

Functionality of Children with Leukemia in Chemotherapeutic Treatment

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Funcionalidade de Crianças com Leucemia em Tratamento Quimioterápico

Funcionalidad de los Niños con Leucemia en Tratamiento con Quimioterapia

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ABSTRACT

Introduction: Leukemia is the most common type of neoplasm diagnosed in children in the world, affecting them in a critical period of their neuro-psychomotor development. Once diagnosed with a life-threatening disease, those children need palliative care concurrently with curative care. **Objective:** Assess the functionality of children with leukemia during chemotherapy treatment and compare it at the beginning and after one year of ongoing treatment. **Method:** Cross-sectional observational analytical study with 37 children evaluated with interviews performed with their parents, utilizing an investigation form and the Pediatric Evaluation Disability Inventory (PEDI). The statistical analysis was carried out with Student's t-test and Mann-Whitney test. **Results:** The results indicated there were no statistically significant differences in their functionality before and after 1-year treatment and all of them presented functionality below the expected for the age range. **Conclusion:** It is suggested the creation of a palliative care rehabilitation program for this group since the diagnosis as a way to avoid delays and/or irreversible deficits in the development of these children.

Key words: leukemia/drug therapy; disability evaluation; palliative care; child.

RESUMO

Introdução: A leucemia é o tipo de neoplasia mais comumente diagnosticada em crianças no mundo, afetando-as em um período crítico do desenvolvimento neuropsicomotor. Estando diagnosticadas com uma doença ameaçadora da vida, essas crianças necessitam, concomitantemente aos cuidados curativos, de cuidados paliativos. **Objetivo:** Avaliar a funcionalidade de crianças com leucemia durante o tratamento quimioterápico e compará-la no início e depois de um ano de tratamento em curso. **Método:** Estudo de corte transversal, do tipo observacional analítico, com 37 crianças avaliadas por meio de entrevista com os pais, utilizando um formulário de pesquisa e o Inventário de Avaliação Pediátrica de Incapacidade (PEDI). A análise estatística foi realizada pelos testes *t* de Student e de Mann-Whitney. **Resultados:** Não foram encontradas diferenças estatisticamente significantes entre a funcionalidade de crianças no início e depois de um ano de tratamento, estando todas com a funcionalidade abaixo do esperado para a faixa etária. **Conclusão:** Como forma de evitar possíveis atrasos e/ou déficits irreversíveis no desenvolvimento dessas crianças, sugere-se a criação de um programa de reabilitação em cuidados paliativos nos serviços especializados para cuidar desse público desde o diagnóstico.

Palavras-chave: leucemia/tratamento farmacológico; avaliação da deficiência; cuidados paliativos; criança.

RESUMEN

Introducción: La leucemia es el tipo de neoplasia que se diagnostica con mayor frecuencia en niños de todo el mundo y los afecta en un período crítico del desarrollo neuropsicomotor. Al ser diagnosticados con una enfermedad potencialmente mortal, estos niños necesitan cuidados curativos concomitantes, cuidados paliativos. **Objetivo:** Evaluar la funcionalidad de los niños con leucemia durante el tratamiento de quimioterapia y compararla al inicio y después de un año de tratamiento en curso. **Método:** Se trata de un estudio transversal, tipo analítico observacional, donde se evaluó a 37 niños a través de entrevistas con los padres, utilizando un formulario de encuesta y el Inventario de Evaluación de la Discapacidad Pediátrica (PEDI). El análisis estadístico se realizó utilizando la prueba *t* de Student y la prueba de Mann-Whitney. **Resultados:** En los resultados, no se encontraron diferencias estadísticamente significativas entre la funcionalidad de los niños al inicio y al año de tratamiento, todos con una funcionalidad por debajo de lo esperado para su grupo de edad. **Conclusión:** Como forma de evitar posibles retrasos y/o déficits irreversibles en el desarrollo de estos niños, se sugiere la creación de un programa de rehabilitación en cuidados paliativos en servicios especializados para atender a este público desde el diagnóstico.

Palabras clave: leucemia/tratamiento farmacológico; evaluación de la discapacidad; cuidados paliativos; niño.

