ISSN 1561-6894

NR 2(204) 2020

Nauka i Studia

Przemyśl
Nauka i studia
2020

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APPLICATION OF SYSTEMIC-EFFECT ANTIBACTERIAL MEDICATIONS IN THE MODERN PERIODONTOLOGY

(LITERATURE REVIEW)

Abstract: Numerous studies have established that pathological processes in the periodontium are accompanied by a series of changes that are induced by various microorganisms. This paper provides a review of the literature on the application of systemic antibacterial medications in the practice of a periodontist. Medications that are created for suppressing and eliminating periodontal pathogens are used for the implementation of the preventive-therapeutic effect in the complex treatment of periodontal diseases.

Keywords: periodontal diseases, antibacterial medications, treatment

Periodontal diseases are chronic infectious and inflammatory conditions that are characterized by an active inflammatory process in periodontal tissues followed by the destruction of the periodontal ligament, progressing resorption of the alveolar bone and the migration of the connective tissue epithelium along the tooth surface. The formation of periodontal pockets creates favorable conditions for the emergence and proliferation of anaerobic pathogenic microflora. The microorganisms of the colonies of the sub-gingival plaque are the main etiological factor in the development of inflammation and the subsequent destruction of periodontal tissues. The immune-inflammatory reaction of periodontal tissues to microorganisms and their metabolic products, the synthesis of pro-inflammatory and pro-osteoporotic cytokines, and microcirculation disturbance all stimulate bone tissue resorption processes and those of the destruction of the alveolar bone. As the deep periodontal pockets are formed, a predominantly aggressive anaerobic microflora begins to prevail in them, in which microorganisms that are pathogenic for periodontal tissues, i.e. the so called

periodontal pathogens, are distinguished (*Actinobacillus actinomycetemcomitans, Poiphyrornonas gingi- valis, Prevotella intermedia, Fusobacterium nucleatum, Bacteroi- des forsythus*) [1].

Therapeutic measures for patients with periodontal diseases should be comprehensive: etiological, pathogenetic and symptomatic ones. Etiological treatment is aimed at identifying and eliminating predisposing factors and causes of the development of the disease [2]. Pathogenetic treatment is aimed at reducing the activity of inflammatory processes in periodontal tissues and preventing the resorption of the alveolar bone. Symptomatic treatment is aimed at eliminating the clinical manifestations of the disease [1].

Antibacterial medications are widely used in dentistry: for the treatment of periodontal tissue diseases, in the maxillofacial surgery, and when doing endodontic interventions. In most cases, diseases of the oral cavity are caused by associations of microorganisms and are a combination of several types of infections. Numerous studies indicate the role of poly-microbial synergism in the development of dental diseases.

When prescribing antibacterial medications, a physician should remember that most microorganisms in the oral cavity are combined into a microbial biofilm. The optimum choice of those medications for the treatment of infectious and inflammatory processes of the oral cavity should be based on the results of modern scientific studies proving the clinical and microbiological efficiency, as well as safety of a particular drug. Antimicrobial drugs are recommended in addition to mechanical plaque and tartar removal (Lindhe et al., 2003).

A systemic antibiotic therapy involves the intake of active substances by their absorption into the gastrointestinal tract, through the circulatory system into the tissues of the oral cavity, into the crevicular fluid and the saliva. In case there is a systemic pathway, antibiotic intake occurs uniformly and simultaneously in the entire oral cavity, as well as throughout the body. A necessary condition for the rational antimicrobial therapy as the most important initial link in the complex treatment of patients with the general periodontitis (GP) is the monitored identification of periodontal pocket microorganisms with the subsequent determination of their sensitivity to antibacterial medications [4]. Despite the sufficient amount of data on the sensitivity of the periodontium-related pathogenic bacteria to various antibiotics [4-7], that data requires constant in-depth research due to the significant variability of the microorganisms' properties, the formation of new microbial associations, increases in

the number of antibiotic-resistant strains, which all determines the relevance, the theoretical and practical significance of further microbiological studies in the field of clinical periodontology [8].

