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Orofacial dysfunctions in infants and young children with acute leukemia

Disfunções orofaciais em pacientes infantojuvenis com leucemia aguda

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ABSTRACT

Purpose: To Identify the occurrence of orofacial dysfunctions in young children and adolescents with acute leukemia who are undergoing remission chemotherapy. **Methods:** Over a period of 16 months, 40 three to eighteen year -old patients with acute leukemia were admitted to the Amazonas State Hemocenter. Of these, 23 were included in the cross-sectional study and submitted to the evaluation of orofacial functions using the Nordic Orofacial Test-Screening, between D30 and D33 of the remission induction phase. The presence of oral manifestations was also evaluated via clinical examination. **Results:** Orofacial dysfunction was observed in approximately half of the evaluated cases (n=11). Of these patients, all had alterations in the Dryness of the Mouth (VI) domain and 81.8% (n=9) showed alterations in the Chewing and Swallowing (IV) domain. Mucosites on lips, tongue, floor of the mouth and the oropharynx were the most commonly found oral lesions after the remission induction phase. According to the NOT-S, there was an association between the occurrence of oral lesions in the evaluated patients and the presence of orofacial dysfunction (95% CI, p-value = 0.027). **Conclusion:** It is suggested that orofacial dysfunction is frequent in the remission induction phase in children and adolescents with acute leukemia. Studies regarding these orofacial dysfunctions in this population, as well as their relationship with oral lesions, are needed in order to fully understand their functional impact.

Keywords: Acute leukemia; Orofacial dysfunction; Oral manifestations; Stomatognathic system; Dysphagia

RESUMO

Objetivo: Identificar a ocorrência de disfunções orofaciais em pacientes infantojuvenis com leucemia aguda, submetidos à quimioterapia de remissão. **Métodos:** Em um período de 16 meses, 40 pacientes com leucemias agudas, entre 3 e 18 anos de idade, foram admitidos em um hemocentro no estado do Amazonas. Destes, 23 foram incluídos neste estudo transversal e submetidos à avaliação das funções orofaciais, por meio do *Nordic Orofacial Test-Screening* (NOT-S), entre o trigésimo (D30) e o trigésimo terceiro dia (D33) da fase de indução da remissão. A presença de manifestações orais também foi avaliada por meio de exame clínico. **Resultados:** Disfunção orofacial foi observada em, aproximadamente, metade dos casos avaliados (n=11). Destes pacientes, todos tiveram o domínio Secura de Boca (VI) alterado e 81,8% (n=9) apresentaram alteração no domínio Mastigação e Deglutição (IV). Mucosites em lábios, língua, soalho e orofaringe foram as lesões orais mais encontradas após a fase de indução. Houve associação entre a ocorrência de lesões orais nos pacientes avaliados e a presença de disfunção orofacial, segundo o NOT-S (IC 95%, p-valor = 0,027). **Conclusão:** Sugere-se que a disfunção orofacial seja frequente na fase de indução da remissão em pacientes infantojuvenis com leucemias agudas. Estudos sobre as disfunções orofaciais nessa população, bem como sua relação com as lesões orais são necessários para melhor esclarecimento e compreensão dos impactos funcionais.

Palavras-chave: Leucemia aguda; Disfunção orofacial; Manifestações orais; Sistema estomatognático; Disfagia

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INTRODUCTION

Acute leukemias are among the most common malignant hematological neoplasms in childhood. In pediatric patients it is highly curable and, with the advances in chemotherapy treatment, survival rates have increased significantly. The causes of acute leukemias are still unknown, but the literature reports some possible causes such as viral infections, radiation and exposure to chemical substances[1].

In Brazil, between the years 2018 and 2019, there were about ten thousand cases of the disease, placing it among the most prevalent cancers in the country. In the northern region, the incidence rate presented was from nine to ten cases per 100 thousand inhabitants, with 160 cases diagnosed in 2018[2]. The Amazonas Hematology and Hemotherapy Foundation (HEMOAM) is the reference center for the diagnosis and treatment of hematological diseases in the region, among them leukemias.

The treatment of acute leukemias involves the adoption of prolonged chemotherapy regimens, which can vary between two and three years and, in cases of resistant neoplasms or relapses, bone marrow transplantation is also used. Although the chemotherapy protocols applied in the blood centers may differ, the most current ones possibly include the following five phases: induction of remission, intensification-consolidation, re-induction, prevention of leukemia in the central nervous system and maintenance[3,4].

