MINISTRY OF HEALTH OF THE REPUBLIC OF UZBEKISTAN

TASHKENT STATE MEDICAL UNIVERSITY

TREATMENT OF CANDIDAL STOMATITIS IN CHILDREN.

MONOGRAPH

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The monograph is based on the analysis of our own research results,and the effectiveness of the drug "Citeal" in the treatment of candidal stomatitis in children is studied

The monograph is intended for 5th-year students, dentists and specialists dealing with this problem, as well as for pediatricians and infectious diseases specialists.

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References.

LIST OF ABBREVIATIONS

sJgA-secretory immunoglobulin

HIV – human immunodeficiency virus

WHO – World Health Organization

GI-hygienic index

GNL-Helium-neon laser

DNA-deoxyribonucleic acid

IRL- interferon reaction of white blood cells

MMSI – Moscow Medical Dental Institute

SPL stimulator with a semiconductor laser

PMA-papillary-marginal-alveolar

MMOC – Mucous membrane of the oral cavity

AIDS-acquired human immunodeficiency syndrome

UT-ultrasound therapy

US-ultrasonic spraying

PhI – phagocytic index

GT – the gastrointestinal tract

Introduction

Topicality of the topic:

In recent years, there has been a steady increase in the number of diseases associated with a violation of the biological balance between the macroorganism and various populations of microbial flora. The oral microflora is a highly sensitive indicator system that responds with qualitative and quantitative shifts to changes in the state of various organs and systems of the body [154]. Studies have shown that the barrier-protective mechanisms of the oral cavity are closely related to the microflora living in it. The variety and activity of microflora often determines the pathology of the oral cavity. Currently, fungal infections are one of the most common and poorly controlled [146]. So there are more than 400 types of fungi that cause various pathological changes in the body in humans. According to WHO fungal infection over the past decades, the number of diseases caused by opportunistic fungi of the genus Candida has been progressively increasing worldwide. One of the most important problems of dentistry in recent years is candidiasis of the oral mucosa (MMOC), the share of which in the structure of pathology of SOPR has reached 40.0-45.0%. This is mainly due to the introduction of new medical technologies and a significant increase in the number of patients with immunodeficiency, which is manifested in children by the development of a dysbiotic state of the oral cavity [108].Traditional methods of oral cavity treatment, when various chemicals such as potassium permanganate, menthol, and elixirs are used, do not have a pronounced bacteriostatic effect, and aggravate the dysbiotic manifestation.Therefore, new broad-spectrum drugs are being searched for. One of these drugs that meet modern requirements for medicines used for the treatment of candida stomatitis of the MMOC is the drug "Citeal".

Citeal is an antiseptic foaming solution. It is a synergy of three active components: chlorhexidine, hexamidine diisetionate, and chlorkresol. A drug with a wide spectrum of action: antiparasitic, antibacterial, antiviral, fungicidal. Good tolerance – does not irritate the skin of the face, mucous membranes, children's skin, has a pleasant smell, forms foam, does not cause photosensitization, does not violate the ecology of the skin and mucous membranes.

The drug "Citeal" was used in the treatment of candidal stomatitis in children, and the following was demonstrated:

1. The state of non-specific oral protective factors in children with candidal stomatitis was assessed over time during treatment with "Citeal" and compared with traditional treatment methods.

2. To conduct a comparative assessment of the effect of "Citeal" on quantitative and qualitative indicators of oral microflora in the treatment of patients with candidal stomatitis.

3. To establish a correlation between the clinical efficacy of treatment methods and the state of the oral microflora and non-specific oral protective factors in patients with candidal stomatitis.

4. The effectiveness of Citeal in the treatment of oral mucosal diseases was established.

Our study examined Citeal and its effect on the oral microflora in children with candidal stomatitis.

The drug's effect on local oral immunity was demonstrated.

This study is based on clinical, laboratory, and bacteriological studies, and a method for using Citeal in the treatment of candidal stomatitis in children was developed.

Direct and inverse relationships were established between quantitative parameters of the microbiota and immunological parameters of the oral cavity in children with candidal stomatitis before and after treatment with Citeal.

Clinical and immunobacteriological studies have identified qualitative and quantitative changes in the oral microflora and local immune system in children with candidiasis. Traditional treatment for candidiasis has been shown to be ineffective in completely eliminating the identified changes in the immune and microbial balance in the oral cavity, which are the cause of relapses and chronicity of the disease.

A method for using Citeal for the treatment of candidal stomatitis in children has been developed.

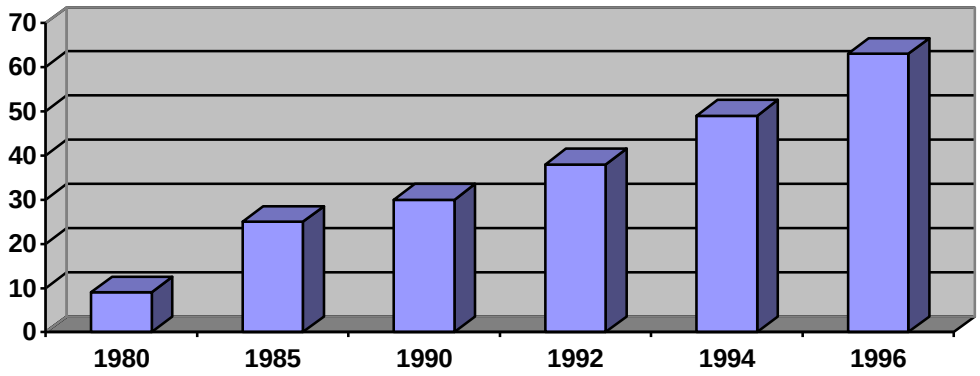
The cost-effectiveness of Citeal treatment, compared to traditional treatment, is due to a reduction in treatment duration by 1-2 days when using Citeal monotherapy.

CHAPTER I.

1. Acute pseudomembranous candidal stomatitis.

Fungal infection has increased dramatically over the past 20 years. This is mainly due to the introduction of new medical technologies and a significant increase in the number of patients with immunodeficiency. According to domestic and foreign authors and scientists from the CIS countries, the spectrum of mycoses is rapidly expanding. Thus, more than 400 fungal species that cause disease in humans are currently known [87,95]. If previously mainly mild cases of candidiasis were recorded, mainly thrush in children, now severe visceral and generalized forms are significantly common. This corresponds to the opinion of some foreign authors [166,171,182,183], who in 1953 considered candidiasis as a disease of the future.

Incidence of candidiasis in different years (%).



According to the authors [18, 69, 139, 143], candidiasis is the most common mycotic complication. The incidence of systemic candidiasis alone in individuals with various types of acute leukemia, in some clinics, reaches 11%, in patients with hematosarcomas-1% [15]. First of all, the mucous membrane of the oral cavity and esophagus is affected with the greatest frequency.

Candidiasis accounts for 1/3 of all SOPR diseases [129, 159,160, 162]. It is known that candidiasis develops against the background of certain physiological

changes in the human body of various pathological conditions, as well as as a result of adverse effects (long-term use of cytostatics, antibiotics, hormonal drugs).

A retrospective analysis of the prevalence of candidiasis of MMOC reveals a sharp increase in its share among other nosologies.

Candidiasis is a disease caused by yeast-like fungi of the genus Candida, which turn from conditionally pathogenic when the immune system of a macro-organism is weakened into pathogenic microorganisms [95]. They form pseudomycelia-filaments of elongated cells. They belong to imperfect fungi-deuteromycetes, which make up an independent genus with more than 80 species. C. albicans, C. tropicalis, C. psevdotropicalis, C. crusei, and others are more common in medicine [92, 93].

All etiological factors are divided into endogenous and exogenous.

Exogenous factors include local factors:

- eruption of baby teeth, violation of the integrity of the MMOC, chemical burns with arsenic paste, formalin, resorcinol [95, 159].

Endogenous factors include:

- metabolic disorders, hypovitaminosis, acute and chronic infectious and non-infectious severe diseases, diseases of the female genital organs. Children are especially susceptible to candidiasis. "Compress" candidiasis can develop when infants overheat, wear tight fitting clothes, tight nightwear, high humidity and temperature lead to maceration of the skin and the development of candidiasis [31, 32, 76, 147].

Fungi of the genus Candida mainly enter the human body from household items, dishes, toys, and food. The source of infection in children in maternity hospitals is medical personnel, equipment, diapers, oilcloths, pacifiers, needles, syringes, and catheters. In 56.4% of cases, the source of infection is mothers with vaginal candidiasis or urogenic candidiasis, which is observed in 25% of women in labor. Later infection of the newborn from the mother is carried out from the oral mucosa, from the skin of the nipple and hands [59, 95, 148].

Nosocomial and HIV-associated infection is usually oral candidiasis. According to the literature [138], 84% of the etiology of modern candidiasis occurs in the species C. albicans, 9% in C. parapsilosis, 2% in C. tropicalis and C. krusei, and 1% in C. clabratc. The leading triad of C. albicans, C. parapsilosis, and C. tropicalis species sensitive to modern antimycotics accounted for more than 95% of candidiasis in all localities.

Irrational long-term use of drugs can change the species composition of normal microflora, which leads to inhibition of the vital activity of microbes, sterilizes the mucous membrane of the oral cavity and intestines, weakens the human immune system, thereby releasing fungi of the genus candida.

In the pathogenesis of candidiasis, the main role is assigned to the failure of cellular immunity – a violation of the function of T-lymphocytes, the interaction of T and B lymphocytes, as well as a violation of the phagocytic activity of neutrophils, monocytes, and eosinophils. In chronic candida infection, the autoantibody titer increases, which is one of the most important links in the complex chain of immunological disorders in the state of the macroorganism [138, 149]. Due to long-term sensitization by products of vital activity of candida fungi, cells and tissues of the body are damaged – an autoimmune response. In chronic and severe forms of candidiasis, the level of blood antibodies and immunoglobulins, in particular Ig G, is increased. Antibodies delay candida filomentation and prepare for subsequent intracellular destruction.

In their works Volosevich L. I. and Sheremet Z. A. 1991 [36] note that the development of candidiasis of SOPR depends on the functional state of the mechanisms of specific and non-specific protection of the macroorganism. An important role belongs to the degree of pathogenicity of fungi of the genus Candida. The main role in this case is played by factors of aggression of the pathogen.

There are 5 levels of interaction between fungi and body cells due to the severity of immunodeficiency:

1. location of the fungus on the surface of the epithelium of the skin and oral mucosa without disturbing the cells of penetration of the fungus deep into the tissues;

2. damage to the epithelium by a fungus with the development of cellular reactions occurring on the surface of the skin and mucous membranes;

3. penetration of the fungus through the epithelium and its interaction with macrophages and neutrophils of tissues;

4. interaction of the fungus with cells of the liver, spleen and other organs with the formation of epithelioid cell granulomas;

5. penetration of the pathogen into the blood and the development of candidemia or candidonemia with multiple lesions in the brain, heart, kidneys and other organs.

Acute superficial candidiasis "thrush" begins asymptomatically. Later, children become restless and do not sleep well. When eating, there is a burning sensation, pain. Regional lymph nodes are enlarged and painful. The temperature is subfebrile. On the mucous membrane of the oral cavity, groups of mother-of-pearl-white spots are found, gradually increasing and merging with each other, forming a white film that rises above the level of the mucous membrane and resembles curdled milk. The plaque may change in color, become yellowish, dirty gray. The fungus initially develops on the surface of the MMOC and therefore is easily removed with a swab, soon penetrates into the surface and then deep layers of the epithelium. Such a plaque is removed with difficulty, and when the film is forcibly rejected, the bleeding erosive surface is exposed. The fungus can spread from the mouth to the respiratory tract and digestive tract. The spread of fungi by contact, hematogenic or lymphogenic means leads to generalized candidiasis, in which almost all organs and systems of the child's body are affected.

1.2. Microbiology and immunology of the oral cavity in children suffering from candidiasis.

The generally accepted position that the disease is easier to prevent than to treat remains relevant in the new economic environment. A great economic effect can be obtained if the prevention of diseases, including dental ones, begins from childhood. However, due to the transition of the Republic of Uzbekistan to market relations, dental care for children is in a worse position. As is well known, it has always been financed from the state budget, and even in the pre-perestroika period there were not enough funds for it, and today the situation has worsened even more [6, 112].

Man and the environment represent a single ecological system that is in a state of biological equilibrium. Symbiont microbes that are part of the macroorganism ecosystem not only form the normal composition of the child's microflora, but also take a direct part in the regulation of many physiological reactions and processes to maintain homeostasis [32, 37, 39].

From modern positions, the normal microflora of a child is considered as a set of microbiocenoses of various parts of the body. Normoflora includes hundreds of diverse species with a total numerical composition of more$^{\text{than 10-14}}$ cells, which are able to form a stable structure of the microbial landscape, and their qualitative (specific) and quantitative composition depends on localization [59, 83, 99].

At the same time, the set of microbiocenoses of a macroorganism is referred to as normobiocenosis, or eubiosis, although recently the term microecology is more often preferred, which is a more capacious concept, since it includes not only data on the qualitative and quantitative equilibrium of various populations of microbial flora of individual organs and systems of a macroorganism, but also their biochemical, metabolic and immunological state. state [46, 78, 153].

However, it should be remembered that when the threshold value of exo - and endogenous factors affecting the body is exceeded, microbiocenoses go out of the state of biological equilibrium, which, in turn, is accompanied by the

occurrence of microecological and immune disorders. This, in turn, leads to the dominance of potentially pathogenic microbes in the biotope, increased genetic exchange, and the formation of altered clones, which often include genes that determine the adhesive and cytotoxic properties of bacteria [23, 141, 153].

Recent studies show that these processes can lead to serious consequences, both functional and structural, that is, to the appearance of dysbiosis [23, 153].

In turn, dysbacteriosis can be formed due to a direct ecopathogenic effect on the microflora of the child with simultaneous violations in the factors of the immunological aspect [113, 141].

Moreover, it has been proven that this is accompanied by species selection of microorganisms, as well as changes within the biological species due to the survival in the habitat of more resistant strains that can cause or maintain diseases [113, 141].

Microbiological studies conducted in recent decades show that bacteria occupy the dominant place both in terms of the diversity of species living in the oral cavity and in terms of the number. Thus, according to various researchers, the number of bacterial species in this ecological niche in children ranges from 120 to 200. The number of oral bacteria in terms of the number of species and content per unit of material competes with the gastrointestinal tract. The content of microorganisms in saliva (oral fluid) is from 4 million to 5 billion CFU / ml, in plaque (plaque) it is even higher and ranges from 10 to 100 billion per gram of material [23, 33,81, 113, 117, 141].