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INTRODUCTION

Childhood and adolescent cancer (0 to 19 years of age) affects mainly blood cells and connective tissues, the most frequent are central nervous system (CNS) tumors and lymphomas¹. Leukemia is the most commonly diagnosed in children younger than five years of age worldwide and in younger than 14 years in Brazil². Leukemias are divided in lymphoid or myeloid (according to the blood cell affected) and acute or chronic (depending on the speed of its evolution)¹. Still of unknown etiology and difficulty to determine, this disease affects children in a critical period of their development, essential for neuropsychomotor apprenticeship^{3,4}.

Cancer is the first cause of death by non-infectious disease in children and adolescents (from 1 to 19 years) in Brazil, accounting for 8% of them according to the National Cancer Institute José Alencar Gomes da Silva (INCA)¹, but an important progress occurred in its treatment for this population. In the last 50 years, a therapeutic breakthrough was achieved resulting in a cure rate of 80% for children with ALL (acute lymphoid leukemia), the most common in childhood^{1,5}. Eventually, it resulted in a high rate of survivors needing a multidisciplinary team to meet preventive, curative and palliative demands this population has for better quality-of-life since diagnosis through post-treatment^{2,3}.

Even with scarce literature evidences that multidisciplinary rehabilitation significantly impacts the functioning of children with cancer, recent studies concluded that early rehabilitation in adults is beneficial to these patients^{6,7}. The proposal is to include this program in palliative care of children soon after cancer diagnosis concomitantly with palliative care⁸.

The body functions (mental, sensorial, speech, systemic, mobility and skin) integrated to the individual's capacity of performing relevant daily routine activities, allowing its participation in the society are defined as functionality⁹. It is important to evaluate these aspects in children with cancer and in treatment as further to the disease itself, chemotherapy can be debilitating and impact the development and neuropsychomotor apprenticeship of this population⁸.

A study conducted in the United States of America (USA)¹⁰ draws attention to the risk of changes of neurocognitive functions of children with leukemia in chemotherapy treatment due to possible leukoencephalopathy. Acute and/or chronic effects affecting the CNS and mental functions are important concerns today as cognitive difficulties have already been reported in children submitted to this treatment, in addition to seizures, dementia and modifications

of neuroimages because of the chemotherapy-related toxicity¹⁰⁻¹².

The neurocognitive alterations directly affect the neuropsychomotor development of the children who start to need specific monitoring and stimulation. It is known that children with delayed development have decreased performance of their daily activities and communicate poorly, unable or not knowing to express their feelings or wishes which can compromise the treatment routine and overload the caregiver¹³.

This study has the objective of evaluating the global functioning (selfcare, mobility and social functioning) of these patients in chemotherapy treatment because of the necessity of identifying early neuropsychomotor delays and initiate the follow-up of children diagnosed with leukemia in view of their high survivorship and analyze the impact of chemotherapy on functioning.

METHOD

Cross-sectional, analytical study developed at the Pediatric Oncology of the "Instituto de Medicina Integral Professor Fernando Figueira (IMIP)", in Pernambuco, a national and international reference of childhood cancer¹⁴.

The study was conducted from May 2018 to February 2019. The inclusion criteria were age between 3 and 6 years old, diagnosed with leukemia, in chemotherapy treatment at IMIP.

As children are diagnosed with leukemias usually from 2 to 4 years of age⁴ and this evaluation comprehends children from 6 months to 7 and half years old, it was decided to conduct the study with 3-6 years old children diagnosed and in treatment because in this range the child is in pre-school¹⁵, all of them in the same age of development.

Children with pre-leukemia comorbidities as neurological sequelae, cognitive and/or motor deficits, heart problems, genetic syndromes and visual compromise were excluded.

The population was divided in two groups according to the time of chemotherapy treatment: group 1 (G1) – children diagnosed with leukemia in chemotherapy for less than one year at the time of data collection; group 2 (G2) – children diagnosed with leukemia in treatment for one year or more at the time of data collection.

Convenience sampling method was chosen for both groups according to the demand, frequency and assiduity of the patients at the outpatient facility where the study was developed; information about the children with the study profile in treatment during the collection period were collected.