Indications for the use of antibacterial drugs

General periodontitis in the acute stage, with a pronounced inflammatory and destructive component in the form of abscesses, suppuration, progressing alveolar bone tissue resorption and the aggressive course of the disease.

General periodontitis in adolescents and young people: localized periodontitis, aggressive periodontitis.

General periodontitis in patients with a severe concomitant pathology, where therapeutic manipulations can complicate the course of the main disease (rheumatoid arthritis, endocarditis).

Periodontitis that is refractory to the traditional periodontal treatment. In the absence of a successful outcome of the initial periodontal treatment, three months later, the sensitivity of the microflora of periodontal pockets to antibiotics is determined (culture infection test).

Before and after surgery on periodontal tissues.

For the treatment of the periimplantitis:

- ulcerative necrotic gingivitis, severe course, with the signs of a systemic disease;

- gingivitis, severe course, with the signs of a systemic disease.

Antibacterial medications in periodontal treatment:

Penicillins. Pharmacotherapeutic group: amoxicillin and amoxicillin/clavulanate.

Amoxicillin is a polysynthetic antibiotic with a wide spectrum of antibacterial action against many gram-positive and gram-negative microorganisms. The antibacterial effect of this drug lies in the inhibition of the bacterial cell wall synthesis. Amoxicillin is sensitive to beta-lactamase secreted by microorganisms, and degrades under its impact. The action spectrum of amoxicillin does not therefore include microorganisms synthesizing that enzyme.

Clavulanic acid combined with amoxicillin blocks beta-lactamase enzymes and restores the sensitivity of pathogens to the bactericidal action of amoxicillin. Clavulanate provides insignificant antibacterial effect but its combination with

amoxicillin constitutes an antibacterial drug with a wide spectrum of action in relation to a wide range of microorganisms: *Corynebacterium, Enterococcus faecalis, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus agalactiae, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus, Streptococcus viridans spp.*; gram-positive anaerobes: *Clostridium spp., Peptococcus spp., Peptostreptococcus spp.*; gram-negative aerobes and gram-negative anaerobic bacteria *Bacteroides spp.*

Fluoroquinolones. Pharmacotherapeutic group**:** ciprofloxacin.

Ciprofloxacin is a synthetic broad-spectrum antibacterial drug of the fluoroquinolones class. It has a bactericidal effect due to the inhibition of the action of the bacterial DNA gyrase enzyme with the disruption of the DNA synthesis, the microorganisms' growth and reproduction. This medication provides a quick and pronounced bactericidal effect on microorganisms that are both in the breeding phase and in the resting one. It is highly efficient against almost all gram-negative and gram-positive pathogens. Ciprofloxacin is efficient against bacteria producing beta-lactamases. The drug is also active against microorganisms that are resistant to almost all antibiotics, sulfonamide and nitrofuran drugs; it can be a good alternative in helping to eliminate periodontal pathogens (Guentsch et al., 2008; Ardila et al., 2010). Ciprofloxacin can be combined with metronidazole or beta-lactam compounds to treat mixed anaerobic periodontal infections.

Tetracyclines. **Pharmacotherapeutic group:** tetracycline.

It is a broad-spectrum antibiotic, active against gram-positive (staphylococci, including those that produce penicillinase; streptococci, pneumococci, clostridia, listeria, anthrax bacilli) and gram-negative bacteria (gonococci, bordetella, Escherichia coli, enterobacteria, klebsiellas, salmonella and shigellas), as well as spirochetes, rickettsia, leptospira, also against trachoma and ornithosis pathogens. The bacteriostatic effect of the drug is conditioned by the inhibition of the ribosomal protein synthesis by a microbial cell.

Lincosamides. **Pharmacotherapeutic group:** Lincomycin.

