Quality of Life and Oral Health in Children undergoing Antineoplastic Therapy

Qualidade de Vida e Saúde Bucal em Crianças submetidas à Terapia Antineoplásica
Calidad de Vida y salud Oral de los Niños sometidos a Terapia Antineoplásica

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ABSTRACT

Introduction: Cancer is a burdensome disease whose treatment protocol can produce severe psychosocial and physical side effects. The main effects of antineoplastic treatment may affect the oral cavity, especially in children, compromising theirs and their family quality-of-life. **Objective:** To identify and describe side effects-related antineoplastic treatment and to assess its impact on the children's and their families' quality-of-life. **Method:** Qualitative and cross-sectional study, with the participation of 117 children, preschoolers, consulted at a referral hospital in the State of Paraíba, through the B-Ecohis questionnaire, dental clinical exams and medical records. The statistical treatment was based on descriptive analysis and Poisson Regression with robust variance in the Stepwise method (p<0.05). **Results:** The most common manifestations were mucositis and xerostomia (66.7% and 54.7% respectively). The impact on the children's quality-of-life affected mostly the domain of functional limitation with mean of 3.0 (±1.8) and 1.0 (±1.0) for the family function in the family. **Conclusion:** The impact on the quality-of life in children was weak and not significant in the family.
Key words: neoplasms; antineoplastic agents/adverse effects; oral manifestations; quality of life; child.

RESUMO

Introdução: O câncer é uma doença grave cujo protocolo de tratamento pode produzir severos efeitos colaterais de ordem psicossocial e física. Os principais efeitos do tratamento antineoplásico podem acometer a cavidade oral, especialmente em crianças, comprometendo a sua qualidade de vida e a do núcleo familiar. **Objetivo:** Identificar e descrever as lesões bucais relacionadas aos efeitos colaterais produzidos pelo tratamento antineoplásico e avaliar seu impacto sobre a qualidade de vida da criança e da sua família. **Método:** Estudo qualitativo e transversal, com a participação de 117 crianças pré-escolares atendidas em hospital de referência (Paraíba), por meio do questionário B-ECOHIS, de exames clínicos odontológicos e de prontuários médicos. O tratamento estatístico fundamentou-se na análise descritiva e regressão de Poisson com variância robusta no método Stepwise (p<0,05). **Resultados:** As manifestações mais observadas foram mucosite e xerostomia (66,7% e 54,7%, respectivamente). Relativo ao impacto na qualidade de vida da criança, o domínio de maior média foi limitação funcional 3,0 (±1,8) e, na família, função familiar 1,0 (±1,0). **Conclusão:** O impacto na qualidade de vida das crianças se revelou fraco e, no núcleo familiar, não foi significativo.
Palavras-chave: neoplasias; antineoplásicos/efeitos adversos; manifestações bucais; qualidade de vida; criança.

RESUMEN

Introducción: El cáncer es una enfermedad grave cuyo protocolo de tratamiento puede producir efectos secundarios psicosociales y físicos graves. Entre los principales efectos del tratamiento antineoplásico, algunos afectan la cavidad bucal, especialmente en los niños, comprometiendo su calidad de vida y el núcleo familiar. **Objetivo:** Identificar los efectos secundarios producidos por el tratamiento antineoplásico y evaluar su impacto en la calidad de vida del niño y su familia. **Método:** Estudio cualitativo y transversal, con la participación de 117 niños, preescolares, atendidos en un hospital de referencia (Paraíba), mediante el cuestionario B-Ecohis, exámenes clínicos dentales y registros médicos. El tratamiento estadístico se basó en análisis descriptivo y Regresión de Poisson con varianza robusta en el método Stepwise (p<0,05). **Resultados:** Las manifestaciones más observadas fueron mucositis y xerostomía (66,7% y 54,7% respectivamente). En cuanto al impacto en la calidad de vida del niño, el dominio con mayor promedio fue la limitación funcional 3,0 (±1,8) y la función familiar 1,0 (±1,0) en la familia. **Conclusión:** El impacto en la calidad de vida de los niños fue débil y en la familia no significativo.
Palabras clave: neoplasias; antineoplásicos/efectos adversos; manifestaciones bucales; calidad de vida; niño.

