

RATIONAL ANTIBIOTIC THERAPY IN THE COMPLEX TREATMENT OF PATIENTS WITH GENERALIZED PERIODONTITIS

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SUMMARY

The article treats the problem of the application and choice of antibiotics when carrying out antimicrobial therapy in inflammatory diseases of the periodontium. Based on data obtained from the bacteriological test of the content of periodontal pockets, in 75% of the patients with generalized periodontitis with a different degree of severity, there are discovered aerobic – anaerobic – fungal associations with primarily obligate and facultative anaerobes. In view of the results from the determination of sensitivity of various bacterial strains to antibiotics of various classes, the most prospective preparation for the suppression of the growth of the whole specter of pathogenic flora, located in the periodontal pockets in patients with periodontitis, is Clindamycin MIP. The data about the high clinical and bacteriological efficiency of Clindamycin, obtained from the clinical and microbiological tests, give us grounds to recommend it in the complex treatment of severe forms of generalized periodontitis.

Key words: antibiotic therapy, periodontitis, periodontium, clindamycin

INTRODUCTION

There are incontestable data about the role of microbial factor in the development of inflammatory diseases of the periodontium. Associative interrelations of the micro-ecological systems in the oral cavity with the local and general indicators of antibacterial protection formulate the basic principles of antibacterial therapy in generalized periodontitis (GP). These data, however, need constant thorough checks, in view of the considerable variability of the properties of microorganisms, formation of new microbial associations, substantiated by the increasing effect of tissue damage, and the change in the sensitivity of bacteria to the changing antimicrobial preparations, increase in the quantities of strains that are resistant to antibiotics.

The recognition of dental plaque as a leading etiological factor in the development of inflammatory and dystrophic– inflammatory diseases of the periodontium,

determine the role of antimicrobial therapy as the most important initial unit in the complex treatment of GP. The objective of antibacterial therapy – aetiotropic action that blocks the cascade of inflammatory changes on the level of exogenous microbial mediators.

In the inflammatory diseases of the periodontium (gingivitis and periodontitis) local antimicrobial therapy has prior significance, assisted by the most common preparations in clinical periodontology – 0.05-0.3% solution of chlorhexidine, 0.02% solution of decametoxine, 1% water solution of iodolium, 0.25% alcoholic solution of chlorfilip and other solutions, which are used as applications, for rinsing the mouth and gargle or which are included as ingredients of healing periodontal dressings. In spite of this, in some cases it is appropriate to carry out additional systemic antibiotic therapy. Indications for the systematic application of antibiotics are: GP severe degree, exacerbated discharge (multiple periodontal abscesses); atypical forms of periodontitis – early progressive, localized and generalized juvenile and post-juvenile, rapidly progressing periodontitis in adults, periodontitis resistant to treatment effects (refractory); symptomatic ulcerated – necrotizing gingivitis; preparation for periodontal surgery; in patients of risk groups (with cardiovascular disorders, diabetes mellitus, immunodeficiency conditions etc.). Nowadays, the choice of antibacterial preparation, the dose and duration of treatment are determined primarily empirically and in view of the clinical effect. In the national and international literature there are data about the clinical efficiency of the following preparations: Lyncomicine, Metronidazole, Tetracycline, Doxycycline, Cefotaxime, Amoxicillin, Azithromycin, Roxithromycin etc. In spite of that, as evident from the results of the microbiological tests and the determination of sensitivity of the microflora to antibiotics, the effect of the selected preparation on the microorganisms in the periodontal pocket and the oral cavity in general is not always adequate, which on its turn not only does not improve the patient's condition, but also entails considerable damage to the microbiocenosis – reduction in

the factors of the local and general immunological reactivity, deficiency and elimination of the obligate microflora in the oral cavity. This determines the importance and necessity to carry out bacteriological tests in order to establish a final diagnosis and to plan the treatment, to substantiate the indications for application and evaluation of efficiency of a complex antimicrobial therapy in diseases of the periodontium and the mucous membrane of the oral cavity.

When antibacterial treatment is carried out in patients with a stomatological profile, the following basic principles have to be complied with: presence of indications for prescribing an antibiotic, ascertaining the reasons obstructing the application of rational antibiotic therapy; identification of microorganisms and determination of their sensitivity to preparations; choice of optimal schemes in view of the localization of the infection process or the type of pathogenic agent; rational combination of antimicrobial means; choice of optimal dose and method of application of the medical preparation; determination of the duration of antimicrobial therapy.

