

Childhood Cancer patients and dentist registers from a hospital: a 15-year study

Pacientes com câncer na infância e registros dentários de um hospital: um estudo de 15 anos

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ABSTRACT

The antineoplastic therapy side effects on buccal mucosa may affect patients' life quality, mainly in children and teenagers. This cross-sectional study assessed the frequency of up to 19-years-old patients treated at Hospital de Câncer de Cascavel – UOPECCAN (Cascavel Cancer Hospital) among 2000-2014, only those assisted by the institution dentist. Neoplasm, treatment, and the oral manifestations were determined. Medical records focused on gender, age, cancer classification, and treatment. Dental exams and years of assistance were collect too. From 100 patient who matched criteria the results were: male (57%), female (43%), < 1-year-old (5%), 1-4 (42%), 5-9

(25%), 10-14 (23%), and 15-19 (5%). Leukemia (48%), rhabdomyosarcoma (10%), and neuroblastoma (7%) were the most prevalent as well chemotherapy (55%). Eight six people developed oral manifestations: mucositis (34%), gingivitis (9%), caries (33%), herpetic gingivostomatitis (11%), herpes labialis (7%), candidiasis (9%), and other mixed dentition stage-related (primary tooth exfoliation and edema- 8%). The dental sector increased the number of assistance over the years. The dentist assisted half of the patients. Most of them were children under 4-year-old. Leukemia and chemotherapy were more prevalent and 86% of the sample developed oral manifestation.

Keywords: Neoplasms, Child, Adolescent, Oral Manifestations.

RESUMO

Os efeitos secundários da terapia antineoplásica na mucosa bucal podem afectar a qualidade de vida dos pacientes, principalmente em crianças e adolescentes. Este estudo transversal avaliou a frequência de pacientes com até 19 anos tratados no Hospital de Câncer de Cascavel - UOPECCAN (Hospital do Cancro de Cascavel) entre 2000-2014, apenas os assistidos pelo dentista da instituição. Foram determinados o neoplasma, o tratamento, e as manifestações orais. Os registos médicos centraram-se no sexo, idade, classificação do cancro, e tratamento. Também foram recolhidos exames dentários e anos de assistência. De 100 pacientes que corresponderam aos critérios os resultados foram: homens (57%), mulheres (43%), < 1 ano de idade (5%), 1-4 (42%), 5-9 (25%), 10-14 (23%), e 15-19 (5%). Leucemia (48%), rabdomiossarcoma (10%), e neuroblastoma (7%) foram os mais prevalentes, bem como a quimioterapia (55%). Oito seis pessoas desenvolveram manifestações orais: mucosite (34%), gengivite (9%), cárie (33%), gengivostomatite herpética (11%), herpes labial (7%), candidíase (9%), e outras relacionadas com o estágio de dentição mista (esfoliação primária dos dentes e edema - 8%). O sector dentário aumentou o número de assistência ao longo dos anos. O dentista prestou assistência a metade dos pacientes. A maioria deles eram crianças com menos de 4 anos de idade. A leucemia e a quimioterapia foram mais prevalentes e 86% da amostra desenvolveu manifestação oral.

Palavras-chave: Neoplasmas, Criança, Adolescente, Manifestações Orais.

1 INTRODUÇÃO

The antineoplastic therapies (AT) target malignant cells, preferably those in mitosis¹. As buccal mucosa cells present similar state, secondary effects^{2, 3} might worse patients' life quality^{1, 2}, particularly children and teenagers^{3, 4}. So, the injuries' gravity the internment time tends to increase, as well as the treatment costs².

Recently, a study showed oral manifestation in 40% who underwent AT, which percentage increased to 90% for those under 12-year-old⁴. The younger the greater the chance of injury given children's growth and development⁵.

As far as we know, a wide range of oral AT related lesions was reported: mucositis, temporary xerostomia, immunodepression⁶⁻⁸, taste changes, dysphagia, trismus, radiation caries, osteoradionecrosis^{3,5}, gingival bleeding¹, dental germs development disturbs¹. In addition, the

deciduous to mixed dentition transition may difficult to maintain buccal hygiene and predispose other problems³.

