

Application of Autoplasma Enriched with Platelet in the Treatment of the Abscesses and Phlegmon of the Maxillofacial Area in Patients with Diabetes Mellitus

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Abstract The article is dedicated to the advanced multimodality therapy of the patients with odontogenic osteomyelitis of the jaws and its complications with local application of platelet enriched with plasma in the patients with diabetes mellitus taking into account the nature of the course of the inflammatory process. Platelet autoplasma is a highly active biological stimulator of regeneration processes owing to various growth factors contained in alpha granules of platelets, acting on all structural units of the surrounding tissue and stimulating regeneration processes. The article defines the use of platelet autoplasma and their advantage in the treatment of abscesses and phlegmon of the maxillofacial area in patients with diabetes mellitus.

Keywords Phlegmon, Osteomyelitis, Autoplasma, Immunity, Diabetes mellitus, Antibiotic, Growth factor, Infiltrate, Glycemia, Pus, Infection, Detoxification

1. Introduction

The frequent development of abscesses and phlegmon in the head and jaws is due to the high prevalence of chronic focal odontogenic, tonsilogenic infection, as well as infectious and inflammatory wounds of the skin and oral mucosa. The most common form of septic inflammation is odontogenic suppurative inflammatory disease. In recent decades, interest in acute infections of the face and neck has increased due to an increase in the number of patients with these diseases and the number of severe intracranial and extra cranial complications [1].

Unfortunately, the problem of odontogenic infection to date remains significant. According to most researchers, this is due to the following reasons:

- With an increase in the number of patients with odontogenic pyoinflammatory diseases in specialized clinics, they range from 45% 55% [2].
- With the development of new resistant strain microorganisms, the species composition of pathogens of pyoinflammatory diseases has changed, the dominant role of the anaerobic component is eminent.
- The majority of authors consider the reason for this course of the disease to be a decrease in immunological

reactivity, a distortion of the immune response against the background of preliminary sensitization of the body from the focus of a chronic infection.

Topographical and anatomical features of this area play an vital role in the course of pyoinflammatory diseases of the maxillofacial area: the complexity of the relationship between the tissue spaces, the abundance of collaterals to anastomoses with the vessels of the brain, the underdevelopment of venous valves and their incomplete closure determines the possibility of reflux the toxins into the head of the inflammation brain [3].

The combination of odontogenic infection with diabetes forms a vicious cycle in which the infection negatively affects metabolic processes, exacerbating insulin deficiency and increasing acidosis, and metabolic disorders and microcirculation worsen the course of reparative processes in the focal lesion.

Insulin deficiency develops disorganization of carbohydrate metabolism, hyperglycemia, glycosuria, a decrease in glycogen content in tissues, primarily in the liver of the patients with diabetes. Due to a disorder in liver function, water-salt and protein metabolism subsequently change. Disorder of protein metabolism develops in a decrease in its synthesis and the increase in its breakdown. As a result, there increases the formation of glucose from amino acids. Ketone bodies and acetone accumulate in the body of patients on the ground of an almost complete loss of the ability to synthesize fats, which leads to ketoacidosis. In our opinion, the severe results of these patients at the previous stages of treatment were due to the relationship of

poorly treated purulent infection with uncompensated diabetes.

This is the basis of "The syndrome of mutual aggravation", which means a new form of the disease with a specific adverse course, requiring, in our opinion, a fundamentally new approach to treatment [2,7–9].

A known fact is the mismatch of the healing time of bone tissue and mucous membrane. Sometimes, after a qualitatively performed operation in the area of the interdental papillae, healing takes place by secondary intention, which causes washing –out the osteoplastic material and ingrowth into the periodontal recess of the epithelium, and, consequently, the absence of further regeneration and inhibition of reparative processes in periodontal tissues [13].

Numerous studies, conducted over the past decades, have clearly shown that the clinical course of inflammatory disease and the state of reparative processes are significantly affected by such mechanisms of regulation of immune responses as the function of immunocompetent cells, the production of cytokines, the level of production of pathogenic immune complexes and adhesive molecules [18].

An increased susceptibility to infections in patients with diabetes is associated with impaired protective functions of the immune system, increased cell adhesion of microorganisms, the presence of micro- and macroangiopathy, neuropathy, as well as an increased frequency of conservative and surgical interventions [3,7–9, 11,12]. An additional factor is the susceptibility to catabolic processes. As a result, the purulent process is accompanied by severe intoxication and metabolic disorders, which leads to functional disorders of the liver and kidneys. Symptoms of intoxication are observed very early, when local development of the inflammatory process is still slightly seen [2,7,8]. At the same time, secondary immunological insufficiency develops, in particular, antibody synthesis changes, the phagocytic activity of macrophages and leukocytes decreases, the regenerative ability of all tissues decreases on the whole, and the barrier function of the mucous membranes decreases [1,2,7–9]. Due to the reduced resistance of patients with diabetes to infection in wounds, necrotic processes predominate, the typical symptoms that characterize inflammation are sometimes minor, and some may be absent. Suppurative processes can acquire a dystrophic nature, which is based on tissue acidosis.