Lincomycin is an antibiotic produced by *Streptomyces lincolnensis* or other actinomycetes and it belongs to the group of lincosamides. Lincomycin hydrochloride has a bacteriostatic and/or bactericidal effect depending on the concentration of the drug and the sensitivity of a respective microorganism to it. It is efficient against

anaerobic non-spore forming gram-positive bacteria, including *Actinomyces spp; Propionibacterium spp. i Eubacterium*; anaerobic and microaerophilic cocci, including *Peptococcus spp., Peptostreptococcus spp.* and microaerophilic streptococci; aerobic gram-positive cocci including *Staphylococcus spp.; Streptococcus spp.* (except for *S. faecalis*), including *Streptococcus pneumoniae*.

***Clindamycin*. Pharmacotherapeutic group:** Clindamycin.

Clindamycin is a semi-synthetic lincosamide antibiotic (Rang & Dale, 2007; Clindamycin, 2011). It has a wide spectrum of action, can act as bactericidal or bacteriostatic medication, which depends on the sensitivity of the respective microorganism and the concentration of the said antibiotic. Clindamycin is a highly efficient drug in the treatment of anaerobic infections. It acts on such forms of microorganisms as aerobic gram-positive cocci: *Staphylococcus aureus, Staphylococcus epidermidis* (strains producing and not producing penicillinase). The use of this medication is recommended for patients with penicillin allergies. In cases of anaerobic infections, clindamycin is considered the drug of the first choice.

***Macrolides*. Pharmacotherapeutic group:** clarithromycin, azithromycin.

Clarithromycin is a semi-synthetic antibiotic of the macrolide group. The drug is highly efficient *in vitro* against a wide range of aerobic and anaerobic gram-positive and gram-negative *moniae, Streptococcus pyogenes*; aerobic gram-negative: *Haemophilus influenzae, Neisseria gonorrhoeae*; anaerobic gram-positive: *Clostridium perfringens, Peptococcus niger, Propionibacterium acnes*; anaerobic gram-negative – *Bacteriodes melaninogenicus*; other microorganisms).

Another antimicrobial agent similar to clarithromycin is azithromycin. This antimicrobial agent has the same properties as clarithromycin, because it is absorbed by neutrophils, macrophages and fibroblasts and is slowly released. (Hirsch et al., 2010). Azithromycin provides powerful antibacterial activity against gram-negative bacteria, is capable of penetrating into the biofilm and accumulating in the gingival sulcus. Other positive properties of this agent: with systemic intake, azithromycin is concentrated in periodontal tissues, where it persists for at least 14 days. (Hirsch et al., 2010).

***Nitroimidazoles*. Pharmacotherapeutic group:** metronidazole.

Metronidazole is a derivative of the imidazole. It provides an antiprotozoal and bactericidal effect (Felleskatalogen, 2011; Metronidazole 2011). Sensitive to the drug

are: anaerobic gram-negative bacteria (*Helicobacter pylori, Bacteroides spp.*, including the *Bacterioides fragilis, Fusobacterium spp.* group), anaerobic gram-positive bacteria (*Clostridium spp.* and sensitive strains of *Eubacterium*), anaerobic gram-positive cocci (including *Peptoco'ccus spp.* and *Peptostreptoccus spp.*). In relation to aerobic bacteria, as well as fungi, the drug is not active.

The choice and clinical efficiency of the antibiotics' application for the treatment of periodontal diseases depend on the dose, the administration rhythm and the duration of the course of treatment, where the concentration of the drug in the blood and the gingival fluid should be 2 to 8 times higher than the minimum inhibitory concentration, while a decrease in the duration of therapy reduces the risk of toxic and allergic phenomena development. Of great importance nowadays are the interaction of the prescribed medications with the human body and that of the medications with each other.

Antibacterial medications are prescribed within 1 to 2 days of the sub-gingival removal of dental deposits and the curettage of the sub-gingival calculus in patients with the general periodontitis at the stage of exacerbation and abscess formation. Patients with a chronic course of the general periodontitis, if there is a purulent exudate when probing the sub-gingival calculus, are also prescribed antibiotics.

