

ORIGINAL ARTICLE

Oral complications in hospitalized children during antineoplastic treatment

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Abstract

Introduction: Normal cells are also affected during antineoplastic treatment, including oral mucosa cells, which potentially causes oral complications.

Objective: This study aimed to assess the prevalence of the main oral complications and the oral hygiene index in children and adolescents aged 5 to 12 years, who received chemotherapy and/or radiotherapy.

Methods: It is an observational prevalence study performed in a hospital in Southern Brazil. Data were collected from 21 hospitalized patients with a self-application questionnaire for the responsible persons of children and with an intraoral clinical examination. The indicators used were DMFT (decayed, missing, and filled teeth) for dental caries, SOHI (simplified oral hygiene index) for oral hygiene, and the presence of mucositis, xerostomia, and candidiasis.

Results: Most of the sample was male (57.1%) with average age of 8 years (sd 2.92), diagnosed with leukemia (47.6%). All patients received chemotherapy as treatment of choice and 38.1% received radiotherapy as part of the treatment. The results showed the presence of 61.9% of mucositis in patients and 28.6% of xerostomia. No patient presented candidiasis during clinical examination. As for dental caries, 66.7% of patients showed a DMFT from 4 to 16, which is considered high, and 38.1% of patients showed the presence of bacterial plaque and dental calculus.

Conclusion: It is concluded that the main oral complications in children during antineoplastic treatment were mucositis and xerostomia. It was observed a high rate of dental caries as a consequence of an inadequate oral hygiene.

Keywords: chemotherapy, radiotherapy, oral health, mucositis, xerostomia.

What is the purpose of this study?

The present study aimed to evaluate the prevalence of the main oral complications and the oral hygiene index in children and adolescents aged 5 to 12 years submitted to chemotherapy and / or radiotherapy in order to demonstrate the importance of the dental surgeon as a member of pediatric multidisciplinary oncological team.

What researchers did and found?

Oral clinical examination was carried out in patients undergoing cancer treatment. It was reported that the main oral complications in children and adolescents during the antineoplastic treatment were mucositis and xerostomia. Regarding oral health conditions, children and adolescents have a high caries rate, often associated with brushing difficulties due to oral complications of treatment.

What do these findings mean?

Due to the presence of oral problems related to the treatment of cancer, the presence of the dentist in the oncological team is vital for reducing the morbidity of these lesions. Longitudinal and full-time monitoring of the pediatric patient is necessary because of the risk of recurrence of some complications, even after ending the antineoplastic treatment.

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■ INTRODUCTION

Cancer is responsible for countless deaths worldwide, and it is the second most frequent cause of death of children older than one year¹. In Brazil, from the year 2000 to 2005, cancer was among the ten most common causes of deaths of children and adolescents aged 1 to 18 years². Nevertheless, the evolution of medicine has allowed a significant progress in cancer treatment and currently, 70% of children may be cured when diagnosed early¹. The most prevalent neoplasias in children are leukemia, lymphomas, and tumors in the central nervous system^{3,4}.

The antineoplastic treatment, like chemotherapy, has the capacity to induce cellular damage in the epithelium, oral mucosa and salivary glandular structures, impairing their functions and, consequently, promoting quantitative and qualitative alterations, which are manifested as a stomatologic complication in cancer patients⁵. Among antineoplastic treatment modalities, radiotherapy and chemotherapy, when performed mainly in the head and neck region, are characterized for nonspecifically restraining the exacerbated proliferation of neoplastic cells.

This consequently interferes with cell multiplication of tissues that physiologically require accelerated replacement, such as the oral mucosal epithelium,³ as well as affects vascularization potential and osteoblastic activity^{6,7}. Due to these and several other side effects, a number of oral complications such as mucositis and osteoradionecrosis, as well as opportunistic infections such as candidiasis, xerostomia, periodontal diseases, loss of or decreased taste, and trismus become common in patients subjected to these treatment modalities,^{8,9,10} which are responsible for creating a major discomfort to the patient, especially to children^{7,11,12}.