According to various researchers, the share of anaerobic and microaerophilic oral flora in children accounts for 60 to 80 % of the microbial landscape. The remaining part is made up of facultative species: staphylococci, streptococci, Enterobacteria, Neisseria, Acinetobacteria and others [118, 191, 196, 203].

According to the results of studies led by Academician N. N. Bazhanov (1985) and Professor I. I. Oleinik (1990), conducted using the technique of anaerobic cultivation, it was found that the share of Staph. aureus accounts for no

more than 15 percent of all strains isolated from inflammation of the oral mucosa, even less often isolated coagulase-negative strains of staphylococci: St. epidermidis, St. saprophiticus.

At the same time, the isolation of streptococci (Str. pyogenes, Str. faecalis, Str.viridans) in inflammatory processes in the oral mucosa slightly exceeds 20-30 percent. Although it is necessary to take into account separately the frequency of isolation of microaerophilic streptococci of the oral cavity in children, which occupy an intermediate position between anaerobes and aerobes [172, 176, 186].

It should be especially noted that microaerophilic streptococci: Str. sanquis, Str. salivarius, Str. mitis, Str. mutans, Str. millari are quite often found in the pathological material of inflammatory diseases of the oral cavity in children, especially in periodontitis, abscesses, phlegmon, etc. [172,176,186].

It is well known that the mother's birth canal is non-sterile and during birth the child receives the microflora located there. However, not all types of the maternal organism colonize the oral cavity of the newborn, which is determined by the peculiarities of its genotype and physiology. 6-8 hours after birth, there is a rapid increase in the number of bacteria in the oral cavity. During this period, as a rule, various aerobic and facultative anaerobic species are identified: Neisseria, sarcina, lactobacilli, streptococci, staphylococci, corynebacteria, etc. [107, 208].

At the same time, the maximum diversity of the oral microflora reaches at the age of 2-4 months of life. In this case, the following bacteria are sown from the oral cavity: Neisseria, streptococci, including Str. salivarius, as well as yeast-like fungi of the genus Candida. Obligate anaerobes, such as Veilonella and some fusobacteria, appear in the folds and crypts of the mucosa [107, 108, 121].

An important stage in the dynamics of the formation of oral microbiocenosis is the period of teething. Teeth create conditions for the growth of obligate anaerobic species and bacteria with high adhesive abilities in relation to enamel: streptococci (Str. mutans, sanguis, actinomycetes). In preschool children, the microflora of the oral mucosa and gingival groove resembles the microflora of adults and includes bifidobacteria, peptostreptococci, fusobacteria and spirilli. At

the same time, most children usually lack representatives of the group of bacteroids, spirochetes, and protozoa [107, 108, 121].

A remarkable fact is the interaction of normal microflora with the child's immune system, which is confirmed by the detection of antibodies to many types of microbes. Since these data mainly fall on age groups older than 1 year, which coincides with the time of teething, it seems likely that this interaction is also associated with an inflammatory reaction in the gum during teething [13, 54, 146].

Many studies have established that saliva contains the most important molecular: lysozyme, lactoferrin, lactoperoxidase and other enzymes and cellular factors of nonspecific resistance of the body. The protective activity of various saliva substances is related both to their direct action on microbes and inhibition of tooth adhesion and enamel or mucosal epithelium [19, 40].

Lysozyme is an N – acetyl-muramyl hydrolase enzyme that is active in weakly acidic and neutral environments. Causes hydrolysis of the glycoside bond in the peptidoglycan molecule of the bacterial cell wall. It is produced by lymphocytes, granulocytes, macrophages, and some bacterial species [19, 94, 104].

At the same time, cellular factors of nonspecific resistance – macrophages and microphages (granulocytes) – perform a phagocytic function on the mucosal surface, in the gingival groove and submucosal layer. However, in children, due to the hypotonic environment of the oral fluid, the active role of leukocytes is significantly limited, and the picture of "incomplete phagocytosis" is often observed. Apparently, it is possible that such a mechanism is biologically justified from the point of view of maintaining equilibrium with the resident flora or stimulating the antigen-presenting function of macrophages in the immune response [14, 28, 88, 135].

It is interesting to note that active contact with the environment, carried out by our body through the oral cavity, in particular, the ingestion of a wide variety of antigens, determines that it is the "theater" of action of various affective and effector mechanisms of the human immune system. It has been established that all the most important functions of the immune system are implemented to varying

degrees at the level of the mucous membrane, submucosal layer of the oral cavity, and the lymphoid apparatus of the maxillofacial region [25, 53].

Undoubtedly, a particularly important role in this process is played by secretory IgA (sIgA), whose concentration in saliva is 1000 times higher than their concentration in blood serum. sIgA is a dimeric or trimeric macromolecule protected from the action of salivary proteolytic enzymes by a secretory component of a glycoprotein nature. Due to these features, for a long time sIgA was considered the only antiviral and antibacterial factor in saliva. However, recently it has been established that IdM and IgG can also retain their activity in saliva, although their concentration is lower than sIgA [61, 122, 155].

Immunological studies have established that changes in the described defense systems are detected already in the first days of the development of opportunistic infections in the oral mucosa, and sometimes precede the clinical manifestations of the disease. This gives grounds to consider defects of non-specific resistance and immunological reactivity as a trigger factor for acute inflammatory diseases of the oral mucosa [91, 192].

As noted by Loe H [192], the most common cause of weakening of human resistance to infection is considered to be a defect in phagocyte function. It turned out that the insufficiency of the cellular defense link activates yeast-like fungi, some bacilli, streptococci, actinomycetes, protozoa, oral cavities, and their population size is controlled by these mechanisms.

Loe H [192] also notes that lysozyme deficiency is accompanied by activation of gram - positive obligate and facultative anaerobic bacteria: peptostreptococci, actinomycetes, staphylococci, streptococci, whose peptidoglycan herpes is destroyed by sufficient activity of this enzyme.

Thus, it is necessary to recognize that the nature of developing local disorders in the focus of inflammation also depends on the type of opportunistic microbes that are activated, the breadth and possibility of implementing their pathogenic properties. This determines the need to consider individual genera and

types of oral flora, their pathogenicity factors in the development of acute and chronic inflammatory diseases of the oral mucosa.

It should be noted that among the huge variety of infections characteristic of humans, a special place is occupied by infections caused by bacteria, viruses and fungi. Among bacterial infections that occur, as a rule, with damage to the oral mucosa, these are: diphtheria, tuberculosis, scarlet fever, syphilis, at the same time, among viral infections, these include viruses of chickenpox, influenza, measles, herpes and others, and most often especially in children there are fungal lesions – candidiasis.

Lesions of the oral mucosa in children, as it was already emphasized above, there is an increase in cases of damage to the oral cavity by fungi of the genus Candida, i.e. candidiasis. In most cases, the disease is caused by C. albicans. This type is found in the oral cavity in about 60 % of adults, with a high frequency in women and men who smoke [138].

However, against the background of existing non - communicable diseases, HIV infections and AIDS, the carriage of Candida species other than C. albicans increases, and sometimes more than twice. A trend towards a decrease in the proportion of C. albicans in the oral flora was observed in the 1990s [138].

Human infection with candida fungi, as a rule, is exogenous and endogenous, newborn children are most often infected from their mothers. In these cases, infection with microorganisms that populate the mother's birth canal (especially in patients with vaginal candidiasis) may occur during childbirth, but more often it is caused by transmission through the hands of the mother and service personnel.

Observations have shown that the main source of neonatal thrush is the oral cavity of the mother and nurses of maternity hospitals [49].

According to the latest statistics, oral candidiasis occurs in 5% of newborns and almost 10% of infants. In healthy adults, this is a fairly rare disease, occurring almost exclusively in predisposed subjects. For various reasons, the

prevalence of oral candidiasis in the elderly is again close to 10%, although it increases to 60% in permanent prosthetic wearers [62].

Mycological studies of recent years indicate that the probability of Candida carriage in the oral cavity changes with age. Candida – can be detected in the oral cavity in more than 90% of newborns (according to foreign authors, in 45% of healthy newborns). In children older than this age, carriage is less common than in adults and does not exceed 45-65%. By the age of 10, its frequency reaches that of adults (in healthy people-30-45%). By the age of 80, the content of Candida in the oral cavity increases sharply [138].

According to the data of Romanyuk F. P., Chistyakova A. I., Bubnova L. N. [75] Candida carriage in the oral cavity in the 40-60s of the XX century averaged 40-50%, and at the same time by the age of 90 it averaged 60-70% in the entire population.

Individuals with oral diseases, salivation disorders [71], or other disorders of the oral ecosystem are predisposed to candida colonization. First of all, it is caries and periodontitis . Candida colonization of the oral cavity is also significantly increased in diabetes mellitus up to 67%, Down syndrome up to 69%, lichen planus and leukoplakia up to 76-82%, respectively, Sjogren's disease, tumor chemotherapy, HIV infection and AIDS up to 72-84% [13, 91, 138], including exfoliative cheilitis and other conditions. With HIV infection, the carrier is persistent.

However, it should be noted that the percentage of colonization increases significantly in elderly patients who wear dentures (about 60%) and use dentures [80]. Fungi are most often isolated from the surface of the prosthesis. Moreover, what is most interesting is that colonization is more likely to occur in those individuals who do not follow the rules of oral hygiene, leave dentures in their mouths overnight and do not sterilize them.

In addition, in recent years, it has been proven that candidiasis can be associated with blood type, so according to data [7, 15, 69], it is more common in people with the first (0) blood type.

Of great importance is the statement of a number of scientists [138] who claim that the use of antibiotics, especially broad-spectrum drugs and their combinations, leads to an increase in candida colonization by an average of 20% [203] and is considered as a factor most contributing to the development of oral candidiasis in adults. Due to these facts, antibiotic therapy largely determines the inclusion of oral candidiasis in the number of nosocomial infections.

At the same time, many mycologists believe that oral candidiasis is most often found in people with immunodeficiency conditions, apparently this is traditional for opportunistic infections in the state-HIV infection and AIDS and other oncological diseases with their radio and chemotherapy, treatment with corticosteroid hormones, including their inhaled forms, as well as severe exhaustion with poor nutrition.

Statistics show that oral candidiasis occurs in one-third of HIV-infected people and more than 90% of AIDS patients. Xerostomia from the use of a number of drugs is considered no less significant than a reduced number of $DM4_4$+lymphocytes, a factor predisposing to candidiasis in AIDS.

Apparently, it is quite justified to consider oral candidiasis as an HIV-associated disease; in the classification of HIV infection, oral candidiasis, including previously treated ones, is assigned to category B, although in the previous classification, persistent oral candidiasis for more than 2 months was considered in category D [138].

It is practically established that the initial event in the development of candida colonization or infection is considered to be the adhesion of a fungal cell to any surface in the oral cavity. Once in the oral cavity, the cell of any microbe finds itself in a complex ecosystem, its habitat is heterogeneous and depends on the influence of various factors.

According to histological data, the oral cavity has different types of epithelium lining the surface of the gums, tongue, cheeks or palate, teeth, dentures, require different abilities in adhesion to them. In addition, different areas of the oral cavity maintain different acidity, redox potential, oxygen content, carbon

dioxide and nutrients. Apparently, these factors create conditions for the colonization of different parts of the cavity by those microbial associations for which these conditions are most acceptable [98]. At the same time, the interaction of candida with other microbes in the oral ecosystem can be both beneficial and harmful for the former [138].

It is interesting to note that coagulation together with other oral microbes, Enterobacterium and Actinomyces, Streptococcus and others in the presence of saliva is considered one of the factors affecting the adhesion of C. albicans. This is determined by the amount and composition of bacterial flora, which can both significantly impair candida adhesion [138] and promote biofilm formation. The expression of candida adhesins to the mucosa and bacteria seems to occur simultaneously.

It is proved that microbes can break down macroorganism substances with the help of their own enzymes, thereby helping other microbes that do not have such enzymes. Candida was found to be resistant to the action of calcium hydroxide, which, along with the ability to survive together with some bacteria, may explain their excretion in chronic periodontitis [138].

The antagonistic influence of bacteria includes competition for adhesion receptors and nutrients, the creation of an unfavorable habitat due to the products of their own vital activity, and the production of microbocidal substances. It is assumed that some bacteria inhibit the growth of candida by producing fungicidal substances, which, in particular, include hydrogen peroxide and nitrite. Currently, an approximate composition of the oral flora that suppresses candida growth has been established [138].

Medical experience shows that the use of antibacterial drugs leads to a rapid change in the quantitative and qualitative composition of the oral microflora with the predominance of certain types of microbes, including candida fungi [106]. Deprived of competitors and antagonists, fungi get the opportunity for adhesion, accelerated growth and colonization.

It is known that the adhesion of candida to the oral mucosa is carried out by complex ligand-receptor interactions. As a rule, some salivary proteins promote adhesion, as well as the action of neuraminidase [138].

Successful adhesion is not yet a guarantee of future colonization. In order to conquer the ecosystem of the oral cavity, fungal cells need to survive and multiply. Various factors contribute to and prevent this.

Mycologists have found that the oral cavity, with its pleasantly low acidity and regular supply of easily digestible sugars, is a suitable habitat for fungi. An acidic environment ensures the existence, and with an abundance of carbohydrates, rapid reproduction in the yeast phase, as well as the activity of proteinases that destroy the protective factors of the macroorganism. The activity of candida proteolytic enzymes in oral candidiasis is significantly higher than in healthy people [138]. Temporary glucose deficiency promotes the formation of the mycelial phase and adhesion, and in the presence of glucose, biofilm formation is stimulated. Some sugars contribute to the survival of fungal cells under the influence of microbicidal factors.

Well-known mycologists Kindelan S. A., 1998; Ener B., 1992; McCarthy G. M., 1992; indicate that saliva, in addition to its physico-chemical properties and antimicrobial factors contained in it, has an antifungal effect of a mechanical nature. First, with saliva, candida cells that have not managed to gain a foothold on the surface are removed. Secondly, by flowing around the hard surfaces of the oral cavity, saliva interferes with adhesion to them. Third, saliva removes the remaining nutrients, especially carbohydrates. Apparently, these properties of saliva explain the fact that hyposalivation and xerostomia contribute to candida colonization. In addition, there is evidence that individuals with xerostomia tend to eat carbohydrate-rich foods.

