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INFLUENCE OF VARIOUS GROUPS OF ANTIBIOTICS ON SOCKET REGENERATION AFTER TOOTH EXTRACTION: REVIEW OF LITERATURE

Abstract. At the present stage, patients make high demands on the healing time of the wound process after tooth extraction. The main wishes are: no pain during extraction, short healing time, high quality and availability. Due to untimely access to a dentist, the root of the tooth becomes inflamed in patients, so the processes of removing and restoring the socket become more time-consuming. These patients are prescribed antibiotic therapy to relieve inflammation and eliminate the development of infection. The use of antibacterial drugs effectively reduces the number of postoperative infectious complications.

Keywords: tooth extraction, regeneration, healing, antibiotics, tissue.

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ВЛИЯНИЕ РАЗЛИЧНЫХ ГРУПП АНТИБИОТИКОВ НА ПРОЦЕСС РЕГЕНЕРАЦИИ ЛУНКИ ПОСЛЕ ЭКСТРАКЦИИ ЗУБА (ОБЗОР ЛИТЕРАТУРЫ)

Аннотация. На современном этапе пациенты предъявляют высокие требовании ко времени заживления раневого процесса после удаления зуба. Основными пожеланиями являются: отсутствие боли при экстракции, короткие сроки заживления, высокое качество и доступность. Из-за несвоевременного обращения к врачу-стоматологу у пациентов воспаляется корень зуба, поэтому процессы удаления и восстановления лунки становятся более трудоемкими. Данным пациентам назначается антибиотикотерапия, чтобы снять воспаление и устранить развитие инфекции. Применение антибактериальных препаратов эффективно снижает число послеоперационных инфекционных осложнений.

Ключевые слова: удаление зуба, регенерация, заживление, антибиотики, ткань.

Relevance. Various areas are developing in dentistry, such as implantology, periodontal surgery and others. However, tooth extraction is the most common and, in view of this, the most medically relevant operation in practical dentistry. The management of sockets after tooth extraction is a rather complicated procedure the dental surgeon deals every day with.

Currently, a large number of unfavourable healing outcomes have been recorded: slow regeneration of the socket after tooth removal, inflammatory-infectious and non-inflammatory complications, deficient formation of bone tissue around the extraction site. All this poses a grave risk for the patient’s health. In addition, this impedes orthopedic treatment. The solution of the

problems mentioned above will help to eliminate them altogether or significantly improve the existing state of affairs.

The goal of the study: to make an analysis of all the phases of socket healing on the basic of the Russian and foreign medical literature and to study the effect of various antibiotic groups on the process of socket regeneration.

Material and methods. A review of the literature was made in order to analyse the present-day ideas on the socket healing process and to determine the prospects for applying the acquired knowledge to elaborate therapeutic strategy and choice of antibiotics that are able to improve the therapeutic outcome.

Results and discussion. Multiple studies and clinical trials have given evidence that the index of the inflammatory process may change depending on the age, concomitant diseases, the living conditions and other social characteristics of the contingent under study. But, irrespective of this index has always been high, with a tendency to rise [6].

Tooth extraction may lead to local and functional changes. In most cases, the patient perceives tooth extraction as a tooth loss, but there after local changes begin to rise and promote deformation of the soft and hard tissues of the alveolar ridge. This is accompanied by damaging the integrity of the oral mucous membrane, circular binding of the teeth, amages to the vessels, alveolar periosteum, the nerves and the bone structure of the socket. Even a minimally traumatic tooth extraction may cause considerable changes in the nervous, cardiovascular, endocrine and immune system [3].

After tooth extraction, anatomo-functional changes occur both on the site of alveolar maxillary process and in the adjacent teeth. It should be noted, that due to the use of contemporary osteoplastic materials, like synthetic (Cerasorb, SintoGraft, Maxresorb) and natural bones of the cattle (Bio-Oss, Cerabone, SmartBone) it is now possible to preserve the socket's anatomy after a non-traumatic removal of a tooth [12].

The local changes that occur during the close-up of the wound and the restoration of the tissue integrity are called «socket healing». The alveolar bone tissue loses its volume after tooth extraction. So, modeling and remodeling of the bone are inevitable processes that occur during the socket healing of the extracted tooth [14].

After tooth extraction, the regeneration process takes place, triggered by primary and secondary strain. There are 3 phases in the socket healing process that take place under normal conditions: 1) the phase of inflammation; 2) the phase of proliferation; 3) the phase of modeling/remodeling of the bone tissue.

The phase of inflammation is subdivided into 2 stages: the formation of a blood clot and migration of the immune cells.