Such acute complications because of the antineoplastic treatment may have a high impact on quality of life, oral health, and general health of patients, leading to the interruption of oncological treatment and consequently increasing the risk of disease persistence;^{13,14} they also increase the difficulty in maintaining oral hygiene and accepting dental treatment^{3,4,6}. The adoption of a sugar-rich and extremely cariogenic diet is quite common among pediatric patients, due to hyposalivation and loss of or decreased taste. These factors, associated with the direct result of radiation on dental tissues, lead to an increase in caries occurrence^{3,9}.

The dentist becomes essential for monitoring pediatric hospitalized patients, because of the ability for diagnosing and treating these oral complications, considering they may further aggravate the clinical condition of the patient and serve as a trigger for secondary infections, directly affecting the oncological treatment and the quality of life of the child^{8,11}.

Adopting protocols for planning the oncological treatment, primarily focusing on control and careful oral hygiene before the antineoplastic treatment, is essential for maintaining oral health, preventing the occurrence of caries and periodontal diseases. Adequacy of the oral environment and removal of potential sources of

trauma such as poorly adapted restorations, orthodontic appliances, and fractured teeth are vital for preventing the occurrence of mucositis and other complications^{4,10}. The dentist is also responsible for handling infections, bleeding prevention, and discomfort relief for better nutritional condition, thus improving the quality of life of patients with such morbidities and significantly reducing complications caused by oral inflammatory processes^{3,9,14}.

The guidance of parents and/or legal guardians of children that go through oncological treatment concerning the required procedures of oral hygiene is the foundation for preventing mucositis, caries, periodontal diseases, spontaneous bleeding, among others. The presence of the dentist in the oncological team is vital for reducing the morbidity of these lesions. Longitudinal and full-time monitoring of the pediatric patient is necessary because of the risk of recurrence of some complications, even after ending the antineoplastic treatment^{10,14}.

Therefore, after defining the importance of the dentist as part of the pediatric oncological multidisciplinary team, the present research aimed to assess the prevalence of the main oral complication and the oral hygiene index in hospitalized children and adolescents aged 5 to 12 years, who received chemotherapy and/or radiotherapy.

■ METHODS

The present study is quantitative and observational¹⁵ with prevalence design. The sample was selected by convenience, assessing children submitted to chemotherapy and/or radiotherapy admitted to Hospital São Vicente de Paulo (HSVP) in the city of Passo Fundo, RS, Brazil, from August to December 2015. Hospital São Vicente de Paulo is located in the city of Passo Fundo upstate Rio Grande do Sul, Brazil, which is the largest city in the North region of the state and it is considered a health center, assisting patient demands from the entire state of Rio Grande do Sul. This hospital is equipped with an important and modern radiotherapy and chemotherapy center of Southern Brazil.

The oncological team of HSVP includes dentists, they monitor treatment development by performing interventions in the dental area; they also perform diagnosis, prevention, and oral health promotion of patients.

Only children and adolescents aged 5 to 12 years were included, regardless of gender or ethnicity, who were under radiotherapy or chemotherapy treatment, either associated or not. Children with undefined diagnosis or in terminal stages were removed from the sample because they could not be assessed, which resulted in 21 children for assessment.

Before data collection, the research was approved by the Scientific Commission of HSVP and by the Research Ethics Committee of Faculdade Meridional, under protocol 1.176.032. All patients and their legal representatives signed the Informed Consent Form and the Consent Term accepting to participate in the research.

For collecting clinical data of the 21 children

selected, an intraoral examination was performed in patients (clinical observation) and medical records were analyzed in order to verify changes in oral mucosa (mucositis, xerostomia and candidiasis) and confirm the average number of decayed, missing, and filled teeth (DMFT) and the Simplified Oral Hygiene Index (SOHI).

Mucositis examination was performed through detailed clinical observation in the entire oral mucosa (tongue, palate, gingiva), and a score of zero (0) was assigned for absence and one (1) for presence.

Presence of xerostomia was assessed according to patient reporting and medical record analysis performed by the dentist of oncological team, and a score of zero (0) was assigned for absence and one (1) for presence.