Indeed, preparing the oral environment previously to the AT reduces the complication risk and impacts the internment time⁹. In this sense, the dental surgeon in the cancer treatment team is an urgent demand^{1,2,4} so is the investigation of oral manifestations of children who were assisted by a dentist during AT.

Thus, the percentage and the demographic profile from childhood cancer (CC) patients assisted by a dentist of a cancer hospital for 15 years were assessed. The neoplasm and treatment types, oral manifestations, and mixed dentition related changes not described previously were determined.

2 METHODOLOGY

State University of West Paraná (2.958.385) and Hospital de Câncer de Cascavel – UOPECCAN (Cascavel Cancer Hospital) Ethics Committees approved this cross-sectional study, according to Resolution 466/12 of the Health National Council.

2.1 STUDY DELIMITATION AND PATIENT SELECTION

All children and teenagers up to 19-year-old medical reports (printed and electronic) diagnosed and treated for any topography primary malignant neoplastic disease from that hospital between 2000 and 2014 were checked. Only those who have been assist by the dentist were eligible. Diagnosis confirmation was mandatory: histopathological, cytopathological, hematological/blood count, exploratory surgery, image, clinical, or any other exam¹⁰. The exclusion criteria were: 1) benign or uncertain behavior tumors; 2) who started AT in another hospital (missing diagnosis reports), and 3) patients transferred to other hospitals.

2.2 DATA COLLECT

Data were collected among October 2018 to July 2019:

- a)** Gender: male (M) or female (F);
- b)** Age (Brazilian Cancer National Institute Age Classification): < 1-year-old; 1 to 4; 5 to 9; 10 to 14 and 15 to 19¹¹;
- c)** Neoplasm type - International Classification of Childhood Cancer (ICCC) based on the International Classification of Diseases (ICD)¹²;
- d)** AT [chemotherapy (CT); radiotherapy (RT); surgery (S); bone marrow transplant (BMT)].
Dentist records provided clinical exam data and attendance year.

2.3 STATISTICAL ANALYSIS

The data were tabulate in Microsoft Excel (2010) and presented by descriptive statistics.

3 RESULTS

Out of the 247 reports/cases presented by the hospital, 201 followed matched the sample criteria. Only 100 were assist by the dental service, and all after the antineoplastic therapy: 57% male and 43% female. The age group results were < 1-year-old (5%), 1-4 (42%), 5-9 (25%), 10-14 (23%), and 15-19 (5%). Lymphoid leukemias affected 48 patients (48%), rhabdomyosarcomas 10 (10%) and neuroblastomas 7 (7%) (Table 1). The most used AT was CT-only (55%) or in association to other one (41%) (Table 2).

Tables 3 and 4 present oral manifestations by gender, age-group, and AT, seen in 86% reports; 7% unallowed the exam. The most prevalent was labial dryness (43%), mucositis (34%), and caries (33%). Sometimes they had more than one (greater than 100%). Only 7% were oral manifestations-free. Graphic1 shows the patient percentage by year.

4 DISCUSSION

Overall results highlight trained dentists¹³ should be part of the CC treatment team^{3,4} especially the pediatric dentist¹⁴. Providing ongoing care to the patients would be mandatory since 86% presented oral changes (Tables 3 and 4). Although half of the included patients had received dental care (Table 3), the appointment number throughout the years (Graphic 1) illustrate the UOPECCAN-Cascavel commitment with the effect of AT over oral health, emphasized since last century¹⁵. It is possible whom unallowed dental evaluation (Table 3) may have resorted to external assistance. When no longer under control or uncontrolled, systemic organic disorders and or oral manifestations could have worse their general condition^{3,4}.

