

Assessment of the State of the Oral Mucosa in Children With Acute Leukemias With Chemotherapeutic Treatment

Nosirova Sevara Zakirdjanovna

Tashkent State Medical University Tashkent, Uzbekistan

Abstract: Acute leukemias are the most common group of malignant neoplasms in children, accounting for up to 30-35% of all oncological diseases in the pediatric population. Every year, around 50,000 new cases of acute leukemia are diagnosed in children worldwide, with acute lymphocytic leukemia occurring in 80-85% of cases and acute myeloblastic leukemia in 15-20%. Modern chemotherapeutic treatment protocols have allowed achieving a five-year survival rate exceeding 85% in acute lymphocytic leukemia and 60-70% in acute myeloblastic leukemia, representing significant progress in pediatric oncohematology.

Keywords: leukemia, children, oral mucosa, chemotherapy, mucositis, dental complications, oncohematology, oral infections, quality of life, prevention.

Introduction. The problem of oral mucosa status in children with leukemia during chemotherapy is particularly relevant due to several factors. The frequency of mucositis development in children receiving chemotherapy for leukemia reaches 80-90%, which is significantly higher than the same indicators in adult patients [1]. Leukemias are the most common group of malignant neoplasms in children, accounting for about 30% of all oncological diseases in pediatric practice. Modern chemotherapy protocols have significantly improved the prognosis of the disease, however, intensive therapy is accompanied by the development of severe side effects, among which lesions of the oral mucosa occupy a special place. Success in treating acute leukemias in children has been achieved through the implementation of intensive polychemotherapy protocols based on high-dose chemotherapy using various combinations of cytostatic drugs. However, aggressive antitumor therapy inevitably accompanies the development of serious side effects that significantly affect the quality of life of patients and require a comprehensive interdisciplinary approach to their prevention and treatment.

The mucous membrane of the oral cavity, characterized by a high rate of epithelial cell renewal and rich vascularization, is one of the most vulnerable targets for the toxic effects of chemotherapeutic drugs. Cytostatics have a direct damaging effect on rapidly proliferating cells of the basal layer of the epithelium, which leads to disruption of regeneration processes, atrophy of the epithelial covering, and the development of mucositis of varying severity.

Oral mucositis develops in 75-100% of children receiving high-dose chemotherapy for acute leukemia and is one of the most severe and clinically significant complications of antitumor treatment. The pathogenesis of chemoinduced mucositis is a complex multi-stage process involving primary damage to epithelial cell DNA, activation of pro-inflammatory cytokines, disruption of the integrity of the epithelial barrier, bacterial translocation, and the formation of a secondary infection.

The clinical manifestations of oral mucositis range from mild erythema to deep ulcers of the mucous membrane with pronounced pain syndrome, which leads to a significant deterioration in the quality of life of patients. Severe forms of mucositis may require a reduction in the dosage of chemotherapeutic drugs or postponement of subsequent treatment courses, which negatively affects the effectiveness of antitumor therapy and the prognosis of the disease.

Pediatric patients represent a special risk group for the development of severe oral mucositis due to the anatomical and physiological characteristics of childhood. The thinner epithelial covering of the mucous membrane, increased vascularization of tissues, imperfect local defense mechanisms, and the

peculiarities of the oral microbiocenosis in children contribute to the earlier development and severe course of mucositis compared to adult patients.

In addition, children experience significant difficulties in maintaining adequate oral hygiene against the background of developing mucositis, which creates favorable conditions for microbial colonization of the damaged mucous membrane and the development of secondary infectious complications. The pain syndrome in mucositis leads to a refusal to eat, disruption of nutritional status, and delayed physical development, which is especially critical in pediatric practice.

