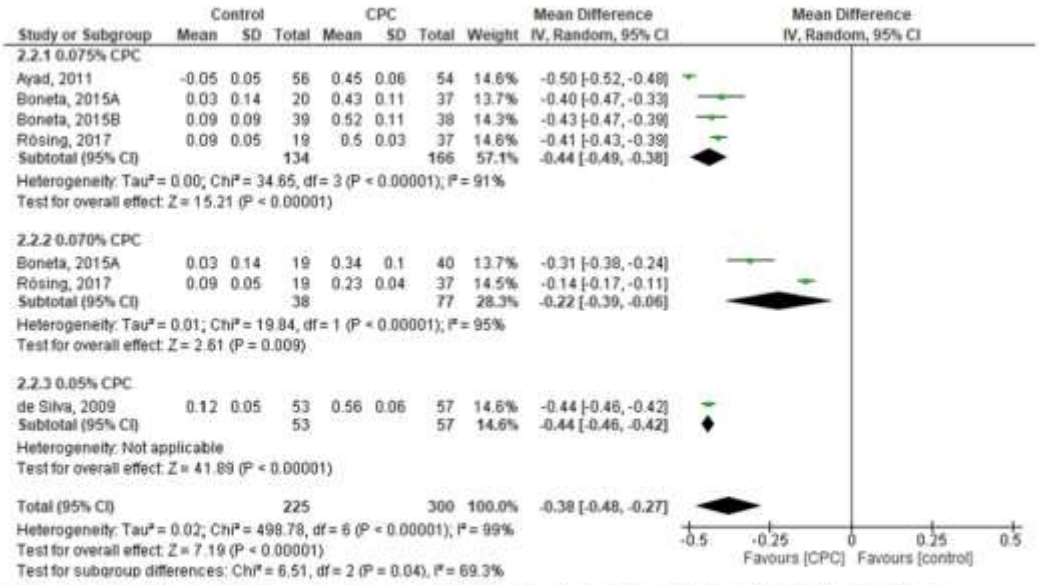

Fig. 4 Forest plot for the meta-analysis of the interproximal gingival index, considering the different concentrations of CPC as subgroups

addressed the interproximal area. It is important to mention that, in abovementioned systematic review, studies using interproximal devices for oral hygiene were also included.

Regarding the anti-plaque efficacy, all nine included studies demonstrated significant reduction when CPC was compared to placebo regardless of the concentration of CPC used. From the results observed in this review, the meta-analysis for anti-plaque efficacy, seven studies [9, 14, 15, 31–35] were included and, in the CPC groups, a statistically significant higher reduction of 0.70 (95%CI: − 0.83 to − 0.57) scores in plaque index was observed when compared to the control group. Regarding the anti-gingivitis efficacy, the five [9, 31–34] included studies showed that in the CPC group, a significantly higher reduction of 0.38 (95%CI: − 0.47 to − 0.28) was observed when compared to the control group. A high risk of bias was detected in only one study.

When comparing the anti-plaque and anti-gingivitis effect in those using or not interproximal cleaning devices, one study instructed the volunteers to use dental floss during the experimental period [36]. Conversely, the other studies did not allow interproximal cleaning or did not provide specific oral hygiene instruction for these devices. Due to the high heterogeneity, the abovementioned study [36] was not included in the meta-analyses.

Past studies claimed that the majority of the patients were not capable of removing biofilm effectively from the interproximal sites [38], which leads to the development of gingivitis in this area. These findings suggest that daily use of "therapeutic chemical agents" to help reduce plaque accumulation would be of value [39]. Clinical indications for mouthwash solutions include patients with a lack of dexterity for tooth brushing, patients with temporary or continuous impaired motor function, as an adjunct to mechanical biofilm control or halitosis treatment, during postoperative oral procedures, or as a pre-procedural mouthwash for reducing bacteria in dental aerosols [40].

Various concentrations of CPC are effective both in whole-mouth and interproximal areas for anti-plaque and anti-gingivitis efficacies [9, 14, 15, 31–35]. In the present study, different concentrations of CPC, as well as components added to the formula, have shown to lead to better clinical results. For instance, one study added zinc lactate to the CPC formulation, improving clinical outcomes when compared to a solution with CPC only [9]. This result was even more interesting in the interproximal area.

Among all interdental cleaning methods, interdental brush and dental floss [41–44] are the most used. The interdental brush is undoubtedly more efficacious when comparing all the interdental cleaning devices [45–47]. However, a space between the teeth is needed to accomplish hygiene with this specific device. When this gap is not available, clinicians rely on dental floss. The results of a Cochrane systematic review, published in 2011, showed the limitations of dental floss in preventing caries and periodontal diseases as the included studies were weak or low quality [3]. This finding is also supported by a study [48] in which schoolchildren were evaluated. The addition of flossing to brushing was assigned to each experimental group in each phase of 21 days; oral hygiene instruction in brushing and flossing was provided. This study showed that the introduction of a regimen of brushing was efficient in reducing plaque and gingival bleeding when considering separately or in association. However, when including flossing to the regimen, no additional significant plaque removal or decrease in gingival bleeding was observed. The authors declared that the addition of flossing into this brushing regimen showed no significant improvement in the parameters evaluated in young schoolchildren. Additionally, the inclusion of supervised flossing for a relatively short period did not improve gingival inflammation. Herein, the effect of tooth brushing in the interproximal area should not be ruled out. It is important to study new possibilities and/or solutions to compensate for these difficulties addressed by the studies of dental floss in the prevention of the most prevalent oral diseases.

In addition to chemical solutions, toothbrushes have shown the potential capacity of interproximal biofilm removal when different characteristics of the bristles or designs are tested. Clinical trials have shown that toothbrushes with tapered soft bristles have shown reduced plaque level in the interproximal area when comparing to other bristles [10, 49]. These results show progress in the promotion of plaque and gingivitis control even if they are not specific for the interproximal region.

As demonstrated in this systematic review, the included studies have reported similar data about the ability of CPC-containing chemical agents to reach the interproximal biofilm and reduce gingival levels of inflammation. Slightly different concentrations were used in the included studies. It is likely that the addition of zinc lactate brought additional clinically relevant effects when compared to other solutions. This possibility was illustrated in Rösing et al. [9], where the addition of zinc lactate was responsible for better results in the whole mouth and especially in the interproximal area. Zinc salts have additional benefits in oral health, including the effect on halitosis [50].

Overall, CPC demonstrated higher plaque and gingival inflammation reductions when compared to the placebo group. This outcome was supported by the plaque and gingival meta-analysis. The findings bring a clear vision of how much a CPC-based mouthrinse with or without added components, as an adjunct to toothbrushing can bring better clinical results. Furthermore, the possibility of compensating for the limitations of the use of dental floss should be considered. The clinical results presented in the included studies about CPC are similar to the results found in other reviews [8, 37, 51], in which CPC-containing mouthrinses in addition to toothbrushing seem to be effective in controlling dental plaque and

gingivitis in intermediate or long-term trials. However, none of the referred reviews had directly compared the effect in the interproximal area.

