

Oral Mucositis in Children Suffering from Acute Lymphoblastic Leukaemia

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ABSTRACT

Background: Oral mucositis is the most commonly reported side effect observed in neoplastic patients treated with chemotherapy and radiotherapy of the head and neck region as well as in patients who have received a haematopoietic stem cell transplant. The aim of the study was to assess the oral mucosa status in children with acute lymphoblastic leukaemia (ALL) during antineoplastic therapy.

Material and methods: The clinical examination included 127 children aged 5-15 with ALL. The clinical examination was conducted using the dental diagnostic instrument. The condition of the oral mucosa was determined using the WHO scale for oral mucositis.

Results: In the first period of antineoplastic therapy the pathological lesions of the oral mucosa of the mucositis type were observed among the examined patients. The lesions had various levels of intensity. Pain was found to be the primary symptom of oral mucositis. In this study the following were observed: local erythema of the oral mucosa in 10%, ulcerative lesions in 5%.The remaining 85% patient who could not eat or drink because of pain and soreness.

Conclusion: Local treatment of oral mucositis with polyantibiotic-antifungal mixture, supporting antifungal systemic treatment, and improving the overall peripheral blood conditions in children suffering from acute lymphoblastic leukaemia improve the condition of the oral mucosa.

Key words: oral mucositis, acute lymphoblastic leukaemia (ALL).

INTRODUCTION

Pathological changes of the oral mucosa defined as oral mucositis are caused by cytotoxic effects of chemotherapy and local radiotherapy of the head and neck region. Oral mucositis symptoms are also observed in 40-100% of patients who have had stem cell transplantation. Oral inflammation caused by stomatotoxic chemotherapy is painful and restricts oral administration of drugs, also increasing the risk of infection of the intrinsic oral cavity flora. It is a serious problem, which results in decreased doses of administered drugs and may increase the cost of tumor treatment. General incidence of mucositis may differ and depends on the diagnosis and the patient's age, previous condition of the oral cavity, as well as the type, dose and frequency of administration of pharmacological medicines. WHO distinguishes five grades of oral mucositis severity (Table 1):

Table 1: WHO Classification of oral mucositis

<i>Grade</i>	<i>Symtoms</i>
0	no symptoms of oral mucositis
1	redness, erythema, soreness
2	erythema and ulceration, patient can swallow solid food
3	ulceration and erythema, patient cannot swallow solid food
4	ulceration and pseudomembrane formation of such severity that alimentionation is not possible

Development of oral cavity inflammation defined as mucositis is claimed to be a complex pathological process, in which proinflammatory cytokines play an essential role. In a five-phase model of mucositis pathogenesis, the primary cause and trigger of the inflammatory process, is microvascular injury to quickly dividing basal epithelial cells during radiation and chemotherapy, which results in production and release of free oxygen radicals, which in turn activates cytokines, including tumor necrosis factor-alpha, produced mainly by macrophages and interleukin-1 and -6. Developing ulcers in the mucosa are a base for development of bacterial microflora leading to secondary infections. The fifth and last phase is healing, which is characterised by epithelial cell proliferation, tissue differentiation and recovery of epithelial integrity ^(1, 2).

Among patients treated according to the protocol for high risk patients, severe mucositis occurs in more than 60%. Half of those patients experience deterioration of the oral mucosa condition, which is so serious that it requires changes in the antitumor treatment and/or administration of parenteral analgesia. Observations reveal that oral mucositis occurs more often in children than in adults with a similar tumor disease. Oral inflammation is also more often observed in patients after bone marrow transplantation ^(2, 3, 4)

AIM OF THE STUDY

The aim of the study was to assess oral mucosa

in children suffering from acute lymphoblastic leukaemia during anti-tumor treatment.

MATERIAL AND METHODS

The study included 127 children aged from 5 to 15 suffering from acute lymphoblastic leukaemia (ALL) (Table2). All patients diagnosed by physicians (Table 3).

Table 2: Age and, gender distribution for (127) patients with ALL

Age	F	%	Males		Females	
			F	%	F	%
5-7	20	16	10	8	10	8
8-9	55	43	35	27	20	16
10-12	30	24	18	14	12	9
13-15	22	17	12	9	10	8
Total	127	100	75	58	52	32

Table 3: Methods of diagnosis for (127) patients with ALL

Categories	F	%
Core biopsy lymph node	40	31
Blood tests	20	16
Biochemical tests	15	12
Ultra sound abdomen	12	9
Bone marrow biopsy	40	31
Total	127	100

The study group collected from different areas in Iraq (Table 4).

Table 4 : Residence for (127) patients and place of hospital with ALL

Categories	F	%	Hospitals			
			W.T.H *		C.C.T.H **	
			F	%	F	%
Center	25	20	13	10.23	12	9.44
North	25	20	12	9.44	13	10.23
East	18	14	16	12.29	2	1.57
West	19	15	10	7.87	9	7.08
South	40	31	30	23.62	10	7.87
Total	127	100	81	63.77	46	36.22

*W.T.H: Walffer Teaching Hospital (Medical City)

**Central Child Teaching Hospital

In the study group, forty children had swollen lymph node, 15 fatigue and weakness, 12 complaining from recurrent infection, 10 had easy bruising, 30 bone and joint pain (Table5).