Objective of the research – comparative study of the efficiency of a number of antibacterial preparations used in the treatment of GP, as well as determination of the nature and sensitivity of the microflora of the periodontal pocket and evaluation of the clinical and bacteriological efficiency of Clindamycin (Clindamycin MIP 600 mg) in the complex treatment of GP.

SUBJECT AND METHODS OF RESEARCH

It was held a clinical and microbiological test of 50 patients aged 18-68 with GP in various stages. The clinical test included: study of the history of their lives and of the disease; evaluation of the condition of the periodontal tissues visually (how close it fits, contour of the marginal edge of the gum, presence of oedema, expressed hyperemia, puss discharge from the periodontal pockets, condition of the teeth) and aided by Paraclinical indices – PMA, periodontal (PI), blood flow, looseness of teeth, depth of periodontal pocket, recession of the gum, contact x-ray and orthopantomographies; determination of indications for surgical treatment and elaboration of a plan for treatment. Laboratory tests: general blood analysis, determining the glucose content in blood, calcium in blood plasma; microbiological test of the substance contained in the periodontal pockets, placed in a sterile container in transport medium, inoculation of media for aerobes, anaerobes and fungi cultivated in a thermostat for 3-5 days at 37°C (anaerobes - in microanaerostats), isolation of clean cultures and their identification based on biochemical and morphological characteristics, as well as using the test system of a microbiological analyzer. The sensitivity of different bacterial strains to antibiotics was determined using the disc diffusion method.

20 patients, aged from 18 to 50, were selected, who

had indications for systematic antibiotic therapy: 6 – with GP of severe degree in an acute stage (numerous periodontal abscesses), 5 – with rapidly progressive periodontitis, 3 – with GP, complicated by ulcerative – necrotizing gingivitis, 1 – with insulin-dependant diabetes mellitus, before surgery osteogingivoplasty, 5 – in a period of preparation for surgeries of the periodontium. We applied basically (professional hygiene of the oral cavity, removal of local periodontal pathological factors), local antibacterial therapy using 0.1%-0.05% solution of chlorhexidine and 0.25% solution of chlorfilipt, anti-inflammatory treatment of periodontal pockets and the gum edge, polyvitamins, adaptogens, antioxidants, if necessary – immune-corrective or osteotropic preparations, as well as Clindamycin (Clindamycin MIP 600 mg). Clindamycin was prescribed as follows: one pill three times per day (daily dose 1800 mg) in the first two days, after which twice a day (1200 mg). The course of treatment which we preferred was between 6-8 days, depending on the severity and nature of the inflammatory-dystrophic process of the periodontal tissues. The efficiency of the treatment with Clindamycin was evaluated on the basis of the changes in the indices of the clinical and microbiological tests carried out after the course of treatment; clinical – based on the change in the symptoms of the diseases; general state of the patients, pain and oedema of the gum, the discharge from the periodontal pockets (puss discharge), change of their depth, looseness of teeth. The bacteriological efficiency of Clindamycin MIP 600 mg in patients with GP was judged on the basis of a repeated bacteriological test of the periodontal pockets or of the granulates, removed during surgery by means of a lambo from the deep bone pockets (in 12 patients).

RESULTS AND DISCUSSION OF RESULTS

The results of the microbiological test evidence the polymicrobial constitution of the periodontal pocket flora in patients with GP: in 80% there were aerobic – anaerobic-fungal associations, in 17.3% - anaerobic-fungal associations, in 2.7% - aerobic-anaerobic ones. On the average, in the contents of the periodontal pocket of one patient there were isolated associations of 3-6 microorganisms, and staphylococci prevailed among the aerobic and facultative bacteria (in 57% of the patients), enterobacteria – E.colli (in 21.3%) and Klebsiella (in 14.7%); among the facultative anaerobes – Capnocytophaga spp. (in 21.3%), among obligate anaerobic fusobacteria (in 30.7%), Prevotella spp. (in 18.7%) and peptostreptococcus (in 17.03%). There was ascertained a considerable concentration in the periodontal pockets of yeast fungi of the Candida type of about 10-10 KOE/ ml which is considerably more than the permissible level of Candida content (to 10 KOE/ ml). In 74.7% there were ascertained pathogenic fungi of the type Cryptococcus neoformans – the main cause of cryptococcosis, in individuals with expressed

immunodeficiency (patients with AIDS).

Upon analysis of the isolated microorganisms depending on the clinical picture of the disease, it was noted a consecutive change of the microbial associations: at the beginning – predominant aerobic and facultative anaerobic microflora with a light degree of GP, afterwards – predominant obligate anaerobes and pathogenic fungi in the deep periodontal pockets in the cases of severe GP.