In the remission induction phase, the goal of chemotherapeutic drugs is to eliminate all the leukemic cells (blasts) present in the blood[5]. In the oral cavity, the action of chemotherapeutic drugs in this phase can generate several manifestations and complications, among them, mucosites, candidiasis, periodontitis, gingivitis, xerostomia and dysphagia[6,7].

Chemotherapy is highly toxic due to the excretion of the drugs by the salivary glands and their systemic circulation, and it can affect all oropharyngeal structures and, consequently, compromise orofacial functions. Some neurological complications may also be present in acute leukemias. Among these complications, there are reports in the literature of alterations in tongue mobility, difficulty swallowing, hypotonia of the masticatory muscles and sensory alterations involving the lips and tongue[5-7].

Difficulty when swallowing can contribute to reduced food intake and malnutrition. When not identified or not properly managed, it leads to a difficulty swallowing that tends to be prolonged due to muscle atrophy as a result of lack of nutrients[8]. Understanding the impacts on chewing and swallowing functions in this population is essential, since the treatment itself is affected due to the patient's difficulty in feeding due to the difficulty the patient may have when feeding, either due to mechanical issues or due to the hypersensitivity generated by oral lesions, which may compromise nutrition and quality of life.

Therefore, in relation to oral manifestations, the evaluation of stomatognathic functions by a speech therapist is essential for the diagnosis of orofacial dysfunctions within a multidisciplinary approach. The knowledge of anatomical and functional aspects allows the speech therapist to establish clinical reasoning and plan therapeutic strategies for rehabilitation of the patient[9].

Based on our research in the literature, and up until the conclusion of this study, references to orofacial dysfunctions in patients with acute leukemia undergoing chemotherapy are scarce, and are composed of case reports unrelated to orofacial dysfunctions, and only cite them as symptoms[10,11]. In addition, there are no protocols for screening or evaluating these dysfunctions in this population. Therefore, the objective of this research was to identify the occurrence of orofacial dysfunctions in infants and young children diagnosed with acute leukemia and that are undergoing remission chemotherapy.

METHODS

This research represents an observational, cross-sectional and descriptive/analytical study organized according to the STROBE checklist - *Strengthening the Reporting of Observational Studies in Epidemiology*[12]. This study was approved by the Research Ethics Committee of the Fundação Hospitalar de Hematologia e Hemoterapia do Amazonas (HEMOAM), under protocol 4.353.177 (CAAE: 19053619.0.0000.0009). All patients and/or guardians signed the informed consent form (ICF) or informed assent form (IAF).

In this study, a convenience sample was adopted that was composed of children aged between 3 and 18 years of age, of either of the gender, who had been diagnosed with acute leukemia in the remission induction phase, and were under two therapeutic protocols throughout the collection, namely the Brazilian Treatment Group for Childhood Leukemia (GBTLI LLA-2009) and German Berlin-Frankfurt-Munich Group (ALL IC-BFM 2009). All patients were hospitalized in the Hematology Center in the state of Amazonas between September 2019 and December 2020. The sample was subdivided into two groups: pediatric patients, aged 3 to 12 years, and adolescent patients, aged over 12 years. This subdivision has only a descriptive character and served as a basis for the characteristics and craniofacial development.

Patients who had already started their chemotherapy treatment, cases restarted due to relapse of the disease, syndromic patients, who had had head and/or neck surgery, with a history of neurological alterations, with a nasoenteral probe and/or tracheostomy, as well as absence of incisor teeth or molars/premolars during the evaluation period, patients who had died, were transferred or were discharged before the last day of the remission induction phase were all excluded from the study. (Figure 1).

During the first contact with the patient, which occurred in the second week after the start of treatment (D15), socio-demographic data and body weight parameters were obtained. The percentages of weight loss during remission induction (D0 and D33) were obtained from the patients' records and subsequently analyzed considering as a cut-off point any significant loss greater than 5% in one month[13].

Between D30 and D33, the patients were evaluated by the dental surgeon at the hematology center. The data obtained in the dental evaluation were related to oral hygiene conditions, type of dentition, delay in dental eruption, presence of soft tissue lesions and oral mucositis score based on the World Health Organization's toxicity scale (WHO)[14].