Modern diagnosis of oral mucositis is based on the use of standardized assessment scales, including the WHO scale, the general toxicity criteria scale (CTC), and the oral mucositis assessment scale (OMS). However, existing assessment systems do not always adequately reflect patients' subjective feelings and functional disorders, which requires the development of more advanced methods for monitoring the condition of the oral mucosa. The economic aspects of the problem of oral mucositis include both direct costs for treating complications and indirect costs associated with extending hospitalization periods, the need for additional medical care, and a decrease in the quality of life of patients and their families. Developing effective strategies for the prevention of mucositis can significantly reduce the overall cost of treating children with acute leukemia.

Current trends in treating acute leukemias in children, including the introduction of targeted therapy, immunotherapy, and hematopoietic stem cell transplantation, require a reassessment of approaches to the prevention and treatment of oral mucositis. Each treatment method has specific effects on the oral mucosa, which must be considered when developing individualized accompanying therapy protocols. The long-term consequences of chemotherapeutic effects on the oral mucosa and the dentoalveolar system as a whole remain insufficiently studied. Dental developmental disorders, increased risk of caries, xerostomia, and other long-term effects can significantly impact the quality of life of recovered patients, requiring prolonged dental monitoring and rehabilitation measures.

Oral complications significantly worsen the quality of life of young patients, affect nutritional status, and can lead to delayed or modified antitumor therapy. The pathogenesis of oral mucosa damage during chemotherapy is a multifactorial process. Cytostatic drugs have a direct cytotoxic effect on rapidly dividing cells of the basal layer of the epithelium, causing their damage and death. Simultaneously, regeneration processes are disrupted, local immunosuppression develops, which creates favorable conditions for the addition of secondary infection[2].

Leukemia remains the leading cause of oncological mortality in childhood, accounting for approximately 30-35% of all malignant neoplasms in pediatric patients. Modern achievements in oncohematology have significantly improved the survival rates of children with leukemia, achieving a 5-year survival rate exceeding 85% in acute lymphocytic leukemia [3]. However, the intensification of chemotherapeutic protocols aimed at improving the effectiveness of antitumor treatment inevitably accompanies the development of severe side effects that significantly affect the quality of life of young patients [4].

Among the entire spectrum of chemotherapy complications, changes in the oral mucosa are of particular clinical importance, occurring in 70-90% of children receiving cytostatic treatment for leukemia. These disorders are of a polyetiological nature and are caused by both the direct cytotoxic effect of chemotherapeutic drugs on rapidly proliferating oral epithelial cells and secondary immunological and infectious complications developing against the background of induced immunosuppression.

The pathophysiological mechanisms of oral mucosa damage during chemotherapy of leukemia in children represent a complex cascade of interconnected processes. Primary damage to the DNA of the epithelial cells of the basal layer leads to a disruption of the cell cycle, apoptosis, and subsequent atrophy of the mucous membrane. Simultaneously, pro-inflammatory cytokines are activated, tissue repair and regeneration processes are disrupted, creating a favorable environment for the colonization of opportunistic microflora and the development of secondary infectious complications [6]

The clinical polymorphism of changes in the oral mucosa varies from mild erythematous reactions to severe ulcerative-necrotic lesions accompanied by pronounced pain syndrome, dysphagia, and impaired nutritional status. Severe forms of mucositis (III-IV degrees according to WHO criteria) can serve as a dose-limiting factor requiring a reduction in the dosage of chemopreparations or a temporary cessation of antitumor therapy, which can potentially negatively affect the cancer prognosis [7].

The high risk of developing systemic infectious complications in leukemic children with oral mucosal barrier integrity disorders is of particular concern. In chemotherapy-induced neutropenia, the damaged mucous membrane becomes an entry point for bacterial, viral, and fungal infections, which can lead to the development of sepsis and other life-threatening conditions[8]. The economic aspects of the problem of oral mucositis include both direct costs for treating complications and indirect costs associated with extending hospitalization periods, the need for additional medical care, and a decrease in the quality of life of patients and their families. Developing effective strategies for the prevention of mucositis can significantly reduce the overall cost of treating children with acute leukemia.