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INTRODUCTION

The rate of morbimortality of childhood cancer demands substantial attention in human health. For each year of the triennium 2020-2022 it is estimated the occurrence of 8,460 new cases of cancer, the incidence for childhood and adolescence is approximately 276 thousand new cases per million children[1].

Most of the children diagnosed with neoplasms is submitted to antineoplastic treatment involving chemotherapy, radiotherapy and surgery[2]. Chemotherapy agents in special, depending on the dosage and frequency can affect the oral mucosa and provoke buccal alterations. These oral manifestations as consequence of the intense immunosuppression caused by chemotherapy can interfere in the results of medical therapeutic, causing relevant complications and significantly increasing the length of hospital stay, treatment costs and directly affecting the quality-of-life of the child and its family[3,4].

Quality-of-life is defined as the individual's perception of its position in life in the context of culture, values, expectations and objectives[1]. Among the instruments created to measure the oral health related quality-of-life (OHRQoL), the Early Childhood Oral Health Impact Scale (ECOHIS) is the most utilized to evaluate pre-school children and their parents. It was validated and is available to be utilized in Brazil (B-ECOHIS) and allows to measure the impact of oral disorders/diseases and experiences of dental treatments in the OHRQoL of children and parents[5,6].

Considering the impact the cancer diagnosis in its own provoked in the family and child, further to the invariably long and painful treatment with biopsychosocial consequences, it is justified to evaluate the quality-of-life of children and their families in these conditions and identify the most frequent oral manifestations.

METHOD

Quantitative, cross-sectional study with secondary data carried out from June 2019 to March 2020, at the philanthropic *Hospital Napoleão Laureano* and referral for blood diseases and cancer treatment in the municipality of João Pessoa (PB), upon approval by the Institutional Review Board of "*Universidade Federal de Campina Grande*" with the participation of "*Faculdade São Leopoldo Mandic*", number 3.269.555/2019, CAAE: 10933119.2.0000.5575 in compliance with Resolution 466/2012[7] of the National Health Council.

Children in the age-range from two to six years old registered at the hospital and submitted to antineoplastic therapy whose parents signed the Informed Consent Form (ICF) and accepted to join the study were evaluated. The children who were in the first cycle of chemotherapy when the study was in course were excluded because they had no oral manifestations as xerostomia, mucositis and fungicide and viral infections.

The questionnaires were applied with the parents in an individual interview to ensure all questions were responded. Prior to the application of the questionnaire B-ECOHIS, the investigator guided the parents about the questions which addressed their children oral health, the importance and differences among apparently similar questions to minimize misinterpretations and eliminate the variables that could potentially compromise the acquisition of the data. In average, 30-minutes six weekly interviews were conducted.

The questionnaire with information about sex, age, tumor site, number of chemotherapy cycles, medication utilized and baseline diseases was collected from the patients' charts.

The 13-questions form utilized assessed the parents' perception about OHRQoL, with nine questions on the domain of the section "Impact on the Child": symptoms – one question; impairment – four questions; psychological – two questions; self-image and social interaction – two questions; four questions were included in the section "Impact on the Family": parents' distress – two questions; family function – two questions.

The responses were categorized and coded as: 0 (never); 1 (almost never); 2 (sometimes); 3 (frequent); 4 (very frequent) and 5 (don't know). The total score was calculated from the sum of the responses.

Zero was the lower score, that is, no influence of oral health on the quality-of-life of the children and the maximum score, 56, strong influence of oral health on the quality-of-life of preschoolers. The classification of the impact according to the total score was: 0 (no impact); $0<x<18.67$ (mild impact); $18.67<x<37.34$ (average impact) and $37.34<x\leq56$ (strong impact).