Table 5: Chief compliants for (127) patient with ALL

Categories	F	%
Swollen lymph node	40	31
Fatigue and weakness	15	12
Recurrent infection	12	9
Easy bruising	10	8
Bone and joint pain	30	24
Abdominal pain	20	16
Total	127	100

RESULTS

In our own study , lesions of the mucositis type were observed in ALL children in the period from 48 hours to 6 months, having various intensity and with periods without pathological lesions, which was related to the intensity of the chemotherapy. Mucosa opacity followed by redness usually occurred within 2-4 days from the treatment by (etoposide, cytosar, zofran) (Table 6).

Table 6: Therapy 2 weeks (14 days)

days		grade									
		0		1		2		J		4	
		F	%	F	%	F	%	F	%	F	%
1	H	0	0	0	0	0	0	0	0	0	0
2	0	0	5	4	0	0	0	0	0	0	0
3	0	0	5	4	0	0	0	0	0	0	0
4	0	0	3	2.5	0	0	0	0	0	0	0
5	0	0	0	0	J	2.5	0	0	0	0	0
6	0	0	0	0	3	2.5	0	0	0	0	0
7	0	0	0	0	0	0	6	5	0	0	0
8	0	0	0	0	0	0	0	0	20	15.5	0
9	0	0	0	0	0	0	0	0	30	24	0
10	0	0	0	0	0	0	0	0	30	24	0
11	0	0	0	0	0	0	0	0	22	16.5	0
12	0	0	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0	0	0

The most severe lesions of the oral mucosa were observed after the first month of chemotherapy. Wounds and ulcers difficult to heal were related to blood parameters. It was observed that healing was faster, especially with regard to oral mucosa ulceration, when blood morphological parameters were improved. Lesions of the mucositis type were also dependent on the level of neutropenia. Each child with neutropenia also had fungal complications in the oral mucosa weeks from the implementation of treatment, and were mostly dependent on blood morphology and haematological therapy, as well as on the oral cavity hygiene prior to treatment. Lesions in oral mucosa were the most persistent in children with bone marrow aplasia (up to 3 weeks) and in children with neutropenia. Difficult healing was also observed following chemotherapy infusion.

DISCUSSION

Severe type of oral mucositis may be the cause of antitumor treatment postponement or modification, which results in decreased effect of the therapy^(5, 6). Most frequently, changes of the mucositis type are observed 2-4 days after administration of chemotherapy. Lesions usually develop on buccal and tongue mucosa, as well as on the lips. The average time of development of mucositis-like lesions and ulcers was about 10-16 days of chemotherapy.

Problems in the oral cavity occurred independently of the chemotherapy protocol^(7, 8). Patients with aplasia or neutropenia are especially exposed to dangerous fungal complications. Therefore, introduction of antifungal prevention in the form of 100 mg of fluconazole daily may significantly reduce occurrence of pathological changes^(9, 10). Proper function of bone marrow and improvement in blood morphology parameters lead to regression of changes in the oral mucosa⁽¹¹⁾.

According to Karolewska et al. (2004, 2008), problems of the oral mucositis type in children with leukaemia are related to a great extent to a reduced level of S-IgA, myeloperoxidase, salivary peroxidase and to almost half the level of the total protein in saliva in comparison to patients with acute leukaemia without symptoms of oral mucositis^(12, 13). The intensity of oral inflammation significantly depends on oral hygiene, which was confirmed by McGaw et al. (1985), who observed less intense and shorter symptoms of oral mucositis in subjects using mouthwash with chlorhexidine⁽¹⁴⁾. Studies conducted by Hameralak(2004) indicate a correlation between development of oral mucositis following

intensive cytostatic treatment with alkaline increase in saliva pH in children with leukaemia. Irrigation of the oral cavity during chemotherapy with solution compatible with the saliva Ph of the child resulted in a reduced intensity of inflammatory necrotic changes⁽¹⁵⁾. The authors, who had observed poor oral hygiene in children prior to bone marrow transplantation, included the patients in routine dental care in order to minimise the occurrence of complications and infections in the oral cavity. The procedure included teaching the children to brush their teeth and to clean them with dental floss, as well as fluoride varnish^(16, 17).

An important problem related to oral mucositis is pain, which leads to poor nourishment and insufficient hydration of the patients and increases the risk of local infections, especially systemic ones, which may pose a threat to life. Complications in the oral cavity may also prolong treatment and increase its cost^(18, 19, 20).

Among preparations able to decompose dental plaque and prevent development of a new one, chlorhexidine seems to be the most effective. Numerous authors confirm chlorhexidine efficacy in 0.1% or 0.12% solution in the treatment of oral inflammatory conditions^(3, 7, 8, 14, 21). Certain researchers, however, do not recommend chlorhexidine preparations for children, claiming that mouthwashes containing fluoride compounds or saline have comparable therapeutic effects. Especially chlorhexidine solutions 0.2% or 0.3% are not recommended for children with acute lymphoblastic leukaemia, due to their flavour and tendency to discoloration. According to some researchers, both chlorhexidine and benzydamine have a positive effect on reduction of oral mucositis during chemotherapy, but only in children over 6 years of age^(22, 23, 24).

All physicians agree that the most important factor lowering the risk of oral complications is regular, at least twice a day, brushing of teeth, mouth washing and effective motivation of the patient to clean dental surfaces and oral tissues of the oral cavity. Some studies recommend that during chemotherapy, the toothbrush should be placed in a 2% chlorhexidine solution after each use, and thoroughly rinsed prior to use^(23, 24, 25, 26, 27).

In conclusion: local treatment of oral mucositis with a polyantibiotic and antifungal mixture supported by antifungal general treatment and improvement in blood morphology in children suffering from acute lymphoblastic leukaemia improves the condition of the oral mucosa.

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