Evaluation of Handgrip Strength and Children's Quality of Life with Cancer Submitted to Chemotherapy with Vincristine

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Avaliação da Força de Preensão Palmar e Qualidade de Vida de Crianças com Câncer Submetidas à Quimioterapia com Vincristina

Evaluación de la Fuerza de Asimiento Palmar y Calidad de Vida de Niños con Cáncer Sometidos a la Quimioterapia con Vincristina

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Abstract

Introduction: With chemotherapy, patients may have several changes. Among them: polyneuropathy and change in the quality of life, both the children and the family. **Objective:** To evaluate the handgrip's power and the life quality in these children and teens with cancer undergoing to chemotherapy with vincristine. **Method:** This is a study in which patients responded the questionaries of anamnsis and *PedsQL™ 3.0 Cancer Module* in three different moments of the treatment. One of your responsible was invited to answer separately the same questionarie. The handgrip's power was measured by dynamometer, in the same moments. **Results:** The sample was composed for seven patients with average 7 (5-15 years); The most of them were girls, residing in Porto Alegre-RS, with a prevalent diagnostic of Acute Lymphoid Leukemia and who were hospitalized in the first week after the diagnosis of cancer. The handgrip's strength show significant reduction for all of the limbs (p=0,0018, right upper limb; p=0,0030, left upper limb). Although of not show significant results, in most areas of the questionnaire of quality of life ocurred decline in the answers, mainly in the parents awnsers. **Conclusion:** The chemotherapy with vincristine, decrease in the peripheral muscle strength in the patients with cancer, in the first 30 days. In relationship of quality of life, there was no significant diference, however we could perceive some trends. Therefore, it is clear the importance of the continuous monitoring of physiotherapy with a team prepared for these patients and their families.

Key words: Hand Strength; Quality of Life; Neoplasms; Child; Adolescent.

Resumo

Introdução: Com a quimioterapia, os pacientes podem apresentar diversas alterações; entre elas, polineuropatia e mudança na qualidade de vida, tanto à criança como aos familiares. **Objetivo:** Avaliar a força de preensão palmar e a qualidade de vida de crianças e adolescentes com câncer submetidos à quimioterapia com vincristina. **Método:** Trata-se de um estudo, no qual os pacientes responderam aos questionários de anamnese e *PedsQL™ 3.0 Câncer Module*, em três momentos diferentes do tratamento. Um dos seus responsáveis foi convidado a responder ao mesmo questionário. A força de preensão palmar foi aferida por meio de um dinamômetro, nos mesmos momentos. **Resultados:** A amostra foi composta por sete pacientes com mediana 7 (5-15 anos); com predomínio de meninas, residentes em Porto Alegre, RS, e diagnóstico prevalente de leucemia linfoide aguda, internados na primeira semana após o diagnóstico de câncer. A força de preensão palmar apresentou redução significativa para ambos os membros (p=0,018, membro superior direito; p=0,030, membro superior esquerdo). Apesar de não apresentar resultado significativo, na maioria dos domínios do questionário de qualidade de vida, ocorreu declínio nas respostas, principalmente nas dos pais. **Conclusão:** A quimioterapia com vincristina reduz a força muscular periférica em pacientes com câncer, nos 30 primeiros dias. Em relação à qualidade de vida, não foi apresentada diferença significativa. Porém, dentro dos domínios, pôde-se perceber algumas alterações. Sendo assim, fica clara a importância do acompanhamento contínuo da fisioterapia junto a uma equipe preparada para esses pacientes e seus familiares.

Palavras-chave: Força da Mão; Qualidade de Vida; Neoplasias; Criança; Adolescente.