One evaluator trained by a stomatologist conducted one clinical oral exam. Most common oral manifestations arising from antineoplastic treatment were: mucositis, mouth ulcer, xerostomia and candidiasis. The World Health organization (WHO) scale to diagnose oral mucositis was adopted: grade 0 – none; grade 1 – erythema, irritation and pain; grade 2 – erythema, ulcers (solid diet); grade 3 – ulcers (liquid diet) and grade 4 – oral alimentation impossible.

Oral exam was performed with children at admission after the second cycle of antineoplastic treatment in a secluded room of the hospital and with children hospitalized. The exams were tactile and visual with disposable wood spatulas, sterile tongue depressor sticks

and gauze compress if needed, with flashlight. The evaluator and assistant were wearing caps, gloves and disposable masks according to biosafety norms. Intraoral data collected in the evaluation were recorded in a form, indicating the cancer site, oral manifestations, prescribed medication and type of treatment.

The Statistical Package for the Social Sciences (SPSS, Chicago, IL, USA), version 20.0 was utilized to analyze the information. The domains and totals score of B-ECOHIS were considered dependent variables. The other clinical conditions and socioeconomic variables were classified as independent variables. Descriptive analysis was performed for the data with absolute frequencies, percentage, mean and standard-deviation, minimum and maximum values and percentiles. The chi-square test was adopted to associate the qualitative variables. The value of $p<0.05$ was significant.

The test Kolmogorov-Smirnov was utilized to determine that the pattern of distribution of the instrument B-ECOHIS was non-normal, with value of $p<0.05$ considered significant. To verify the impact of the sociodemographic aspects and clinical conditions on the OHRQoL, the Mann-Whitney and Kruskal-Wallis tests were utilized. The value of $p<0.05$ was considered significant.

Poisson regression with Stepwise robust variance was adopted to determine the associations between impact of OHRQoL with independent variables. The magnitude of the association was evaluated by the prevalence ratio (PR), adjusted rate ratio (aRR), confidence intervals (CI 95%) and values of p. The variables with values of $p\leq0.20$ in the univariate analysis were included in the adjusted model. Only the variables with values of $p<0.05$ remained in the final model.

RESULTS

The final sample consisted in 117 children, mostly males (55.6%) with 6-years of age (29.1%). Other data are described in Table 1.

Table 2 shows oral manifestations, standing out mucositis + mouth ulcer and xerostomia + mucositis in 21.4% and 20.5% respectively, the classification G3 was predominant (31.6%).

Table 3 shows the responses after application of the instrument B-ECOHIS about the impact to the child and family. 46.2% of the children reported frequent or very frequent "oral/dental pain" and 47% had frequent or very frequent "difficulty drinking". Regarding family impact, 2.2% of the individuals missed their jobs frequently or very frequently and 21.4%, felt upset frequently or very frequently.

Table 1. Descriptive analysis of the profile of children submitted to antineoplastic treatment at an oncologic treatment clinic in Paraíba (n=117)

Variable		n	%
Age	2	13	11.1
	3	18	15.4
	4	26	22.2
	5	26	22.2
	6	34	29.1
Sex	Female	52	44.4
	Male	65	55.6
Local	Capital (João Pessoa)	37	31.6
	Countryside	80	68.4
Zone	Urban	97	82.9
	Rural	18	15.4
	Did not respond	2	1.7
Type of treatment	Chemotherapy	98	83.8
	Chemotherapy + surgery	13	11.1
	Chemotherapy + radiotherapy	4	3.4
	Chemotherapy, radiotherapy and surgery	2	1.7
Type of chemotherapy	Curative	88	75.2
	Adjuvant	13	11.1
	Neoadjuvant	6	5.1
	Palliative	9	7.7
	No information	1	0.9
Baseline disease	Diabetes	1	0.9
	Hypertension	1	0.9
	Cardiopathy	20	17.1
	Total	**117**	**100.0**

The total score of B-ECOHIS ranged from 0 to 16 with mean 8.0, with greater impact of OHRQoL in the domain functional impairment (mean 3 and standard-deviation 1.8) and subsequently, psychological domain (mean 1.6 and standard-deviation 0.9) as shown in Graph 1.