Quite often, in these patients there is a reactive course of the purulent process or a flaccid, protracted course of the wound infection after the removal of acute effect [1,7–12].

Presently, varieties of methods are used in the treatment of acute odontogenic pyoinflammatory diseases of the maxillofacial area, aimed at both the local focus of inflammation and the microorganism as a whole. Local methods can be a very important connection in the treatment of inflammatory diseases of the maxillofacial area stimulation of soft tissue regeneration processes.

Active research is currently being done to explore ways to increase the effectiveness of existing bone materials and

membranes. A favorable method in solving this problem is plasmolifting, developed by R.R. Akhmerov and R.F. Zarudy- the injection inserted into the body tissue of platelet-rich plasma (P.R.P.) obtained from the blood of the patient himself [14].

The complexity of the treatment of inflammatory periodontal diseases lies in the fact that the known and standard methods (antibacterial and local therapy) do not always give a positive result and a long period of remission [15]. Therefore, it is necessary to introduce new innovative treatment methods into dental practice to improve the quality of medical care for patients with periodontal pathology [16].

Platelet autoplasma is a highly active biological stimulator of regeneration processes due to the various growth factors contained in alpha granules of platelets, acting on all structural units of the surrounding tissue and stimulating regeneration processes.

In addition, the use of autologous plasma eliminates the possibility of allergic reactions.

The technical result of the method is achieved through the use of a new technique, namely: venous blood sampling in a patient becomes in a volume of 9-36 ml, depending on the extent of inflammation, then the blood is centrifuged with an acceleration of 1000G for 5 minutes, after centrifugation 3,0 ml of the obtained platelet autoplasma are taken with a luer-lock system syringes from the tube, then the platelet autoplasmic syringes are placed in a thermostat and kept to obtain a gel, while for the introduction into a purulent wound, the autoplasma is kept at a temperature 85°C for 6 minutes, after which the resulting gel is cooled in a sterile tray for 2 minutes, and then the gel is introduced into the infiltration area via syringe connector.

The autoplasma obtained by centrifugation contains high concentration platelets, which means the following growth factors:

- IGF (insulin-like growth factor) - stimulates the differentiation of stem cells, enhances bone metabolism and collagen synthesis. PDGF (platelet-derived growth factor) - activates the proliferation and migration of mesenchymal (osteogenic) cells, stimulates angiogenesis. PDEGF (platelet-derived endotheliocyte growth factor) - has a stimulating effect on endothelial cells and has an angiogenic effect. VEGF or PDAF (platelet-derived growth factor of vascular endothelium): there are 4 types of factor VEGF-A, B, C and D. It is involved in angiogenesis, induces proliferation of vascular endothelial cells. EGF (epidermal growth factor) - stimulates the synthesis of proliferation of fibro and osteoblasts, stimulating the synthesis of fibronectin.
- TGF- β (the "family" of transforming growth factor) is a multifunctional factor that causes many cellular and intercellular responses, including other products of growth factors.
- FGF (fibroblast growth factor) - causes expression in bone tissue, angiogenesis, ossification, induces the

production of TGF in osteoblastic cells.

2. The Aim of the Study

Was to evaluate the effectiveness of the use of PRP-therapy in patients for the treatment of odontogenic inflammatory diseases of the MFA (maxilla facial area).

3. Materials and Methods

There were 153 patients aged 17 to 70 years with odontogenic purulent-inflammatory diseases of the maxillofacial region on the background of diabetes in the clinic of maxillofacial surgery in the Bukhara regional multifield medical center, from 2015 to 2019. Among them were 64 men and 89 women. The duration length of diabetes mellitus ranged from 3 to 18 years. In 70 patients, insulin-dependent diabetes was determined, in 83 - non-insulin-dependent diabetes. Odontogenic phlegmon was diagnosed in 93 patients, abscess in 24 patients, odontogenic osteomyelitis in 15 patients, odontogenic maxillary sinusitis in 21 patients.

4. Results of the Study

In the general structure of patients with purulent-inflammatory diseases of the maxillofacial area in the presence of diabetes, more than half (56.6%) of the patients were observed moderate and severe disease. All these patients were older than 50 years. In most of them, the course of the underlying disease was aggravated, in addition to diabetes mellitus, by two or three concomitant diseases: 60% suffered from hypertension, 48% from angina pectoris and atherosclerosis, and 40.5% from obesity. Most patients were admitted to hospital in the later stages from the onset of purulent surgical disease. Prior to hospitalization, 95 patients took oral hypoglycemic agents, 53 people took parenteral insulin, and 5 patients had no data on the treatment of diabetes in the case report. After studying the glycemic profile and endocrinologist's consultation at the clinic, all patients underwent correction of hypoglycemic therapy. Patients who received the tablet form of the drug were prescribed insulin for parenteral introduction.