Resumen

Introducción: Con la quimioterapia, los pacientes pueden presentar varias modificaciones. Entre ellas: polineuropatía y cambio en la calidad de vida, tanto del niño y de los familiares. **Objetivo**: Evaluar la fuerza de asimiento palmar y la calidad de vida de niños y adolescentes con cáncer sometidos a la quimioterapia con vincristina. **Método:** Se trata de un estudio, en el cual los pacientes respondieron a los cuestionarios de Anamnesis y PedsQLTM 3.0 Cáncer Module, en tres momentos diferentes del tratamiento. Uno de sus responsables fue invitado a responder el mismo cuestionario. La fuerza de asimiento palmar fue evaluada por medio de un dinamómetro, en los mismos momentos. **Resultados**: La muestra fue compuesta por siete pacientes con mediana 7 (5-15 años); teniendo más niñas, residentes en Porto Alegre-RS, con diagnóstico prevalente de leucemia linfoide aguda y que estaban internadas en la primera semana después del diagnóstico de cáncer. La fuerza de asimiento palmar presentó una reducción significativa para ambos miembros (p=0,018, miembro superior derecho, p=0,030, miembro superior izquierdo). A pesar de no presentar resultados significativos, en la mayoría de los dominios del cuestionario de calidad de vida ocurrió declinación en las respuestas, principalmente en la respuesta de los padres. **Conclusión**: La quimioterapia con vincristina reduce la fuerza muscular periférica en pacientes con cáncer, en los 30 primeros días. En cuanto a la calidad de vida, no se presentó una diferencia significativa. Sin embargo, dentro de los dominios se pode percibir algunos cambios. Por lo tanto, queda claro la importancia del acompañamiento continuo de la fisioterapia junto a un equipo preparado para esos pacientes y sus familiares.

Palabras clave: Fuerza de la Mano; Calidad de Vida; Neoplasias; Niño; Adolescente.

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INTRODUCTION

Childhood cancer consists of a group of various diseases that have in common the uncontrolled proliferation of abnormal cells and that can occur anywhere in the body. The most frequent tumors in childhood and adolescence are leukemias, tumors of the central nervous system, and lymphomas. Children and adolescents can also present neuroblastoma, Wilms tumor, retinoblastoma, germ cell tumor, osteosarcoma, and sarcoma[1].

In Brazil, cancer is already the leading cause of death from disease (8% of the total) among children and adolescents 1 to 19 years of age. According to the National Cancer Institute José Alencar Gomes da Silva (INCA)[1], the estimate for the year 2018 was 12,500 new cases of pediatric cancer.

The objectives of cancer treatment are: cure, prolonging life when cure is not possible, and palliation of symptoms. When treatment (chemotherapy, radiotherapy, and/or surgery) cannot result in cure, it should lead to improvement in well-being and quality of life[2].

Vincristine is a chemotherapeutic drug that is present in nearly all the protocols, and the main limitation is dose-dependent neurotoxicity, leading to episodes of polyneuropathy[3]. Corticoids are essential with chemotherapy for these patients, and they also have important side effects when used in high doses, frequently leading to major musculoskeletal complications such as muscle weakness, myopathies, osteoporosis, fractures, and osteonecrosis[4]. Patients end up presenting lower levels of physical aptitude and bone mineral density when compared to healthy children[5,6].

Treatment usually involves long hospitalization time, besides various therapeutic interventions, for which special attention for patients and their families is necessary and fundamentally important. The right to play and to physical, affective, social, and personal growth must be safeguarded by the team to constantly improve care, aimed at promoting satisfactory quality of life[7].

There is still no consensus on the moment in the chemotherapy in which children or adolescents begin to present alterations in muscle strength and quality of life. This emphasizes the need to monitor these patients during chemotherapy and to establish a physical therapy schedule in order to minimize such complications. The current study thus aimed to assess handgrip strength and quality of life in children and adolescents with cancer undergoing chemotherapy with vincristine.

METHOD

This was a study of children and adolescents monitored for 30 days during chemotherapy, approved by the Institutional Review Board of the University Hospital of Porto Alegre (HCPA) (CAAE: 53521615.0.0000.5327) and the Institutional Review Board of the Methodist University Center - IPA (CAAE: 53521615.0.3001.5308), according to the Brazilian National Health Council Resolution CNS 466/12. Permission was obtained from the *MAPI Research Institute* to apply the questionnaire *Pediatric Quality of Life™ (PedsQL™) Cancer 3.0 Module*.