The evaluation of orofacial functions followed the Brazilian version of the validated protocol NOT-S (Nordic Orofacial Test-Screening), which was performed at the end of the remission induction phase, after the dental evaluation. The individualized evaluations were performed by the researcher according to the protocol available at Leme et al.[15].

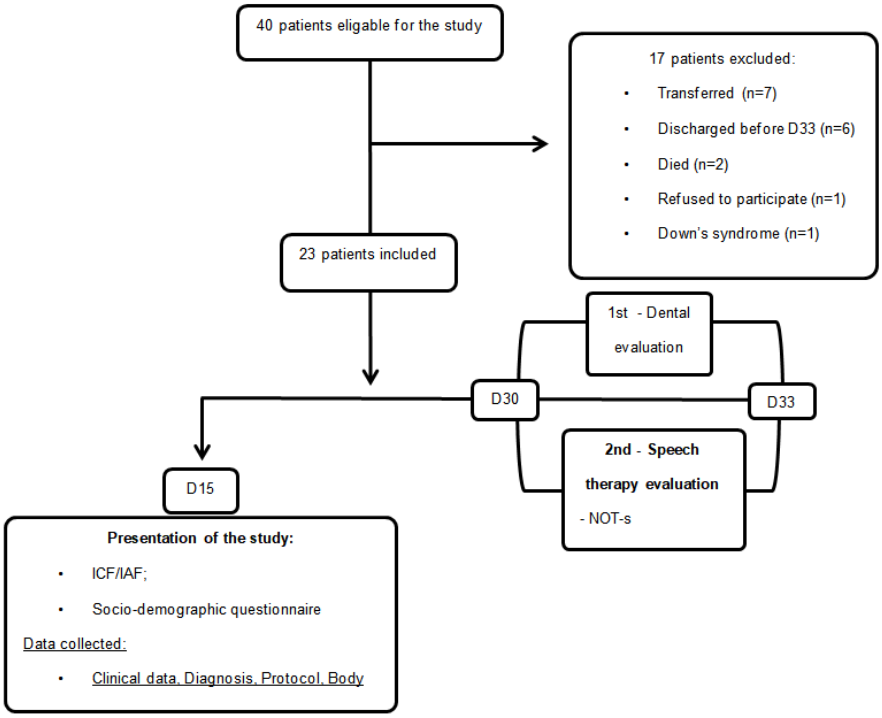

Figure 1. Study flowchart
Subtitle: n = number of patients; D15: Fifteenth day of treatment in the remission induction phase; ICF/IAF: Informed consent form and informed assent form; D30: Thirtieth day of treatment in the remission induction phase; D33: Thirty-third day of treatment in the remission induction phase; NOT-S: Nordic Orofacial Test-Screening.

The NOT-S protocol is subdivided into two stages: structured interview and clinical examination (Chart 1), and both contain six domains each, totaling 12 domains. The first stage (interview) was carried out with the parents or guardians of the participants under the age of 12 years, or directly with the participants over the age of 12 years, with the support of the parents/guardians. Initially, the first stage addressed questions already established in the protocol itself. The questions described in the protocol referred to observations and daily habits of the minor, intraoral sensitivity, snoring/apnea, presence of deleterious oral habits, coughing during meals, difficulty with more solid foods, sialorrhea, xerostomia and pain in the oral mucosa. Then, in the second stage (clinical examination), the following aspects were evaluated: posture, mobility and tonicity of the intra and extraoral muscles, respiratory mode, mobility and tonicity of the chewing and swallowing muscles, articulation and pneumophonoarticulatory coordination (PPAC).

The NOT-S instrument consists of twelve domains, scored as 1 when an alteration is found. Therefore, its total score can range from 0 to 12. Each of these twelve domains, composed of one or more questions, is considered altered if at least one of them is scored as a positive. According to the protocol, the presence of orofacial dysfunction in infants and young children occurs when the patient has a score greater than or equal to 4.

All data were analyzed using Epi Info software (version 7) and IBM-SPSS (version 26). The descriptive statistics presented the measurements of position (mean), dispersion (standard deviation) and absolute and relative frequency of the variables. Categorical variables were submitted to the chi-square/Fisher's exact test with a confidence interval of 95%.

RESULTS

Of the 40 young patients identified, 23 of them were included in the survey. The mean age of the patients was 9.5 years (min. 3 years and max. 16 years) and 56.5% (n = 13) were female (Table 1). In addition, in a descriptive manner, the 23 patients evaluated were subdivided into two groups: pediatric patients and adolescent patients, according to their anatomo-functional peculiarities.