It is well known that the microbiocidal factors contained in saliva are divided into specific and non-specific. The main specific factor is secretory immunoglobulin A (s-IgA), which is produced strictly against candida antigens, when the macroorganism comes into contact with them. Non-specific factors are

constantly produced against many microbes. Such factors are mucins, lactoferrin, lysozyme, peroxidase, etc.

It is interesting to note that the gingival slits are washed not with saliva, but with gingival fluid, which is similar in composition to blood plasma. The gingival fluid contains immunoglobulins of classes A, M and G, complement components, and transferrin. Cellular elements are mainly represented by polymorphonuclear leukocytes (90%), which also synthesize peroxidase and lysozyme; B lymphocytes predominate among mononuclears. Gingival fluid stimulates the activity of its neutrophils to a lesser extent than saliva [52, 57, 65].

One of the well-known immunologists Challacombe S. J., 1994; notes that currently sIgA is considered as one of the key factors opposing microbial colonization in the oral cavity. At the same time, one of the main mechanisms of its action is to prevent the adhesion of fungal cells by binding to adhesins. The effect disappears when mannose or anti-JgA is added to the medium.

The effects of sIgA also include suppression of germination in C. albicans, and the cell wall of fungi contains factors that prevent the action of sIgA . Serum IgA does not have this effect.

There is an opinion that sIgA is effective mainly in the fight against candida colonization, in the early stages in acute forms of oral candidiasis. However, despite the fact that the secretory component protects sIgA from destruction by microbes, C. albicans and C. tropicalis can lyse sIgA. In candida infection, especially in its chronic stage, cell factors, phagocytes, and T-lymphocytes are more actively involved in the fight against microbes [106, 138].

Most researchers believe that oral neutrophils are more capable of phagocytosis mediated by an alternative pathway of complement activation. Although, there is evidence that sIgA can have a negative effect on this process by shutting down fungal receptors [65].

Kurnatowski P., Kurnatowska A. J., 1999 (189) note that in oral candidiasis, the content of sIgA in the number and function of T-lymphocytes decreases. Increased sIgA correlates with the degree of colonization observed in

HIV infection and is most pronounced in AIDS. Among the factors that weaken candida phagocytosis in oral candidiasis, the effect of fluoride contained in many toothpastes was noted [106].

Thus, infection, i.e. oral candidiasis, is usually understood as a stage of the process following colonization and representing an invasion, the introduction of a fungal cell into the tissue of a macroorganism. The depth of invasion can vary from minimal, which is observed in most cases and is limited to epithelial layers, to pronounced, reaching the submucosal and muscular membranes [138].

It should be noted that currently, leading dental scientists in many countries, together with mycologists, pharmacologists, are developing special tools for the prevention of candidiasis and other oral diseases in children and predisposed individuals. These include miconazole varnish for dentures, acting on fungi and bacteria. For patients suffering from hyposalivation, special gels are offered and used, artificial saliva containing histatins is developed. The possibility of using probiotic bacteria that make up the normal ecosystem of the oral cavity is being studied [106, 138].

1.3. Modern approaches to the treatment of diseases of the oral mucosa in children.

Treatment of oral candidiasis.

Treatment of candidiasis requires an individual approach to each case, as candidiasis usually develops as a secondary disease caused by a decrease in immunological protection, which can be due to various reasons.

All treatment is divided into general and local. A diet with the exclusion of sweets and restriction of carbohydrates, rich in vitamins and proteins, is prescribed. With a mild degree, local alkalinization is used, which is an obstacle to the vegetation of mushrooms, in the form of irrigation and washing the oral cavity with 1-2% sodium bicarbonate. It is rational to use nystatin powder [87].

Leshchenko, G. N., 1985 [93] believes that aniline dyes 1-2% water and alcohol solutions of methylene blue, diamond green, 0.25% silver nitrate solution, Lugol's solution, fucorcin (Castellani liquid), nystatin, levorin, and decamine ointments are effective for treating surface forms.

Based on the failure of the immune system, Kashkin P. N., Sheklakov N. D. [72] recommend a candida vaccine: monovalent, polyvalent, and auto-vaccine. For the same purpose, pyrimidine derivatives can find a place in the arsenal of medicinal products – pentoxyl 0.2 g 3 times a day for 3 weeks, methyluracil 0.5 x 3 times a day, the course of treatment is 3-4 weeks. The drugs stimulate the production of antibodies, phagocytic activity, activate leukopoiesis, increase the content of gamma globulin in the blood serum, and increase the regenerative ability of tissues.

Lukinykh L. M., 2000 [95] suggests gamma-globulin, histoglobulin 2 ml 2 times a week for a course of 7-10 injections. After 2-3 months, the course of treatment is repeated. T-activin 40 mcg per day subcutaneously or intramuscularly. The course of treatment is 7-10 days.

Kem-tonon 0,2-3 times a day for 14 days. Or diuciphone 0.1-2 times a day for 6 days. Conduct 2-3 such courses with an interval of 1-3 days under the control of biochemical and immunological blood parameters.

Levamizole (decaris) 150 mg 1 time a day for 3 days, spend 2 courses with an interval of 3-6 days. Repeat the course of treatment after 2-3 months [69].

A.V. Shumsky, M. M. Pozharitskaya, and E. V. Yurchenko, 1996 [163] suggest antifungal immunomodulatory lymphotropic therapy. In this case, levorin is administered in a horizontal position of patients subcutaneously in the middle third of the lower leg after a preliminary injection of lidase, after which a cuff is placed on the thigh for 2-2. 5 and pressure is created up to 45-50 mm Hg.An immunocorrector thymogen is injected into the submandibular and chin lymph nodes. The course of treatment included 5-6 courses. After treatment, the state of the SOPR normalized, the contamination of the mucous membrane with yeast cells sharply decreased, the content of substances with an average molecular weight in

mixed saliva decreased, and cellular and humoral immunological indicators normalized.

Lukinykh et al., 2000 [84, 95] recommend polyene antibiotics – nystatin, levorin for 500 thousand rubles. UNITS 4-8 times a day, so a daily dose of 2-4 million units of the drug, for a course of treatment of 56 million units for 14 days. It is advisable to chew and absorb the tablet, since polyene antibiotics are poorly absorbed in the gastrointestinal tract. Regression of clinical symptoms is observed on day 5-6: hyperemia, edema, loosening of the SOPR decreases, epithelialization of erosion is observed. In case of ineffectiveness of nystatin and levorin [157], amphotericin B is recommended.The dose is set individually at the rate of 100-250 u/kg, gradually the dose can be increased to 400-500 u/kg IV, for a course of 20-25 infusions.

Glazkova L. K. [69] believes that amphoglucalin has a similar effect, the course of 14 days is 600 thousand rubles. UNITS up to 1 million units per day. Canesten 60 mg / kg of body weight, the course of treatment is 10-14 days.

Il'in I. I. [69] suggests demikainovuyu caramel 0.00015 g for 1 caramel 6-8 times a day for 14 days. Nizoral 2 tablets a day, a course of 10 days, lamizil 250 mg a day, a course of 2 weeks, diflucan 100 mg 1 time a day, a course of 7-14 days.

Multivitamins with trace elements [9] 2-3 tablets a day for 1 month. Vitamins of group B – B2,- B6, C, PP and others. Vitamin B2 (riboflavin) has a certain antifungal effect, regulates redox processes, and takes part in the processes of carbohydrate, protein, and fat metabolism.

A number of authors (16, 17, 76) recommend using calcium supplements (calcium gluconate, calcium glycerophosphate, calcium lactate) 0.5 g 3 times a day for 1 month as a general tonic and hyposensitizing.

Pantothenic acid preparations-calcium pantothene 0.1 g-3-4 times a day for 1 month. Since candidiasis disrupts iron metabolism, iron preparations are recommended for 1 month-ferroplex, conferon, reducing iron tablets. Desensitizing

therapy is also mandatory: diphenhydramine, suprastin, pipolfen, fencarol for 1-1. 5 months [72].

Polyene antibiotics [134] in the form of applications on the oral and lip mucosa are used every day, 3-4 times a day, and the course of treatment is 14 days. Levorin and nystatin ointments, clotrimazole and canesten, mycoseptin and mycoheptin, amphotericin and decamine ointments can be prescribed in the form of 20-minute applications. To enhance the penetrating power of polyene antibiotics, the applicator is pre-moistened with a 10% dimexide solution, and an ointment base is applied on top. Topical application of polyene antibiotics leads to changes in the cytoplasmic permeability of cells, thereby exerting a fungicidal and fungistatic effect [144].

Alkaline mouthwashes – 2-4% sodium bicarbonate solution, sodium tetraborate, 2% boric acid solution, which can stop the reproduction and growth of candida fungi [144].

To stop the growth and reproduction of candida fungi [95], the authors suggest iodine preparations – 1% iodinol solution, 0.1% iodine solution, Lugol solution, which can be applied topically, in the form of mucosal quenching.

Aniline dyes – 1-2% methylene blue solution, diamond green, Castellani liquid, 1-2% fuchsin solution, methylene violet, crystal violet, gentian violet in the form of quenching of the oral mucosa, 1-2 times a day, preparations have a fungistatic effect, stop the growth and reproduction of the candida genus fungus [75, 162].

Keratoplastic medicines: vinilin, Tezan emulsion, aloe juice and kalanchoe juice, vitamin A and E in oil, rosehip oil, carotolin, olive and sea buckthorn oil, aekol, aloe liniment and kalanchoe liniment in the form of applications on the oral mucosa, for 20 minutes 3-4 times a day, from 4-5 days from initiation of general and local treatment with polyene antibiotics. [138].

CHAPTER II

Microbiological and immunological studies of children with candidal stomatitis

2.1 General characteristics of the clinical material.

We examined 70 children. With candidal stomatitis - 60 children. 10 healthy children from kindergarten N419 formed the control group. The studies were conducted in children aged 3 months to 6 years, not burdened with any common diseases. There were isolated cases of 10, 11, and 14-year-olds. The examined children are divided into 3 groups and 4 subgroups:

I-control group 10 people	II-children with candidal stomatitis 60 people

Traditional treatment for 20 people	Lech.citealom 40 people

$$PMA = \frac{\text{sum of indicators}}{\text{number of teeth x 3}} \text{ x } 100$$

The evaluation was performed using the following codes:

0 points – no inflammation

1 point – inflammation of the gingival papilla

2 points – inflammation of the gum margin

3 points – inflammation of the alveolar gum

The severity was determined by the following criteria:

Up to 30% - light grade

30-60%-medium degree

more than 60%-severe stage

The degree of oral hygiene was determined by the method of Fedorov. Yu. A. and Volodkina. V. V., 1972; by staining the lower frontal teeth with Lugol's solution according to the following formula

GI=Sum of plaque scores/n number of examined teeth.

Assessment of the intensity of plaque staining on each tooth is carried out using the following codes:

1 point – no staining

2 points-staining 1/4 of the tooth crown surface

3 points – staining 1/2 of the tooth crown surface

4 points-staining 3/4 of the tooth crown surface

5 points – staining of the entire tooth surface.

Score criteria

1.1-1.5 points – good oral hygiene

1.6-2.0 points – satisfactory oral hygiene

2.1-2.5 points – poor oral hygiene

2.6 – 3.4 points – poor oral hygiene

3.6-5.0 points – very poor oral hygiene.

5. The period of clinical recovery is characterized by complete recovery of impaired functions

2.1.1. Candidal stomatitis.

In children with candida stomatitis, mainly mild and moderate forms of the clinical course of candida stomatitis were registered - this group consisted of 60 people, of which 20 were allocated to the treatment control group, who received the traditional method of treatment.

Candidal stomatitis according to the clinical classification of mycoses proposed by N. D. Sheklakov in 1976, there are

- superficial candidiasis of the mucous membranes, skin, nails

- chronic generalized granulomatous candidiasis
- visceral systemic candidiasis of various organs.

Acute and chronic candidiasis are distinguished by the course of the disease:

- acute pseudomembranous candidiasis (thrush),
- acute atrophic candidiasis,
- chronic hyperplastic candidiasis,
- chronic atrophic candidiasis.

The disease begins asymptomatically, later children become restless, do not sleep well, and lethargically suck the breast. Older children complain of an unpleasant taste in the mouth, a burning sensation, then pain appears during meals, especially sharp and hot. Regional lymph nodes can be painful. The temperature is within the normal range or subfebrile.

On examination, groups of pearlescent – white spots ranging in size from fractions of a millimeter to 1 – 1.5 mm of a round shape were found on the unchanged or hyperemic mucous membrane of the tongue, lips, cheeks, and palate. As the fungus multiplied, the affected areas slowly increased in size and, merging with each other, formed a white film that rises above the level of the mucous membrane and resembles curdled milk. Sometimes the plaque is coarser, cheesy, tiny or frothy, containing threads of pseudomycelia, budding mushroom cells, desquamated epithelium, white blood cells, and food residues. The plaque changed in color, becoming yellowish, dirty gray, and when blood hit – brown. The fungus initially developed on the surface of the mucous membrane and therefore was easily removed with a swab, but after penetration into the surface, and then into the deep layers of the epithelium, the plaque was removed with difficulty. When the film was forcibly rejected, a bleeding erosive surface was exposed. It is possible that the fungus penetrates into the underlying connective tissue and even sprouts the walls of blood vessels, followed by hematogenic dissipation of candidiasis. The fungus can spread from the mouth to the respiratory tract and digestive tract. Young children often have yeast skin lesions in the genital, cervical, and

interdigital folds, which is important to consider as a source of repeated infection of the oral cavity.

Due to the introduction of new medical technologies and a significant increase in the number of patients with immunodeficiency, the number of fungal and herpetic infections has increased dramatically. Therefore, for the treatment of stomatitis, we need more effective drugs that can respond to the invasion of infectious agents, which can stop the infectious process. One of these drugs that meet modern requirements for medicines used in the treatment of diseases of the SOPR is the drug Citeal.

2.2. CHARACTERISTICS OF THE DRUG CITEAL.

Citeal is a foaming antiseptic solution with antibacterial, antifungal and antiparasitic properties.

The composition of the drug includes chlorhexidine-cationic antiseptic, synthetic biguanide, hexamidine - cationic antiseptic from the group of diamidines, chlorocreosol-antiseptic from the group of halophenols.