The authors are aware of the strengths and intrinsic limitations of this review. Studies in which interdental hygiene devices were allowed were also included, although only one met all the inclusion criteria. Adjunct use of floss did not contribute to a further reduction in interdental plaque/gingival inflammation control if compared to toothbrushing alone, as has been shown in some published clinical trials in the literature [47, 52]. Therefore, the inclusion of studies in which interdental devices were allowed [37] adds more information when comparing different protocols of adjunct use of mechanical and chemical oral hygiene. Moreover, it is important to emphasize that the reason for the lack of effect of dental floss in patients that report its usage might be due to either the manual complexity of the technique or the usual lack of patient compliance in regards to flossing. Additionally, the daily use of chemical methods to control biofilm can lead to known side effects, as cited in the present study, which should be considered in their indication.

Another limitation of the present study is the high heterogeneity detected in the within-subgroups analyses for both anti-plaque and anti-gingivitis. Variables other than CPC concentrations may explain these findings. For example, mean plaque at baseline ranged from 2.70 [31] to 4.03 [32] in the included studies. Meanwhile, for the gingival index, one study detected a mean of 1.73 [9], and another had a mean of 2.21 [34], which may explain the high heterogeneity. Unfortunately, due to the low number of included studies, a meta-regression could not be performed to further address this heterogeneity.

Patients have shown willingness to use mouthrinses in oral hygiene habits. In evidence-based dentistry, dental professionals must make a well-considered decision about the advice given to each patient. The clinical expertise, patient values, available instruments, and experimental evidence must be taken into consideration [53] to make a well-informed decision. A systematic review carries weight because of its level of evidence. It is a systematic assessment of the available literature for the effects of healthcare interventions, an assessment intended to help the professional in this process.

It is important to note that no oral hygiene instruction was provided in the included studies, which probably reflects the patients' daily habit of oral hygiene. Studies have reported that supervised oral health promotes better results in school children [48]. These results show that when individuals participate in an oral hygiene program, better clinical results are seen on all tooth faces.

The 2011 Cochrane systematic review concluded that there is still weak evidence that supports the prevention of caries and periodontal diseases when flossing is used in adjunct to toothbrushing [3]. The present study points to a different perspective to compensate for flossing in adjunct to toothbrushing to prevent caries and periodontal diseases.

Conclusion

The use of CPC mouthrinses can reduce interproximal plaque in both non-users and users of interproximal cleaning devices. This effect is observed independently of the periodontal condition, whether limited to plaque accumulation with gingival inflammation or in individuals with periodontitis. Consequently, lower levels of interproximal gingival inflammation are detected in individuals using CPC mouthrinses.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Ethical approval does not apply to systematic reviews.

Informed consent Informed consent does not apply to systematic review.

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ARTIGO 5

ANTI-PLAQUE AND ANTI-GINGIVITIS EFFICACY OF CETYLPYRIDINIUM CHLORIDE WITH ZINC LACTATE IN COMPARISON TO ESSENTIAL OILS MOUTHWASHES: RANDOMIZED CLINICAL TRIAL

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ANTI-PLAQUE AND ANTI-GINGIVITIS EFFICACY OF CETYLPYRIDINIUM CHLORIDE WITH ZINC LACTATE IN COMPARISON TO ESSENTIAL OILS MOUTHWASHES: RANDOMIZED CLINICAL TRIAL

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ABSTRACT

Objective: This study aimed to evaluate the clinical anti-plaque and anti-gingivitis effects of three oral hygiene regimens: 1) toothbrushing with standard fluoride toothpaste, manual toothbrush and a mouthwash containing cetylpyridinium chloride, zinc lactate and fluoride in an alcohol-free base (CPC+Zn+F); 2) toothbrushing with standard fluoride toothpaste, manual toothbrush and a mouthwash containing essential oils in an alcohol-free base (EO); and 3) toothbrushing with manual toothbrush and standard fluoride toothpaste (CONTROL). **Material and Methods:** Individuals (n=120) were randomly assigned to study groups and followed the assigned regimens twice daily for six weeks. Volunteers were examined by a calibrated examiner for the Quigley-Hein Plaque Index (Turesky modification) and Löe-Silness Gingival Index (GI) at baseline, weeks four and six. Statistical analyses were performed separately for plaque and gingival indices, by ANOVA, paired t-test and ANCOVA (α=0.05). **Results:** At week four, CPC+Zn+F group presented additional reductions in dental plaque of 21.4% ($p<0.001$) and 31.4% ($p<0.001$), as compared to EO and CONTROL, respectively. After six weeks, these values were 26.7% ($p<0.001$) and 44.8% ($p<0.001$). For GI, additional reduction in CPC+Zn+F, as compared to EO, were 10.6% ($p<0.001$) and 13.7% ($p<0.001$), at four and six weeks, respectively. In comparison to CONTROL, these reductions were of 13.6% ($p<0.001$) and 17.8% ($p<0.001$). **Conclusion:** The regimen including a mouthwash containing CPC+Zn+F presented higher anti-plaque and anti-gingivitis effects as compared to EO and CONTROL regimens. **Practical Implications:** A mouthwash containing cetylpyridinium chloride, zinc lactate and fluoride is an effective protocol for the control of dental plaque and gingivitis.

KEY WORDS: Mouthwashes; Cetylpyridinium; Essential Oils; Gingivitis; Dental Plaque.

INTRODUCTION

The importance of the removal of supragingival plaque has been well-established in the literature regarding oral health care. Rates of caries, periodontal disease and tooth loss have been shown to be lower in populations with good standards of plaque control.(4, 26) The most widely-used method of mechanically disrupting supragingival biofilm is with toothbrushes and, overtime, this practice results in improved oral health.[3] In addition to mechanical toothbrushing, mouthwashes have been used with varied formulations to chemically control biofilm in an effort to compensate for the limitations associated with toothbrushing.[4] Literature reports that patients with motor or cognitive problems, those with a lack of motivation, patients in postsurgical phases, and those with orthodontic devices may benefit from the use of mouthwashes containing antimicrobials.[5, 6]

Studies have shown potential antibacterial effects, with limited adverse events, of mouthwashes containing cetylpyridinium chloride (CPC), which is one of the types most commonly used.[7] For example, additional oral health benefit result when CPC is added to Sodium Fluoride rinsing solutions in comparison with mouthwashes containing only NaF.[8, 9] A systematic review of the literature has demonstrated a small but significant anti-plaque and anti-gingivitis effect of CPC as an adjuvant to routine mechanical oral health hygiene.[9]

In a recent published systematic review that evaluated the efficacy of adjunct use of chemical agents and mechanical plaque control in systemically healthy individuals, it was demonstrated that, after 6-months, anti-septic agents were clinically efficacious in terms of reducing gingival index.[10] No clear evidence is detected in the literature regarding who would benefit the most from these agents. However, when analyzing the results from the published studies, in patients with higher accumulation of dental plaque, the use of these agents may provide benefits in a long term (>6 months) regarding dental plaque and gingivitis reduction.[10] Despite of that, side effects may be expected, mostly dental staining.[11]