Due to the shrinking of the circular binding after tooth extraction the edges of the wound start to together. Simultaneously, there starts bleeding in the alveolus and the socket fills with blood. After that, a blood clot is formed that blocks several vessels and stops bleeding. Two or three days later, a large number of the immune cells migrate into the wound «to clean up» a side for the generation of a new tissue. A complex, made up of the immune cells, immature fibroblasts and generating vessels promotes on days 3 to 5 the formation of a highly vascularized granulation tissue. This tissue is rich in leukocytes, mesenchymal cells and fibroblasts. Simultaneous with the formation of the granulation tissue, progresses the vegetation of the epithelium from the gum edges. On days 7, 8 the granulation tissue replaces most of the blood clot. On days 12 to 14 the alveolus becomes wholly filled-in with maturing granulation tissue. After the wound has become sterile, the granulation tissue is replaced with provisional connective tissue, rich in collagen fibres and cells. The blood clot is destroyed by fibrinolysis [11].

The phase of proliferation may be conventionally divided into two stages: fibroplasias and bone tissue formation. Fibroplasia is rapid formation of the connective tissue. The vessels and cells that generate the bone tissue penetrate into the connective tissue in the form of sprouts embedded along blood vessels. Afterwards, these sprouts surround the vessels completely, thus forming the primary osteon. In some cases, the primary osteons may be strengthened by coarse-fiber bone tissue. Immature bone tissue starts to generate inside the healing socket from week 2 after tooth extraction and stays in the wound for several weeks. The immature bone tissue is not under stress and is later replaced with mature bone tissue (lamellar bone and bone marrow) [11].

So, a sequential replacement of the granulation tissue occurs, with the osteoid tissue and, later, with the bone tissue. Simultaneously with the latter process, the edges of the alveolar socket undergo resorption to one-third of the root length. The bone is subjected to lacunar resorption at the site where it was damaged during the surgery [10].

The bone tissue modeling involves alterations of the form and architectonics of the bone. Remodeling is reconstruction of the bone tissue without changes of its form and architectonics. The remodeling process is an outcome of osteoblast and osteoclast activities. The formation of the bone and its further remodeling depend on proliferation of blood vessels and blood supply in this area. The replacement of immature bone tissue with lamellar bone and bone marrow is a process of remodeling, while the resorption occurring in the alveolar walls is a modeling process that leads to dimensional alterations in the alveolar ridge. Therefore, the remodeling and resorption of the alveolar ridge after tooth extraction are natural processes of socket healing [11]. The modeling process precedes remodeling and it proceeds in such a way, that the two-thirds of it occur in the first 3 months of healing. In its turn, the bone tissue remodeling lasts from several months to several

years. Both processes lead to alterations in the extraction site, with dimensional reduction of the alveolar ridge [10].

If the blood clot has not been formed: the phase of inflammation: the socket is healing due to the formation of the granulation tissue on the side of the socket bone walls. Gradually, the gum edges over the socket come together and the socket is first filled in with the granulation tissue and, later, with osteoid tissue. The phase of proliferation and of modeling/ remodeling: like under normal conditions.

In the presence of inflammatory processes: the phase of inflammation: initially, a blood clot is formed. Thereafter, on days 10 to 14 the granulation tissue is formed. The phases of proliferation an of modeling/remodeling: like under normal conditions.

In traumatic tooth extraction, with rupture of the gum and damage to the alveolar walls: the phase of inflammation: a more pronounced delay in the wound epithelization and in bone formation. Therefore, the edges of the gum do not come together for a long time. The wound epithelization is completed on days 30 to 50. The phase of proliferation: a significant part of the alveolus is filled in with the osteoid tissue on day 60, which is gradually replaced with mature bone. The phase of modeling/remodeling of the bone tissue: like under normal conditions.

From all of the above it follows, that, in norm, the socket regeneration lasts for 40 days on average: from the point of blood clot formation to the connective-tissue formation and filling-in of the socket with not yet fully formed bone tissue. Sixty days thereafter, the alveolus is filled in with young bone tissue on the lower jaw and 90 to 120 days afterwards-on the upper jaw. The bone tissue gradually becomes mature [11].

As a rule, if the tooth extraction is followed by inflammatory processes, antibiotics are prescribed in the majority of cases, to prevent complications and unfavourable consequences. The selection of an antibiotic drug is made individually, on the basis of medical indications and contraindications. Also, on drug administration modes, bacterial sensitivity, pharmacological characteristics, side effects, interaction with other drugs, the cost and the patient's compliance [13].