According to B-ECOHIS, in the association between the median value of the domains and total score with sociodemographic and clinic variables, it was found relation between sex and oral symptoms (p=0.018), between type of treatment and psychological domain (p=0.029), between mucositis and domain functional impairment (p<0.001) and total score (p=0.019). Also, it was found association between mouth ulcer (p=0.038) and total score of B-ECOHIS. (Table 4).

Table 2. Descriptive analysis of oral manifestations in pediatric patients in chemotherapy treatment in an oncologic treatment clinic in Paraíba (n=117)

	Variable	n	%
Type of oral alteration	Not reported	17	14.5
	Mucositis + mouth ulcer	25	21.4
	Xerostomia + mucositis	24	20.5
	Mucositis	6	5.1
	Xerostomia	14	12.0
	Mouth ulcer	4	3.4
	Mucositis + mouth ulcer + xerostomia	23	19.7
	Xerostomia + mouth ulcer	3	2.6
	Candidiasis	1	0.9
Grade of mucositis	G0	24	20.5
	G1	27	23.1
	G2	29	24.8
	G3	37	31.6
	Total	**117**	**100.0**

DISCUSSION

The relation of antineoplastic treatment and development of oral alterations is well recognized in the medical and odontology literature. The type and degree of cancer malignancy, the prescribed drug dose, the frequency of chemotherapy, age and oral hygiene of the child are determinant factors for the onset and severity of oral lesions[2,8].

Oral diseases are important aggravating factors of systemic diseases impacting the medical treatment, prolonging hospital stay and compromising the quality-of-life of the child and its family[9,10].

To evaluate the influence of oral lesions post-antineoplastic treatments on the quality-of-life and the consequences to the child and its family life routine is paramount to address health initiatives to minimize their suffering.

The current study revealed that among oral manifestations, mucositis was the most prevalent and the great impact on the quality-of-life occurred in the domain functional impairment of the child but to the family, it was weak. The results of this study concur with

Table 3. Responses of the Brazilian version of instrument B-ECOHIS in children submitted to antineoplastic treatment (n=117)

		Never	Almost never	Sometimes	Frequent	Very frequent	Don't know
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Child Impacts						
Domain oral symptoms	Oral/dental pain	2 (1.7)	20 (17.1)	41 (35.0)	53 (45.3)	1 (0.9)	0 (0.0)
Domain functional impairment	Difficulty drinking	6 (5.1)	20 (17.1)	36 (30.8)	28 (23.9)	27 (23.1)	0 (0.0)
	Difficulty eating	21 (17.9)	34 (29.1)	40 (34.2)	21 (17.9)	1 (0.9)	0 (0.0)
	Difficulty pronouncing words	98 (83.8)	18 (15.4)	1 (0.9)	0 (0.0)	0 (0.0)	0 (0.0)
	Missed pre-school	26 (22.2)	53 (45.3)	34 (29.1)	3 (2.6)	1 (0.9)	0 (0.0)
	Missed some daily activity	51 (43.6)	20 (17.1)	45 (38.5)	1 (0.9)	0 (0.0)	0 (0.0)
Domain psychological	Trouble sleeping	56 (47.9)	4 (3.4)	41 (35.0)	16 (13.7)	0 (0.0)	0 (0.0)
	Irritated	2 (1.7)	16 (13.7)	85 (72.6)	14 (12.0)	0 (0.0)	0 (0.0)
Domain self-image/social interaction	Avoided smiling	64 (54.7)	27 (23.1)	26 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)
	Avoided talking	72 (61.5)	34 (29.1)	11 (9.4)	0 (0.0)	0 (0.0)	0 (0.0)