The addition of zinc lactate in the composition of the rinse was also seen to be safe in an oral environment, with beneficial potential for various oral conditions (e.g. reduction of plaque and gingival inflammation) and a decrease in oral malodor.[7] Additionally, the anti-gingivitis effect of the combination of CPC and zinc lactate was shown to be significantly greater when the mouthwash was used as an adjuvant with a toothbrush in a six-week clinical trial, in comparison

with a formulation without the zinc lactate. In addition to the abovementioned benefits of Zinc, one *in vitro* study showed that this substance has antimicrobial properties when tested against bacteria associated with halitosis.[12] The benefits of zinc was also demonstrated by a randomized clinical trial (RCT), which showed that a zinc-based mouthrinse may have similar clinical benefits, in terms of halitosis reduction, when compared to a chlorhexidine mouthrinse.[13] This formulation was also shown to be more effective at reaching interproximal areas than comparison groups.[14] Another study observed that the effect of CPC is comparable with the same seen in chlorhexidine as a pre-procedural rinse.[15]

Essential oils (EO) are also used in combination with mechanical plaque removal. A systematic review has shown their potential to remove significantly more plaque and reduce gingival inflammation compared to both a placebo and a CPC formulation without zinc lactate.[16] Studies assessing the efficacy of mouthwashes containing CPC and zinc lactate simultaneously compared with mouthwashes containing EO have not been published. The concept of the present study relies on a possible synergistic effect of zinc lactate and CPC. As such comparison between this combination and EO has not yet been undertaken, the aim of this study was to evaluate the clinical efficacy of three oral hygiene multi-component regimens in controlling established dental plaque and gingivitis over a six-week period of use: (1) a commercial-available regular fluoride toothpaste, an adult soft-bristle manual toothbrush and a mouthwash containing 0.075% CPC and 0.28% zinc lactate and fluoride in an alcohol-free base, (2) a commercially-available regular fluoride toothpaste, an adult soft-bristle manual toothbrush and a mouthwash containing EO in an alcohol-free base, and (3) a commercially-available regular fluoride toothpaste and a soft-bristle manual toothbrush.

MATERIAL AND METHODS

Study Design

This study was designed as a phase III randomized, single-center, three-cell, examiner-blind and parallel-group clinical study. This study followed the Consolidated Standards of Reporting Trials (CONSORT) statement.

Ethical Considerations

The protocol was approved by the Institutional Review Board of the Federal University of Rio Grande do Sul, Brazil, and all the volunteers signed an informed consent form.

Sample Size Estimate

The sample size of 120 (40 per group including attrition) was determined based on the standard deviation for the response measures of 0.58, a significance level of α=0.05, and an 80% level of power. This study was powered to detect a mean difference between groups of 15% in dental plaque. The sample size calculation utilized historical data from a previous pilot study, and 32 individuals were considered necessary.

Sample Population

The sample consisted of 121 male and female individuals, aged 21-70 years, who were recruited by convenience, and 120 were randomized into one of the three treatment groups (Figure 1). The study was conducted from August to September of 2018, at the School of Dentistry of the Federal University of Rio Grande do Sul. Inclusion criteria were comprised of good general health, availability for the six-week duration of the study, an initial mean Plaque Index score of at least 1.5 as determined by Turesky modification of the Quigley-Hein Plaque Index,[17 18] a mean Gingival Index score of at least 1.0 as determined by the Löe-Silness Gingival Index,[19] and a minimum of 20 natural teeth, excluding third molars.

Individuals were not included in the study if they presented with any of the following conditions: orthodontic bands; partial removable dentures; tumors or significant pathology in the soft or hard tissues of the oral cavity; moderate or advanced periodontal disease; five or more carious lesions requiring immediate care; antibiotics use at any time one month prior to entry into the study; pregnant or breastfeeding women; individuals who received a dental prophylaxis in the

past two weeks prior to the baseline examination; a history of allergies to oral or personal care consumer products or their ingredients; any prescription medicines that might interfere with the study outcome; any medical condition which requires not eating, drinking or chewing gum within four hours of their scheduled visit; or history of alcohol or drug abuse.

Experimental Procedures

Qualifying individuals attended the clinical study site after refraining from any oral hygiene procedures for twelve hours, and from eating, drinking or smoking for four hours. The baseline examination consisted of soft and hard tissue evaluation of the oral cavity and perioral region, followed by plaque and gingivitis assessments.

Supragingival plaque examination was then performed with plaque disclosure rinsing with 10ml – 0.04% basic fuchsine solution (Replasul; Iodontosul, Porto Alegre – RS, Brazil). The supragingival plaque examination was performed with the modified Quigley and Hein Index.[17, 18] Plaque was assessed in six sites per tooth and scored from 0 (no plaque) to 5 (plaque covering 2/3 or more of the side of the crown of the tooth). Individual scores were calculated by summing all scores for all sites and dividing by the total number of sites scored.

Gingival inflammation was scored at six sites per tooth according to the criteria of the Gingival Index (GI) system.[19] Individual scores were calculated by summing all scores for all sites and dividing by the total number of sites scored. Furthermore, gingival severity was calculated by the percentage of sites scored two or three, which represents sites that bleed on marginal probing.[20]

Subjects were randomized into one of three 40-individuals groups. The randomization list was computer-generated. Allocation concealment was the responsibility of an external researcher, and products were covered with white over-wrapping paper in order to conceal product identity. The material was numbered sequentially and kept inside opaque plastic bags.

The experimental group regimens were:

1. A test group given mouthwash containing 0.075% CPC and 0.28% Zinc lactate with 0.05% sodium fluoride in an alcohol-free base (Colgate-Palmolive Co., New Jersey – USA)

together with an adult soft-bristle manual toothbrush and standard fluoride toothpaste (CPC+Zn+F group).

2. A positive control group containing EO in an alcohol-free base (Johnson & Johnson Co., New Jersey – USA) together with an adult soft-bristle manual toothbrush and standard fluoride toothpaste (EO group).
3. A negative control group containing an adult soft-bristle manual toothbrush and standard fluoride toothpaste (CONTROL group).

Individuals were instructed to brush their teeth twice daily with the standard commercially-available sodium fluoride toothpaste and the adult soft bristle manual toothbrush for two minutes (morning and evening). In addition, the CPC+Zn+F and EO groups were instructed to rinse for 30 seconds with 20ml of their assigned mouthwash for a period of six weeks. The subjects were instructed to refrain from using any other type of oral hygiene product or method, such as mouthwash or interproximal cleaning devices (dental floss or interdental brushes), for the duration of the study period. These instructions were given to participants after the baseline examination by a researcher uninvolved in the clinical examination. The first rinse was performed at this time, at the clinic and under supervision.