The young children (n=13), aged from 3 to 11 years, had a slightly higher prevalence in the evaluated patients, with 56.5%, while the adolescent group (n=10, 43.5%) was composed of patients aged 12 to 18 years. In addition, 91.3% (n=21) of the patients evaluated were diagnosed with acute lymphoid leukemia (ALL). Of the 23 patients, 60.9% (n=14) lived in the rural area of the state of Amazonas and 73.9% (n=17) had a family monthly income lower than one minimum wage.

The mean score of all patients evaluated using the NOT-S protocol was 3.35 (2.17). The occurrence of orofacial dysfunction, according to the protocol, was associated with some socio-demographic variables and it was possible to observe a higher occurrence of orofacial dysfunction among patients in the pediatric group, aged between 3 and 11 years (53.8%, n=7). Among the associations, only the gender variable, specifically the female gender (69.2%, n=9), presented significant statistics when associated with orofacial dysfunction, according to the NOT-S ($X^2_{(1)}=5.490$; $p=0.036$) (Table 1).

The result of the NOT-S protocol showed that 47.8% (n=11) of the patients evaluated presented orofacial dysfunctions at the end of induction. Each of the 12 domains addressed in NOT-S presented peculiarities. In the domains of the interview (I-VI),

Chart 1. *Nordic Orofacial Test-Screening* domains

NOT-S Interview
I – Sensory Function
A- Does brushing your teeth make you feel like vomiting?
B- Do you put so much food in your mouth that it becomes difficult to chew?
II – Breathing
A- Do you breathe normally or do you use any type of breathing support?
B- Do you snore a lot when you sleep?
III – Habits
A- Do you bite your nails, or suck your fingers or other objects every day?
B- Do you suck or bite your lips, tongue or cheeks every day?
C- Do you clench your teeth hard or grind them during the day?
IV – Chewing and swallowing
A- Does not eat with the mouth
B- Do you find it difficult to eat foods with a certain consistency (harder foods)?
C- Do you take more than 30 minutes to eat a full meal?
D- Do you swallow large pieces of food without chewing?
E- Do you cough often during meals?
V – Drooling
A - Do you get saliva in the corner of your mouth or on your chin every day?
VI – Dry mouth
A- You need to drink some kind of liquid to be able to eat a cracker?
B- Do you feel pain in the mucous membrane (skin) of the mouth or tongue?
NOT-S Clinical examination
1 – Face at rest
A- Asymmetry
B- Deviant lip position
C- Deviant tongue position
D- Involuntary movements
2 – Nasal breathing
A- Close your mouth and take 5 deep breaths through your nose (smell)
3 – Facial expresssion
A- Close your eyes tightly
B- Show your teeth
C- Try to whistle (blow)
4 – Masticatory muscles and mandibular function
A- Bite hard with your back teeth
B- Open your mouth as wide as you can
5 – Oral motor function
A- Stick your tongue out as far as you can
B- Lick your lips
C- Fill your mouth with air and hold for at least 3 seconds
D- Open your mouth wide and say ah-ah-ah!
6 – Speech
A- Does not speak
B- Count out loud to ten
C- Say PATAKA, PATAKA, PATAKA

Subtitle: NOT-S: *Nordic Orofacial Test-Screening*
Source: Leme et al.[15]

the ones that had a greater occurrence in these patients were, respectively, Dry mouth (VI) in 100% of cases (n=11), Chewing and swallowing (IV) 81.8% (n=9) and Habits (III) and Sensory function (I), in 54.5% (n=6) for both. While in the domains of clinical exam (1-6), the most prevalent were Facial expression (3) and Masticatory muscles and mandibular function (4) in 72.7% (n=8) of cases for both (Table 2).

In the patients evaluated, 30.4% (n=7) presented oral lesions at the end of the induction phase. Mucositis (n=4) was observed in the lips, tongue, floor of the mouth and oropharynx, herpes simplex on the gums (n=1) and hard palate and gum (n=1), as well as mucositis on the lips and the mucosa (n=1) and morsicatio buccarum on the mucosa (n=1). In addition, most (60.9%, n=14) presented poor/regular oral hygiene and 78.3% (n=18) mixed/permanent dentition, though all of which had adequate eruption chronology (Table 3).