Certainly, treatment is CC classification related. The high prevalence of acute lymphoid leukemia (ALL)^{10,16,17} (Table 1) and the number of CT^{1,18} (Table 2) shows it. Therefore, we focused on oral CT effects. The exclusion of non-assisted patients by dentist at the hospital may support the neoplasms frequency divergences^{10,16,17}.

CT impacts on the childhood cancer survivors' life quality are known^{3,4,15,19,20}. It raises the treatment cost at both private and public health levels because of the risk of developing other diseases²¹. Besides the common symptoms,⁶ others were observed: infections (of dental origin as well as bacterial, fungal, and viral), soft/dental tissues changes, and findings related to dentition transition or poor oral hygiene (Table 3). Local trauma, oral microbiota changes, compromised immune system^{1,7,10,14,22} also predispose the development of such manifestations.

Viral and fungal disease data (Table 3) illustrate dental evaluation previously to AT and control of children's immunosuppression are fundamental. Infections pre-exist in 60% of cases². Also, the selectivity and severity of CT related immunosuppression depend on the nature and specificity of the agents²². In this respect, neutropenia makes them more vulnerable to oral cavity opportunistic infections^{2,23} interfering in the therapeutic protocols and worsen the systemic condition². Although this not yet evaluated association, the present study has observed some infection records (Table 3): herpetic gingivostomatitis (HGS) (11%), recurrent herpes labialis (HSV) (7%), and candidiasis (9%)^{4,6,7,19}. The higher prevalence of the HGS in comparison to the HSV contrasts to another study¹⁹. Probably it is due to the under 5-year-old children on the sample (Table 3). HSG (the primary HSV manifestation)²⁴ is common this age. Despite the low frequency of candidiasis (Table 3), fungal septicemia may lead to death². Oral mucosa integrity damages and xerostomia increase the risk of infections⁷.

Mucositis is the most prevalent complication caused by AT in patients with CC^{2,6,7}. It is related to CT in high doses, head and neck RT, and BMT²⁵. However, the low prevalence observed (34%) (Table 3) seems not to reflect reality. No-specified oral injury (24%) and the erythematous mucosa (6%) registers might have underestimated mucositis frequency. Once the oral epithelium basal cells destructed, edema, reddish inflammation areas, and bleeding occur. Advancing to ulcers causes intense pain, discomfort, dysphagia, sleep disorders, eating difficulties, and poor oral hygiene; consequently, systemic debilitation^{2,6}. Thus, adopting a proper protocol to assess and follow-up mucositis would simple diagnosis.

Xerostomia is also a frequent effect^{8,26} but was low prevalent. This result probably agrees to the most affected age group (5-year-old above) (Table 3) because younger children sometimes unsuccessful report xerostomia sensations²⁷. Although uncommon and transitory in children, xerostomia may be seriously in advanced cancer²⁸. Besides, literature reports other related conditions: odynophagia (5%), burning mouth (2%), taste change (1%), hypersensitivity (1%) and halitosis (1%)^{6,7}. Thus, dentists should equally investigate the salivary function and subjective sensations.

Less than half of the patients showed labial dryness (Table 3), which is easy for themselves, dentist, and guardians to detect. Despite the high prevalence reported¹⁹, it seems uncaused exclusively by AT, because this condition involves the geographical climate region and water intake habits, among others.

Caries lesion was prevalent and progression related infection focus (residual root, pulp necrosis, fistula, and abscess) was found (Table 3). Mature dental biofilm, gingivitis, gingival bleeding, dental calculus formation, and tongue coating would be the pain cause (in mouth, gingiva

or, teeth) (Table 3)^{6,7}. It is inappropriate to comment that when dental evaluation previous to AT is unavailable^{3,29,30}. So, there is a need for dentists to register, control, and follow up all caries related changes, and cariogenic diet¹. Oral health orientations toward toothbrushing and flossing to prevent periodontal diseases³¹ should have been mandatory¹ (at the hospital or back home). Therefore, the risk of mucositis, fever, and bacteremia³² would be lower. Planned periodontal treatment in the CT cycle intervals would reduce febrile neutropenia too^{31,32}.