From the point of view of pharmacology, the purpose of antibiotic prophylaxis is to achieve an efficient level of antibiotics in the tissues prior to microbial contamination and to maintain the drug activity throughout the surgical treatment and subsequent 3 to 4 hours. This time period is crucial for triggering the mechanisms of the inflammatory-infections process in the wound [9].

Currently, there are 20 classes of antibacterial drugs and over 200 antibiotic drugs have been registered in Russia. «Antibiotic activity is aimed against the microorganisms which multiply very fast; this determines the selection of drug resistance» [4].

Since ancient times, odontogenic infectious processes were the most widespread infections in the human body. These infections may be followed by life-threatening complications, and for this

reason there is a need of a careful evaluation of the infections and timely treatment: drainage and an appropriate antibiotic therapy. Currently, a variety of antibacterial drugs have been used the groups: penicillins, cephalosporins, macrolides, clindamicines, tetracyclines, nitroimedasoles [7].

According to S.E. Brodsky's research, the antimicrobial drugs commonly used in dental practice have a varying extent of activity against the causative agents of inflammatory-infectious complications after dental surgery. Least active are macrolides of the first generation, sulfanilamides and aminoglycosides. A moderate activity is typical for tetracyclines, imidasoles, lincosamides, fluorquinolones of the second – third generation. The highest activity is observed in fluorquinolones of the fourth generation and present-day macrolides [1].

Penicilline. The mechanism of its action is associated with inhibiting the synthesis of a bacterial cell wall. It is highly efficient against aerobic gram-positive bacilli; anaerobic gram-positive and gram-negative cocci, but it is weakly efficient against aerobic gram-negative bacilli. Penicillin is an antibiotic of choice for treating odontogenic infections in recommended dose 1500000 ME every six hours, fasting, or not earlier than 2 hours after taking meals, within 10 days. In recent years there has been an increasing number of cases of resistance to penicillin in some bacterial species (Bacteroides and Prevotella). For this reason this antibiotic has been rejected.

Semisynthetic derivatives of penicillin – amoxicillin and ampicillin have the same mechanism and an antimicrobial spectrum of action as penicillin. Recommended dose perorally is 500 to 1000 mg every 6 to 8 hours for ampicillin and 500 mg every 8 hours for amoxicillin.

Over the last few years a wider use of the combinations of semisynthetic penicillins with varying β-lactamase inhibitors has come into practice, such as amoxicillin with clavulanic acid and ampicillin with sulbactam. This leads to an expansion in the activity spectrum of mentioned antibiotics. Recommended doses: for peroral intake: 375 to 750 mg, every 12 hours for ampicillin/sulbactam and 625 mg every 8 hours for amoxicillin/clavulonic acid, for 10 days. The use of this-group drugs is restricted due to arising reactions of hypersensitivity, up to an anaphylactic shock [13].

The mechanism of action of cephalosporins is identical to that of penicillin. Comparing their antimicrobial efficiency, we have to state that perorally ingested cephalosporins of the first generation (cephalexine, cephazolin, cephadioxyl) have no great advantage over penicillin and ampicillin while a peroral intake of the second generation cephalosporins (cephatrisine, cephaclor, loracarbef, cephprozil, cephuroxime, cephoranid and cephoxitine) are resistant to β-lactamases, that neutralize ampicillin. They can be used as alternative medications, including cases of absent patient's response to penicillin. Present-day cephalosporins of the third generation administered perorally (cephetamet, cephixime, cephtibuten and cephpodoxime), resistant to β-lactamases are

potentially efficient against *Enterobacteriaceae*, but not against anaerobes. Therefore, they should not be prescribed for treating oral odontogenic infections that pass without complications [13].

According to V.V. Labis research, cephtibuten has a pronounced antimicrobial effect against the microflora involved in contaminating wounds in the jaw bones, including the types that produce collagenase. The efficacy of this antimicrobial drug is higher than that of other cephalosporin-group antibiotics. For systemic antibiotic prophylaxis, cephtibuten should be taken 60 min prior to the surgery and 4 days post the surgery (dose 0.4 g, once per 24 hours, irrespective of food intake) [8].

In his study S.E. Brodsky [1], compared the traditional schemes of cephasoline and cephepime. He noted that a distinctive teature of cephipime is its efficacy not only against non-clostridial anaerobes, but also against common representatives of enterobacteria and staphylococcus that cause wound infection. Another significant advantage of cephepime is its favourable effect on the cytokinic profile of the patients, observed at several stages of the study. This means, that the clinical use of these medications reliably decreases, the number of inflammatory complications [1]. The side effects of cephalosporins are similar to those of penicillins [7].