The presence of oral manifestations characterized by lesions in these structures, as previously shown, were statistically significant when associated with the result of the NOT-S. Fisher's chi-square/exact test indicated that there is an association between oral lesions and the presence of orofacial dysfunction ($X^2_{(1)}$=5.789; p=0.027). Of the patients with oral lesions at the end of the induction phase 85.7% (n=6) presented orofacial dysfunctions, according to the NOT-S.

Between D0 (day zero) and D33 (day 33), 47.8% (n=11) of patients with acute leukemia in the remission induction phase had suffered weight loss, which we considered as significant when greater than 5% in one month. Of these, 63.6% (n=7) had orofacial dysfunctions according to the NOT-S and 81.8% (n=9) had alterations in the domains Chewing and Swallowing (IV) and Dry mouth (VI).

DISCUSSION

In acute leukemias, oral manifestations and systemic changes due to chemotherapy are relatively common. These factors can contribute directly or indirectly to changes in orofacial functions and, consequently, in quality of life. Due to the short interval between the manifestation of the first symptoms and the diagnosis, some socioeconomic and demographic aspects, such as place of residence, level of education and socioeconomic status of the family have direct impacts on the treatment of the disease[16,17].

The sociodemographic data evaluated in this study showed that patients under the age of eleven years have a higher occurrence of orofacial disorders, according to the NOT-S, with a greater tendency of the feminine gender for orofacial dysfunctions at the end of the remission induction phase. In addition, more than half of the patients evaluated lived in the rural area of the state of Amazonas, the largest Brazilian state, and lived on less than one minimum wage per month. This reinforces the importance of speed in the detection of initial symptoms and referral of the patient to the nearest hematology center, in this case located in the city of Manaus, in addition to the follow-up of the entire multidisciplinary team both during and after the patient's discharge.

During chemotherapy, the presence of oral manifestations such as mucositis, candidiasis, periodontitis and gingivitis is relatively frequent[6]. However, one study, which was conducted in the same blood center as this research as this research, showed that oral mucositis was rarely observed, though the presence of other nonspecific oral manifestations, such as petechiae, dry lips, ecchymosis, mucosal pallor and pericoronitis was common[14].

In this study, the casuistry of oral lesions was also relatively low, with the presence of mucositis, herpes simplex and biting of the mucosa. It is worth mentioning that this result could possibly be justified by the presence of a dental team working at the HEMOAM Foundation, with the application, whenever possible, of a prophylactic laser therapy protocol, using a low intensity laser, in patients undergoing chemotherapy, in order to reduce the chances of worsening of oral lesions, or, may even, be probably due to the low toxicity of the chemotherapeutic protocols adopted.

Table 1. Socio-demographic and body weight characterization of younger patients in remission chemotherapy for treatment of acute leukemia

Characteristics	n = 23 N(%)	No dysfunction (NOT-s) N = 12 (52.2)	Dysfunction (NOT-s) N = 11 (47.8)	*p-value*
Gender				
Male	10 (43.5)	8 (80)	2 (20)	0.036[a]
Female	13 (56.5)	4 (30.8)	9 (69.2)	
Age group				
3-11 years	13 (56.5)	6 (46.2)	7 (53.8)	0.68[a]
12-18 years	10 (43.5)	6 (60)	4 (40)	
Leukemia				
ALL	10 (47.6)	10 (47.6)	11 (52.4)	0.478[a]
AML	2 (100)	2 (100)	0 (0)	
Family income*				
Up to one minimum wage per month (< R$ 998.00**)	17 (73.9)	9 (52.9)	8 (47.1)	1.000[a]
Over one minimum wage per month (> R$ 998.00)	6 (26.1)	3 (50)	3 (50)	
Resides in:				
Urban zone	9 (39.1)	5 (55.6)	4 (44.4)	1.000[a]
Rural zone	14 (60.9)	7 (50)	7 (50)	
Weight (kg)	**Mean ±SD**		**Min – Max**	
D0	32 ±14.4		14 – 60	
D33	30.4 ±14.3		14.3 – 59.2	

[a]Pearson Chi-square Test/ Fisher Exact Test *According to the census of the Brazilian Institute of Geography and Statistics (2019)
Subtitle: n = number of patients; % = percentage; ALL = Acute Lymphoid Leukemia; AML = Acute Myeloid Leukemia; Min = minimum; Max = maximum; DP = standard deviation; NOT-s = *Nordic Orofacial Test-Screening*; < = less than; > = greater than; D0 = Start of remission induction phase; D33 = End of remission induction phase **(US$ 192,29)