Exfoliation and erupting tooth stages predispose to dental biofilm accumulation³ might cause inflammation gingival (Table 3). This condition in CC patients was so far absent in the literature. It is a time to reinforce using flossing and toothbrushing to minimize or even prevent systemic issues periodontal disease development related^{1,4}. Moreover, changing the oral hygiene subjective evaluation data to indexes would be more consistent for retrospective studies.

Evidence supports CT affects odontogenesis: microdontia, macrodontia, root or crown malformation, premature apexification, unerupted teeth, and taurodontism, among others^{26,33,34}. We found agenesis in a 5-year-old child and so ankylosis in a 12-year-old one. Only 7% had dental color change^{4,29}. Thus, long-term follow-ups are needed³³.

Undergo AT patients challenge dentists to be prepared to diagnose, prevent, and treat oral manifestations. We emphasize the importance of dental assistance at the treatment beginning^{13,25,34} to adhere better to the treatment of improving individuals life quality²⁰.

5 CONCLUSION

The dentist assisted half of the patients. Most of them were children under 4-year-old. Leukemia and chemotherapy were more prevalent and 86% of the sample developed oral manifestation.

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ATTACHMENTS

Table 1 – Frequency of neoplasia types in patients seen by the dentist (n=100).

Parameter	n	%
Leukemia, myeloproliferative diseases and myelodysplastic diseases		
Lymphoid leukemias	48	48.00%
Acute myeloid leukemias	4	4.00%
Reticuloendothelial lymphomas and neoplasms		
Hodgkin lymphoma	3	3.00%
Non-Hodgkin lymphoma (except Burkitt lymphoma)	1	1.00%
Burkitt lymphoma	2	2.00%
CNS tumors and different intracranial and intraspinal neoplasms		
Astrocytomas	1	1.00%
Embryonic intracranial and intraspinal tumors	4	4.00%
Other specified intracranial and intraspinal neoplasms	1	1.00%
Non-specified intracranial and intraspinal neoplasms	1	1.00%
Neuroblastoma and other peripheral nerve cells tumors		
Neuroblastoma and ganglioneuroblastoma	7	7.00%
Renal tumors		
Nephroblastoma and other non-pelvic renal tumors	4	4.00%
Hepatic tumors		0.00%
Hepatoblastoma	2	2.00%
Malignant bone tumors		
Osteosarcomas	2	2.00%
Soft tissue and other extraosseous sarcomas		
Rhabdomyosarcomas	10	10.00%
Other specified soft tissue sarcomas	1	1.00%
Non-specified soft tissue sarcomas	1	1.00%
Germ cell tumors, trophoblastic tumors and gonadal neoplasms		
Intracranial and intraspinal germ cell tumors	1	1.00%
Malignant gonadal germ cells tumors	2	2.00%
Other malignant epithelial neoplasms and malignant melanomas		
Adrenocortical carcinomas	3	3.00%
Other non-specified carcinomas	2	2.00%
Total	100	100%

CNS: Central Nervous System

Table 2 – Frequency of the treatment made in patients seen by the dentist (n=100).

<u>Treatment</u>	<u>N</u>	<u>%</u>
CT	55	55.00%
CT + RT	9	9.00%
CT + RT + surgery	8	8.00%
CT + RT + BMT	2	2.00%
CT + surgery	17	17.00%
CT + BMT	5	5.00%
RT	1	1.00%
RT + surgery	1	1.00%
<u>Surgery</u>	<u>2</u>	<u>2.00%</u>
<u>Total</u>	<u>100</u>	<u>100%</u>

CT: chemotherapy; RT: radiotherapy; BMT: bone marrow transplant

Table 3 – Frequency of the oral changes diagnosed by the dentist divided by gender and age group (n=100).

