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EFFECTIVENESS OF BACTERIOPHAGE THERAPY IN INFLAMMATORY DISEASES OF THE ORAL MUCOSA IN CHILDREN

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Abstract
This article describes methods for treating stomatitis that develops against the background of viral diseases in children, as well as the practical application of improved and refined techniques in this field of medicine. The ways of improving the treatment of stomatitis developing against the background of viral diseases in paediatric dentistry are analysed from a scientific standpoint. A comparative analysis of this treatment method with the treatment approaches currently used in practice is also carried out, and its practical significance is demonstrated.

Keywords: Viral infections, stomatitis, bacteriophage, drug, microflora, antiseptic treatment, disinfection, antiviral therapy, regeneration, immunity.

Introduction

In children with viral infections, stomatitis accompanied by inflammation of the oral mucosa is frequently encountered in dental practice. As a result of decreased immunity following acute respiratory viral infections (ARVI) and other viral diseases, erosions and aphthae appear in the oral cavity. This condition causes pain, difficulty eating and a deterioration of the general state of the child.

Owing to the anatomical and physiological features of the oral mucosa in children and the immaturity of the children's immune system, inflammatory processes run a more severe course. Disturbance of local immunity and changes in the microbial balance create conditions for secondary infection, which significantly alters the clinical course of stomatitis and prolongs the duration of treatment.

In the study, clinical examination, history taking and assessment of the condition of the oral mucosa were used in children with signs of stomatitis. During treatment, local antiseptic and antiviral agents and preparations accelerating epithelialization were applied.

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Materials and Methods

This study was conducted at the Department of Prevention of Dental Diseases of Tashkent State Medical University and included the clinical observation and treatment of children with signs of stomatitis that had developed against the background of viral infections.

The study included children aged 3 to 12 years with clinically confirmed stomatitis that had developed against the background of viral diseases (ARVI, herpesvirus infection and others). The total number of patients was 40. According to the treatment method applied, all patients were divided into two groups:

–study group (n = 20) – patients who received complex therapy including a bacteriophage preparation;

–control group (n = 20) – patients who received standard treatment without a bacteriophage.

Inclusion criteria: presence of clinical signs of stomatitis (erosion, aphthae, hyperaemia of the mucosa, pain syndrome); a recently suffered viral infection in the history.

Exclusion criteria: severe somatic diseases; immunodeficiency states; intake of systemic antibiotics during the study.

Before the start of the study, informed consent to participate was obtained from the parents or legal representatives of all patients.

All patients underwent a comprehensive clinical examination including:

–history taking (nature and duration of the illness, presence of viral infection, patient complaints);

–visual examination of the oral cavity and assessment of the condition of the mucosa;

–determination of the location and number of pathological elements;

–assessment of the degree of hyperaemia and oedema;

–assessment of the pain syndrome on the visual analogue scale (VAS).

Particular attention was paid to oral hygiene status and to the factors leading to the inflammatory process.

Treatment of the patients was carried out on an outpatient basis and involved a comprehensive approach aimed at eliminating the inflammatory process, reducing the pain syndrome, accelerating regeneration and preventing secondary bacterial infection.

In both groups, the oral cavity was treated locally with antiseptic solutions, using 0.05% solutions of chlorhexidine or miramistin. Treatment was performed 3–4 times a day by irrigation or by application with sterile tampons.

When the viral aetiology of the disease was confirmed by clinical signs, patients were prescribed aciclovir in age-appropriate doses. Depending on the patient's condition, the drug was applied as an ointment or systemically.

To reduce the pain syndrome and decrease inflammation, local preparations in ointment form (Kamistad, Cholisal) were used. They were applied 2–3 times a day after antiseptic treatment.

To accelerate epithelialization of the mucosa, Solcoseryl adhesive paste was used. The preparation was applied to the affected areas twice a day onto the previously cleaned mucosa.

All patients were prescribed vitamin–mineral complexes as well as symptomatic therapy (antipyretics where necessary). A diet excluding irritating foods was recommended.

In the study group, a bacteriophage preparation was additionally applied in the form of a spray or solution. The preparation was applied to the oral mucosa 2–3 times a day after antiseptic treatment. When the solution was used, the application method was employed: a sterile tampon soaked in

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bacteriophage was placed on the affected area for 5–10 minutes. The treatment course was 5–7 days depending on the clinical situation.

The data obtained were processed using methods of variation statistics. Mean values (M) and standard deviation (SD) were calculated. The reliability of differences between the groups was assessed using the student t-test. Differences were considered statistically significant at $p < 0.05$.