to be continued

Table 3. continuation

		Never	Almost never	Sometimes	Frequent	Very frequent	Don't know
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
	Family impact						
Domain family stress	Been upset	55 (47.0)	29 (24.8)	8 (6.8)	25 (21.4)	0 (0.0)	0 (0.0)
	Felt guilty	87 (74.4)	5 (4.3)	25 (21.4)	0 (0.0)	0 (0.0)	0 (0.0)
Domain family function	Time off work	11 (9.4)	39 (33.3)	41 (35.0)	26 (22.2)	0 (0.0)	0 (0.0)
	Financial impact	37 (31.6)	47 (40.2)	27 (23.1)	6 (5.1)	0 (0.0)	0 (0.0)
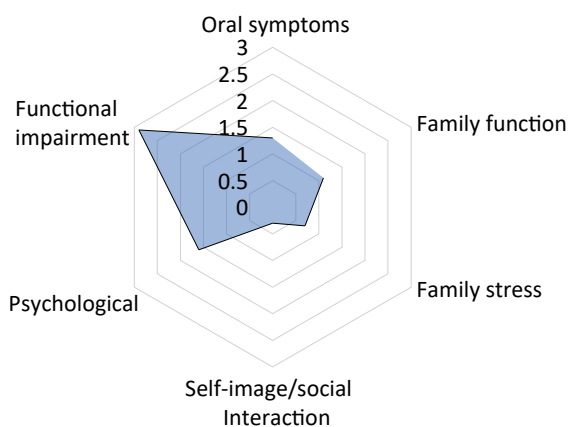
Graph 1. Diagram of Kiviat of the means of the scores of the dimensions of B-ECOHIS in children submitted to antineoplastic therapy (n=117)

other investigations[6,11] when effects of oral conditions in children and their families are compared, showing a strong influence on children, especially in the domains functional impairment and oral symptoms.

It is possible to infer the association of mucositis with functional impairment of the children, considering that it is caused by chemotherapy as it is the prevalent manifestation in the population investigated producing ulcers, discomfort and pain, similar to other articles[12-15].

The decline of the quality-of-life may be related to the joint onset of mucositis-mouth ulcer-xerostomia with oral symptoms and functional impairments (difficulty feeding and drinking) also concluded in the present article. These facts can be explained by the quanti-qualitative reduction of salivary flow, which makes deglutition difficult and the presence of painful mouth ulcers because of the absence of epithelial surface and exposure of nerve terminations[13,16-18]. The negative impact on psychological domain is evident (difficulty sleeping and irritation).

The impact was low in the domain self-image of the children evaluated. Nevertheless, 45.3% reported "dental pain" which, despite without significant statistical data, can potentially and negatively interfere in the child's quality-of-life. Studies comparing the quality-of-life of oral health of children diagnosed with cancer and healthy children reached similar results[9,10], possibly due to the humanized reception by the caretakers, health professionals and institutional[17,19-22].

As a reference for onco-pediatric treatment the hospital provides the required dental care and complementary approaches as art therapy, music, dance, psychotherapy, mind-body therapy and prayers. These measures can minimize the treatment adverse effects improving the quality-of-life of the child and the family[23,24].

The study limitation is its cross-sectional design, which does not include the causality relation that a longitudinal design could address. In addition, children with cancer may not relate the disease with adverse effects due to immaturity and level of cognition. The methodological care and rigor while collecting the data, nevertheless, counterbalanced these restrictions.

The results of this study ensured a broad understanding about the repercussions of the antineoplastic treatment on the child and family and brought relevant information for health professionals that deal with the children in their conditions. Despite treatment side effects and complications, these professionals should reinforce that the treatment is necessary and unquestionable for the benefit of health. The encouragement will potentially reduce the negative impacts of the therapeutic approach and will play a key role to improve the quality-of-life, educating the child and family to recognize the benefits. The presence of the dental-surgeon in the multiprofessional team providing oncological care to the pediatric patient is mandatory for target-interventions about the necessity and importance of oral health within educative, preventive and curative perspectives.