Upon evaluation of the ratio of the level of concentration in the periodontal pockets of anaerobic and aerobic bacteria in cases of GP of medium and severe degree, it was ascertained that the level of KOE anaerobic bacteria in 1 ml of material exceeds such aerobic bacteria 1000-10000 times, and in 17.3% of the patients there were isolated only obligate and facultative anaerobes. As per the data provided by D.Zambrano (1993), the ratio anaerobes/aerobes in saliva within the normal rates is 1:1, on the tooth surface (in the dental plaque) – 1:1, and in gum liquid – 1000:1. Therefore, the nature of the microflora in the periodontal pocket has to be taken in consideration in the specific tactics of antibacterial therapy in patients with periodontitis. It is necessary for a combined therapy to be carried out, aimed at various components of microbial associations (including pathogenic fungi), however, preference is to be given to preparations which are most efficient with respect to anaerobes.

There were carried out tests in order to determine the sensitivity *in vitro* of isolated bacterial cultures to the modern antibacterial preparations that are most commonly used in clinical periodontology – Gentamicin, Azithromycin (Sumamed), Clindamycin (Clindamycin MIP 600 mg), Lincomycin, Metronidazole, Rovamycine. The results of the test evidence various activity with respect to the representatives of the aerobic and anaerobic flora. In particular, 75% of the strains of Streptococcus spp., 60% - Porphyromonas gingivalis and 56% - Prevotella spp. are resistant to Gentamicin, even though the aerobic and facultative bacteria – staphylococci, enterobacteria and Escherichia coli in most of the cases (85-100%) were sensitive to its action, i.e. Gentamicin may be prescribed to suppress the aerobic bacteria in microbial associations in combination with anti-anaerobic preparations.

As regards Metronidazole, a classical anti-anaerobic medicine, 53% of the strains of Prevotella spp., 40% - Fusobacterium spp., 39% - Capnocytophaga spp. and 38% - Bacteroides spp. were resistant. This makes Metronidazole inappropriate as a choice of medicine in the various forms of periodontitis. This preparation may be applied in combination with other preparations if in the periodontal pocket there is oral trichomonad and/or amoeba gingivalis.

Upon evaluation of the sensitivity of the microflora to Lincomycin, it was ascertained weak antimicrobial activity to all isolated bacterial strains. Resistant to the effect of this antibiotic were: 75% - Bacteroides spp., 60% -

Staphylococcus aureus, 43% - Porphyromonas gingivalis and 40% Fusobacterium spp. A much more considerable bacterial efficiency has the derivative of Lincomycin – Clindamycin. It is efficient in 71-100% of the strains of the obligate and facultative anaerobes and 88-100% of the staphylococci strains. This is why our first choice of a preparation for systematic antibiotic therapy in patients with generalized periodontitis was Clindamycin MIP 600 mg. As compared to Lincomycin, Clindamycin had a wider specter, higher antimicrobial activity, better absorption in the digestive tract and is less toxic. The basic mechanism of action of Clindamycin is that it connects to the 50S-subunit of ribosomes and blocks the protein synthesis in the elongation phase. Clindamycin has mainly a bacteriostatic effect, but depending on the concentration in the place of infection and the sensitivity of the pathogenic agent, it may have a bactericidal effect. Clindamycin can concentrate in the granulocytes of the polymorph nuclear cells and the macrophages (40 times higher concentrations in the granulocytes, as compared to those in the serum). This aids the increase of chemotaxis, opsonization and phagocyte activity of these cells, by reducing the expression of the factors of virulence and pathogenicity of bacteria (Glycocalyx etc.). Furthermore, this allows the antibiotic to reach the regions with lower blood supply, such as bone and necrotized tissue (inflammation foci, abscesses) and to achieve high concentrations there.

During the course of treatment there were not reported any serious undesirable reactions to the medicines. Two of the patients (2/20, 10%) reported gastrointestinal discomfort which died down several days after the therapy was terminated. Good tolerability can be explained with the fact that the medicine is in the form of film tablets which gradually release the medical substance, thus avoiding high local concentrations and protecting patients with more sensitive gastrointestinal mucous membranes. There were not established any diagnoses of pseudomembranous colitis. A slight allergic reaction was observed in one of the patients (1/20, 5%) which died down after taking Clemastine. The preparation does not contain lactose and is suitable for patients with lactase insufficiency. The data obtained show good tolerability of the preparation owing to the special galenics used by the manufacturer.