Macrolids and fluorquinolons. Erythromycine and new macrolids (claritromycine, roxytromycine, azitromycine and diritromycine) inhibit biosynthesis by microbial cells on ribosomal level. Their antimicrobial spectrum includes gram-positive anaerobis and aerobic cocci found in the oral cavity. Gram-negative anaerobes and aerobes are resistant to the drugs of this group. So, this group of drugs is a good alternative for the treatment of odontogenic infections not followed by complications and also for patients allergic to β-lactame [13]. Moxifloxotin, hemifloxotin and gatifloxatin are far more advantageous by their activity than other drugs from the fluorquinolons group and than the antibiotics commonly used in dental practice [5].

According to Brodsky's research, an antibacterial drug from the fourth generation fluorquinolone group-moxifloxotin has a wide spectrum of action against obligate-anaerobic, microaerofilic and facultative-anaerobic bacteria which are common for odontogenic infection. Moxifloxacin can be used for post-surgery antibiotic prophylaxis in dental practice. The dose for cases of conventionally pure and contaminated surgical interventions in oral cavity is: 400 mg in a single dose, 2 hours before surgery; if infection is present: 400 mg 2 hours before surgery followed by a 400 mg single dose a day for 4 days [1]. The side effects: gastrointestinal disorders [7].

Clindamycine. Its mechanism of action is similar to that of macrolids; it is highly efficient for treating sever and resistant odontogenic infections, but not efficient against gram-negative aerobic bacilli. Recommended peroral dose: 300 mg every 8 hours for 10 days. The side effects: antibiotico-associated diarrhea and pseudo-membraneous colitis.

Tetracyclines (tetracycline hydrochloride, oxitetracycline, minocycline and doxycycline) are bacteriostatic drugs that inhibit the protein biosynthesis of microbial cells at the level of ribosomes.

They are highly effective against aerobes and anaerobes of the oral cavity. Doxycycline and minocycline are more efficient against anaerobes than other tetracycline-group drugs. They are fully absorbed after peroral intake; so, they may be taken 2 times a day (100 mg every 12 hours) due to a more prolonged half-life of this drug within 10 days [13].

According to the study [2], a combined medication «Doxycycline with glucosamine» as compared with separately used components, manifests more pronounced antiexudative properties. The obtained findings give evidence of the feasibility of prospect for this drug to be used in clinics for treating infectious diseases and preventing post-surgical complications. Its side effects are similar to those of macrolides, plus impaired vestibulocochlear nerve (dizziness) [7].

Nitroimidazoles (metronidazole and ornidazole) have a fast bacterisidal effect against gram-negative and gram-positive anaerobes. However, they should not be used as sole drugs for treating ondogenic infections. Standard peroral dose: 500 mg every 8 hours for metronidazole and 500 mg every 12 hours for ornidazole for 10 days [7].

The study of the wound process dynamics and monitoring of microbial contamination after surgery in patients with the inflammatory diseases of the maxillofacial area evidenced a very high efficacy of the following drugs: cephepime, doxycycline, amoxyclaw, levofloxacine. The clinical uses of these drugs have demonstrated a reliable decrease in a number of clinical parameters: temperature, presence of purulent discharge, soft-tissue swelling, enlargement of regional lymph nodes, the pain syndrome (in a trial with a control group) [1].

Conclusion. Established, that the course of the wound process depends on the initial state of a tooth. Normally a blood clot in the alveolus is replaced with the granulation tissue on days 3, 4; in case of the inflammatory processes in the alveolus, wound healing takes from 10 to 14 days; in case of a traumatic tooth extraction with a gum rupture and damage to alveolar walls, the process of epithelization lasts 30 to 50 days. Antibiotic drugs are administered in the presence of focal infection in order to decrease body temperature, prevent proliferation of the infection and as therapy for a significant focal infection. The dentist may also prescribe the infection therapy to avoid complications and relieve inflammation. There are two modes of injections: intramuscular and intraoral. An example of an intraoral injection: half an ampoule of an anesthetic and 4 mg of dexamethasone to be used after tooth extraction for 2, 3 days, one injection per 24 hours.

The use of various antibiotic drugs according to the described schemes has proved their efficacy for decreasing the number of post-surgical infectious complications.

Consequently, the antibiotic therapy is, undoubtedly, very important far all kinds of infections pathologies: sepsis, necrosis, inflammation of the root. This kind of therapy plays an important role in inhibiting the spread of infection and in preventing its hematogenic spreading. It is owing to the antibacterial drugs that our body fights these infections and speeds up wound healing.

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