Interviews with the parents or main caregivers in a secluded room were conducted and after the signature

of the Informed Consent Form (ICF), it was applied the study questionnaire to characterize the sample and the Pediatric Evaluation of Disability Inventory (PEDI) in its original version¹⁶.

The Brazilian version of the PEDI was adapted by Mancini¹⁵, validated in Brazil for parents of children from 6 months to 7 and a half years old, consisting in three fields of performance to be evaluated: selfcare, mobility and social functioning. Each one of these fields will be reviewed in three parts: “functional skills”, “caregiver assistance” and “modifications”¹⁷.

Each item of “functional skills” is evaluated with score 0 (zero) if the child is unable to perform tasks or 1 (one) if it is able. Scores from 0 to 5 are attributed to “caregiver assistance” (0 – total; 1 – maximum; 2 – moderate; 3 – minimal; 4 – overlook; 5 – independent)¹⁷. The total score is the sum of the items of each scale that can be converted in normative and/or continuous score.

The item “modifications” was not addressed in the study. The normative, of all the instruments’ scores, was utilized in the present investigation because it shows the performance per age matched to the typical development. The normative score between 30 and 70 indicates that the child’s development is satisfactory to the age-range while lower values mean delay¹⁷.

Descriptive analyzes were carried out for socioeconomic conditions, the software SigmaStat 4.0[®] was utilized for statistical calculations with the variables (normative scores extracted from PEDI) of the two groups. The non-parametric Kolmogorov-Smirnov test was adopted to compare the two groups. Student’s *t* test was applied to compare variables with parametric distribution and the Mann-Whitney test to compare variables with non-parametric distribution ($p < 0.05$).

The Institutional Review Board (IRB) of IMIP approved the study in compliance with Ordinance 466/12¹⁸ of the National Health Council of the Ministry of Health, report number 2,836,582 and CAAE (Submission for Ethical Review) 91196318.6.0000.5201.

RESULTS

Thirty-seven (37) (100%) children were evaluated, 18 (48.65%) of G1 and 19 (51.35%) of G2, nearly the entire sample diagnosed with ALL, except one child of G2 diagnosed with acute myeloid leukemia (AML). 15 children of G1 and 8 children of G2 were males.

Of the 37 children in oncologic treatment, 27 were not residents of the state’s capital and 25 were not attending day care or school. Children not attending school at data collection period but who attended before, stopped because of the treatment (17 of the 25 not attending

school or day care). Those who were never enrolled at the school or day care initiated the treatment before 4 years old at a pre-school age and had ever attended day care (Table 1).

Table 1. Distribution of the frequencies of sociodemographics of children with less than one year of treatment (G1) and children with one year of treatment or more (G2). Recife, 2019

	Categories	G1 % (n=18)	G2 % (n=19)
Gender	Female	16.7	57.9
	Male	83.3	42.1
Attends school	Yes	11.1	52.6
	No	88.9	47.4
Residence	Recife	27.8	26.3
	Another city of Pernambuco	72.2	73.7

Captions: G1 = less than one year of treatment; G2 = one year or more of treatment.

All the study families earned less than one minimum wage, 16 of them below deprivation (less than ¼ of the minimum wage) and 17 below poverty line (less than ½ minimum wage)¹⁹. Most of the families were recipients of government aide but six of G1 and two of G2 had none.

After the Kolmogorov-Smirnov test, the fields “functional skills–social functioning” and “caregiver assistance – selfcare” presented parametric distribution (comparison of two groups by Student’s *t* test) and the other fields had non-parametric distribution by the Mann-Whitney test (Table 2).

With the results of PEDI for G1 and G2, the number of children with delay was greater in comparison with those with satisfactory grading (expected functionality for age), except the field “caregiver assistance – selfcare” in G2, when only seven children presented delay (Table 2), delay was detected in both groups and no statistically significant difference was found between them.

The arithmetic means of the results of PEDI for both groups are shown in Table 3, most of them below 30, indicating development delay. For two fields alone, “caregiver assistance – selfcare” and “caregiver assistance – social functioning”, the mean was 31.253 and 30.800, respectively, both in G2.