Data collection took place from July to October 2016, and the study sample was non-probabilistic. Eligibility criteria were children and adolescents of both sexes, from 5 to 17 years of age, treated at the HCPA Pediatric Oncology Service, from the first to seventh day of hospitalization, with diagnostic confirmation of cancer, and capable of performing the proposed tests (dynamometry and the questionnaire). Patients were included who agreed to participate in the study after reading the free and informed consent form, authorized by their parents or guardians, and were about to initiate treatment with vincristine (all the patients were part of the same chemotherapy protocol). The sample excluded individuals who chose not to continue to participate, for any reason, during the evaluation.

Initially, having considered the inclusion criteria, the children and adolescents underwent an evaluation with a patient history form containing data on personal identification, laboratory tests, medications, anthropometric variables, results of complementary tests from the patient chart, and current vital signs: heart rate (HR), respiratory rate (RR), and oxygen saturation (SpO_2).

Next, the handgrip strength test was performed using a *Gripper* type dynamometer for Electronic Count (*Camry®*, model EH01-17), with a capacity of 90 kg. Patients were instructed as to the correct position, according to the American Society of Hand Therapists (ASHT)[7]. Three attempts were made to obtain maximum handgrip strength, with 60-second intervals in order to avoid a decline between the first and the last measurement. The highest measurement was recorded, and patients were told to maintain that hold for five seconds.

Assessment of quality of life used the questionnaire *PedsQL™ Cancer 3.0 Module*, applied to the child or adolescent and one of the parents, who answered separately but simultaneously. This questionnaire is divided into 27 items distributed across eight domains: pain and hurt (2 items), nausea (5 items), procedural anxiety (3 items), treatment anxiety due (3 items), worry (3 items), cognitive problems (5 items), perception of physical appearance (3 items), and communication (3 items). The scale consists of five possible answers: 0 = "never", 1 = "almost never", 2 = "sometimes", 3 = "often", and 4 = "almost always"

(these items are inverted and transformed into 100, 75, 50, 25, and 0). The adapted versions for children 5 to 7 years of age included just three possible answers, "never", "sometimes", "almost always" (100, 50, 0), and uses a faces scale. In the final sum, a lower score corresponded to worse quality of life.

The complete questionnaire took approximately 30 minutes. Data collection was done in the hospital at the following moments: days 0 to 7 (pre-chemotherapy) (T1), day 15 (T2), and day 30 (post-chemotherapy) (T3), with the latter two performed either in the outpatient setting or during hospitalization (if the patient was still hospitalized).

Quantitative variables were expressed as the median (minimum and maximum). Qualitative variables were described as absolute and relative frequencies. Comparison of the three moments used the Friedman test, complemented by the Wilcoxon test. Associations between the answers by the parents and children on the quality of life questionnaire were assessed by the Spearman correlation coefficient. Significance was set at 5% ($p<0.05$), and the analyses were performed in SPSS version 21.0.

RESULTS

We assessed handgrip strength and quality of life in seven children and adolescents with cancer. Median age (minimum and maxim) was 7 years (5-15). Six of the seven patients in the sample were girls (85.7%). The predominant diagnosis was acute lymphocytic leukemia (ALL), with 71.4%. Table 1 shows the other variables.