Candidiasis was diagnosed through clinical observation of the entire oral mucosa, verifying the presence of white or yellowish plaques that were removable by scraping, which would be confirmed by the positive response to the antifungal therapy. However, there were no cases for analysis.

Periodontal condition was assessed with the SOHI proposed by Greene and Vermillion¹⁶, which measures the existence of plaque and calculi on the buccal surface of teeth 11, 31, 16, and 26 (maxillary right central incisor, mandibular left central incisor, first maxillary molars) and on the lingual surface of elements 36 and 46 (first mandibular molars). In deciduous teeth, the buccal surface of teeth 51, 71, 55, and 65 were analyzed, as well as the lingual surface of teeth 75 and 85. The Simplified Oral Hygiene Index is the combination of plaque and calculus indexes. The scales for plaque and calculus range from zero to three. In case the teeth required for examination are decayed, missing, or filled, the subsequent teeth are used to replace them. Plaque and calculus indexes are calculated separately through the sum of degrees assigned and the posterior division by the number of surfaces examined. The result of the Simplified Oral Hygiene Index is represented by plaque and calculus indexes.

Results were classified according to the following scores: 0 - satisfactory oral hygiene, and from 0.1 to 1.5 - regular oral hygiene. For assessing this index, children mouth was washed with 5 ml of plaque disclosing solution Eviplac (Biodinâmica, Ibiporã, RS, Brazil) for one minute, and all content accumulated inside the mouth was eliminated after mouth washing.

Table 1: Description of demographics, diagnosis, and cancer treatment variables of children and adolescents admitted to HSVP, in the city of Passo Fundo, 2015.

Demographics, diagnosis, and treatment variables	n (21)	% (100)
Sex		
Female	9	42.9
Male	12	57.1
Age		
5 to 8 years	11	52.4
9 to 12 years	10	47.6
Cancer diagnosis		
Brain stem glioma	1	4.8
Leukemia	10	47.6

For dental caries, the DMFT index proposed by Klein and Palmer¹⁷ was used. Index values were classified as low to moderate DMFT (0.0-3.0) and high DMFT (4.0-16.0)¹⁷.

Patients were examined by a dentist, who was previously trained and had performed a 2-month hospital internship in the oncology department, along with the multidisciplinary team of the hospital. Ten children from 5 to 12 years old were examined in the dental clinic of Instituto Meridional in order to train the examiner and perform the Kappa test for DMFT and SOHI indexes. The inter-examiner result by the Kappa test for dental caries was $K=0.87$, which was considered excellent. For bacterial plaque and dental calculus, the result was $K=0.79$, which was considered good. The clinical examination was performed complying with biosafety rules, aided by a disposable mouth opener, a flashlight, and full PPE - lab coat, head cover, mask, and gloves, in an illuminated area, with patients seated in a hospital chair while waiting for the medical appointment. Clinical examination was performed in children while they received chemotherapy drugs at the chemotherapy department of said hospital.

Besides clinical examination, a self-application questionnaire based on previous studies^{4,13,18} and modified by the author was applied, including questions directed to the patient and/or their legal representatives, in order to classify patients according to their age, gender, type of cancer, oral hygiene habits, and signs and symptoms of oral complications before and after treatment.

After collection, data were statistically managed by the software SPSS 20.0 for Windows to perform descriptive analyses and variables prevalence. The results are shown in a table with relative and absolute values to verify the frequency distributions found.

RESULTS

From the 21 individuals assessed in the study, the majority was male (57.1%) with average age of 8 years (sd 2.92). From the total individuals, 10 were diagnosed with leukemia (47.6%), while the remaining 11 were diagnosed with varied types of tumors. Table 1 describes variables such as cancer diagnosis and antineoplastic therapy modality performed in children admitted to HSVP.

Continuation - Table 1: Description of demographics, diagnosis, and cancer treatment variables of children and adolescents admitted to HSVP, in the city of Passo Fundo, 2015.