Due to the combination of different three components in it, Citeal has a wide range of activity, which includes

1. Gram-positive bacteria Streptococci, Staphylococci.

2. Gram-negative bacteria Proteus, Pseudomonas aeruginosa, E. coli, Neisseria gonorrhoeae.

Cytéal

ЦИТЕАЛ МЕХАНИЗМ ДЕЙСТВИЯ

Цитеал представляет собой пенообразующий раствор, который благодаря трем своим компонентам оказывает:

- ✓ бактерицидное действие
- ✓ фунгистатическое действие
- ✓ бактериостатическое действие

СИНЕРГИЗМ ТРЕХ АКТИВНЫХ КОМПОНЕНТОВ

- ХЛОРГЕКСИДИН
- ГЕКСАМИДИН ДИИЗЕТИОНАТ
- ХЛОРОКРЕЗОЛ

ЦИТЕАЛ
ШИРОКИЙ СПЕКТР ДЕЙСТВИЯ

ПРОТИВО-ПАРАЗИТАРНЫЙ
Trichomonas vaginalis,
Treponema palidum

ПРОТИВО-ГРИБКОВЫЙ
Candida albicans
Trichophyton rubrum
Microsporum canis

АНТИ-БАКТЕРИАЛЬНЫЙ
Грам + : Streptococci, Staphylococci
Грам - : Proteus, Psedomonas aeruginosa, E. coli, Gardnerella vaginalis
Chlamydia Trachomatis, Neisseria Gonorrhea, Mycoplasma.

ПРОТИВО-ВИРУСНЫЙ
Herpes type I
Herpes type II
HIV

Cytéal
ЦИТЕАЛ

ИДЕАЛЬНЫЙ АНТИСЕПТИК ДЛЯ НАРУЖНОГО ПРИМЕНЕНИЯ

- ✓ Эффективен в биологических средах (гной, кровь, серозная жидкость и др.)
- ✓ Образует пену с приятным запахом
- ✓ Не раздражает кожу лица, детскую кожу, слизистые оболочки
- ✓ Уменьшает кожный зуд
- ✓ Не вызывает фотосенсибилизацию
- ✓ Не нарушает экологию кожи и влагалища
- ✓ Сохраняет терапевтический эффект в течении 18 часов

ТРИ АКТИВНЫХ КОМПОНЕНТА ЛУЧШЕ ЧЕМ ОДИН

3. Candida albicans fungi.

4. Protozoa Trichomonas vaginalis.

Citeal also inactivates the herpes simplex virus (type 1-2)

The drug retains its activity in the presence of biological substances (pus, keratin, blood, serous fluid).

Its effect lasts up to 18 hours after a single application. The drug also has an antipruritic effect.

The main active substance of Citeal is chlorhexidine.

Citeal does not irritate tissues and skin, does not cause photosensitization and discoloration of the skin, does not violate the ecology of the skin.

Citeal has both curative and preventive effects.

All sick children in the dynamics of their observation were studied using clinical and laboratory methods. Dental examination of children was performed on the first day of their admission. Concomitant and acquired diseases, the duration of the underlying disease, the extent to which the child owns and how individual oral hygiene care is performed were investigated. Clinical examination of the oral cavity was performed on a dental chair using dental instruments in natural light. When studying the dental status, the condition of the hard tissues of the teeth, periodontal, oral mucosa, the presence of rashes, aft, erosions, swelling, pasty plaque on the tongue, and the condition of the papillae of the tongue were taken into account. The diagnosis of acute herpetic stomatitis was established on the basis of complaints from sick children, their parents, objective and laboratory data. The severity of the disease was determined by the severity of the temperature reaction, the presence of rashes on the oral mucosa, on the skin of the face and in the oral region. According to the severity of the clinical course, sick children were divided into three groups and each group was treated according to an individual method:

Most microorganisms do not have their own metabolic system, but use the metabolic system of the macroorganism cell for life and reproduction. At the same

time, a number of new protein compounds are formed in the body, which cause intoxication and allergization of the macroorganism. Often there are concomitant dyspeptic phenomena. Secondary infection also plays an important role.

It is necessary to adjust the function of the intestines, ensure proper nutrition, prescribe gastric juice, vitamins, especially C and group B, with neuralgic pain – amidopyrine. In a serious condition of the child, as well as with a sluggish, prolonged course of the disease, general tonic treatment is used.

2.3. Microbiological studies.

Along with dental research methods, we conducted microbiological and immunological studies in the same children.

For this purpose, oral fluid was collected from all examined children during the examination period 2 hours after eating in sterile test tubes. Serial dilutions were prepared from the obtained material in the laboratory, then a certain amount of which was sown on the surface of differential diagnostic nutrient media: agar for anaerobes, Endo medium, milk-salt agar, Kalina medium, blood agar, MPC-4 medium, Saburo medium, and others.

It should be noted that the Laboratory of Microbiology (TMA), since 2004, has been using new highly selective nutrient media obtained from the company Hi Media, which opened the Uzbek-American joint Venture Phoenix International in Uzbekistan.

Crops on blood agar, Endo, milk-salt agar, Saburo were cultivated under normal conditions for 18-24 hours, at a temperature of 37^0C, and the cultivation of crops for the isolation of anaerobes was carried out by the method of "sealed" polyethylene bags (Somov L. A. et al., 1987) filled with main natural gas (Adylov Sh. K., 1988). Cups with crops on MPC-4 were placed in a desiccator with a candle in a thermostat at 37^0C for 24-48 hours. Packages filled with gas from Blaurocco crops were also placed in a thermostat at 37^0C for 3-5 days. After the specified time, the seeded cups were removed from the thermostat, the grown colonies were counted, the group and species belonging of isolated

microorganisms were determined based on microscopy data of Gram-stained smears, the growth pattern on selective and differential diagnostic media in accordance with the Order of the Ministry of Health of the USSR No. 535 of 1985 "On the unification of microbiological research methods". Belonging to the Micrococcaceae family was determined by morphological characteristics and the presence of catalase.

The generic identity of Staphylococcus and Micrococcus was determined by the following tests: the presence of pigment, microscopy data, and glucose breakdown under anaerobic conditions.

To differentiate staphylococci of golden and epidermal origin, tests were used: ability to produce hemolysin, plasma coagulase, lecithinase, and ferment mannitol under anaerobic conditions. In the presence of all these properties, the studied cultures were classified as staphylococci aureus. Epidermal staphylococci did not have similar properties.

Group D streptococci included strains that ferment mannitol, produce growth in 40% bile, 6.5% sodium chloride, and reduce 1% blueness in milk.

Table 1. Volume of microbiological and immunological studies performed.

#	Group	of children examined	total	Microbiological studies Immunological studies
1	Control group	10	10	10
3	Children with oral candidiasis after traditional treatment. therapy sessions.	20	18	17
5	Sick children with oral candidiasis	40	20	20

	after special treatment. "Citealom".			
Total		70	48	47

When working according to the modified method, the result was taken into account according to the last dilution in which bacterial growth was obtained, the number of microorganisms was calculated according to the following formula:

K = A x 200 x P (CFU / ml)

Where, K is the number of bacteria of a certain type.

A is the number of colonies on the plate in the last dilution, where there is microbial growth;

200 – coefficient that leads to loop seeding (volume is 0.005 ml) in accordance with 1 ml.

P – the degree of dilution.

The number of bacteria of each species was expressed in lg CFU / ml.

Taking into account the numerous literature data on the pathogenic role of conditionally pathogenic autoflora, the presence of pathogenicity factors was determined in the selected representatives of the salivary microflora.

To study pathogenicity enzymes, conventional methods were used to study hemolytic properties, plasma coagulation ability, fibrinolytic, lecithinase, and hyaluronidase activity.

Cultures with two or more pathogenicity factors were considered the most likely agents in the realization of potential pathogenicity.

2.4. Immunological research methods.

In parallel with microbiological studies, immunological indicators were studied in the same children. To determine the phagocytic activity of neutrophils in saliva, saliva sampling and processing were performed according to the method of M. A. Temurbaev (1984) modified by Antonov A.V. (1996). To do this, the selected saliva was cleaned, washed with buffered solution and centrifuged at 1000

rpm for 10 minutes: the supernatant was drained, and 0.5 ml of saline solution was added to the sediment. To 0.2 ml of the resulting mixture, 0.1 ml of suspended latex particles ($5x10^8$ in 1 ml) with a diameter of 0.8 microns were added in a test tube. The mixture was incubated in a wet chamber for 30 min, at 37^0S, shaking constantly. Subsequently, smears were prepared from this mixture and stained according to Romanovsky-Giemsa. At least 100 neutrophils with and without latex were counted in each preparation, the phagocytic index was determined, i.e., the % of phagocytic leukocytes counted, and the phagocytic number-the average number of absorbed latex particles per phagocytic cell.

The activity of lysozyme in saliva was determined by us using the method proposed by Aliyev Sh. R. (1994), which included the use of sterile paper disks. For this purpose, saliva was collected on an empty stomach in sterile test tubes, then paper disks (similar to antibiotic disks) were taken with tweezers and thoroughly soaked in saliva, then these disks were placed on the surface of nutrient agar (Diff'ko agar) in Petri dishes sown with lawn with a daily culture of Micr. lysodenticus (strain 2665 GKI im. L. A. Tarasevich) crops were incubated in a thermostat at a temperature of 37^0C, the activity of lysozyme in saliva was determined by the agar diffusion method.

Determination of class A immunoglobulins-secretory fraction. The method is based on the Mancini method (1964), which is based on measuring the diameter of the precipitation ring formed when oral fluid is introduced into wells cut in an agar layer in which monospecific antiserum is preliminarily dispersed. Under standard experimental conditions, the diameter of the precipitation ring is directly proportional to the concentration of immunoglobulin.

To determine the level of immunoglobulin in the test saliva, the following procedure was performed: the diameter of the precipitation ring of the test oral fluid was plotted on the abscissa axis, the perpendicular was restored to the intersection with the calibration curve, and then the straight line was projected onto the ordinate axis. The obtained value corresponded to the level of immunoglobulin, which was expressed in IU / ml.

2. 5. Statistical processing of the obtained data.

The resulting digital material was processed statistically. The arithmetic mean, their errors, and confidence intervals were calculated with 95% probability.

The arithmetic mean was calculated by the formula:

$$M = \frac{E_x}{n}, \text{ where}$$

E_x – the sum of the results of individual definitions.

n – total number of definitions.

The standard error was found by the formula:

$$m = \sqrt{\frac{E\,(x_2 - x_1)^2}{n\,(n-1)}}, \text{ where}$$

$E\,(x2_2 - x_1)^2$ – sum of squared deviations of the results of individual measurements from the arithmetic mean;

n – number of individual dimensions.

Reliability was determined by the formula:

$$t = \frac{M_1 - M_2}{\sqrt{m_1^2 + m_2^2}}, \text{ where}$$

M_1 ; M_2 – comparative arithmetic averages.

m_1, m_2 – errors in arithmetic means.

the correlation coefficient between the studied parameters was calculated using the algebraic correlation formula:

$$r = \frac{M_1 \text{ x } M_2 - M_1 \text{ x } M_2}{SM_1\, SM_2}$$

$M_1\ M_2$ – the average value of the products of the arithmetic mean values.

$M_{M1}\ x_{M2}$ – product of the arithmetic mean values.

$SM_1\ SM_2$ – standard deviations from the arithmetic mean values.

Calculations were performed using JBM P / C computing equipment.

Chapter III. Clinical and laboratory evaluation of treatment results

3.1. Clinical study of the oral mucosa in children with candidiasis.

During the period of work from 2003-2005, 70 sick children were under our supervision. Of these, 60 children and 10 healthy children had candida stomatitis in the control group.

3.1.1. Clinical study of SOPR in acute pseudomembranous candidiasis [thrush].

Thrush is the most common form of damage to the oral mucosa. Infants and weakened children are more likely to get sick.

The group of patients with candidal stomatitis consisted of 60 people. When examining this group of sick children, we noted on the oral mucosa pearlescent-white spots ranging in size from fractions of a millimeter to 1-1.5 mm of rounded shape, located on the tongue, cheeks and soft palate. As the fungus multiplies, the affected areas slowly increase in size by 1-1. 5 mm and, merging with each other, formed a white film that rises above the level of the mucous membrane and resembles curdled milk. It was found that the plaque was sometimes coarser and resembled curd-like masses, tiny or foamy, consisting of threads of pseudomycelia, budding fungal cells, desquamated epithelium, leukocytes, and food residues (Figs. 6, 7). We noted that depending on the composition, the plaque can change color, become yellowish, dirty gray and when blood gets brown. The fungus initially develops on the surface of the mucous membrane and therefore the plaque is easily removed, and a hyperemic area is found under it. When the fungus sprouts into the deep layers of the epithelium, the plaque is removed with difficulty, and when the film is forcibly rejected, the bleeding erosive surface is exposed. At the same time, all areas of the oral mucosa can be affected

Figure 5. A sick child with candidal stomatitis

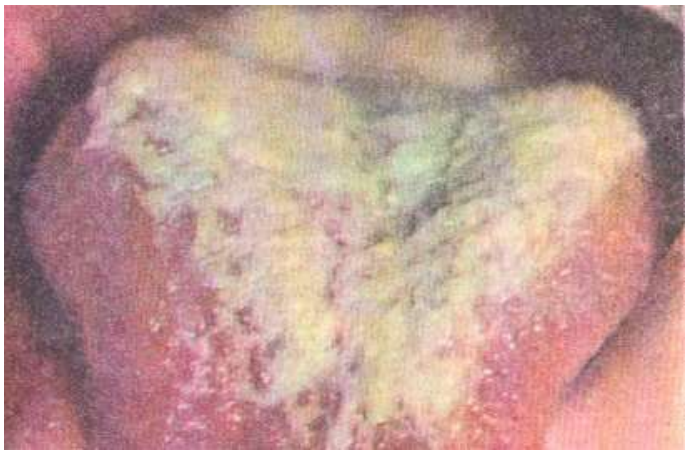


Figure 6. A sick child with candida stomatitis

Figure 7. A sick child with candida stomatitis

mouth, palate, tongue, lips, cheeks. The process can spread to the larynx, pharynx and esophagus. It is possible that the fungus penetrates into the underlying connective tissue and even sprouts the walls of blood vessels, followed by hematogenic dissimilation of candidiasis. If acute pseudomembranous candidiasis is not treated, it can develop into an acute atrophic form.

Children clinically ill with candidiasis refuse to breastfeed and eat, become sluggish and moody.

Observations have shown that young children often have yeast skin lesions in the genital, cervical, and interdigital folds, which is important to consider as a source of repeated infection of the oral cavity.