Handgrip strength showed a significant reduction in both limbs (p=0.018, right upper limb; p=0.030, left upper limb). (Table 2)

The *PedsQL™ Cancer 3.0 Module* did not show statistically significant results, perhaps due to the small sample size. However, overall there was a drop in the scores from the first seven days to day 30. In most of the domains in the questionnaire there was a gradual decrease in the scores over time, especially for the parents' answers, while the patients' self-report showed a reduction up to day 15 and an improvement by day 30. (Table 3)

Table 1. Characteristics of a sample of pediatric patients in chemotherapy that included vincristine

Variables	n=7
Age (years) – md (min-max)	7 (5-15)
Sex – n (%)	
M	1 (14.3)
F	6 (85.7)
Diagnosis – n (%)	
Acute lymphocytic leukemia	5 (71.4)
Others	2 (28.6)
Time since diagnosis – n (%)	
0 to 7 days	3 (42.9)
8 to 30 days	3 (42.9)
More than 30 days	1 (14.3)
Origin – n (%)	
State capital	6 (85.7)
Interior of the state	1 (14.3)

Key: md (median); min (minimum); max (maximum).

Analysis of the associations showed a significant difference between the answers by the parents and children at T2 (p=0.04; r=0.77) for the domain "treatment anxiety". The answers to the same questions were thus worded differently comparing children and their parents in most of the domains. The parents saw greater difficulties in the children than the children themselves, but these differences were not significant as in the other domains.

DISCUSSION

The most prevalent diagnosis in these seven patients was ALL, corroborating data from the National Cancer Institute José Alencar Gomes da Silva (INCA)[1]. Meanwhile, the predominant sex (female) was the opposite of that in some studies[8,9], reporting a predominance of males.

The current study found a decrease in muscle strength, measured by the handgrip strength test, from the moment chemotherapy began up to day 30. According to Moura[10], it is essential to measure handgrip strength in order to determine not only the integrity of the upper limbs, but

Table 2. Comparison of anthropometric data and handgrip strength over time

Variables	0-7 days T1	15 days T2	30 days T3	*p*
	md (min-máx)	md (min-máx)	md (min-máx)	
Weight (kg)	29 (18- 62)	28.3 (18-57)	28 (17-59.8)	0.56
BMI (kg/m2)	17.4 (13.8-23.6)	17.0 (13.9-24)	17.2 (14.1-22)	0.56
Right HGS (kg)	10.8 (5.8-36.3)	10 (4.8-34.4)	9.8 (4-20.8) ¥	0.01*
Left HGS (kg)	8.1 (5.5-35.2)	7.4 (4.5-30.6) €	7.8 (4.3-20.9) ¥	0.03*

Key: Md (median); min (minimum); max (maximum); body mass index (BMI); handgrip strength (HGS). *p<0.05 Friedman test; ¥ p<0.05 T3-T1 Wilcoxon text; € p< 0.05 T3-T2 Wilcoxon test.

Table 3. Comparison of quality of life results at three moments in the assessment, according to children and parents

Variáveis	0-7 days T1	15 days T2	30 days T3	*p*
	md (min-max)	md (min-max)	md (min-max)	
Children				
Overall quality of lif	1,775 (950-2,300)	1,500 (1,150-2,325)	1800 (1,150-2,475)	0.36
Pain and hurt	150 (50-200)	200 (150-200)	150 (100-200)	0.27
Nausea	450 (400-500)	450 (250-500)	350 (200-500)	0.16
Procedural anxiety	150 (0-300)	225 (0-300)	250 (0-300)	0.49
Treatment anxiety	250 (100-300)	275 (175-300)	300 (225-300)	0.18
Worry	150 (50-250)	100 (0-175)	150 (50-300)	0.43
Cognitive problems	350 (150-500)	325 (100-450)	325 (200-500)	0.86
Perception of physical appearance	225 (100-300)	200 (50-270)	150 (100-300)	0.46
Communication	200 (0-275)	150 (0-275)	125 (50-275)	0.73
Parents				
Overall quality of life	1,625 (1,075-2,150)	1,550 (1,250-2,100)	1,425 (900-2,100)	0.63
Pain and hurt	150 (100-200)	175 (0-200)	175 (100-200)	0.95
Nausea	500 (250-500)	350 (200-500) π	300 (0-400) ¥	0.01*
Procedural anxiety	75 (0-150)	175 (0-250)	150 (25-250)	0.22
Treatment anxiety	100 (0-300)	150 (125-300)	225 (150-300)	0.09
Worry	150 (0-300)	150 (25-250)	100 (25-300)	0.95
Cognitive problems	325 (125-500)	350 (275-400)	350 (225-500)	0.85
Perception of physical appearance	175 (0-250)	150 (125-300)	200 (25-250)	0.55
Communication	125 (50-250)	150 (75-250)	125 (25-300)	0.31