At weeks four and six individuals were instructed to return to the clinical study site with the products, and any adverse events were recorded. When an adverse event was reported, an oral examination was performed in order to provide proper treatment or explanation to the participant. The allocation concealment was kept unbroken during the entire study. Additionally, participants were examined for dental plaque and degree of gingival inflammation, using the same procedures employed at baseline. These evaluations were performed by the same trained and calibrated examiner (CKR), who remained blind to product assignment during the course of the study. Intra-examiner reproducibility was assessed prior to the study for both plaque and gingival inflammation, with appropriate levels of reliability (Kappa>.7).

Statistical Analysis

Statistical analyses were performed separately for dental plaque and gingivitis assessments. Whole-mouth mean values and interproximal mean values were also calculated and separately analyzed. Comparisons of the treatment groups with respect to baseline GI scores and Plaque Index

scores were performed using an analysis of variance (ANOVA) in a per-protocol approach. Within-treatment comparisons of the baseline versus follow-up gingival and Plaque Index scores were performed using paired t-tests. Comparisons of the treatment groups with respect to baseline-adjusted gingival and plaque scores at the follow-up examinations were performed using analyses of covariance (ANCOVA's). All statistical tests of hypotheses were two-sided, and employed a level of significance of $p<0.05$.

RESULTS

Of the initial 120 randomized individuals, 110 subjects completed the six-week clinical study. The flowchart of the study, with reasons for exclusion, is shown in Figure 1. Table 1 contains a summary of gender, age and baseline characteristics of the study population. Throughout the study, eight adverse effects on the oral hard or soft tissues of the participants were observed by the examiner or reported by the study subjects. No adverse events were reported in the CPC+Zn+F group, three were reported in the EO group and five were reported in the CONTROL group. The reported adverse events comprised dentin hypersensitivity (one in EO and one in CONTROL group), gingival bleeding (one in EO and one in CONTROL group), palate and tongue burning (one in EO group), headache (two in CONTROL group) and swelling and gingival bleeding (one in CONTROL group).

Clinical Results

Clinical results will be given separately for plaque and gingivitis. Figure 2 displays the mean Plaque Index (full-mouth) at different study periods. At baseline, no statistically significant difference among groups was observed for Plaque Index ($p=0.115$). CPC+Zn+F, EO and CONTROL groups presented a mean (±standard deviation) Plaque Index of 4.15±0.44, 4.32±0.41 and 4.08±0.63, respectively. At weeks four and six, a higher reduction in plaque was observed for the CPC+Zn+F group, followed by EO and CONTROL groups. At week four, the additional reductions in dental plaque for the CPC+Zn+F group as compared to EO was of 21.4% ($p<0.001$), and were 31.4% ($p<0.001$) as compared to CONTROL. After six weeks, these values were 26.7% ($p<0.001$) and 44.8% ($p<0.001$), respectively. When the mean interproximal Plaque Index was analyzed, the same results were obtained. The CPC+Zn+F group reached the highest reduction in interproximal plaque, followed by the EO and CONTROL groups. Statistically significant differences were observed among all groups (Figure 3).

Figure 4 shows mean full-mouth GI scores for experimental groups at different study periods. The mean GI did not display any statistically significant difference at baseline; CPC+Zn+F, EO and CONTROL groups presented a mean (±standard deviation) GI of 1.69±0.15, 1.68±0.15 and 1.67±0.18, respectively. These values were reduced in all groups throughout the

study, and both at weeks four and six higher reductions were observed for the CPC+Zn+F group as compared to EO and CONTROL groups. EO performed better in terms of GI reduction as compared to CONTROL. For GI, the additional reduction in the CPC+Zn+F as compared to EO was of 10.6% ($p<0.001$), and to CONTROL of 13.6% at week four. At week six, these values were of 13.7% ($p<0.001$) and 17.8% ($p<0.001$), respectively.

When the GI was dichotomized and bleeding sites were analyzed, baseline values of 69%, 68% and 67% were obtained for CPC+Zn+F, EO and CONTROL groups, respectively. The CPC+Zn+F group had these values reduced to 28% and 20% at weeks four and six, respectively. EO group reduced bleeding sites to 43% and 39% and CONTROL group reduced to 47% and 46% at weeks four and six, respectively. The analysis of these results revealed the same result as the mean GI, with better performance for the CPC+Zn+F group. Results related to GI for interproximal surfaces are displayed in Figure 5. No statistically significant difference was observed at baseline. At weeks four and six, the highest interproximal GI reduction was achieved with the use of the CPC+Zn+F regimen, as compared to EO and CONTROL. EO displayed a higher reduction in interproximal Gingival Index as compared to CONTROL.

DISCUSSION

This randomized and examiner-blind clinical study provided an investigative comparison of the efficacy, with respect to dental plaque and gingivitis reduction over a six-week period, of an oral hygiene multi-component regimen encompassing a commercially-available regular fluoride toothpaste, an adult soft bristle manual toothbrush and a mouthwash containing 0.075% CPC and 0.28% zinc lactate with fluoride in an alcohol-free base, as compared to a positive control (similar regimen, with a mouthwash containing EO in an alcohol-free base) and a negative control (only brushing with commercially-available regular fluoride toothpaste and a soft bristle manual toothbrush). The results generally demonstrate that the CPC+Zn+F group displayed higher reductions in plaque and gingivitis (that is, a higher anti-plaque and anti-gingivitis effect) over the study period, as compared to both groups.

The research design was a phase III randomized controlled clinical trial. RCT studies are considered one of the best ways of demonstrating the efficacy of oral hygiene regimens, and are used also as primary data for systematic reviews, the highest level of evidence for clinical decision making.[4] It is important that the present study made comparisons to EO and CONTROL groups, which provides perspective on the real efficacy of the regimen, as compared to one proven efficacious agent or to the absence of a source of benefit. In addition, a blind examiner, allocation concealment, and randomization were taken into consideration, further proving the validity of the results. Regarding compliance, all individuals were asked about their product usage and reported they had used the mouthwashes. They returned with the unused liquids, which were discarded according to legal regulations.

Oral hygiene regimens traditionally include solely the use of toothbrushing with dentifrice and, in some cases, flossing. The efficacy of flossing has been recently questioned, especially since the available evidence does not include studies in which flossing performed effectively in, for example, long-term supervised studies.[21] It is also noteworthy that the consumer consumption of dental floss, despite an increase over time, is still low.[22] In an attempt to compensate for the lack of use (or lack of correct use) of dental floss, the use of mouthwashes has been studied.[14] Also, different toothbrush designs have proven to increase the efficacy of toothbrushing.[23]

CPC has been demonstrated to be efficacious since the classical study by Gjermo et al.[7] However, its clinical efficacy was limited due to lack of substantivity, which is the ability of an

antimicrobial agent to retain its effect in the mouth for an extended period. Meta-analyses of clinical studies have confirmed a high heterogeneity in the benefits of the use of CPC.[4, 9] Recently, the addition of zinc lactate has been proposed to increase the capacity of CPC mouthwashes in terms of both plaque and gingivitis reduction. A RCT demonstrated that this association substantially increased CPC's anti-plaque and anti-gingivitis effects when compared to a mouthrinse with CPC only.[14] In the studied formulation, the presence of fluoride probably has no effect on plaque and gingivitis; however, it is interesting in terms of fluoride availability for caries prevention.