3.2. The state of oral microflora in sick children with candidal stomatitis.

It is known that in the human body, the oral cavity contains the largest number of bacterial species compared to other cavities, not including the colon. According to various authors, the number of bacterial species, including anaerobes, ranges from 100 to 200. This is due not only to the fact that bacteria enter the oral cavity with air, food, water, etc., so-called transit microorganisms, but here we are talking about the resident bacterial flora of the oral cavity, which forms a rather complex and stable ecosystem.

Numerous studies conducted both in our country and abroad have proved that in the vast majority of cases, pathological processes in the oral cavity are usually accompanied by dysbiotic changes in the microflora of the oral fluid, which in turn leads to a violation of the state of the immune system indicator.

According to current data, human herpesviruses type 1 and 2 belong to the Alphagerpesvirinae and are characterized by effective destruction of affected cells, a relatively short reproductive cycle, and the ability to remain latent in the ganglia of the nervous system. The virus is contained in saliva both in the presence of lesions of the oral mucosa, and without them, when the disease is asymptomatic. Clinically expressed primary herpetic infection is observed more often in children

aged 6 months-5 years and less often in adults. In children, the most common form of primary herpes is aphthous stomatitis, accompanied by extensive damage to the oral mucosa /Shuvalova E. P., 1999/.

Given the associative nature of the "Microbial Landscape" in various pathological processes in the oral cavity, the question naturally arises about the role of individual representatives of microflora in the development and course of the disease, and this will help us to study the quantitative and qualitative ratio of individual representatives of microbial flora.

Table 2. Characteristics of normoflora
oral cavities in children and adults.

Lg M±m CFU / ml

№	Groups of microbes	Microbial groups Number of microbes in 1 ml of saliva	
		Norm in adults	Norm in children
1	Total number of anaerobes	7,60±0,41	5,69±0,15***
2	Lactobacilli	5,90±0,14	4,60±0,14***
3	Peptostreptococci	6,00±0,39	3,77±0,11***
4	Total number of aerobes	6,30±0,41	5,30±0,17*
5	Staphylococci aureus	--	-
6	Staphylococci saprophytic	-2.15	2,15±0.51
7	Staphylococci epidermal	3,15±0,30	4,15±0,14***
8	Streptococci gr A.	--	-
9	Enterococci	4,30±0,19	5,15±0,15***
10	Escherichia Lp	-	2.30±0.17
11	Escherichia LN	-	-
12	Candida River	fungi 1.30±0.25	2.15±0.18***

Note: * - the presence of confidence (P >0.5) in comparison with the control

***- presence of confidence (P >0.001) in comparison with the control

3.2.2. Features of candidal stomatitis.

It is known that inflammatory processes in the oral cavity most often occur under the influence of endogenous infections as a result of violation of physiological protective devices. The course of odontogenic inflammatory processes, like any other, can be different and the composition of the microbial flora largely depends on this.

The development and widespread introduction of immunological research into clinical practice in the last decade show that the frequency of numerous diseases of the oral cavity, especially various inflammatory processes in children, is directly or indirectly dependent on the state of both general and local factors of oral immunity.

Along with viral infections, fungal diseases have also become widespread in recent years, among which candidiasis occupies a special place. As most mycologists point out, candidiasis accounts for the vast majority of cases of mucosal lesions, among which candidiasis of the oral cavity in children plays a significant role. The widespread prevalence of candidiasis is not surprising, given that Candida albicans are found on the mucous membranes and skin of more than half of the entire population of the planet /Sergeev V. P., 2001/.

According to the majority of mycologists, the significant increase in the incidence of candidiasis observed in the last decade is primarily due to the fact that this infection is opportunistic, and therefore affects primarily a weakened body, and this probably explains the most frequent oral lesions in children whose immune system has not yet fully matured.

Candidiasis develops due to the introduction of fungi into the tissues, which are normal inhabitants of the mucous membranes. The transition of Candida to a parasitic state and the occurrence of visceral candidiasis contribute to severe general diseases, chronic diseases of the respiratory system and gastrointestinal tract. Also of great importance are immunodeficiency, irrational use of antibiotics, corticosteroid drugs, immunosuppressants, etc. Candidiasis of the oral mucosa in children – thrush or yeast stomatitis-is manifested by damage to the mucous

membranes of the cheeks, palate of the tongue, gums, corners of the mouth (jamming). It develops more often in infants. On the oral mucosa, white and bluish-white spots appear-plaque-like and curd-like masses, the accumulation of which in different areas is not the same.

We have studied the state of oral microbiocenosis and the immune system in children suffering from candida stomatitis. The data obtained in these studies are presented in Table.№6. The table shows that in sick children suffering from candida stomatitis, dysbacteriosis is detected at the stage of applying to the polyclinic.

A characteristic feature of these dysbiotic changes in the oral cavity in children is a significant decrease in the anaerobic group of microorganisms, but against this background there is a sharp increase in the amount of captcha flora. So, the total amount of aerobes was lg 8.60±0.69 CFU / ml, which is 3 orders of magnitude more than anaerobes.

It is noteworthy that in the oral cavity of these children, microbes appear that are not characteristic of this biotope, such as staphylococci aureus, pyogenic streptococci, lactose-negative Escherichia strains. Moreover, it should be noted that these are mostly those groups of microbes that, as a rule, have a large set of pathogenicity enzymes. But, we were especially surprised by the condition of the mushrooms, the initial sowing from the usual dilutions actually gave a continuous growth (fig. 12), when we prepared a smear from them, it turned out to be typical strains of Candida fungi (Fig.13).

Table 6. The state of oral microflora in children of sick children candidal stomatitis. lg M±m CFU/ml.

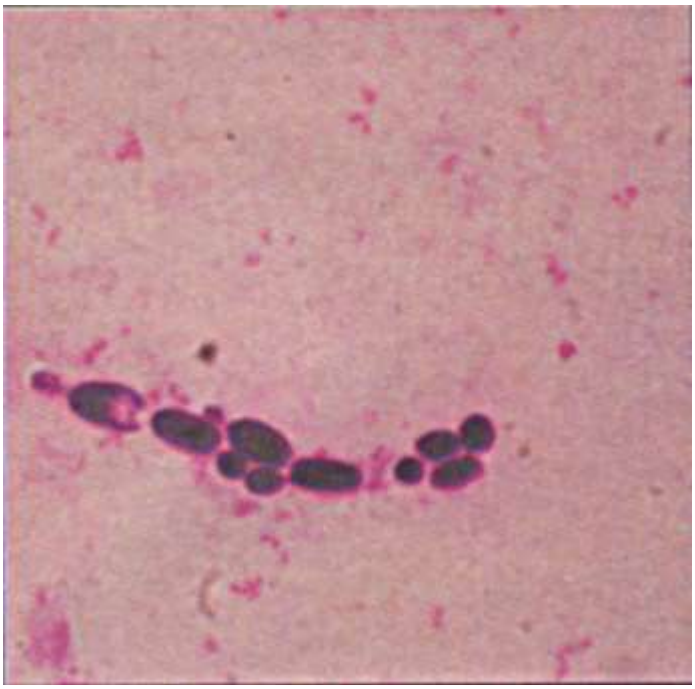
№	Group	of microbes Number of microbes in 1 ml of saliva in patients with candida stomatitis		
		Norm	At admission	After traditional treatment
1	Total number of anaerobes	5,69±0,15	4,39±0,21	5,01±0,17**

2	Lactobacilli	4,60±0,14	3,17±0,22	2,17±0,11***
3	Peptostreptococci	3,77±0,11	4,29±0,25	4,37±0,21
4	Total number of aerobes	5,30±0,17	8,60±0,69	7,37±0,69
5	Staphylococci aureus	-2.30	2,30±0.19	2.47±0.13
6	Staphylococci saprophytic	2.15±0.51	3.170.11	3.11±0.17
7	Staphylococci epidermal	4,15±0,14	4,11±0,27	3,41±0,15**
8	Streptococci gr A.	-	4,60±0,27	3,89±0,17**
9	Enterococci	5,15±0,15	5,12±0,39	5,11±0,22
10	Escherichia LPS	2,30±0,17	4,27±0,21	3,60±0,21**
11	Escherichia LN	-5,12	5,12±0,41	3,12±0,19***
12	Candida River	mushroom s 2,15±0,18	7,89±0,52	6,12±0,37**

Note: * * - the presence of confidence (P>0.01) in comparison with the control

***- presence of confidence (P>0.001) in comparison with the control

Figure 12. C. albicans culture growth on Saburo medium



13. C. albicans cells in the preparation. Gram-based coloring

Later, to better calculate the colony, we sowed from higher dilutions, and we obtained a typical growth of a mushroom colony on Saburo medium (Fig. However, we were surprised by the fact that giant fungal colonies with pseudo-mycelia on the body surface appeared on individual plates (Figure 15).

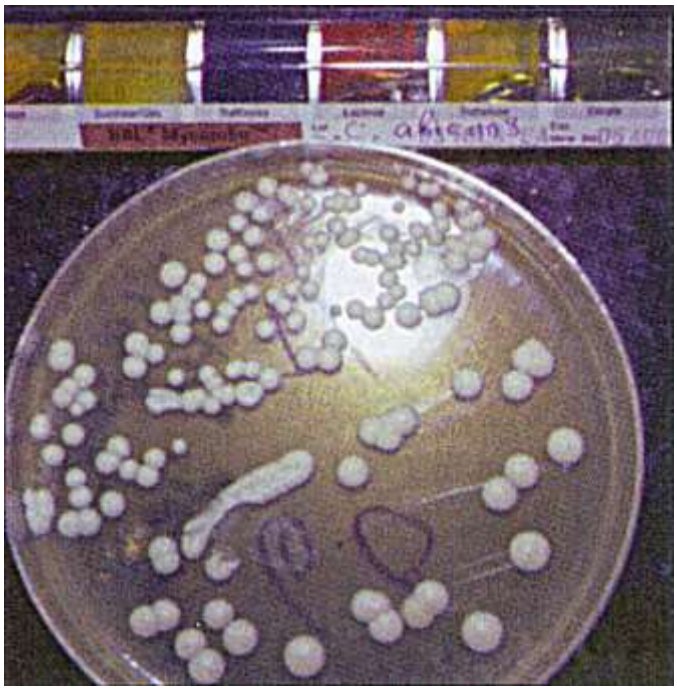
A group of sick children suffering from candida stomatitis underwent traditional therapy, / the method of application is given in the section material and methods/.

After completing the course of traditional therapy, we also studied the microflora of the oral fluid in a group of children, the data obtained are shown in Table No. 6. The table shows that the course of traditional therapy as a whole had a positive effect on the state of the oral microflora in children suffering from candida stomatitis. At the same time, particularly pronounced positive changes were observed in relation to anaerobic flora. This cannot be said with regard to the facultative flora. So the total number of aerobes, although slightly reduced, but there was no need to talk about a full recovery. Especially noteworthy is the stable state of quantitative parameters for such microbes as staphylococci aureus, pyogenic streptococci, and lactose-negative Escherichia coli.

In addition, the most significant indicator of oral dysbiosis in these children remains the quantitative parameters of fungi of the genus Candida, so their number is lg 6.12±0.37 CFU/ml, confidence at the norm of lg 2.15±0.18 CFU/ml, confidence ($P>0.001$), that is, 4 orders of magnitude higher.

All these negative indicators of oral dysbiosis in children suffering from candida stomatitis should be taken into account by the attending dentists when providing medical care, as a chronic form of the disease can form.

Moreover, the quantitative and qualitative changes in the autoflora of the oral cavity in children with candida stomatitis revealed by us are natural



14. Culture of fungi of the genus Candida on the Saburo medium

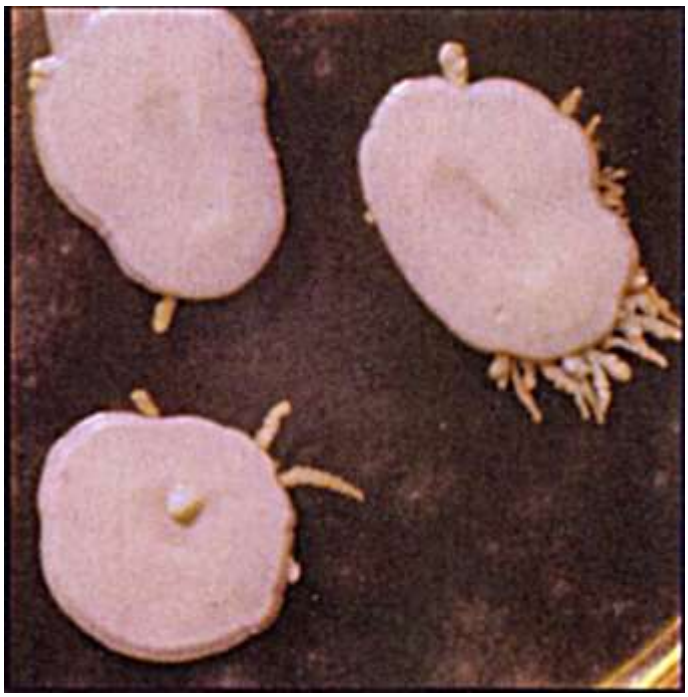


Figure 15. Giant colonies of fungi of the genus Candida in the Saburo environment

they set a task for pediatric dentists to find more effective methods of treating such patients.

3.3. **Immunology of oral fluid in children suffering from candidal stomatitis.**

The development and widespread introduction of immunological assays into clinical practice in the last decade shows that the frequency of numerous diseases of the oral cavity, especially various inflammatory processes in children, is directly or indirectly dependent on the state of both general and local factors of oral immunity.

According to modern data, mixed saliva and oral fluid are a coloid solution constructed of micelles of phosphates and calcium hydrophosphates surrounded by dense water-protein shells. Saliva contains the most important molecular components of the complement system: lysozyme, lactoferrin, lactoperoxidase and other enzymes, and cellular components: granulocytes and macrophages, which are factors of nonspecific resistance of the body. The protective activity of various saliva substances is associated with both their direct action on microbes and inhibition of adhesion to tooth enamel or mucosal epithelium.

It should be noted that the exact mechanism that determines the causal role of opportunistic flora in inflammatory diseases of the oral mucosa has not yet been established. Although, the main postulate is the position on the determining role of regulatory immune and non-immune mechanisms in the balance of all components of the microbiocenosis, the violation of which leads to the development of the infectious process. A clear confirmation of this is the polyethology of opportunistic infections, that is, associations of several types are usually isolated from the inflammatory focus, which is confirmed by the dynamics of the level of antibodies to their antigens.