Demographics, diagnosis, and treatment variables	n (21)	% (100)
Burkitt's lymphoma	1	4.8
Rhabdomyosarcoma	1	4.8
Ewing's sarcoma	2	4.8
Wilms Tumor	1	4.8
Leg tumor	1	4.8
Brain tumor	3	14.3
Kidney tumor	1	4.8
Chemotherapy		
Yes	21	100
No	0	0
Radiotherapy		
Yes	8	38.1
No	13	61.9

Table 2 and Table 3 show the oral hygiene habits variables and oral complications variables of the sample. From the 21 children interviewed, none of them presented any oral change prior to the oncological treatment. However, regarding complications diagnosed for these children, 13 (61.9%) were cases of mucositis and 8 (28.6%) cases of xerostomia. From the patients

examined, 13 (61.9%) did not have bacterial plaque and dental calculus, so their oral hygiene was classified as satisfactory. Nonetheless, when assessing the decayed, missing, or filled teeth index (DMFT), 7 patients (33.3%) showed DMFT from 0 to 3 and the remaining 14 patients (66.7%) presented DMFT from 4 to 16.

Table 2: Description of oral hygiene habits variables of children and adolescents admitted to HSVP, in the city of Passo Fundo, 2015.

Oral hygiene habits variables	n (21)	% (100)
Toothbrushing/day		
Once	4	19
Twice	4	19
Three times or more	13	61.9
Who performs toothbrushing		
Child	14	66.7
Responsible person	4	19
Both	3	14.3
Dental visit		
Yes	18	85.7
No	3	14.3
Frequency of dental visits		
Weekly	1	4.8
Once a year	2	9.5
Every 6 months	4	19
Unknown and/or never visited	15	66.6

Table 3: Description of oral complications variables of children and adolescents admitted to HSVP, in the city of Passo Fundo, 2015.

Oral complications variables	n (21)	% (100)
Eating difficulty		
Yes	5	23.8
No	16	76.2
Diet		
Solid	20	95.2
Soft	1	4.8
Pain when performing oral hygiene		
Yes	4	19
No	17	81
Previous oral change		
No	21	100
Yes	0	0
Burning sensation to food		
Citrus	5	23.8
No	16	76.2
Candidiasis		
No	21	100
Yes	0	0
Xerostomia		
Yes	6	28.6
No	15	71.4
Mucositis		
Yes	13	61.9
No	8	38.1
DMFT		
0 to 3	7	33.3
4 to 16	14	66.7
SOHI		
0.0	13	61.9
0.1 to 1.5	8	38.1

DISCUSSION

In Brazil, leukemia is the most prevalent neoplasia in children younger than 15 years¹⁹. This agrees with the results obtained in this study, in which leukemia was the type of childhood cancer (47.1%) mostly found among the respondents, thus also agreeing with findings from other studies performed earlier with children of the same age group^{4,9,19,20}. According to Santos *et al.*¹⁸ leukemia is characterized as a malignant neoplastic hematologic disease, resulting from the irregular proliferation of a clone of hematopoietic bone marrow cells with changes in cell maturation and apoptosis. The disease may have an acute or chronic clinical condition, considering that 80% of acute leukemia in children are lymphocytic (Acute lymphocytic Leucemia- ALL), and in adults 85% are myeloblastic (Acute Myeloid Leukemia-AML).

A longitudinal prospective study with 28 patients selected in a dental clinic specialized in Oncology

observed adverse effects to the oncological treatment with chemotherapeutics and/or radiotherapeutics, more specifically verifying the presence of oral mucositis²¹.

This study identified that 61.9% of the respondents showed oral mucositis, which was the main complication identified for the antineoplastic treatment. According to Gordón-Núñez *et al.*,¹⁸ and other studies^{4,13}, the treatment for neoplastic diseases is responsible for different stomatological complications, and mucositis is highlighted with rates from 40% to 76% in such researches. Patients report that mucositis is the most debilitating side effect of cancer treatment. For the management of mucositis, maintaining good oral hygiene is important. Regarding the strategies to soften the effects of mucositis, we can mention smoothing the bristles of the toothbrushes in warm water for a few minutes, causing greater comfort during brushing, or even replacement with foam brushes. In addition, it is possible to use treatments such as oral

cryotherapy, low-intensity laser therapy^{22,23}, sodium bicarbonate washes and mouthwash of benzydamine²⁴.