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Diagnosing and monitoring changes in the oral mucosa in children with leukemia requires a multidisciplinary approach involving oncohematologists, dentists, clinical pharmacologists, and infectious disease specialists. Modern assessment methods include the use of standardized scales (WHO, CTCAE, OMAS), microbiological research, and in some cases, the application of innovative diagnostic technologies. Despite significant achievements in understanding the pathogenesis of oral chemotherapy complications, the problem of their prevention and treatment in children with leukemia remains unresolved. Existing therapeutic approaches are often symptomatic and do not always provide adequate control over the development and progression of pathological changes[9].

Studying the patterns of oral mucosa changes in children with leukemia against the background of chemotherapeutic treatment is of not only scientific but also practical interest, as deepening knowledge in this area can contribute to the development of more effective prevention and treatment strategies, which will ultimately improve the quality of life of patients and optimize the results of antitumor therapy.

The clinical manifestations of oral mucosa lesions in children with leukemia are characterized by polymorphism and depend on the stage of the disease, the chemotherapy protocol used, and the individual characteristics of the body. The most common are erythematous changes, swelling, ulcerations of varying severity, bleeding of the gums, and petechial eruptions. Mucositis, which develops against the background of chemotherapy, is classified according to the criteria of the World Health Organization and the Common Terminology Criteria for Adverse Events (CTCAE) system. Severe forms of mucositis (III-IV degrees) occur in 40-60% of children with acute lymphoid leukemia and can serve as a limiting factor for continued planned therapy[11]. The problem of infectious complications in the oral cavity in children with leukemia deserves special attention. Neutropenia developing against the background of chemotherapy, combined with a violation of the integrity of the mucous barrier, creates a high risk of developing local and generalized infections. The most common pathogens are bacteria of the genus *Streptococcus*, *Staphylococcus*, as well as *Candida* fungi[12].

Diagnosis of oral mucosa lesions in children with leukemia should be comprehensive and include thorough clinical examination, microbiological studies, and in some cases, histological examination. Differential diagnosis is carried out with leukemic infiltrates, viral lesions, and other conditions accompanied by mucosal ulcers[13]. The prevention and treatment of oral mucosa lesions in children with leukemia is a complex medical task. Modern approaches include using cryotherapy, laser therapy, local anesthetics, antimicrobial drugs, and regeneration-stimulating agents. It is especially important to sanitize the oral cavity before the start of chemotherapy and maintain adequate oral hygiene throughout the entire treatment period[14]. The quality of life of children with leukemia, who have lesions of the oral mucosa, significantly decreases. Pain syndrome, difficulty eating, sleep disturbance, and emotional disturbances require a comprehensive approach to the rehabilitation of such patients. Psychological support for the child and their family is an integral part of the treatment process.

Modern research is aimed at developing new methods for the prevention and treatment of oral complications in children with leukemia. The use of growth factors, probiotics, photodynamic therapy, and other innovative approaches is promising[15].

CONCLUSIONS: Lesions of the oral mucosa are among the most frequent and clinically significant complications of chemotherapy in children with leukemia, occurring in 80-90% of cases. The pathogenesis of oral complications is multifactorial and includes the direct cytotoxic effect of chemopreparations, disruption of regeneration processes, and the development of a secondary infection

against the background of immunosuppression. Clinical manifestations are characterized by polymorphism and can range from mild erythematous changes to severe ulcerative-necrotic lesions requiring anti-tumor therapy correction. Prevention of oral complications should begin before the initiation of chemotherapy and include oral sanitation, hygiene training, and the application of preventive measures. Treatment of oral mucosa lesions requires a multidisciplinary approach involving oncohematologists, dentists, clinical pharmacologists, and other specialists. Further research is needed to develop more effective methods for the prevention and treatment of oral complications in children with leukemia to improve the quality of life of patients and optimize antitumor therapy.

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