CONCLUSION

This study demonstrated that the antineoplastic treatment of the population investigated had poor impact

Table 4. Association between the median value of the domains and total score of the instrument B-ECOHIS with sociodemographic and clinical variables in pediatric patients in chemotherapy treatment of an oncologic treatment clinic in Paraíba

Variable		Domain oral symptoms	Domain functional impairment	Domain Psychological	Domain self image/social interaction	Family stress	Family function	Total score
		Median (value minimum-maximum)	Median (value minimum-maximum)	Median (value minimum-maximum)	Median (value minimum-maximum)	Median (value minimum-maximum)	Median (value minimum-maximum)	Median (value minimum-maximum)
Age	2	1.0 (0-2)	4.0 (0-5)	1.0 (0-3)	0.0 (0-2)	0.0 (0-3)	1.0 (0-3)	7.0 (1-13)
	3	1.0 (0-2)	3.0 (0-6)	1.0 (0-4)	0.0 (0-1)	0.0 (0-3)	1.0 (0-3)	8.0 (0-14)
	4	1.0 (0-2)	3.0 (0-6)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	8.5 (2-13)
	5	2.0 (0-3)	3.0 (0-6)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	8.0 (1-12)
	6	2.0 (0-2)	3.0 (0-7)	2.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	9.0 (0-16)
	Value of p**	0.166	0.833	0.750	0.534	0.418	0.895	0.343
Sex	Female	1.0 (0-3)	3.0 (0-6)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	7.5 (0-14)
	Male	2.0 (0-2)	3.0 (0-7)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	8.0 (0-16)
	Value of p*	**0.018**	0.292	0.919	0.310	0.495	0.179	0.087
Local	Capital (João Pessoa)	1.0 (0-2)	3.0 (0-6)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	8.0 (3-13)
	Countryside	1.0 (0-3)	3.0 (0-7)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	8.0 (0-16)
	Value of p*	0.476	0.737	0.253	0.673	0.856	0.484	0.969
Type of treatment	Chemotherapy	1.0 (0-3)	3.0 (0-7)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	8.0 (0-16)
	Chemotherapy + surgery	2.0 (0-2)	2.0 (0-5)	1.0 (0-2)	0.0 (0-1)	0.0 (0-3)	1.0 (0-3)	7.0 (3-11)
	Chemotherapy + radiotherapy	0.5 (0-2)	3.0 (0-4)	1.5 (1-2)	0.0 (0-0)	0.0 (0-3)	0.5 (0-1)	7.0 (1-9)
	Chemotherapy, radiotherapy and surgery	1.0 (0-1)	0.5 (0-6)	1.0 (1-1)	0.0 (0-0)	2.5 (2-3)	2.0 (1-3)	7.0 (6-8)
	Value of p**	0.428	0.187	**0.029**	0.425	0.124	0.479	0.178
Mucositis	Yes	2.0 (0-3)	4.0 (0-7)	2.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	9.0 (0-16)
	No	1.0 (0-2)	2.0 (0-5)	1.0 (1-4)	0.0 (0-1)	0.5 (0-3)	1.0 (0-4)	7.0 (4-13)
	Value of p*	0.080	**<0.001**	0.127	0.190	0.103	0.185	**0.019**
Xerostomia	Yes	2.0 (0-2)	3.0 (0-7)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	8.0 (1-16)
	No	2.0 (0-3)	3.0 (0-6)	1.5 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	9.0 (0-13)
	Value of p*	0.815	0.492	0.923	0.870	0.940	0.321	0.337
Mouth ulcer	Yes	2.0 (0-3)	3.0 (0-7)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	9.0 (0-16)
	No	1.0 (0-2)	3.0 (0-6)	1.0 (0-4)	0.0 (0-2)	0.0 (0-3)	1.0 (0-4)	7.0 (4-14)
	Value of p*	0.216	0.119	0.659	0.858	0.631	0.782	**0.038**

(*) Mann-Whitney Test.
(**) Kruskal-Wallis Test.

in the quality-of-life of the children and was not significant in relation to the family.

CONTRIBUTIONS

All the authors contributed substantially to the study design and conception, analysis and interpretation of the data, wording and critical review. They approved the final version to be published.

DECLARATION OF CONFLICT OF INTERESTS

There is no conflict of interests to declare.

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