Xerostomia appears as the second complication mostly found in this research, affecting 28.6% of patients. According to Lopes et al.,⁴ xerostomia is the main oral manifestation of the antineoplastic treatment; it is described as mouth dryness for being a transitory change in the functioning of salivary glands caused by antineoplastic treatments. Similarly, Kreuger *et al.*,²⁴ identified xerostomia as the main complication found in 46 of 86 medical records analyzed, as well as the study by Sera *et al.*,²⁶ in which 80.9% of patients complained about xerostomia. Such variation may be linked to different dental care protocols of pediatric patients from the institutions of the aforementioned studies, as well as to previous care obtained by the dental team before starting the antineoplastic treatment. In addition, variations of tumors and chemotherapeutics used for the treatment of these neoplasias may also cause such differences.

According to Górdon-Núñez *et al.*,¹⁹ 50% of oral infections in cancer patients corresponds to candidiasis. Lopes *et al.*,⁴ affirm this is the main fungal infection, it is evidenced by white and removable plaque on oral mucosa, tongue, and palate. In the present study, none of the children showed this condition during the period of clinical examinations. Lopes et al.,⁴ found that 41.6% of cases reported the lesion, 50% in a study by Hespagnol²⁷ and 52.3% for Sera *et al.*,²⁶ Therefore, a high discrepancy may be noticed between the results obtained in this research and similar studies. Thus, consequently facing the circumstances found, it is possible to suggest that the satisfactory oral hygiene of most children (61.9%) and proper diet habits (76.2%) may be responsible for the non-identification of candidiasis cases in the patients investigated. This fungal infection is characterized for affecting pediatric patients in neutropenia and immunosuppression status associated with poor hygiene, as well as poor nutrition from difficulties in food intake³.

Although not every patient of this research showed good oral hygiene - 38.1% had regular hygiene -, more concerning rates were identified in a study performed by Mouchrek Júnior and Trovão,¹² who identified the presence of bacterial plaque in all children examined, proving the lack of oral hygiene. Azher and Shinggaon²⁸ similarly identified the lack of oral hygiene as the main problem found in their research with hospitalized children with leukemia, aged 2 to 14 years. Thus, it may be proposed there is a satisfactory rate of oral hygiene among the children interviewed, which is caused by good education from parents and children, as well as the effective work of the dental team of the hospital where this study was performed.

As for dental caries, seven patients presented DMFT from 0 to 3, while the remaining 14 presented DMFT from 4 to 16. The high rate of caries is directly related to oral hygiene difficulties caused by complications from the treatment, such as mucositis that causes a lot of pain, or even xerostomia, considering that saliva is important for caries prevention. Lopes *et al.*,⁴ reported that mucositis is more accentuated in patients with poor oral hygiene, because the action of virus, fungi, and bacteria aggravates

the condition and causes a vicious cycle, suggesting that patients cannot perform hygiene.

When asked about the type of diet, only one patient reported having changed to soft diet, while the remaining 20 continued eating solid food. However, five patients (23.8%) reported feeling some type of difficulty for eating, while the other 23.8% of patients reported feeling their mouth burn when ingesting food such as citrus fruits. Patients did not report change in taste and they were not questioned about it; however, another study⁴ observed that taste dysfunction might occur with chemotherapy. It may be mild, known as hypogeusia, when taste change is limited to some weeks, or dysgeusia, when this change is persistent. Such variations are responsible for insufficient food intake and consequent weight loss during treatment. One study evaluated the detection of umami taste in patients with and without cancer and, although no significant statistical difference was found between umami taste thresholds and presence of cancer, sex, age and nutritional status the authors²⁹ emphasize the importance of nutritional counseling, especially in children, with the objective of not harming treatment, since children undergoing oncological treatments may experience changes in taste and appetite, impacting on nutrient consumption and immune response, affecting their rate of recovery.