The EO group included in the present study was given a solution of essential oils that has been demonstrated to be effective against plaque and gingivitis.[16] An alcohol-free solution of EO was used. The presence of alcohol has been questioned in the literature, although no proven adverse effects, such as increased risk for oral cancer, have been reported. However, the use of alcohol is being limited in clinical settings due to its strong taste and associated burning sensation. Studies comparing chlorhexidine solutions with or without alcohol have demonstrated that patients prefer the taste of non-alcoholic solutions.[24, 25] In a comparative study with other products, the taste of CPC was appreciated better.[26] In order to increase patient compliance with the use of any rinsing solution, especially on a daily basis, taste is of utmost importance.

It should be noted that the response rate of the present study is high, with more than 85% of individuals completing the six-week trial. Taking into consideration that the required number of individuals was achieved in all groups, the internal validity of the study is warranted, with more than 80% of power. Adverse events occurred both in the EO and in the CONTROL groups, but not in the CPC+Zn+F group. All adverse events were of low magnitude and promptly resolved. The loss of individuals for follow-up was due to reasons not related to the protocol. These findings must be compared to the high occurrence of adverse side effects when chlorhexidine, a gold standard agent for plaque control, is used.[27]

The novel element of this study is the direct comparison of an oral hygiene regimen with mechanical toothbrushing together with a CPC+Zn+F mouthwash, with the same regimen including an alcohol-free EO solution. This, to the best of the authors' knowledge, has not been previously performed. The results comprise the study of reductions in plaque and gingivitis in two

experiment periods, at four and six weeks. Such periods are frequently used in oral hygiene regimen studies.[14, 28]

In relation to supragingival biofilm accumulation, it is noteworthy that all three regimens led to a statistically significant decrease in dental plaque at weeks four and six as compared to baseline. Baseline plaque values did not differ among groups. This situation allows for better comparability of the encountered effects. The observed decrease may be related to both the Hawthorne effect[29] (e.g. as observed in the CONTROL group) and the anti-plaque potential of the included substances. It should be emphasized that the CPC+Zn+F group exhibited the best performance in relation to plaque. The literature has previously demonstrated this effect of CPC, although systematic reviews have led to the conclusion that this effect would be of low magnitude.[4, 9] However, the presence of zinc lactate likely increased the anti-plaque capacity of CPC, as demonstrated in a comparison with a mouthwash without the zinc salt.[14] In this respect, the demonstrated effect substantiates the claim that the combination of CPC+Zn+F regimen was superior to EO in an alcohol-free base as well as the control regimen.

The analysis of gingival inflammatory signs is also of utmost importance, since it is even more a reflection of oral hygiene standards than plaque removal. The mean GI values observed in the present study demonstrate that, similarly to plaque analysis, the three regimens were able to decrease gingival inflammation, with the CPC+Zn+F group showing the best performance. Mean GI frequently correlates in research studies with mean Plaque Index, which has been evident since the classical study "Experimental Gingivitis in Men" by Löe et al.[30] In the present study, the mean GI was further reduced in the CPC+Zn+F group, with an additional 10% to 14% as compared to the EO group, and 13% to 17% as compared to CONTROL. This reduction is of clinical interest. Therefore, the observed low-magnitude results in the systematic reviews of the use of CPC have been demonstrated, both in the present study and prior research, to enhance the quality of the performance.[4, 14]

Also of great clinical importance is the analysis of the effect of the three regimens on the presence of gingival bleeding. The GI for this study was dichotomized into bleeding and non-bleeding sites, as proposed by Ainamo and Bay.[31] This dichotomization allows for a more clinically relevant interpretation of the results. The present study also demonstrated a better performance within the CPC+Zn+F group, indicating the superiority of such a regimen in

decreasing gingival bleeding, a classic sign of gingival inflammation that has been a target of the dental profession for decades.

The participants of the present study refrained from flossing during the study period. Even without performing mechanical interdental plaque removal, both plaque and gingival inflammatory signs were clinically reduced at both experimental periods. This effect is important, especially considering the lack of evidence supporting the long-term benefits of flossing.[21] The additional use of mouthrinses demonstrated an effect on interdental surfaces in both the CPC+Zn+F and EO groups. However, this effect was higher in the CPC+Zn+F group. In this respect, both the Hawthorne effect and the chemical effect of the rinsing solutions might be responsible for the encountered results. The superiority of the CPC+Zn+F group was demonstrated, and the comparison with the CONTROL group mitigates the potential influence of the Hawthorne effect. Taking into consideration the need for interproximal plaque control and the higher prevalence of disease in these sites,[22] the present study has demonstrated a clinically relevant finding.

The limitations of the present study are related to the fact that convenience samples in RCT have limited external validity, and that the duration of the study was limited to six weeks. However, the comparisons among the three groups were performed under the same environmental and experimental conditions, which allows for clear conclusions. In addition, the clinical results demonstrated by the present study have an especially interesting characteristic, which is the consistency of the findings in both evaluation periods (after four and after six weeks). Independently of the parameter, the CPC+Zn+F group consistently demonstrated the best performance, with statistically significant differences from the EO group. The EO group showed the second-best performance, and in turn presented statistically significant differences from the CONTROL group. This clearly demonstrates that CPC+Zn+F has better clinical performance than either EO or CONTROL for both supragingival plaque and gingival inflammatory signs. Such a finding, encountered in an RCT and performed with contemporary research paradigm tools, leads to the clinical indication of the regimen in a decision-making process. It is concluded that the regimen including a mouthwash containing CPC+Zn+F presents significantly higher anti-plaque and anti-gingivitis effects as compared to EO and CONTROL, both in whole-mouth as well as in interproximal surfaces.

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Table 1. Summary of age and gender for subjects who completed the 6-week clinical study.