Table 2. Distribution of domains according to the Nordic Orofacial Test-Screening protocol score

		Nordic Orofacial Test-Screening			
		No dysfunction 12 (52.2)		Dysfunction observed 11 (47.8)	
		Alteration in domain	No alteration in domain	Alteration in domain	No alteration in domain
		n (%)	n (%)	n (%)	n (%)
Interview	**I – Sensory Function**	2 (16.7)	10 (83.8)	6 (54.5)	5 (45.5)
	II – Breathing	1 (8.3)	11 (91.7)	1 (9.1)	10 (90.9)
	III – Habits	4 (33.3)	8 (66.7)	6 (54.5)	5 (45.5)
	IV – Chewing and swallowing	7 (58.3)	5 (41.7)	9 (81.8)	2 (18.2)
	V – Drooling	1 (8.3)	11 (91.7)	0 (0)	11 (100)
	VI – Dry mouth	5 (41.7)	7 (58.3)	11 (100)	0 (0)
Clinical examination	**1 – Resting Face**	0 (0)	12 (100)	1 (9.1)	10 (90.9)
	2 – Nasal breathing	1 (8.3)	11 (91.7)	0 (0)	11 (100)
	3 – Facial expression	0 (0)	12 (100)	8 (72.7)	3 (27.3)
	4 - Masticatory muscles and mandibular function	0 (0)	12 (100)	8 (72.7)	3 (27.3)
	5 – Oral motor function	0 (0)	12 (100)	2 (18.2)	9 (81.8)
	6 – Speech	0 (0)	12 (100)	3 (27.3)	8 (72.7)

In the last days of the remission induction phase, it was possible to observe that due to the occurrence of oral lesions in some patients, especially mucositis in non-keratinized mucosa and herpes simplex in keratinized mucosa, it was necessary to adapt the diet for the patients affected by the lesions and, in some cases, only the intake of liquids was possible, thus compromising the nutrition of the patient during the treatment.

Within the HEMOAM Foundation, this research was the first to be carried out in order to highlight the importance of speech therapy within the multidisciplinary team in centers specialized in the treatment of onco-hematological patients, and may contribute, mainly, by signaling a better approach to patients with leukemia.

Table 3. Profile of oral hygiene, dental eruption and oral manifestations presented by pediatric patients with acute leukemia at the end of the remission induction phase

Dental characteristics	n (23)	%
Oral Hygiene		
Bad	4	17.4
Average	10	43.5
Good	9	39.1
Dental eruption		
Deciduous dentition	5	21.7
Mixed dentition	8	34.8
Permanent dentition	10	43.5
Soft tissue injury		
Yes	7	30.4
1. Mucositis (n=4) on lips, tongue, floor of mouth and oropharynx		
2. Herpes simplex (n=1) in gums		
3. Mucositis (lips and mucosa) and Herpes simplex (hard palate and gums)(n=1)		
4. Morssicatio buccarium in the mucosa (n=1)		
No	16	69.6
WHO Oral mucositis scale		
Grade 1 - Pain and erythema	0	-
Grade 2 - Erythema and ulcers	3	13
Grade 3 - Diffuse erythema, ulcerative lesions, liquid diet	2	8.7
Grade 4 - Diffuse ulcers that make feeding impossible	0	-

Subtitle: WHO = World Health Organization

The association between the occurrence of oral lesions and orofacial dysfunctions, according to the NOT-S, showed that most patients with oral lesions at the end of the remission induction phase (85.7%; n=6; p=0.027) also presented orofacial dysfunction. On the other hand, the occurrence of oral lesions (30.4%, n=7) was lower than the presence of orofacial dysfunction (47.8%, n=11) in the evaluated patients.

Due to the direct toxicity of some chemotherapy drugs in the mucosa via their systemic circulation, the oral manifestations presented by some patients may affect the structures of the oropharyngeal tract and compromise some stomatognathic functions. Chewing, swallowing and speech are among the orofacial functions that may be affected by the presence of oral lesions. However, as observed in this research, some cases, even in the face of these lesions, are able to preserve the mechanical process of swallowing; though with a reduction in the volume of food intake.

It is worth noting that oral lesions can favor secondary infections that hinder the process of recovery of the clinical situation, hinder nutrition and prolong treatment. The dental surgeon is the professional who diagnoses and treats these lesions; however, the care of the speech therapist within the multidisciplinary team is fundamental in monitoring the dysfunction related to these oral manifestations[18].