In this study, 61.9% of children reported brushing their teeth three or more times per day. This result is similar when compared to the study by Barbosa *et al.*,⁹ in which 72% of patients brush their teeth three times per day, but different from the study by Sera *et al.*,²⁶ in which only 38.2% of patients do the same. It is worth noting the importance of oral health guidance during the hospitalization of the child for positive results of the oncological treatment. Deficient oral hygiene or the pre-existence of infection sites increases the risk of oral infection during chemotherapy and radiotherapy. Hence, the integration of dentist and oncologist is essential, so that, by maintaining a good level of oral hygiene, complications will be minimized⁴.

The dentist plays a vital role in providing full-time care for the patient, preventing and working on oral complications from antineoplastic therapy. This professional should be prepared to diagnose and treat such adverse effects, always instructing patients regarding oral hygiene care and monitoring their oral health before, during, and after treatment. The dentists included in the team treating these patients work for preventing and treating the different side effects found and they may adopt the use of alcohol-free oral antiseptics, artificial saliva, mouthwashes with antifungal drugs and corticoids, topical anesthetic, and laser therapy, which guarantees the improvement in quality of life and the continuation of oncological treatment^{24,25,26}. The attributions of these professionals include handling infection sites, preventing bleeding and acute oral complications, and relieving local discomfort, avoiding these conditions from interfering with diet habits and nutrition of oncological patients, thus reducing treatment side effects^{4,25,26}. In addition, one study showed that the perceptions of mothers in the chemotherapy treatment of children reflects on the way

the child perceives and adheres to it, so it is important that the dentist include the mothers in the protocols for oral health care during the performance of oncological treatments³⁰. Another strategy that can be used, not only by the dentist, as well as by all the healthcare team involved in the multidisciplinary treatment of cancer patients is the use of play strategies, since studies in this sense have demonstrated that this is able to change the conception of children with respect to the hospital environment, passing this to be perceived as a space that can provide well-being, besides being able to play^{31,32}.

It is important to highlight that outcomes of studies about oral complications in children receiving antineoplastic treatment may be explained by different

designs, diversity of sample sizes, and assessments of several indicators on the adverse effects of the oncological treatment, as well as the different types of tumors and chemotherapeutics used. Thus, the explanations should be carefully applied, not generalizing the results for the population.

■ CONCLUSION

The main oral complications in children and adolescents during the antineoplastic treatment were mucositis and xerostomia. Regarding oral health conditions, children and adolescents show a high rate of caries, which is often associated with toothbrushing difficulties due to the oral complications of the treatment.

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Resumo

Introdução: Durante o tratamento antineoplásico, células normais também são afetadas, incluindo assim, as células da mucosa oral, o que potencialmente causa complicações orais.

Objetivo: O presente trabalho teve por objetivo avaliar a prevalência das principais complicações bucais e índice de higiene oral em crianças e adolescentes submetidas à quimioterapia e/ou radioterapia.

Método: O delineamento é do tipo observacional de prevalência realizado em um Hospital do Sul do Brasil. Foram coletados dados de 21 pacientes de 5 a 12 anos de idade em tratamento, a partir de um questionário auto aplicativo para os responsáveis pelos pacientes e um exame clínico intraoral. Os indicadores utilizados foram o índice CPOD (dentes cariados, perdidos e obturados) para cárie dentária, o índice IHOS (higiene oral simplificada) para Higiene Oral e a presença de mucosite, xerostomia e candidíase.

Resultados: A maior parte da amostra era do sexo masculino (57,1%) média de 8 anos de idade (dp 2,92), diagnosticados com leucemia (47,6%). Todos os participantes receberam quimioterapia como tratamento de escolha e 38,1% receberam radioterapia como parte do tratamento. Os resultados evidenciariam presença de mucosite em 61,9% e xerostomia em 28,6% dos pacientes. Nenhum paciente apresentou candidíase durante o exame clínico. Quanto a cárie dentária, 66,7% tem um CPOD de 4 e 16, considerado alto e 38,1% dos pacientes apresentaram presença de placa bacteriana e cálculo dentário.

Conclusão: As principais complicações bucais evidenciadas durante o tratamento antineoplásico foram mucosite e xerostomia. Foi observado também um alto índice de cárie dentária, consequência de uma inadequada higiene oral.

Palavras-chave: quimioterapia, radioterapia, saúde bucal, mucosite, xerostomia.

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