High therapeutic efficiency of Clindamycin MIP 600 mg in patients with GP was reported as early as the 2nd, 3rd day after the start of taking the preparation. It was noted that pain, oedemas and gum bleeding were considerably reduced, bad breath disappeared, patients became more confident when chewing and their general condition improved. After a course of antibiotic therapy with Clindamycin MIP 600 mg after 6-8 days we could note that the gum edge became thicker, there was no puss discharge from the periodontal pockets and there was a trustworthy reduction in the average indicator for depth of the

periodontal pocket ($p < 0.05$), the condition of loosened teeth improved.

The results of the evaluation of biological efficiency of Clindamycin MIP 600 mg are presented in table 3. As evidence of the data from the microbiological tests, after the course of treatment with Clindamycin MIP the microflora from the periodontal pocket disappeared or was significantly reduced or the quantity of pathogenic microorganisms was less. Bacteria of the type *Prevotella* were isolated in 1 patient out of 6, fusobacteria - in 1 out of 5, *Porphyromonas* spp. - in 1 out of 2, *Capnocytophaga* spp. - in 1 out of 4, *Actinomycetes* - in 1 out of 2, and their concentration in the periodontal pocket was reduced from 10 to 10-10 KOE/ml. *Bacteroides* spp., *Actinomyces naeslundii*, *Peptostreptococcus* spp., *Streptococcus sanguis*, *Staphylococcus* spp. were not isolated which witnesses their eradication under the influence of Clindamycin MIP 600 mg. The complex therapy, including professional hygiene of the oral cavity, deep curettage and rinsing of periodontal pockets with antiseptic solutions, the use of antibiotics with immunomodulating properties (Clindamycin) assisted the increase in the non-specific factors of antimicrobial protection, considerably reduced the frequency and level of concentration of microorganisms in the periodontal pockets such as *Klebsiella* spp., *Escherichia coli*,

Enterobacter aerogenes, *Candida albicans* and *Cryptococcus neoformans* (table 3).

CONCLUSIONS:

1. It was ascertained that there were present aerobic-anaerobic-fungal associations in the periodontal pocket in patients with GP as facultative and obligate anaerobes were predominantly present.

2. Based on determination of the sensitivity of the isolated bacterial strains to antibiotics it was ascertained that Clindamycin MIP 600 mg was the most promising with respect to the whole specter of microflora in the periodontal pocket.

3. Clindamycin MIP 600 mg manufactured by MIP Pharma exhibited good tolerability, adequate compliance and better ratio price/duration of therapy as compared to other preparations on the market.

4. The clinical and laboratory study of efficiency of Clindamycin MIP 600 mg as a preparation used for systematic antibiotic therapy of patients with GP revealed his high clinical and bacteriological efficiency.

5. In case it is impossible to isolate, identify and determine the sensitivity of the microflora in the periodontal pockets to antibiotics, Clindamycin MIP 600 mg may be prescribed as a preparation for empiric antibiotic therapy.

REFERENCES:

1. Kleinfelder J. W., Zappa U. - *Actinobacillus actinomycetencomitans* - assozuerter paradontalerkrankungen. *Prophylaxe-impuls*, 1998, 1: 16 - 23.
2. Gemmel C. G., Lambe D. W., Santos I.I. - 1992 - the influence of clindamycin on the host-parasite relationship. In: D.Zambrano. Clindamycin in the treatment of human infections. Kalamazoo: Upjohn Co., 3 - 1: 3 - 46.
3. Komman K. S. - 1996 - Refractory periodontitis: critical questions in clinical management. *J.Clin.periodontology*, 23: 293 - 298.
4. Loesche W.J. - 1998 - The diagnosis and treatment of anaerobic periodontal infections. *Infect.Med.*, 15(II): 788 - 790, 792 - 797.
5. Quee T.C. - 1989 - The role of systemic antibiotics in periodontal therapy. *J.Can. Dent.Assoc.*, 55: 967 - 970.
6. Slots J., Rams T.E. - 1990 - Antibiotics in periodontal therapy: advantages and disadvantages. *J.Clin.Periodontol.*, 17 (7 Pt. 2): 479 - 493
7. Wolff L., Dahlen G., Aeppli D. - 1994 - Bacteria as a risk markers for periodontitis. *J.Periodontol.*, 25(2): 134 - 144.
8. Zambrano D. - 1993 - The role of anaerobic bacteria in human infections. *Clin.Ther.*, 15(2): 244 - 260.

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