At the same time, it is impossible to ignore the possibility of qualitative changes in the properties of microorganisms themselves, that is, regulatory influences within the microbiocenosis – that is, the pathogenization of residents.

Apparently, and most likely, the first and second factors are closely related at the molecular level of biochemical regulation of microflora.

Table 7. Indicators of non-specific factors of oral protection in healthy people.

№	Indicators	Norm in adults	Norm in children
1	Lysozyme level, mg %	18.0±0.60	19.7±0.70*
2	Phagocytrin. indicator, %	55,3±1,20	58,1±1,50*
3	S Ig A level, g / l	2.0±0.10	1.8±0.30

Note: * - the presence of confidence (P>0.5) in comparison with the control

At the same time, it is noteworthy that the more severe the disease, the deeper the secondary immunodeficiency. Moreover, the table shows that our traditional therapy of these patients does not give proper results. Although, it should be noted that traditional therapy in general has a positive effect on the indicators of the immune system, but it is not necessary to talk about the complete correction of detected immunodeficiency disorders, which becomes one of the reasons for the chronization of the disease.

It is known that most pathogenic fungi have an immunosuppressive effect on our body, in fact, we have found complete confirmation of these postulates in our research.

According to the majority of well-known mycologists, a significant increase in the incidence of candidiasis, which differs in the last decade, is primarily due to the fact that this infection is opportunistic, and therefore affects primarily a weakened body, and this probably explains the most frequent oral lesions in children whose immune system has not yet fully matured.

We have studied the state of non-specific factors of oral fluid protection in children suffering from candida stomatitis, the data obtained in these studies are given in Table No. 9. The table shows that in children with candida stomatitis, there is a significant secondary immunodeficiency in the oral cavity, so the level of lysozyme is 11.3±0.4 mg %, with a norm of 19.7±0.70 mg/%, the phagocytic index

was 41.7±1.2% with a normal value of 58.1±1.50%. At the same time, among all the studied parameters of the immune system, the indicators for secretory class A immunoglobulins were most reduced when its indicator was more than 3 times lower than normal and amounted to 0.60±0.20 g/l.

Table 9. Characteristics of non-specific oral protection factors in children with candida stomatitis.

No	**. Indicators**	**Norm**	**Patients with candidal stomatitis**	
			At admission	**After traditional treatment.therapy**
1	Level of lysozyme mg%	19,7±0,70	11,3±0,4	14,7±0,5***
2	Phagocytrin.indicator %	58,1±1,50	41,7±1,2	45,9±1,2
3	sJgA titer g / l	1,8±0,30	0,60±0,20	1,20±0,12**

Note: * * - the presence of confidence (P>0.01) in comparison with the control

***- presence of confidence (P>0.001) in comparison with the control

It should be noted that any researcher? having received certain scientific data, it is necessary to ask yourself the question, what is the reason for these changes. In our case, most likely, the development of children suffering from herpetic stomatitis and oral candidiasis is necessarily accompanied by an immunosuppressive effect of the virus and fungus on the macroorganism, which leads to the development of immunodeficiency, this is consistent with numerous information available in the literature.

Thus, based on the study conducted in patients with children suffering from herpetic stomatitis and oral candidiasis, comparative analysis shows that both with herpetic stomatitis and candidiasis, the development of dysbiosis and immunodeficiency is observed in the oral cavity, but the degree of severity of these changes is higher in patients with candidiasis. Apparently, these features are a natural evolutionary process that has become fixed in the macroorganism, which should be taken into account in their practical work by pediatric dentists.

I would like to emphasize that based on our research on the study of the microflora and immunology of the oral cavity in children suffering from herpetic

stomatitis and candidiasis, all the above postulates are confirmed. Nevertheless, it is clear from our data that the whole set of microbes associations is determined in the microflora of the oral fluid of sick children, among which the majority are sown in healthy children. However, the whole interest of the conducted studies lies in the fact that there are significant differences, both in quantitative and qualitative parameters.

CHAPTER IV.

COMPARATIVE EVALUATION OF THE THERAPY PERFORMED.

4.1. Evaluation of the clinical efficacy of Citeal in children with candidal stomatitis.

The clinical effectiveness of the treatment was determined by the following indicators: reduction of body temperature, acceleration of epithelialization, reduction of damage to the oral mucosa, improvement of the general condition of the child.

Patients with candidiasis were divided into two groups:

1 A group of children with candidiasis formed a comparison group and received traditional therapy.

1 A group of children with candidiasis formed the main group and received the drug Citeal.

2

4.1.2 Comparative characteristics of current therapy in acute pseudomembranous candidiasis.

We observed 60 sick children with acute pseudomembranous candidiasis (thrush). All children with thrush in the number of 60 people are infants aged from a few days to a year. All children were divided into two groups

40 children were treated with Citeal

20 children were included in the control group, who were treated using the traditional method of treatment.

The group of children who were treated with the drug "Citeal" 1:10 already on the first day showed changes. The oral mucosa turned pale, the amount of plaque decreased. The child began to breastfeed and stopped acting up.

On the second day, there was practically no plaque, no new rashes were observed, only a slightly hyperemic oral mucosa remained. When the mucosa was treated with Citeal solution in combination with sea buckthorn oil for 2-3 days, clinical recovery occurred on 3-4 days. The children became active, cheerful, well-fed, their moodiness and lethargy disappeared.

In the course of treatment of children who received traditional treatment, clinical recovery occurred on days 6-7. The oral cavity was treated with a nystatin solution of 1 tablet - 500,000 units. in 5 ml of mother's milk or in water. Be sure to treat the mother's breast nipple before and after feeding with a solution of iodinol.

It is necessary to conduct a conversation and teach the correct skills for caring for the mother's breast nipple. The negligent attitude of mothers to the regular implementation of hygiene rules leads to the addition of a secondary infection, as well as a relapse of the disease

Treatment of candidiasis requires an individual approach to each case, since candidiasis develops as a secondary disease caused by a decrease in immunological protection, which can be due to various reasons.

Therefore, the main directions in the treatment of a patient with candidal stomatitis are:

- identification of the etiological factor;
- elimination or reduction of further negative impact of these factors;
- pathogenetic therapy;
- general strengthening therapy that reduces mycotic sensitization, stimulates non-specific and specific resistance of the body;

– inclusion of antifungal drugs in complex treatment.

A diet with the exclusion of sweets and restriction of carbohydrates, rich in vitamins and proteins, is prescribed.

It is necessary to carry out the prevention of candidal stomatitis in several directions:

1. Reduction of infection with candida fungi in newborns by detecting and treating urogenital candidiasis and candidiasis in pregnant women by prescribing them antibiotics with a narrow spectrum of action (penicillin, oxacillin, erythromycin).

Identification and treatment of oral candidiasis of the expectant mother, rehabilitation of the oral cavity. Sterilization of teats, pacifiers and other baby care items. The child must have individual sterile dishes, his crib and bed linen, an individual night vase.

Compliance with sanitary and hygienic measures and regulations in maternity hospitals, proper treatment of equipment, baby underwear, hands of medical personnel, ensuring the sterility of bottles, pipettes, instruments, syringes and other things. Training nursing mothers to care for their breasts, nipples, and hygiene manipulations.

2. Refusal of irrational and massive antibacterial therapy, careful use of hormones, under the supervision and as prescribed by the attending physician.

With long-term antibacterial therapy, it is necessary to simultaneously prescribe polyene antibiotics inside, with a course adequate to the antibacterial one. And after antimicrobial therapy, prescribe colibacterin and bifidumbacterin.

Severe general somatic diseases should be accompanied by complex treatment, it is necessary to prescribe large doses of vitamins, increase the body's resistance, and overall immunological reactivity.

3. Timely detection and treatment of dysbiosis.

4. Implementation of the sanitary and hygienic regime at food industry enterprises, at production facilities associated with the possibility of infection with candida fungus, as well as in medical institutions when performing various manipulations, compliance with state standards for sterilization of instruments: tweezers, probes, mirrors, etc.
5. Wide sanitary and educational work among medical personnel, employees of food enterprises, among the population, expectant mothers and dads.

Children and adults should know that self-medication is not harmless, self-uncontrolled use of antibiotics and other medications can lead to the development of dysbiosis and candidiasis.

We have studied the state of non-specific factors of oral fluid protection in children suffering from candida stomatitis, the data obtained in these studies are given in Table No. 9. The table shows that in children with candida stomatitis, there is a significant secondary immunodeficiency in the oral cavity, so the level of lysozyme is 11.3±0.4 mg %, with a norm of 19.7±0.70 mg/%, the phagocytic index was 41.7±1.2% with a normal value of 58.1±1.50%. At the same time, among all the studied parameters of the immune system, the indicators for secretory class A immunoglobulins were most reduced when its indicator was more than 3 times lower than normal and amounted to 0.60±0.20 g/l.

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I would like to emphasize that based on our research on the study of the microflora and immunology of the oral cavity in children suffering from herpetic stomatitis and candidiasis, all the above postulates are confirmed. Nevertheless, it is clear from our data that the whole set of microbes associations is determined in the microflora of the oral fluid of sick children, among which the majority are sown in healthy children. However, the whole interest of the conducted studies lies in the fact that there are significant differences, both in quantitative and qualitative parameters.

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Children and adults should know that self-medication is not harmless, self-uncontrolled use of antibiotics and other medications can lead to the development of dysbiosis and candidiasis.

4.2. Study of the effect of the drug "Citeal" on salivary microflora parameters in children with oral candidiasis.

The barrier-protective mechanisms of the oral cavity are closely related to the microflora of the oral cavity. The variety and activity of the oral microflora often determines the pathology of its hard and soft tissues. Unsatisfactory hygienic conditions of the oral cavity, especially in children, contribute to the development of a dysbiotic state here. Traditional methods of oral cavity treatment, when various chemicals such as potassium permanganate, menthol, and elixirs are used, do not have a pronounced bacteriostatic effect, and therefore new antiseptic drugs are being searched for.

It is well known that the oral microflora is diverse and difficult to study. Bacteria, fungi, viruses and protozoa inhabiting the oral cavity are no exception in this regard. The fact is that the oral cavity, its mucous

membrane and the lymphoid apparatus of the maxillofacial region play a unique role in the interaction of the human body with the surrounding world of microbes.

Based on the above, it is logical that for the treatment of the oral cavity it is necessary to find drugs that would have a wide range of antibacterial, antifungicidal and antiviral effects. All this property meets the drug "Citeal".

The drug "Cyteal "(Evromedex) was developed in 1954 in England, originally created as an antiviral agent. It is a foaming antiseptic solution used for the treatment of mucous membranes and contains three sets: chlorhexidine, hypsamidine, chlorpresol, which are active against gram-positive, gram-negative bacteria, mycobacteria and fungi.

Initially, we studied the sensitivity of some types of microbes, taking into account their occurrence in the oral cavity, to the drug "Citeal"in vitro. For this purpose, on a Petri dish with a nutrient medium, certain types of microbes were seeded with "lawn", then pieces of filtered paper (like antibiotic disks) were taken, soaked in various concentrations of the drug "Citeal" and then placed on the surface of nutrient agar with seeding. The cups were kept in the thermostat at 37C for 24 hours. Then, the cups were removed and the microbial growth inhibition zones around the piece of filtered paper were measured.

The obtained data on determining the sensitivity of microorganisms to the drug "Citeal "in various dilutions are shown in Table 10. The table shows that the drug" Citeal " in concentrated form has a pronounced antibacterial effect on both gram-positive and gram-negative microbes. The table also shows that the drug "Citeal" in concentrated form had the most pronounced effect on staphylococci, streptococci, Escherichia and lactobacilli, and had the least effect on pathogenic staphylococci, lactose-negative Escherichia strains and proteus culture.

At the same time, when diluting the drug, its antibacterial effect is significantly reduced, and as can be seen from the table, when diluting the drug in 1/5 and 1/10, the actual antibacterial action, although reduced, is preserved against all the studied microorganisms. However, in the 1/20 dilution, the antibacterial effect of the drug is sharply reduced, although it should be noted that in this dilution it continues to have an effect on gram-positive microorganisms.

Table 10.

Sensitivity of some oral microorganisms to Cyteal in vitro.

№	Microbe Group No	. "Citeala " concentration"			
		1/5 20%	1/10 10%	1/20 5%	100%
1	Streptococci	15,1±1,2	10,2±0,8	5,4±0,6	17,1±1,4
2	2 Staff. Golden	Color-	-	-	5,1±0,4
3	3 Staff. Epidermal	16,1±1,3	11,1±0,9	5,7±0,7	21,1±1,6
4	4 Staff. Saprofit	12,3±1,1	10,1±1,0	7,2±0,8	22,4±2,1
5	Esherechii LP	10,1±1,0	5,2±0,6	-	12,4±1,1
6	Escherichia LN	5,3±0,4	--	-	7,1±0,7
7	Klebsiel	11,1±1,2	5,6±0,7	-	13,1±1,2
8	Candida River	mushrooms 7,1±0,6	5,4±0,7	-	8,4±0.8
9	Pseudomonas	-	-	-	9,2±0,7
10	Protea	5,3±0,4	--	-	8,6±0,8
11	Lactobacilli	9,1±0,8	8,4±0,07	7,1±0,5	11,5±1,3

(M±m) mm – growth retardation zone

Thus, our studies have fully confirmed the passport characteristics of the drug "Citeal" and we believe that it is best to use the drug in a dilution of 1/5 and 1/10., i.e. 10 and 20% concentration.

Based on the data obtained by us and taking into account the literature sources, we conducted the use of the drug "Citeal" for the

treatment of sick children suffering from candida stomatitis, taking into account the clinical phases of the course. (the treatment method is described in the section materials and methods of research.)

4.2.1 Effectiveness of the study of the drug "Citeal" in the treatment of children with candidal stomatitis.

According to the latest data of mycologists, oral candidiasis occurs in 5% of newborns and almost 10% of infants (A. Yu. Sergeev et al.; 2000). In healthy adults, this is a fairly rare disease, occurring almost exclusively in predisposed individuals. At the same time, in the elderly, the prevalence of oral candidiasis for various reasons is again close to 10%, especially after prosthetics.

In recent years, due to various reasons, the number of children applying to a dental institution for candida stomatitis (thrush) has significantly increased. At the same time, various antimycotic drugs are used to treat such patients, which, as a rule, are not always effective.

In the previous section, we already talked about the antifungicidal effect of the drug "Citeal".