Key: Md (median); min (minimum); max (maximum); body mass index (BMI); handgrip strength (HGS). *p<0.05 Friedman test; ¥ p<0.05 T3-T1 Wilcoxon text; € p< 0.05 T3-T2 Wilcoxon test.

also an idea of overall strength, especially in individuals with chronic diseases. Based on this, one is able to interpret the results and establish adequate treatment targets, aimed at rehabilitation, especially in the patients' daily activities.

The study's results corroborate those of Götte et al.[11], who assessed 47 patients 6-17 years of age during chemotherapy, at the end of the induction phase. The Moon test was performed (for motor performance in pediatric oncology), in which one of the assessments was dynamometry for handgrip strength. The results showed a significant reduction in muscle strength during chemotherapy due to inactivity and the treatment itself, generating deficits in motor performance, possibly resulting in future physical and social problems.

Antineoplastic agents are present in cancer treatment, and vincristine was included in the drug protocols used in this study. It is considered the most neurotoxic of the *Vinca* alkaloids, potentially causing significant motor weakness in the hands and feet, with severe toxic effects in patients. These alkaloids have constituted the basis of treatment for malignant hematological neoplasms for nearly 50 years[12].

This corroborates information from the study by Rodríguez-Reyes et al.[13] showing that vincristine-induced peripheral neuropathy is related to the continuous administration of this drug, producing such symptoms as hypoesthesia, predominantly distal muscle weakness (hands and feet), decreased tendon reflexes, and myalgias. That is, all these alterations end up directly affecting the patients' mobility, thus compromising their quality of life.

In Díaz-Jaime et al.[14], patients with ALL that received vincristine as part of chemotherapy underwent a physical therapy program, with assessment using the nerve conduction velocity test (NCV). The 24 patients were divided into two groups: supervised (regular physical therapy and followed up for three month) and without supervision (receiving the physical therapy program). Both groups underwent NCV tests before the exercises. In the results, in 98% of the cases, the nerve most affected was the peroneal nerve, and in 96% of cases this same nerve presented axonal degeneration, the most frequent neuropathy. The study thus showed the importance of an exercise program as part of supervised physical therapy, performed regularly to minimize the effects of chemotherapy on neuropathies developed during treatment.

Hartman et al.[15] assessed strength in some muscle groups and motor performance of 92 children submitted to chemotherapy with vincristine (mean age 8.9 years and mean time 3.3 years since conclusion of treatment). The authors found a significant decrease in muscle strength of ankle dorsiflexors bilaterally, non-dominant wrist flexors, and handgrip strength bilaterally. Assessment of motor performance found that the decreased muscle strength in the wrist flexors resulted in compromised hand function. The same occurred with handgrip strength, which due to its decrease, specifically compromised motor performance in ball-handling skill, but without compromising other aspects such as hand function and balance.

Another study aimed to assess physical aptitude and possible deficits in physical performance in 18 children with diagnoses of ALL and lymphoma after ten months of chemotherapy, compared to 40 healthy children. Four tests were performed, including dynamometry. At the end, Bianco et al.[6] concluded that children with prior malignancies showed a lower level of physical aptitude, but even so they are fit to participate in regular exercise interventions.

Deisenroth et al.[16] conducted a study aimed at assessing muscle strength and quality of life in children and adolescents with cancer in the early phase of primary treatment. Their findings show a decrease in quality of life and muscle strength since the start of treatment in these children and suggest follow-up with physical therapy to decrease such complications.