	Number of Individuals			Age	
Treatment	Male	Female	Total	Mean (S.D.)	Range
CPC+Zn+F	16	21	37	33.54 (9.18)	21 - 60
EO	20	18	38	32.87 (11.72)	22 - 66
CONTROL	07	28	35	32.23 (9.98)	22 - 56

FIGURE LEGENDS

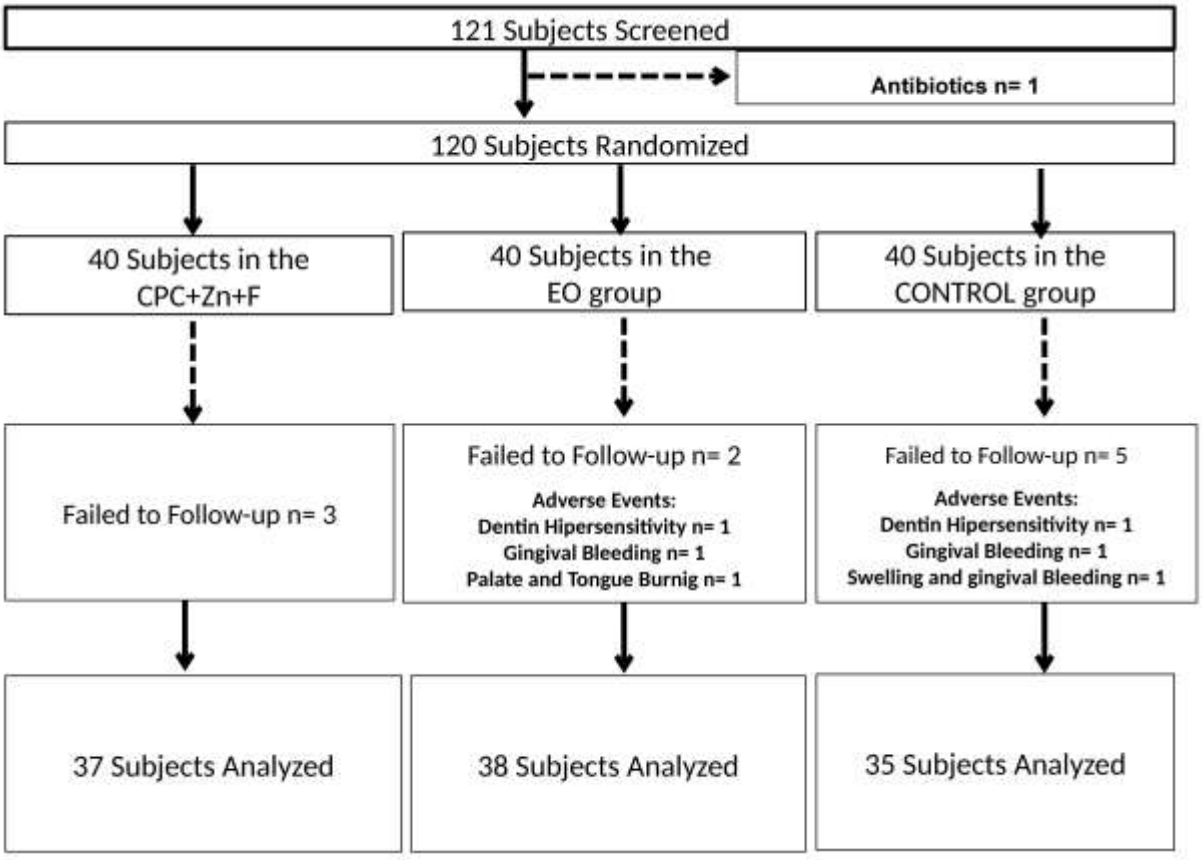
Figure 1. Study Flowchart.

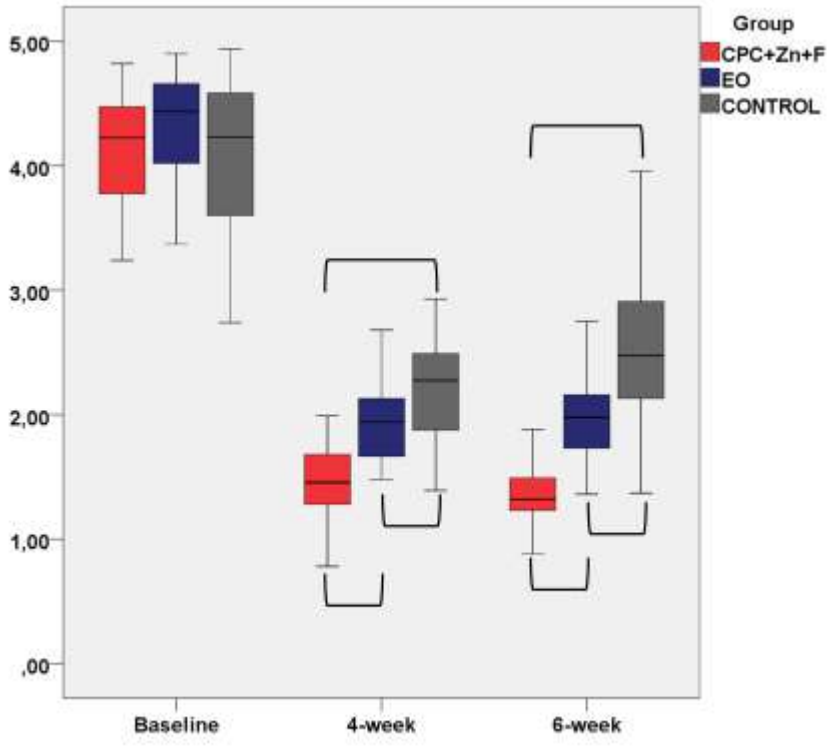
Figure 2. Plaque Index at Baseline, Week 4 and Week 6 Examinations. CPC+Zn+F: cetylpyridinium chloride, zinc lactate and fluoride; EO: essential oil. Brackets represent statistically significant difference for comparisons between groups. All groups demonstrated statistically significant improvements within group (baseline vs. Week 4 and baseline vs. Week 6).

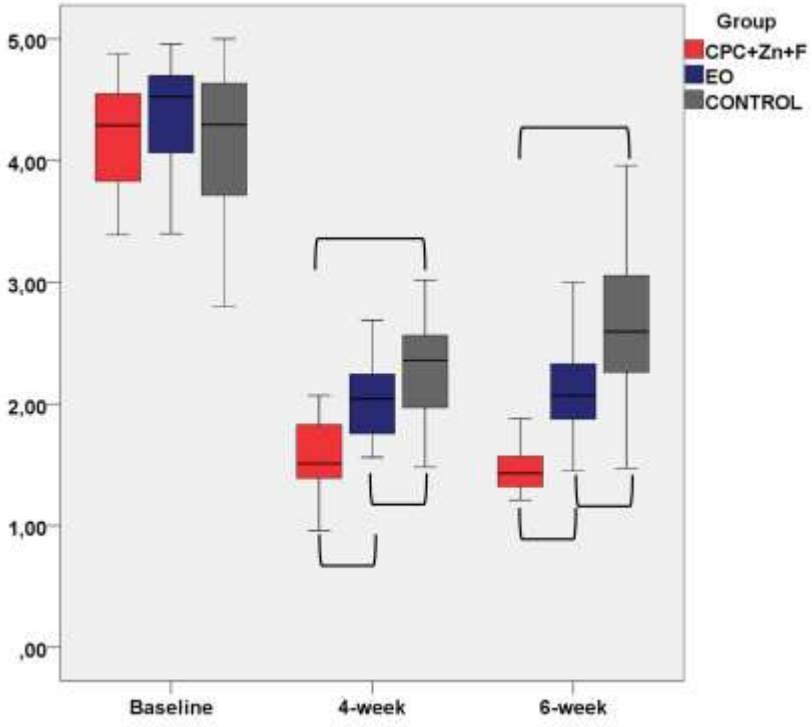
Figure 3. Interproximal Plaque Indexat Baseline, Week 4 and Week 6 Examinations. CPC+Zn+F: cetylpyridinium chloride, zinc lactate and fluoride; EO: essential oil. Brackets represent statistically significant difference for comparisons between groups. All groups demonstrated statistically significant improvements within group (baseline vs. Week 4 and baseline vs. Week 6).