The microbiological data obtained in these studies are shown in Table.14. The table shows that Citeal in the treatment of these sick children also had a positive effect on the quantitative and qualitative indicators of the oral microflora. At the same time, we see almost complete normalization to the control figures of the quantitative indicators of the anaerobic group of microorganisms, for example, the total number of anaerobes was lg 5.57+0.21 CFU/ml, while the norm was lg 5.69+0.15 CFU/ml.confidence($P>0.001$).

However, the most pronounced positive changes occurred in the quantitative and qualitative indicators of the facultative group of microbes. So, the total number of them was lg 5.12+0.31 CFU/ml, while the norm was lg 4.30+0.17 CFU/ml. confidence ($P>0.5$)

Table 14

The effect of treatment with "Citeal" on the state of the oral microflora in sick children suffering from candida stomatitis.

lg M±m KOE/ml.

№	Microbe Group No	. Number of microbes in 1 ml of saliva		
		Norm	After traditional treatment	After treatment with
Citeal 1	Total number of anaerobes	5,69±0,15	5,01+0,71	5,57+0,2
2	Lactobacilli	4,60±0,14	2,17+0,11	3,90+0,34***
3	Peptostreptococcus	3,77±0,11	4,37+0,21	4,11+0,25
4	Total number-during aerobic exercise.	4,30±0,17	7,37+0,69	5,12+0,31**
5	5 Staff. Golden	Color-	2,47+0,13	-
6	6 Staff. Epidermal	2,15±0,51	3,11+0,17	1,90+0,12***
7	7 Staff. Saprofit	4,14±0,14	3,41+0,15	3,17+0,18
8	Strept G. "A"	-3,84	+0,17	-
9	Enterococci	5,15±0,15	5,11+0,22	3,77+0,17**
10	Escherichia LPS	2,30±0,17	3,60+0,21	2,10+0,22**
11	Escherichia LN	-	3,12+0,19	-
12	Candida river	mushrooms 2.15±0,18	6,12+0,37	2,80+0,37***

Note: * * - the presence of confidence (P>0.01) in comparison with the control

***- presence of confidence (P>0.001) in comparison with the control

At the same time, it is necessary to emphasize the normalization of quantitative indicators of fungi, so their number was equal to lg 2.80+0.37 CFU/ml, reliability (P>0.001), while after traditional therapy it was lg 6.12+0.37 CFU/ml, that is, we have a decrease of almost 2 times. It should also be noted that after treatment with Citeal, patients experience complete elimination of microbes with aggressive properties.

Thus, microbiological studies of sick children suffering from candida stomatitis, who used the drug "Citeal" showed that the phenomenon of dysbiosis almost disappeared and in fact the microflora is

close to the control data in all parameters, especially noteworthy is the reduction of Candida fungi and the elimination of anaerobes with aggressive properties. All this taken together allows us to state with a high degree of reliability that the drug "Citeal" turned out to be a highly effective antibacterial and antifungicidal substance and can be recommended for the treatment of candida stomatitis in children. What makes us particularly happy is the fact that our microbiological postulates are fully correlated with clinical data.

4.3. Immunological effectiveness of using the drug "Citeal" in the treatment of candidiasis in children.

Immunological research has traditionally been viewed as something very abstract from the point of view of specialists in the field of therapeutic dentistry. Currently, this is a necessity, which is dictated by the increasing number of patients with aggressive forms that are resistant to traditional influences. Immunological studies are very relevant, since, on the one hand, in combination with microbiological data, they allow us to understand the features of pathogenesis, justify treatment and prevention methods in conditions of adverse effects of adverse factors.

However, when considering the triggering mechanisms of the inflammatory process, we should also take into account the role of endogenous factors and, above all, the state of local and general systems of protection and maintenance of homeostasis. So, for example, it is known that with the development of inflammatory periodontal diseases, in particular with gingivitis, changes in the content of lysozyme and immunoglobulins of the A – secretory fraction (s IgA) in the oral fluid are observed, which are mutually compensated.

Over the past decades, the idea has been formed that in inflammatory processes of organs and systems limited to the mucous membranes, not only general systemic, but also various local specific and non-specific resistance factors play an important role. Moreover, mucosal

immunity is not a simple reflection of general immunity, but has an independent system, especially of sIgA products, which also has a pronounced effect on the formation of general immunity. In this regard, the dentist, along with the general condition of the patient, including the systemic immune status, should be able to assess and correctly interpret the state of local factors of oral resistance. Knowledge of the state of immune mechanisms in a particular patient will help not only in the treatment, but also in the prevention of dental diseases.

It is also obvious that along with the increasingly widespread use of immunological methods for examining patients, it is necessary to study in more depth and take into account the influence of not only internal, but also external factors on the patient's immunological status.

Along with microbiological studies of sick children suffering from candida stomatitis, we studied the immunological parameters in the same children when using the drug "Citeal"for treatment. The data obtained in these studies are shown in Table 15. At the same time, after treating sick children with Citeal, we see that some indicators have become even higher than in a healthy group of children, although it should be noted that Citeal affects the state of secretory immunoglobulin (sIgA).

CHAPTER IV.

STUDY OF THE EFFECTIVENESS OF THERAPY.

4.1. Evaluation of the clinical efficacy of Citeal in children with candidal stomatitis.

The clinical effectiveness of the treatment was determined by the following indicators: reduction of body temperature, acceleration of epithelialization, reduction of damage to the oral mucosa, improvement of the general condition of the child.

Patients with candidiasis were divided into two groups:

3 A group of children with candidiasis formed a comparison group and received traditional therapy.

4 A group of children with candidiasis formed the main group and received the drug Citeal.

Table No. 16

The state of non-specific factors of oral cavity protection in sick children with candidal stomatitis after treatment with "Citeal".

№	Indicators	Patients with candidal stomatitis		
		Norm	After traditional treatment	After treatment with
Citeal 1	Lysozyme level (mg%)	19,7±0,70	14,7±0,50	18,2±0,57**
2	Phagocytic parameters %	58,1±1,50	45,9±1,2	56,5±1,3**
3	Secretory immunoglobulin (s IgA) level. g/l	1,8±0,30	1,20±0,12	1,90±0,11**

Note * * - reliable for the control group (P>0.5)

The same immunological parameters were studied by us in the treatment of Cyteal in sick children suffering from candida stomatitis. The obtained indicators of these studies are presented in Table 16. The table shows that Citeal had a beneficial effect on all indicators of non-specific factors of cavity protection.

Thus, based on the conducted immunological studies, we can assume with a high degree of reliability that the drug "Citeal" can be recommended for the treatment of sick children suffering from acute herpetic infection and candida stomatitis, as a highly effective drug that reduces the degree of chronization of the disease.

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The state of non-specific factors of oral cavity protection in sick children with candidal stomatitis after treatment with "Citeal".

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Note * * - reliable for the control group (P>0.5)

Immunological parameters of Cyteal treatment of sick children suffering from candidal stomatitis were studied. The obtained indicators of these studies are presented in Table 16. The table shows that Citeal had

a beneficial effect on all indicators of non-specific factors of cavity protection.

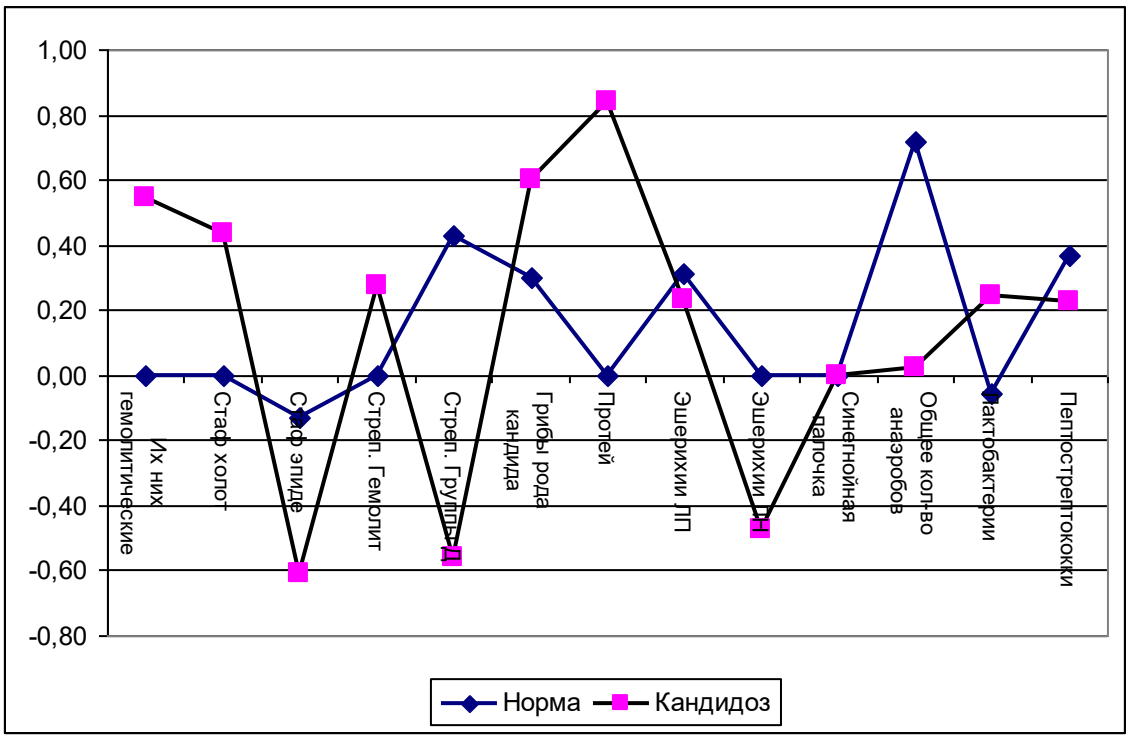
Thus, based on the conducted immunological studies, we can assume with a high degree of reliability that the drug "Citeal" can be recommended for the treatment of sick children suffering from acute herpetic infection and candida stomatitis, as a highly effective drug that reduces the degree of chronization of the disease.

Chapter V. Correlation between changes in the indicators of microflora and immunology of oral fluid during the targeted use of the drug "Citeal" in sick children with candidiasis.

We studied correlations between microbiocenosis indicators and the state of non-specific factors of oral protection in normal conditions and in sick children suffering from candida stomatitis during traditional and specific treatment.

A comparative analysis of the relationship of microorganisms in candida stomatitis in children showed (Figure 19) that a strong direct correlation is characteristic of proteus (r= + 0.84), candida fungi (r= + 0.60), as well as hemolytic and staphylococcus aureus (r= + 0.56 and r= + 0.44, respectively). Group D streptococci (r= - 0.56), epidermal staphylococcus (r= - 0.61), and Escherichia coli (r= - 0.47) have an average feedback.

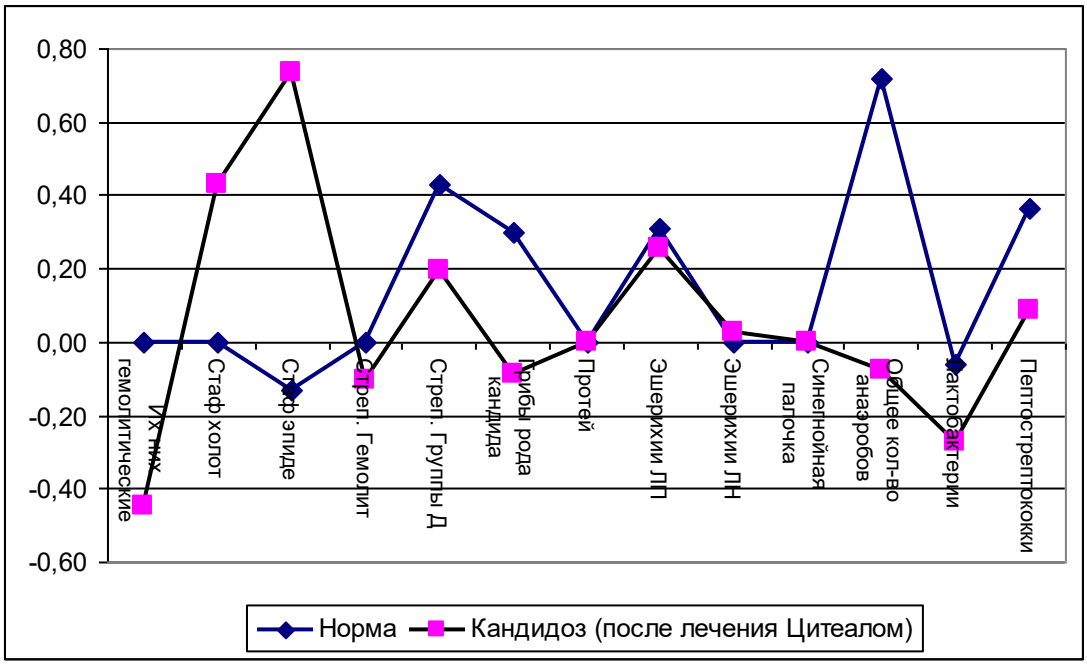
At the same time, after special treatment of candidal stomatitis by using the drug "Citeal", Staphylococcus aureus has the same strength (r= +0.43).



19. Correlation between oral microbes in normal and candida stomatitis patients.

However, the most significant changes in the relationship between the quantitative parameters of oral microorganisms in children suffering from candida stomatitis occurred after special treatment using the drug "Citeal".

Thus, hemolytic microorganisms dramatically changed their status after treatment (Figure 20). Before treatment, they had a direct relationship of medium strength, whereas after treatment, the relationship of hemolytic microorganisms acquired a feedback relationship of medium strength. A similar pattern is observed in epidermal staphylococci (r= + 0.74).



20. Correlation between oral microorganisms in children with candida stomatitis after special treatment.

The most interesting data were obtained when analyzing the relationship between the immunological parameters of the oral cavity in normal children and in patients with candida stomatitis, before and after treatment with the drug "Citeal" (figs. As can be seen from the figures, they normally have an inverse correlation of average strength.