About Bacteriophages

The word "bacteriophage" is of French origin and combines "bacteria" and "phage", meaning "eaters of bacteria". Their size is 23–30 nm, and they consist of nucleic acid and protein. The life cycle of a bacteriophage begins with its binding to a bacterial receptor and the injection of genetic material into the bacterium.

Because bacteriophages are the natural "predators" of bacteria, they are used as a potential therapeutic agent. Owing to their very high specificity, they can act selectively on a particular type of bacterium or even on specific bacterial strains. Since a bacteriophage causes lysis of bacteria, it indirectly stimulates the body's immune system.

The most important advantage of phage therapy is the possibility of adapting it to an individual patient. Bacteriophages are safe for humans; they are natural viruses that have evolved together with bacteria over many centuries. Clinical studies have shown that phages have low toxicity for humans. At present, the efficacy of bacteriophages can be supported by a large body of scientific evidence. They are widely used in hospital-acquired infections, infections of the urinary and reproductive systems, diseases of the respiratory organs, burns and wounds, trophic ulcers, osteomyelitis, infections of the skin and mucous membranes, and infectious diseases of the oral mucosa.

Use of Bacteriophage Preparations in Stomatitis in Children

In viral diseases, damage to the oral mucosa creates a high probability of secondary bacterial infection. For this reason, control of the bacterial microflora is of great importance in complex therapy.

In recent years, the use of bacteriophage preparations in the treatment of stomatitis has yielded good results. Bacteriophages act selectively on specific bacteria, lysing them, while having a minimal negative effect on the oral microbiota.

In the treatment of stomatitis in children, bacteriophage-based sprays can be used as local therapy. The preparation is sprayed onto the oral mucosa 2–3 times a day. A solution form of this preparation is also available, which can be soaked into a tampon or gauze and used to treat the oral mucosa.

Advantages of Bacteriophages

– selective action on pathogenic bacteria;
– low development of resistance compared with antibiotics;
– no negative effect on regeneration of the mucosa;
– good tolerability and safety in children.

The use of bacteriophage preparations within complex treatment contributes to a faster reduction of the inflammatory process, accelerates the epithelialization of aphthous elements and helps prevent secondary bacterial complications.

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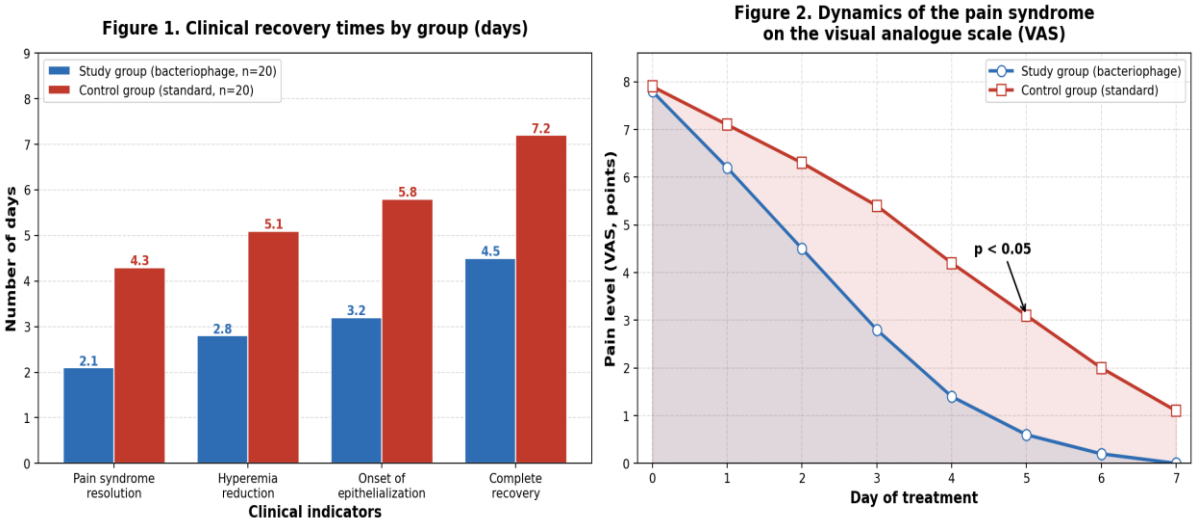
A comparative table of the use of chlorhexidine solution and bacteriophage spray in dental practice is given below.