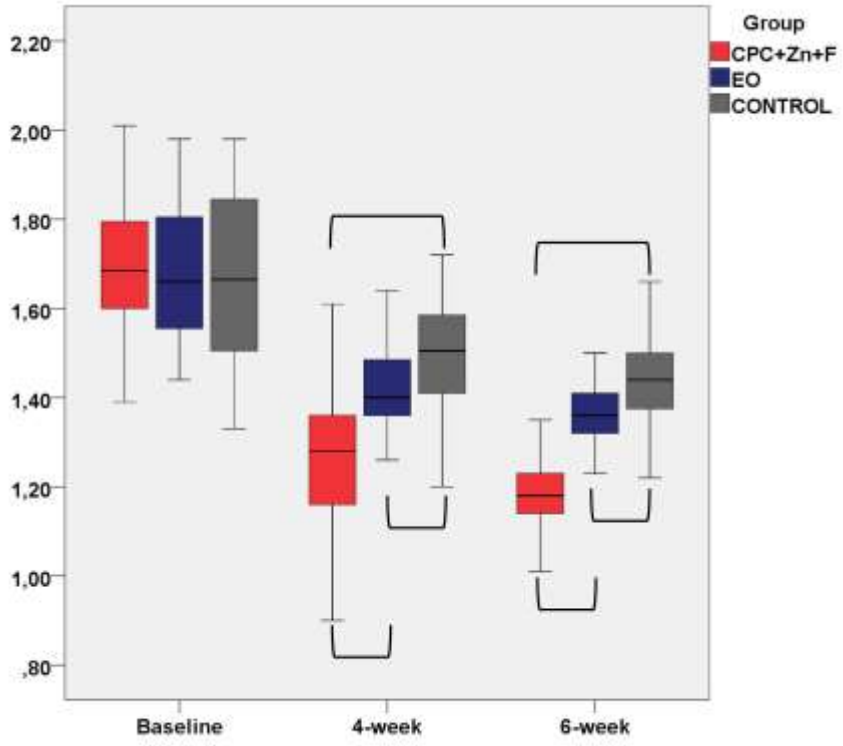
Figure 4. Gingival Index at Baseline, Week 4 and Week 6 Examinations. CPC+Zn+F: cetylpyridinium chloride, zinc lactate and fluoride; EO: essential oil. Brackets represent statistically significant difference for comparisons between groups. All groups demonstrated statistically significant improvements within group (baseline vs. Week 4 and baseline vs. Week 6).

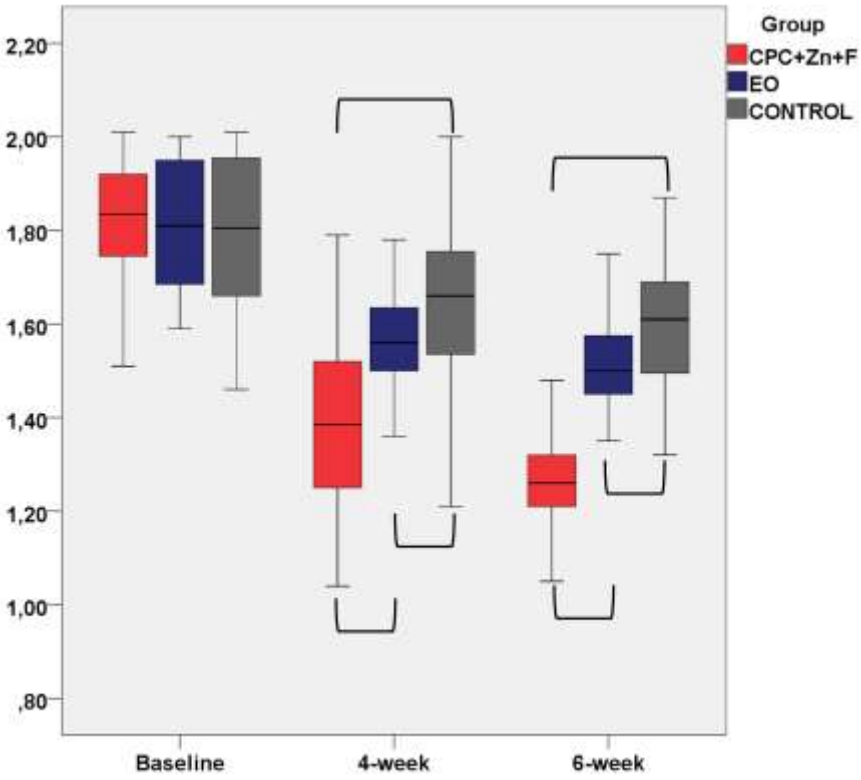
Figure 5. Interproximal Gingival Index at Baseline, 4 Week and 6 Week Examinations. CPC+Zn+F: cetylpyridinium chloride, zinc lactate and fluoride; EO: essential oil. Brackets represent statistically significant difference for comparisons between groups. All groups demonstrated statistically significant improvements within group (baseline vs. Week 4 and baseline vs. Week 6).




Group
CPC+Zn+F
EO
CONTROL
5,00
4,00
3,00
2,00
1,00
,00
Baseline
4-week
6-week


Group
CPC+Zn+F
EO
CONTROL
5,00
4,00
3,00
2,00
1,00
,00
Baseline
4-week
6-week


Group
CPC+Zn+F
EO
CONTROL
2,20
2,00
1,80
1,60
1,40
1,20
1,00
,80
Baseline
4-week
6-week


Group
CPC+Zn+F
EO
CONTROL
2,20
2,00
1,80
1,60
1,40
1,20
1,00
,80
Baseline
4-week
6-week

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CONSIDERAÇÃO FINAIS

O objetivo da presente tese foi de avaliar a eficácia de outros regimes de higiene bucal compensatórios ao fio dental na capacidade de remoção do biofilme interproximal. O primeiro trabalho encontrado nesta tese, serviu de base em que foi possível avaliar a literatura com relação a polemica do fio dental que criou um certo pânico na comunidade odontológica durante os anos de 2015 e 2016, tendo sido colocado nesta mesma revisão a periculosidade de se remover o fio dental como método de manutenção da saúde bucal por este apresentar alguma ineficácia. Tendo sido demonstrado, a partir da revisão da literatura, a clara dificuldade existente na população de realizar o correto uso do fio dental.