Some patients with acute leukemia may have trigeminal and/or facial neuralgia, inability to protrude the tongue, dysphagia, hypofunction of the masticatory muscles, decreased muscle sensitivity and paresthesia in the intra- and extraoral structures. All these myofunctional impacts, such as pain and/or difficulty speaking and swallowing, affect not only the quality of life of the patient during treatment, but also the antineoplastic treatment itself due to patient debilitation and malnutrition due to difficulty with food. These dysfunctions become even more complicated when associated with reduced amounts of saliva[7,19].

Based on the literature[20-22], xerostomia is considered a late complication in treatment and is present in 44.18% of patients undergoing chemotherapy and in more than 95% in the remission induction phase. In these same studies, patients who reported xerostomia and difficulty chewing more solid foods had reduced food intake[19-21]. Saliva is essential for oral health, cleanliness and the mechanics of swallowing. For the full performance of swallowing it is necessary that the cohesive forces between the particles forming the bolus are strong. When this peak of the cohesive forces is not reached due to the viscosity of the saliva, the patient may present problems when swallowing[3,8].

Because of the difficulty when swallowing, change in taste, nausea and/or vomiting, patients undergoing chemotherapy have a reduction of up to 50% of caloric/protein intake because, in addition to the change in taste and smell sensitivity, the reduction of salivary flow can compromise the harmony of the biomechanical process of swallowing[3,23].

In this study, almost half of the patients undergoing chemotherapy presented orofacial dysfunction at the end of the remission induction phase, according to NOT-S protocol. After analysis, it was observed that this dysfunction possibly had a direct impact on oral feeding, as observed during treatment due to the difficulty in ingesting more solid foods and this may have an impact on food intake.

The difficulty in swallowing presented by chemotherapy patients compromises nutrition during treatment. This nutritional deficit has a consequence seen in the loss of muscle mass in these patients (sarcopenia), which further compromises muscle dynamics, and leads to fatigue, asthenia and impaired muscle functions. The loss of muscle mass in pediatric patients during and after the remission induction phase can increase the length of hospitalization, in addition to presenting long-term consequences, such as delay in gross and fine motor development[24,25].

Of the patients with orofacial dysfunction, according to the NOT-S, the domains Mouth Dryness (VI) (xerostomia) and Chewing and Swallowing (IV) were the most altered. It is also worth noting that, in our study, during the remission induction phase, when comparing the body weight measured on the first day of chemotherapy with the weight measured on the day of evaluation (D30-D33), a percentage of weight loss was found in almost half of the patients evaluated that was greater than 5% in one month. Therefore, given the observed data and what is stated in the literature, a greater knowledge of the relationship between and among xerostomia, hypersensitivity due to oral lesions, weight loss and impact on the biomechanics of swallowing is necessary.

This study presented some limitations, such as the low sample number, type of sample, in this case a convenience sample from a single treatment center the temporary limitations regarding collections on account of the COVID-19 pandemic. Another limitation was the absence of data on the presence of orofacial alterations prior to diagnosis, as this is a cross-sectional observational study.

Until the carrying out of this work, no information was found in the literature on orofacial dysfunctions in patients with acute leukemia in the remission induction phase, nor even on the impact of these dysfunctions on the nutritional process and on the antileukemic treatment itself. With the results of this

research, it was not possible to conclude a causal relationship between the oral lesions and orofacial dysfunctions found, much less the impacts of chemotherapy on these structures.

However, this research was the first step towards a better understanding of orofacial dysfunctions in patients with acute leukemia, and raises new questions that will guide future studies. It is necessary to more fully understand the relationship between oral lesions and orofacial dysfunctions in patients with leukemia undergoing chemotherapy, and also discover the possible relationships between these functional impacts and the hypersensitivity resulting from oral lesions, or even the biomechanical consequences resulting from decreased saliva.

CONCLUSION

A high occurrence of orofacial dysfunctions was found in infants and young children diagnosed with acute leukemia at the end of the remission induction phase, which represented about half (47.8%) of the patients evaluated. The greatest trend of orofacial dysfunction occurred in female patients. A relationship between the presence of oral lesions, xerostomia and orofacial biomechanical aspects is suggested, thus indicating the need for future studies that can verify this correlation.

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