For the treatment of infectious and inflammatory diseases in the maxillofacial area, such combination medications as Cifran CT or Azimed are used.

Cifran CT is a combination medication that includes ciprofloxacin hydrochloride (500 mg) and tinidazole (600 mg). It is intended for the treatment of infections caused by aerobic and anaerobic microorganisms. The antibacterial action spectrum of ciprofloxacin encompasses most gram-negative and gram-positive microorganisms, i. e. *E. coli, Klebsiella spp., S. typhi* and other strains, *Salmonella, P. mirabilis, P. vulgarts, Yersinia enterocolitica, P. aeruginosa, Shigellaflexneri, Shigella sonnei, H. dycreyi, H. influenzae, N. gonorrhoeae, M. matarrhalis, V. cholerae, B. fragilis, Staph, aureus* (including methicillin-resistant strains), *Staph, epidermalis, Strep, pyogenes, Strep, pneumonia, Chlamydia, Mycoplasma, Legionella* and *Mycobacterium tuberculosis* [3].

Azimed contains an active ingredient called azithromycin. It represents a group of macrolide antibiotics called azalides. Its molecule is formed as a result of introducing a nitrogen atom into the lactone ring of erythromycin A. The mechanism of azithromycin's action consists in suppressing the bacterial protein synthesis by

binding to 50 S-subunits of ribosomes and inhibiting the translocation of peptides. There is its full cross-resistance to erythromycin, azithromycin, other macrolides and lincosamides among *Streptococcus pneumoniae*, group A β-hemolytic streptococci, *Enterococcus faecalis* and *Staphylococcus aureus*, including methicillin-resistant *Staphylococcus aureus* (MRSA).

Side effects of the antibiotic therapy

When prescribing systemic antimicrobial therapy, the physician should be aware of the possible development of side effects in patients.

The development of bacterial resistance to the medication:

Non-compliance with the indications for the administration of the drug, its dose and the intake regimen.

Conducting systemic antibacterial therapy without adequate local mechanical processing of the sub-gingival space, which may be the cause for the development of periodontal abscesses in the future.

A change in the normal microflora of the oral cavity – the development of a superinfection, i. e. candidiasis (*Candida albicans*) of the oral cavity, the development of which is possible in patients with impaired local and systemic immunity.

Pseudomembranous colitis and diarrhea (anaerobic microflora *of Clostridium difficile*). It most often develops after treatment with clindamycin and ampicillin.

Interaction with other medications.

Decreased efficiency of contraceptive drugs.

Enhanced effect of anticoagulants.

The efficiency of using the antibacterial drugs in question has been proved during the treatment of infectious and inflammatory diseases of the maxillofacial area and periodontal ones. Numerous studies have also proved the dosage regimen and the duration of the drugs' administration [3].

When dealing with periodontal diseases, one can see that antibiotic therapy is characterized by its empirical nature as in case of most infectious diseases, since the symptoms of those pathologies do not give any "clues" as to choosing an antibiotic. For the treatment of periodontitis, antibiotics are prescribed in the event of unsuccessful previous mechanical procedures. If we talk about excessive bacterial growth in the plaque and about subsequent inflammatory diseases, then a broad-spectrum antibiotic capable of destroying as many types of bacteria as possible could

help cope with bacterial contamination. The efficiency of the antibiotic is extremely important in that case, since that antibiotic must offset the problems with controlling the plaque biofilm caused by the poor diffusion into the sub-gingival area. The correct choice of antibiotic therapy depends on the type of bacteria responsible for the development of the periodontitis.

When examining microflora in patients with periodontal diseases, three types of bacteria must be taken into account:

Periodontal pathogens such as *T. denticola* and other spirochetes that refuse to be cultivated and that are sensitive to penicillin. Their distribution levels increase with the increasing severity of the disease (large depth of the gingival pocket). Those levels bear witness to the fact that the periodontitis is an infectious disease.