Parameter	N	%	Gender		Age group					
			M	F	< 1	1-4	5-9	10-14	15-19	
Oral manifestations										
Labial dryness	43	43%	22	21	0	18	12	12	1	
Mucositis	34	34%	20	14	4	12	8	9	1	
Non-specified oral injury	24	24%	13	11	0	11	6	5	2	
Traumatic injury	12	12%	5	7	1	6	2	2	1	
Xerostomia	8	8%	3	5	0	1	2	4	1	
Erythematous mucosa	6	6%	2	4	0	4	0	1	1	
Gingival bleeding	6	6%	1	5	0	3	2	1	0	
Mouth pain	6	6%	3	3	0	2	2	2	0	
Odynophagia	5	5%	3	2	0	1	1	3	0	
Toothache	4	4%	1	3	0	3	1	0	0	
Biting of oral mucosa	3	3%	2	1	0	1	1	1	0	
Gingiva pain	3	3%	1	2	0	2	0	1	0	
Burning mouth	2	2%	1	1	0	1	0	1	0	
Taste changes	1	1%	1	0	0	0	0	1	0	
Gingival peeling	1	1%	0	1	0	0	0	1	0	
Hypersensitivity	1	1%	1	0	0	1	0	0	0	
Halitosis	1	1%	1	0	0	1	0	0	0	
Changes related to oral hygiene difficulty										
Gingivitis	9	9%	4	5	0	2	2	4	1	
Dental biofilm	7	7%	5	2	0	1	1	3	2	
Dental calculus	2	2%	1	1	0	1	0	1	0	
Tongue coating	1	1%	0	1	0	0	0	1	0	
Infections										
Herpetic gingivostomatitis	11	11%	8	3	0	3	4	3	1	
Candidiasis	9	9%	2	7	0	4	2	1	2	
Recurrent herpes labialis	7	7%	5	2	0	2	3	2	0	
Dental abscess	2	2%	1	1	0	0	2	0	0	
Angular cheilitis	1	1%	0	1	0	0	0	1	0	
Mouth stomatitis	1	1%	1	0	0	1	0	0	0	

Non-specified viral infection	1	1%	1	0	0	1	0	0	0
Fistula	1	1%	1	0	0	1	0	0	0
Non-specified infection focus	1	1%	0	1	0	0	1	0	0
Teeth structure changes									
Caries	33	33%	20	13	0	12	10	9	1
Color change	7	7%	1	6	0	4	1	2	0
Crown fracture	3	3%	3	0	0	2	0	1	0
Residual root	2	2%	2	0	0	0	0	1	1
Pulp necrosis	2	2%	1	1	0	2	0	0	0
Agenesis	1	1%	0	1	0	1	0	0	0
Ankylosis	1	1%	1	0	0	0	0	1	0
Factor related to dentition exchange									
Deciduous exfoliation	8	8%	3	5	0	3	3	2	0
Edema in the dental region	8	8%	5	3	0	3	2	3	0
Erupting teeth	5	5%	3	2	2	2	0	1	0
Pericorony hood	3	3%	1	2	0	1	1	1	0
Have not allowed exam	7	7%	1	6	0	6	1	0	0

M: male; F: female

Table 4 – Frequency of the oral changes in the patients seen by the dental sector divided by antineoplastic therapy (n=100).