DISCUSSION

By normative scores of both groups, comparing PEDI’s no statistically significant difference was found, time of treatment caused no influence on children’s functioning. The 3-6 years old children diagnosed with leukemia regardless of the treatment phase, had delays of global

Table 2. Comparison of the results of PEDI of children with less than one year of treatment and with one year or more of treatment. Recife, 2019

Treatment	G1		G2		P
	n (18)	f (%)	n (19)	f (%)	
HF AU satisfactory	6	33.3	8	42.1	0.126 ^β
Delay	12	66.7	11	57.9	
HF MB satisfactory	1	5.6	4	21	0.869 ^β
Delay	17	94.4	15	79	
HF FS satisfactory	6	33.3	9	47.4	0.186 ^α
Delay	12	66.7	10	52.6	
AC AU satisfactory	7	38.9	12	63.2	0.062 ^α
Delay	11	61.1	7	36.8	
AC MB satisfactory	5	27.8	6	31.6	0.824 ^β
Delay	13	72.2	13	68.4	
AC FS satisfactory	8	44.4	8	42.1	0.514 ^β
Delay	10	55.6	11	57.9	

Captions: G1 = children with less than one year of treatment; G2 = children with one year or more of treatment; HF AU = functioning skills – selfcare; HF MB = functioning skills – mobility; HF FS = functioning skills – social functioning; ACAU = caregiver assistance – selfcare; ACMB = caregiver assistance – mobility; AC FS = caregiver assistance – social functioning; f = frequency; α = Student’s t test; β = Mann-Whitney test

Table 3. Arithmetic means of PEDI of children with less than one year of treatment and one year or more of treatment. Recife, 2019

Treatment	G1	G2
HF AU	19.822	25.516
HF MB	13.800	16.684
HF FS	23.194	28.953
AC AU	24.544	31.253
AC MB	20.772	22.263
AC FS	24.428	30.800

Captions: G1 = children with less than one year of treatment; G2 = children with one year or more of treatment; HF AU = functional skills – selfcare; HF MB = functional skills – mobility; HF FS = functional skills – social functioning; AC AU = caregiver assistance – selfcare; AC MB = caregiver assistance – mobility; AC FS = caregiver assistance – social functioning.

functioning or significantly poor performance against children of the same age range without cancer, which may possibly lead to a specific intervention for this population.

For both groups, mobility was the first field of performance where a great number of children had delays, both for functional skills and caregiver assistance,

because if the child is unable to perform (functional skills), the caregiver has to provide more assistance (caregiver assistance). Most likely, this happens because of the disease and treatment-related side effects impacting the children’s activities²⁰. In addition, parents tend to overprotect their children during the treatment for fearing to lose them or attempting to reward them due to the suffering they went through, pulling them away from independent ambulation and exploration of the environment²¹.

Delays were also detected in selfcare. For the age range investigated, children are developing the required skills to perform activities of the daily life, which can be interrupted as a result of the disease and treatment as frequent hospitalizations, asthenia, pain and debilitating periods impacting the routine, possibly hampering the experimentation and training in these skills³. Parents’ overprotection is again a strong influence attempting to spare their children from any effort²¹.

Social functioning is the third domain evaluated, although with delays but with less children below the expected for age, probably because the environment and physical facilities favored the interaction of children in treatment. Even so, school and conviviality with children not in treatment are affected because they may feel excluded for not belonging and fear of being rejected²¹. Nevertheless, it is not possible to compare the results because the literature is scarce in studies with the same evaluation for pediatric oncology.

Sociodemographics revealed that males predominated in both groups but with more females in G2, corroborating the literature with high incidence of leukemia in males^{1,2}. ALL is more frequent in preschoolers (younger than 5 years), with peak of incidence in toddlers². AML is more incident in the first year of life², which did not occur with the only study child diagnosed with this disease at 4 years and 6 months old.

Children diagnosed with cancer whose parents earned less than ¼ of the minimum wage are entitled to Continuing Monthly Benefit (BPC)²². Six of the eight study children who were not receiving this aide had the required profile, most likely still in the bureaucratic approval process which can be long²¹, a condition to continue the treatment as the child needs a full-time companion, often the mother who has no other financial source.