Os quatro seguintes estudos serviram de suporte como artigos originais, nos quais se viu necessário buscar regimes compensatórios ao fio dental, já que vários estudos elucidaram a dificuldade apresentada pelos pacientes em realizar higiene interproximal com o auxílio do fio dental, A ideia subjacente é buscar métodos e dispositivos com foco não interproximal que poderiam de alguma forma suprir a função não alcançada pelos pacientes com o uso regular do fio dental.

Os estudos que abordaram o controle do biofilme com uso das escovas mostram que as escovas de ponta cônica apresentam melhor eficácia na região interproximal assim como já foi apresentado em uma outra revisão sistemática (10). Apesar de tal revisão não apresentar dados clinicamente relevantes nos índices gengivais, apresenta claramente dados de que as escovas de ponta cônica apresentam uma capacidade de remover biofilme interproximal maior que as escovas com certas de ponta arredondada.

Os estudos que abordaram o controle químico do biofilme como adjuvante a higiene mecânica a partir do uso de colutórios apresentam resultados semelhantes a outros estudos, como é o caso da revisão publicada em 2016 (27) em que os óleos essenciais se mostraram eficazes mesmo quando comparados a indivíduos que relatam fazer uso do fio dental. Importante mencionar que os óleos essências apresentaram, em tal revisão, uma eficácia maior que o CPC isolado. E no ensaio clinico aqui apresentado, ficou claro que o CPC quando associado ao lactato de zinco, apresenta melhores resultados de uma forma geral, mas, especificamente nos índices interproximais sendo o que torna um auxílio relevante apresentando também baixos eventos adversos ainda que, usado por longos períodos.

Ainda que os estudos apresentados nesta tese mostrem resultados favoráveis ao uso dos métodos compensatórios, importante que sejam realizados daqui para frente, estudos que tenham maior enfoque em avaliar outros métodos e dispositivos compensatórios, procurando avaliar a eficácia dos mesmos nos índices de placa e inflamação gengival, e mais do que isso, que a longo prazo, esses resultados se mostrem clinicamente relevantes.

Concluindo, fica claro que, é possível manter níveis de saúde mesmo não incluindo o fio dental na rotina de higiene do indivíduo. Talvez, mais do que se indiciar o uso do fio dental, seja importante observar a real necessidade em cada indivíduo.

Após inserção num programa de manutenção periódica em que o indivíduo se apresente com níveis compatíveis com saúde mesmo sem relatar uso de dispositivos interproximais, a indicação destes dispositivos pode ser dispensada e assim, direcionado à pacientes que após treinamento pelo dentista possa fazer uso dos dispositivos de forma correta se beneficiando na sua rotina de higiene.

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ANEXOS

ANEXO 1

The Journal of Evidence-Based Dental Practice

Anti-plaque and anti-gingivitis efficacy of different bristle stiffness and end-shape on interproximal surfaces: a systematic review with meta-analysis

--Manuscript Draft--

Manuscript Number:	
Article Type:	Review Article
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Abstract:	Objective This systematic review aimed to evaluate the efficacy of interproximal plaque scores and gingival inflammation reduction of different toothbrush bristle stiffness and end-shape. Methods Randomized clinical trials evaluating the effect of different toothbrushes on interproximal plaque/gingivitis reduction, with a minimum follow-up of 1 week. MEDLINE-PubMed, Scopus and Embase were searched. Soft tapered-tip bristle toothbrushes were compared to soft end-rounded, medium (any end-shape), or hard (any end-shape) bristle toothbrushes. Two meta-analyses were performed for plaque and gingivitis reduction. For plaque index (PI) and gingival index (GI), a standard mean difference (SMD) and mean difference between baseline and 4 weeks were calculated. In all analyses, random effect models were used. Results Nine studies were included. All included studies demonstrated statistically significant improvement, in at least one parameter, in favor of the tapered-tip bristle toothbrush compared to the end-rounded bristle toothbrush. When analyzing toothbrush stiffness, medium and hard toothbrushes presented significantly higher improvement when compared to soft toothbrushes in all parameters. In the meta-analyses, groups that used soft tapered-tip bristle toothbrushes demonstrated significant greater reductions in PI (SMD -2.64; 95% CI: -4.26 – -1.01) and in GI (MD -0.14; 95% CI: -0.18 – -0.10) when compared to soft end-rounded bristle toothbrushes. Conclusion It is concluded that, when considering interproximal surfaces, better results may be expected for tapered-tip bristle toothbrushes when compared to end-rounded bristles toothbrush. Additionally, better results may be expected in medium or hard toothbrushes, regardless of the bristle end-shape, in non-interproximal cleaners.

ANEXO 2

From: Acta Odontológica Latinoamericana Aol <actaodontologicalat@gmail.com>
Sent: Friday, September 4, 2020 11:14 PM
To: Cassiano Rösing <ckrosing@hotmail.com>
Subject: T954

Estimado Cassiano:
Tengo el agrado de comunicarte que después de las revision realizada, tu trabajo (T954) ha sido aceptado para su publicación. Continuamos ahora con las revisiones técnica e idiomática y te mantendré informado
Saludos cordiales.
Mariel Itoiz

ANEXO 3

Ref.: Ms. No. CLOI-D-20-00871R2
THE EFFECT OF CETYLPYRIDINIUM CHLORIDE MOUTHRINSE AS ADJUNCT TO TOOTHBRUSHING COMPARED TO PLACEBO ON INTERPROXIMAL PLAQUE AND GINGIVAL INFLAMMATION - A SYSTEMATIC REVIEW WITH META-ANALYSES
Clinical Oral Investigations

Dear Dr. Muniz,

It is a pleasure to accept your manuscript entitled "THE EFFECT OF CETYLPYRIDINIUM CHLORIDE MOUTHRINSE AS ADJUNCT TO TOOTHBRUSHING COMPARED TO PLACEBO ON INTERPROXIMAL PLAQUE AND GINGIVAL INFLAMMATION - A SYSTEMATIC REVIEW WITH META-ANALYSES" in its current form for publication in the 'Clinical Oral Investigations'.

Thank you for your fine contribution. On behalf of the Editors of the 'Clinical Oral Investigations', we look forward to your continued contributions to the Journal.

With kind regards

Matthias Hannig, Univ.-Prof. Dr.
Editor-in-Chief
Clinical Oral Investigations

ANEXO 4

24-Sep-2020

Dear Dr. Rosing:

It is a pleasure to accept your revised manuscript entitled "Anti-plaque and anti-gingivitis efficacy of cetylpyridinium chloride with zinc lactate in comparison to essential oils mouthwashes: randomized clinical trial" in its current form for publication in The Journal of the American Dental Association.

The Journal reserves the right to edit all submitted manuscripts and illustrative material to fit JADA's style and format. Once your article has been accepted for publication, it will be typeset and copyedited by JADA's publisher, Elsevier. You will receive a proof from Elsevier to review for accuracy. This will be your final opportunity to make any changes to your article.