We found the same correlation in the indicators of non-specific oral protection factors in patients with candida stomatitis before treatment, with the exception of a direct connection of weak strength in the indicators of phagocytosis (r= + 0.10) in children with candidiasis (Fig

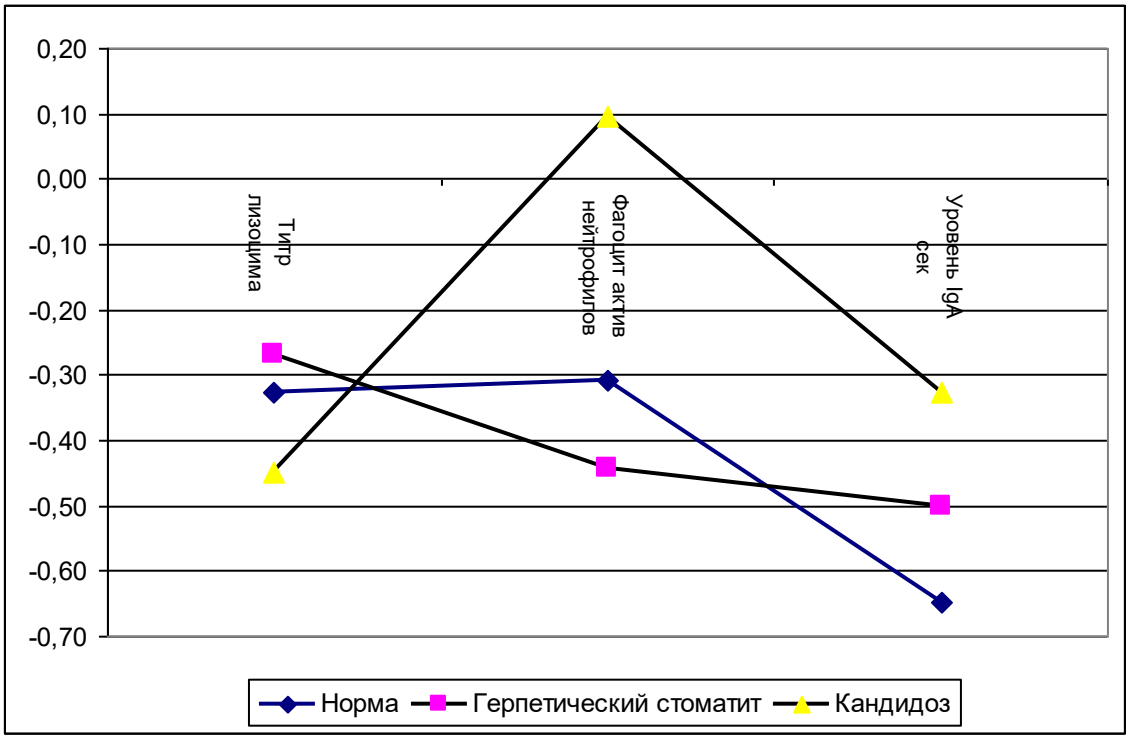
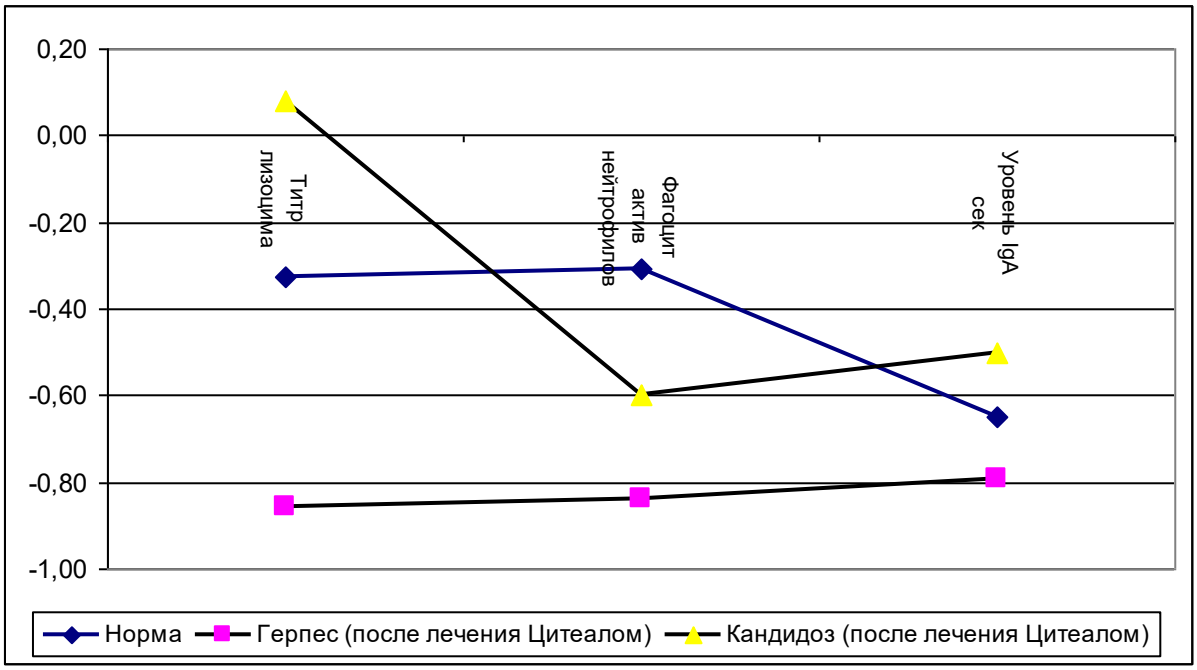


Figure 21. Interrelation of immunological parameters of the oral cavity in children with candidal stomatitis.

At the same time, after a special treatment by using the drug "Citeal", the picture has completely changed. However, the study of these parameters in sick children suffering from candidal stomatitis acquired an inverse correlation of moderate strength (Figure 16), although it should be noted that changes in the lysozyme titer during the treatment of candidiasis did not have a particularly pronounced relationship.



22. Interrelations between immunological parameters in children with herpetic and candida stomatitis after special treatment.

These results indicate the existence of direct and inverse relationships between the quantitative parameters of microbiocenosis and the immunological parameters of the oral cavity in children suffering from candida stomatitis before and after special treatment.

The data obtained allow us to conclude that the generally accepted treatment does not significantly affect the correlation relationships in children suffering from candida stomatitis. On the contrary, there is a decrease and weakening of the relationship between the indicators of microbiocenosis and non-specific protection factors.

All of the above allows us, judging by the correlation analysis, to speak about the most pronounced positive changes in the microbiocenosis and immunological parameters of the oral cavity occur when using the drug "Citeal"for treatment. Based on this, it becomes quite obvious that our dental, microbiological and immunological studies and their interrelationships give us every reason to recommend the drug "Citeal" for the treatment of candida stomatitis in children.

Summing up the results based on the results obtained

In recent years, there has been an increase in diseases of the oral mucosa in children. According to the results of numerous studies by domestic and foreign authors, the most common pathology in childhood is acute candida stomatitis.

Over the past 20 years, the number of mycoses has increased dramatically. The spectrum of pathogens of mycoses is rapidly expanding, currently more than 400 species of fungi are known to cause disease in humans.

The clinical manifestations of fungal infections range widely from relatively harmless, superficial lesions of the mucous membranes and skin to life-threatening, invasive mycoses that can affect almost any organ. The most common form of candidiasis in children is acute pseudomembranous or oral thrush.

Treatment of diseases of the oral mucosa is diverse. But the disadvantage of these methods is the focus of treatment only on eliminating inflammation and affecting the immunity of the oral cavity. Although dysbiotic disorders of the oral microflora have been repeatedly noted in the literature. In this regard, it is advisable to develop new methods of treatment of the oral mucosa, aimed at a gentle effect on the normal flora of the oral cavity.

We observed 60 sick children with candidal stomatitis. Depending on the treatment, the children were divided into 2 groups: Children with candida stomatitis: 20 – received traditional treatment, 40 – with the drug "Citeal".

The clinical diagnosis was established on the basis of anamnestic data, patient complaints, clinical manifestations, and performed index indicators of PMA and GI. The state of oral hygiene was determined by the method of Fedorov Yu. A. - Volodkina V. V. (1972)

Before treatment, patients collected saliva in sterile test tubes. Then the treatment was carried out with a solution of "Citeal" in a dilution of 1: 10 as follows:

The solution "Citeal" was given out on hand for processing at home.

Patients with candida stomatitis were tested for oral microflora in the laboratory.

Microbiological studies were performed in patients with candidal stomatitis. Dysbiotic changes are observed in the oral fluid, which are also characterized by a decrease in the anaerobic group of microorganisms, but against this background, the amount of facultative flora sharply increases. The number of anaerobes is 4.39±0.21 CFU / ml, and the number of aerobes is 8.60±0.69 CFU/ml - this is 3 orders of magnitude more than anaerobes. These children also develop microbes that are not characteristic of this biotope – these are staphylococci aureus, pyogenic streptococci, lactose-negative strains of Escherichia. These are all groups of microbes that have a large set of pathogenicity enzymes.

Along with microbiological studies of oral fluid in sick children, immunological studies were also performed. In sick children with candida stomatitis, a significant secondary immune deficiency is noted, so the level of lysozyme before treatment is 11.3±0.4 mg%, and in the norm 19.7±0.70 mg%, the phagocytic index before treatment is 41.7±1.2%, and in the norm 58.1 ±1.50%.

Among all the studied parameters of the immune system, the indicators for secretory IgA are the most reduced.

All examined children with candidal stomatitis were divided into 2 groups: the first group received traditional treatment, and the second group received treatment with Citeal. So, in children who were treated with the traditional method of treatment, we see that traditional therapy has a positive effect on the state of oral fluid microbiocenosis.

We observed 60 children with candidal stomatitis, who were also divided into 2 groups: 20 children received traditional treatment, 40 - treatment with the drug "Citeal". After completing traditional therapy in this group of children, we studied the microflora of oral fluid. Here we also see that traditional treatment has generally had a positive effect on the oral microflora. Particularly pronounced positive changes were observed in relation to anaerobic flora after treatment with lg 5.01±0.17 CFU / ml, at admission with lg 4.39±0.21 CFU / ml, and at normal 5.69±0.15 CFU/ml. The same cannot be said for facultative flora: at admission -

8.60±0.69 CFU / ml, after treatment-7.37±0.69 CFU / ml, and normally 5.30±0.17 CFU/ml, so the total number of aerobes has decreased, but there is no need to talk about full recovery. Stable condition after traditional treatment of quantitative parameters in such microbes as staphylococci aureus – at admission 2.30±0.19 CFU / ml, after treatment 2.47±0.13 CFU/ml, pyogenic streptococci at admission 4.60±0.27 CFU / ml, after treatment 3.89±0.17 CFU/ml, lactose-negative escherichia at admission 5.12±0.41CFU / ml., after treatment 3.12±0.19 CFU / ml, and normally these strains of microbes are absent.

In addition, the most significant indicator of oral dysbiosis in these children is the quantitative parameters of candida fungi, so their number is lg 7.89±0.52 CFU/ml at admission, lg 6.12±0.37 CFU/ml after treatment, and normally lg 2.15±0.18 CFU/ml, which is 4 orders of magnitude higher.

The quantitative and qualitative changes in the autoflora of the oral cavity identified by us can lead to the chronization of the disease, so it is necessary to find more effective methods of treating such patients.

We studied the effect of the drug in patients with candidal stomatitis. We can see that the drug "Citeal" had a positive effect on both quantitative and qualitative indicators of the oral microflora. Quantitative indicators of anaerobic flora were Ig 5.57±0.2 CFU / ml, and in normal conditions this indicator is 5.69±0.15 CFU/ml. Significant positive changes occurred in the indicators of facultative flora. So the total number of aerobes was 5.12±0.31 CFU / ml, and in healthy children this indicator is 4.30±0.17 CFU/ml. Especially striking is the quantitative indicator of fungi 2.80 ±0.37 CFU / ml, while after traditional therapy their number was 6.12±0.37 CFU/ml, and in normal conditions this indicator was 2.15 ±0.18 CFU/ml. After treatment with the drug "Citeal" comes the complete elimination of microbes with aggressive properties.

Microbiological studies in sick children with candida stomatitis, who used the drug "Citeal" revealed the disappearance of dysbiosis phenomena, and the microflora in all parameters was close to normal.

Along with microbiological studies, immunological parameters were studied in sick children with candida stomatitis.

Thus, based on the dental, microbiological and immunological data obtained by us, we can conclude that the drug "Citeal" has a pronounced antibacterial, antiviral, antifungicidal effect when used in children with oral candidiasis. It should be noted that the results obtained from the use of various methods of therapy, we came to the conclusion that the use of the drug "Citeal" has a pronounced therapeutic, specific, antimicrobial and anti-inflammatory effect, which manifests itself immediately after treatment and retains its effect for a long period. One of the essential aspects of the action of the drug "Citeal" in our patients should be recognized, which increases the local protective barrier of the oral cavity by increasing the activity of non-specific protection factors, thereby ensuring the prevention of relapses of the disease.

All of the above gives us every right and reason to believe that the drug "Citeal" should be widely used as an independent and additional drug for various infectious diseases of the oral cavity, in particular in children. This drug is especially useful in children with fungal diseases of the oral cavity, which, as a rule, are difficult to treat and the available arsenal of antifungal drugs is not economically available for widespread use.

Based on the results of our research, we can show that:

1. In children of patients with candida stomatitis, against the background of violation of the integrity of the MMOC and the development of inflammatory phenomena, there is a sharp deterioration in the PMA and GI indices, which together contribute to the predominance of pathogenic flora and inhibition of local immunity.

2. In candidiasis, traditional therapy improves the clinical picture of patients, but does not completely eliminate the development of dysbiosis and immunodeficiency in the oral cavity in children.

3. The action of the drug "Citeal" is aimed at eliminating the aggression of conditionally pathogenic and pathogenic strains, which helps restore the immunity of the oral cavity and eliminate the conditions of chronization of the disease.

4. It has been established that microflora is a highly sensitive indicator system that responds to qualitative and quantitative changes in diseases of the SOPR. "Citeal" is currently a drug that helps restore biological balance in the system of microflora and non-specific factors of oral protection.

5. There was a direct correlation between the degree of violation of the biological balance of the oral microflora, both on the severity and stage of the course of candida stomatitis. The more severe the disease, the more pronounced the clinical picture and the deeper the shifts in the system of local immunity of the oral cavity.

The work done allows us to recommend:

1. The drug "Citeal" which has both antiseptic, antibacterial, antiviral and fungicidal effects is recommended for wide use in the treatment of candida stomatitis in children.

2. It is recommended to use the drug "Citeal" in a dilution of 1: 10, not only for candida stomatitis in children, but also for other viral and fungal diseases of the MMOC.

3. Taking into account the sparing effect of the drug "Citeal" on the oral microflora in children, it is recommended to use it both in monotherapy and as an additional tool in the treatment of all diseases of the SOPR, as well as in various dysbiotic conditions.