Table 1. Comparative characteristics of chlorhexidine solution and bacteriophage spray

Criterion	Chlorhexidine Solution	Bacteriophage Spray
Composition	Antiseptic agent of the biguanide group (chlorhexidine digluconate)	A complex of bacteriophage viruses acting on specific bacteria
Mechanism of action	Destroys the bacterial cell membrane and kills microorganisms	Selectively lyses pathogenic bacteria
Spectrum of action	Broad-spectrum antiseptic	Selective, precise action against specific bacteria
Effect on microflora	May also destroy beneficial microflora	Acts only on pathogenic bacteria, preserving the normal flora
Method of use	Rinsing or treatment with a tampon	Sprayed onto the oral mucosa; the mucosa is also treated with its solution
Use in children	Used with caution owing to the risk of swallowing	Convenient and safe to use in children
Side effects	Discolouration of tooth enamel, burning in the mouth	Usually well tolerated, side effects very rare
Development of resistance	Some microorganisms may adapt	Development of resistance is very rare
Effect on the mucosa	Prolonged use may dry out the mucosa	Does not hinder regeneration of the mucosa
Efficacy in treating stomatitis	Effective for disinfection	Selectively eliminates secondary bacterial infection and accelerates recovery
Characteristics	Pungent odour, bitter taste, may trigger the gag reflex	Odourless, transparent yellow liquid with a specific taste; does not trigger the gag reflex



Figures 1–2. Clinical recovery times and dynamics of the pain syndrome in the study and control groups

Discussion

The results obtained during the study showed that including bacteriophage preparations in the complex treatment of stomatitis developing against the background of viral infections in children is

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highly effective. It was found that the use of bacteriophages contributes to a faster elimination of the inflammatory process, a reduction of the pain syndrome and an acceleration of epithelialization in the affected areas of the oral mucosa.

One of the main factors determining the severity of the course of stomatitis in children is the addition of a secondary bacterial infection against the background of reduced local immunity. Under conditions of viral damage, the protective (barrier) function of the mucosal epithelium is disrupted and the oral microbiocenosis changes. This creates favourable conditions for the proliferation of pathogenic microorganisms. For this reason, traditional treatment methods, including antiseptic agents, cannot always provide selective control of the pathogenic microflora, since they affect not only pathogenic but also conditionally pathogenic and normal microorganisms.

Unlike antiseptics, bacteriophages have a highly specific action, selectively lysing pathogenic bacteria without disrupting the normal microflora. This mechanism is particularly important in paediatric practice, because maintaining microbiological balance plays a major role in regeneration processes and local immunity. The results obtained showed that the use of bacteriophages was accompanied by a decrease in the frequency of secondary bacterial complications, which is consistent with modern views on the role of the microbiota in the pathogenesis of inflammatory diseases of the oral cavity.

The comparative analysis showed that, in the study group, the clinical recovery times were statistically significantly shorter than in the control group ($p < 0.05$). The faster reduction of the pain syndrome and the acceleration of epithelialization can be explained not only by the direct antimicrobial action of bacteriophages but also by their indirect effect on immune mechanisms. It is known that, during the lysis of bacteria under the action of bacteriophages, bacterial antigens are released, which may stimulate the local immune response.

The very good tolerability of bacteriophage preparations in children deserves particular attention. No clinically significant adverse effects were observed during the study, which confirms their safety and the appropriateness of their use in paediatric dentistry. Unlike some antiseptics, bacteriophages do not irritate the mucosa, do not alter taste sensation and do not have a negative effect on regeneration processes.

It should be noted that the results obtained are consistent with the data of national and international studies, which also report the promise of using bacteriophages in infectious and inflammatory diseases of various localizations. At the same time, despite the positive results, this study has certain limitations, including the relatively small number of patients, the absence of long-term follow-up, and the fact that microbiological examination of the microflora before and after treatment was not carried out.

As a promising direction for further research, it is important to conduct randomized controlled trials with a larger number of patients, as well as to study the interaction of bacteriophages with the oral microbiota using modern molecular-genetic methods. In addition, the development of personalized phage therapy regimens that take into account the individual microbiological profile of the patient is also of great interest.

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Conclusion

The results of the study confirm that including bacteriophage preparations in the complex treatment of stomatitis developing against the background of viral infections in children is a clinically justified and effective approach. It was found that the use of bacteriophages contributes to a faster elimination of the inflammatory process, a reduction of the pain syndrome and an acceleration of epithelialization in the affected areas of the oral mucosa.

According to the results of the comparative analysis, in patients treated with bacteriophage therapy a statistically significant reduction in the duration of treatment was observed compared with traditional treatment methods. In practice, the treatment time was reduced from 7 days to 3 days; of course, this reduction varied depending on the severity of the disease, the clinical course and the individual characteristics of the patient. In addition, the use of bacteriophages made it possible to control secondary bacterial infection more effectively without a negative effect on the normal oral microflora, which is an important advantage in paediatric practice.

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