In an attempt to minimize their discomfort, patients end up curtailing their level of physical activity, thus associating the treatment with prolonged rest and reducing their muscle mass, influencing muscle function, pulmonary function, incapacity, and loss of strength, directly affecting their quality of life[17].

Chemotherapy brings various feelings that become part of the daily routine for children in treatment and their families, including fear, sadness, discouragement, despair, grief, affliction, anguish, restlessness, and impatience. Such feelings are related to the diagnosis, uncertainty as to the prognosis, and complexity of the treatment[18].

The current study used self-report (the patients' own view of their quality of life) and proxy-report (the parents' view of their children's quality of life) in the *PedsQLTM Cancer 3.0 Module* Questionnaire. A comparison of the two views shows that health-related quality of life (HRQoL) according to parent proxy-report declines from the first week of diagnosis to day 30, unlike self-report, which shows a gradual improvement in quality of life from the first week to day 30 of treatment. This information corroborates the study by Matziou et al.[19], reporting that parents tend to associate cancer with worse prognosis and uncertainties as to the future, when compared to the children themselves.

In this study, in the first seven days, the children were more at ease while their parents were highly anxious. At the second moment (day 15), both were anxious. By the third moment (day 30), parents and children were less anxious. According to Matziou et al.[19], treatment anxiety (e.g., visits to the doctor or hospital, or waiting for the doctor) is related to a threatening feeling that precedes moments of danger or tension with unknown causes, depending on maturity and cognitive ability, both of which vary between children and adults.

Again, since parents and children have different impressions related to the cancer treatment, they voiced opposite opinions in the domain of "Communication" (asking whether the patient is able to clear up doubts or answer questions by the hospital team). While the parents felt that the children had difficulties answering questions or clearing up their doubts, the children claimed that it was easy. This clearly highlights the importance of follow-up by a multidisciplinary team in these cases, with parents and patients, with the aim of working together to demystify the concerns.

Matziou et al.[19] studied 149 young patients with cancer followed at the outpatient clinic in a hospital in Greece, divided into two groups: treatment (patients recently diagnosed or in treatment, but without relapses) and without treatment (patients who were still in follow-up after cancer treatment). They used the questionnaire *PedsQL™ 4.0 Generic Core Scales* to observe the agreement between answers by patients and their parents. Young patients reported better quality of life (74.58) (16.68) when compared to their parents' proxy-report (69.18) (17.91), consistent with the current study. Parents often project on their children their own concerns with cancer treatment; in addition, depending on their age, children may not realize what is happening to them (especially in the first days after diagnosis) and do not notice any difference in their HRQoL.

The number of individuals in the study was not addressed, due to the limited time for data collection. In addition, there are few studies on the relationship between prior assessments (physical, behavioral) in children and adolescents that are initiating chemotherapy, thus limiting the discussion. We thus suggest that similar studies be performed to promote adequate treatment for these patients, focusing on both their physical and social well-being.

CONCLUSION

Handgrip strength in children and adolescents with cancer decreased progressively from the start

of chemotherapy with vincristine. Follow-up with physical therapy is thus indispensable for these patients. This group shows good results with such therapy, so it is the duty of the physical therapist to prepare an individualized physical exercise program that provides well-being and improves quality of life for these patients, starting at diagnosis.

Due to the small sample size, there were no statistically significant differences in relation to the quality of life questionnaire. However, analysis of the domains separately identified the moments of greatest instability in the children and parents, highlighting the importance of a multidisciplinary team to work with these patients and their families.

CONTRIBUTIONS

Thayze Bairros da Costa contributed to the study conception and design, data collection, analysis, and interpretation, and writing of the article. Michelle Hagi Frantzeski and Daniela Meirelles do Nascimento contributed to the study conception and design, data collection, analysis, and interpretation, writing of the article, critical revision with intellectual input, and approval of the final version for publication. Lauro José Gregianin contributed to the study conception and design as well as the data collection.

CONFLICT OF INTEREST

None.

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