Parameter	N	%	CT	CT + RT	CT + RT + surgery	CT + RT + BMT	CT + surgery	CT + BMT	RT + surgery
Oral manifestations									
Labial dryness	43	43%	28 28%	0 0%	5 5%	2 2%	7 7%	1 1%	0 0%
Mucositis	34	34%	24 24%	1 1%	3 3%	1 1%	5 5%	0 0%	0 0%
Non-specified oral injury	24	24%	19 19%	0 0%	0 0%	2 2%	2 2%	1 1%	0 0%
Traumatic injury	12	12%	8 8%	0 0%	0 0%	0 0%	2 2%	2 2%	0 0%
Xerostomia	8	8%	4 4%	1 1%	1 1%	0 0%	1 1%	1 1%	0 0%
Erythematous mucosa	6	6%	4 4%	0 0%	1 1%	0 0%	0 0%	1 1%	0 0%
Gingival bleeding	6	6%	5 5%	0 0%	1 1%	0 0%	0 0%	0 0%	0 0%
Mouth pain	6	6%	3 3%	1 1%	0 0%	1 1%	0 0%	1 1%	0 0%
Odynophagia	5	5%	3 3%	0 0%	0 0%	0 0%	2 2%	0 0%	0 0%
Toothache	4	4%	3 3%	0 0%	0 0%	0 0%	1 1%	0 0%	0 0%
Biting of oral mucosa	3	3%	3 3%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
Gingiva pain	3	3%	0 0%	1 1%	1 1%	0 0%	1 1%	0 0%	0 0%
Burning mouth	2	2%	1 1%	0 0%	0 0%	0 0%	1 1%	0 0%	0 0%
Taste changes	1	1%	1 1%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
Gingival peeling	1	1%	0 0%	0 0%	0 0%	0 0%	1 1%	0 0%	0 0%
Hypersensitivity	1	1%	0 0%	1 1%	0 0%	0 0%	0 0%	0 0%	0 0%
Halitosis	1	1%	1 1%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
Changes related to oral hygiene difficulty									
Gingivitis	9	9%	5 5%	3 3%	0 0%	1 1%	0 0%	0 0%	0 0%
Dental biofilm	7	7%	3 3%	3 3%	0 0%	0 0%	0 0%	1 1%	0 0%
Dental calculus	2	2%	1 1%	0 0%	0 0%	1 1%	0 0%	0 0%	0 0%
Tongue coating	1	1%	1 1%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%
Infections									
Herpetic gingivostomatitis	11	11%	8 8%	1 1%	1 1%	0 0%	0 0%	1 1%	0 0%
Candidiasis	9	9%	5 5%	0 0%	0 0%	0 0%	3 3%	1 1%	0 0%

Recurrent herpes labialis	7	7%	7	7%	0	0%	0	0%	0	0%	0	0%	0	0%		
Dental abscess	2	2%	2	2%	0	0%	0	0%	0	0%	0	0%	0	0%		
Angular cheilitis	1	1%	1	1%	0	0%	0	0%	0	0%	0	0%	0	0%		
Mouth stomatitis	1	1%	1	1%	0	0%	0	0%	0	0%	0	0%	0	0%		
Non-specified viral infection	1	1%	1	1%	0	0%	0	0%	0	0%	0	0%	0	0%		
Fistula	1	1%	0	0%	0	0%	0	0%	0	0%	1	1%	0	0%		
Non-specified infection focus	1	1%	1	1%	0	0%	0	0%	0	0%	0	0%	0	0%		
Teeth structure changes																
Caries	33	33%	20	20%	3	3%	2	2%	1	1%	4	4%	2	2%	1	1%
Color change	7	7%	4	4%	1	1%	1	1%	0	0%	1	1%	0	0%	0	0%
Crown fracture	3	3%	3	3%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Residual root	2	2%	0	0%	1	1%	0	0%	0	0%	0	0%	0	0%	1	1%
Pulp necrosis	2	2%	1	1%	0	0%	0	0%	0	0%	1	1%	0	0%	0	0%
Agenesis	1	1%	0	0%	0	0%	0	0%	0	0%	1	1%	0	0%	0	0%
Ankylosis	1	1%	1	1%	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Factor related to dentition exchange																
Deciduous exfoliation	8	8%	6	6%	1	1%	0	0%	0	0%	1	1%	0	0%	0	0%
Edema in the dental region	8	8%	5	5%	1	1%	1	1%	0	0%	0	0%	1	1%	0	0%
Erupting teeth	5	5%	2	2%	1	1%	0	0%	0	0%	2	2%	0	0%	0	0%
Pericorony hood	3	3%	2	2%	0	0%	0	0%	0	0%	1	1%	0	0%	0	0%

CT: chemotherapy; RT: radiotherapy; BMT: bone marrow transplan

Graphic 1 – Year in which the patients were seen by the dental sector (n=100)

Year of the dental care service