Bacteria responsible for the propagation of non-specific bacterial flora and the subsequent development of inflammatory processes (the most common anaerobic species is *Prevotella spp.*).

Oral microbiotas and those microbiotas that enhance bacteremia after dental procedures in patients with periodontitis (the streptococci of the *periodontiti Viridans group,* mainly *S. mitis,* and *S. Oralis*).

When prescribing antibiotic therapy, it is desirable to influence all three of the above-mentioned types of direct- or indirect-effect pathogens [9].

As can be seen from the above, based on the literature review of periodontology practice, taking into account the microbiological research of the sensitivity to identified periodontal pathogens, it is recommended that antibacterial medications of systemic action be prescribed, which would help to eliminate the dystrophic-inflammatory process and prolong the period of remission of a periodontal disease [8].

References

1. I. P. Mazur Clinical and Microbiological Efficiency of the Use of Local Antimicrobial and Antiseptic Medications for the Treatment of Periodontal Diseases / I. P. Mazur, N. A. Bakshutova, D. M. Stavskaya // Modern Dentistry. – 2014. – No.1. – pp. 32-38.

2. Essays in Practical Periodontology / Edited by Professor M. Y. Antonenko // "The Dentist" Physician's Guidebook, 2d Edition. – Kyiv: Health of Ukraine Library LLC, 2017. – 348 p.

3. I. P. Mazur Systemic Antibacterial Medications in Periodontology / I. P. Mazur,
M. V. Slobodyannik / Modern Dentistry. – 2017. – No. 1. – pp. 18-22.

4. V. N. Tsaryov Antimicrobial Therapy in Dentistry: Guidebook. V. N. Tsaryov,
R. V. Ushakov – Moscow: Medical News Agency. – 2004. – 144 p.

5. Modern Aspects of Clinical Periodontology / Edited by L. A. Dmitriyeva. – Moscow: MEDPress, – 2001. – 128 p.

6. Y. G. Chumakova The Effect of the Systemic Antibiotic Therapy on the Condition of Periodontal Tissues When Treating Patients with General Periodontitis / Y. G. Chumakova, V. V. Perekrest // Dentistry Bulletin – 2004. – No. 4. – pp. 36-39.

7. V. F. Kutsevlyak Periodontal Pockets' Microbial Flora Sensitivity to Antibacterial Medications in Patients with the General Periodontitis According to the Results of Bacteriological Studies / V. F. Kutsevlyak, O. V. Lyubchenko // Modern Dentistry. – 2005. – No. 1 – pp. 58-60.

8. Y. G. Chumakova A Comparative Assessment of the Sensitivity of Periodontal Pocket Bacteria to Various Antibiotics / Y. G. Chumakova, A. A. Vishnevskaya // Modern Dentistry. – 2012. – No. 2. – pp.70-73.

9. J. R. Maestre The Role of Bacteria in Periodontal Diseases and the Level of Their Resistance to Antibiotics That Are Used in Dentistry in Spain. J. R. Maestre, A. Bascones, P. Sanchez, P. Matesanz, L. Aguilar, M. J. Gimenez, I. Perez-Balcabao, J. J. Granizo and J. Prieto // Modern Dentistry. – 2012. – No. – pp. 48-52.

10. S. G. Sova Antibiotic Therapy: for Whom, When and Why? S. G. Sova // District Physician.– 2018. – No. 4(64). – pp. 22-24.

11. Dentistry: Textbook: in 2 Books – Book 2 / M. M. Rozhko Dentistry: in 2 Books. – Book 2: Textbook (Higher Education Institution of Accreditation Levels III and IV) / M. M. Rozhko, I. I. Kyrylenko, O. H. Denysenko et al.; Edited by M. M. Rozhko. – 2d Edition – 2018.

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