The low socioeconomic level of the study sample (all the families earned less than one minimum wage) may have negatively influenced the satisfactory development of these children prior to the oncologic diagnosis, only 22.5% of the Brazilian children evaluated to validate PEDI had socioeconomic level similar to the study population¹⁷.

Only two children of G1 were attending school when the scale was applied. Of the 16 not attending school, 11 were beginning treatment because at this phase, frequent hospitalizations and continuous presence at chemotherapy clinics, exams, procedures are routine¹³. In addition, the family is still under the impact of the diagnosis and attempting to deal with cancer stigma and fears, which can also be an obstacle to attend school. After one year, which is the average time children with ALL are absent from school²³, contingent upon the response to the treatment, they are cleared by the doctor and are given guidance by the multidisciplinary team to attend school, making family and children more confident in resuming educational activities.

Nine children were not attending school at G2, six attended before chemotherapy and three were never enrolled. Though a small number, it is still significant in view of the sample size; this occurs because most of these children resided in other cities and needed to travel for long periods to reach the health facilities and/or alternate staying home and attend support houses close to the hospital changing the routine and impacting school activities.

Based in the results of PEDI and the study population, it is important to address palliative care and its role in minimizing the impact of the drop of functioning after the evaluation and on the children's quality-of-life.

Although most of the publications address end-of-life care alone, recent studies suggest that they should begin soon after the diagnosis²⁴, in the course of the disease and concomitant to curative care^{25,26}.

Palliative care should encompass rehabilitation and end-of-life relief of suffering if the disease fails to evolve to cure and including functioning keeping, if needed⁸. It is not possible to predict the repercussions of curative measures over the development of children diagnosed with ALL, therefore, the evaluation of functioning is paramount since the beginning of the treatment; their inclusion in a patient-centered palliative care therapeutic program to keep and/or improve their physical, cognitive, mental and/or social performance in the course of the treatment is essential to preserve their skills or match to the new reality for improved quality-of-life, the core objective of palliative care and to benefit the psychomotor development^{24,27}.

Studies with adult population have proven that early rehabilitation program in individuals diagnosed with cancer improves their functioning and quality-of-life and adherence to the treatment^{6,7}. The program should be structured by a multidisciplinary team to address every complex and diversified demands of the children regarding their development and repercussions of the disease^{8,13,26}.

CONCLUSION

Regardless of the duration of the chemotherapy treatment, most of the children evaluated presented global functioning below the expected for the age range. Based in the high odds of cure of childhood cancer today, specifically children with leukemia, it is important to include in their treatment a therapeutic plan of palliative care for rehabilitation of skills potentially affected after the diagnosis and chemotherapy treatment.

The instrument utilized did not allow to identify whether the delays found are pre-diagnosis and treatment, especially due to the low socioeconomic level of the entire sample, a clear limitation of the study. In addition, it is not conclusive because of the convenience sampling, but suggests the continuation and highlights the importance of full attention to this population.

As the current study has shown, damages to functioning and treatment side effects of children with cancer are expected. A deficit-centered evaluation and intervention as adjuvant to cancer coping are still a shortcoming. As palliative care should be present since diagnosis of a life-threatening disease, rehabilitation has to be one of the objectives of this approach.

It is important to expand the data collection period to continue the study and, if possible, conduct a multicenter study, incorporating other players of the network and another specialized facilities in pediatric oncology. In addition, the socioeconomic condition needs to be incorporated into the results. The scientific community and specialized services should be aware of the specific needs of this population and help the elaboration of new public policies to support these children based in the current study and its potential continuation.

CONTRIBUTIONS

Bruna Negromonte Silva, Maria Soraida Silva Cruz and Tatiany Lisière Brandão Künzler Lima contributed to the study design, acquisition, analysis and interpretation of the data, wording and critical review. Ana Paula Silva de Oliveira and Rafael Moura Miranda contributed substantially to the study design, acquisition, analysis and interpretation of the data. Kaísa Trovão Diniz contributed to the wording and critical review. All the authors approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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