The clinical course of all diseases was characterized by an inadequacy of the mild temperature reaction of the severity of the purulent process: only half of the patients had hyperthermia up to 38.0–38.5°C for 1–3 days before hospitalization. Nevertheless, in most patients, upon admission, clear intoxication, desiccation was observed. A common blood test revealed a tendency to accelerate ESR, a more or less noticeable shift of the leukocyte formula to the left with an increase in the number of stab neutrophils, and a decrease in the number of lymphocytes, which indicated a low reactivity of the patient's body. At the same time, in 75 patients the total number of leukocytes was within

normal limits or slightly higher than physiological boundaries, in the remaining patients it was increased with maximum values of $13-14 \times 10^9 / L$. Noticeable violations of electrolyte metabolism were detected during biochemical studies, the degree of which often depended on the severity of the disease, elevated blood sugar and urine, and acetonuria. In addition to impaired carbohydrate metabolism, severe dysproteinemia was detected in patients due to an intensive decrease in the content of albumin (up to 38%) and an increase in globulin fractions. A clear relationship was determined between blood sugar and the course of the inflammatory process. The higher the glycemia level, the more difficult the inflammatory process was. In severe diabetes mellitus, the development of a purulent process sharply worsened the general condition of the patient. Inhibition of metabolic processes and hypoxia resulted in depression natural resistance of the body and various defects of the immune response characteristic of patients with diabetes. A significant number of these patients developed a sluggish (hyperergic) inflammation with erased clinical development, against the background of functional depletion of the body's protective systems, and a tendency to spread the process. Moreover, in most patients, the formation of abscesses occurred at a satisfactory general condition and normal or mild pyrexia, a tendency to limit the process was not observed for a long time. Treatment of acute purulent surgical diseases of the maxillofacial area (odontogenic abscesses and phlegmon, odontogenic and traumatic osteomyelitis, etc.) in patients with diabetes presents significant difficulties. The purulent process in these patients creates the prerequisites for the destruction of endogenous and exogenous insulin, which leads to an increase in insulin deficiency and thus to the decompensation of diabetes. Patients with diabetes, who have developed a purulent process, need full intensive treatment aimed at both compensating for pathological altered metabolic processes and eliminating the purulent focus from the moment of admission to the hospital. The complex of these measures includes: 1) correction of disorders of carbohydrate metabolism; 2) the prescription of antibacterial drugs, depending on the sensitivity of microflora; 3) detoxification therapy, correction of metabolic disorders; 4) immunocorrective therapy; 5) the use of direct-acting anticoagulants (heparin) of direct effect in prophylactic doses (10,000–20000 units) in connection with severe hypercoagulation in these patients; 6) eutrophic intake, including foods rich in fluids, vitamins, proteins and mineral salts, with a strict restriction of carbohydrates; 7) early active physical lifestyle, breathing exercises, massage; prevention of cardiovascular complications. Since surgical trauma and analgesia cause hyperglycemia, there may be a sharp violation of homeostasis even against the background of compensated diabetes in the postoperative period. In this regard, it is always necessary to involve endocrinologists (diabetologists) in the treatment of this group of patients. In this case, insulin therapy, regularly conducted under the control of a blood glucose test, plays particular importance.

There is no doubt, that the key link in the treatment of purulent-inflammatory diseases of the maxillofacial area is etiotropic antibacterial therapy. From a practical point of view, great attention is drawn to the correct choice of antibiotic. It must be remembered that patients with diabetes require a special care. Let us begin with the microbial area in the foci of inflammation in patients with diabetes that is different from that in patients without diabetes. In addition, diabetic nephropathy, leading to impaired renal excretory function, requires dosage correction of antibacterial drugs. It should be taken account that a number of antibiotics affect the level of glycemia. Therefore, even highly effective antibiotics of the last generation are ineffective against the background of hyperglycemia and other disorders. Thus, timely correction of metabolic disorders, targeted glycemic control and correctly selected sugar-lowering therapy are another key element in the successful treatment of such patients. It is necessary to conduct active detoxification therapy taking into consideration of the obvious intoxication that contributes to hyperglycemia. For this purpose, they use a 4% solution of sodium bicarbonate, succinic acid, glucose-novocaine mixture, reformed, plasmalit and other drugs, combining 2-3 drugs, transfusing them in turn. It is better not to use isotonic sodium chloride solution, because it removes out potassium ions and reduce the fibrinolytic activity of the blood.

Along with traditional methods of infusion detoxification therapy, we widely used such methods of active artificial detoxification as reinfusion of ultraviolet irradiated blood, intravenous laser irradiation of blood, indirect electrochemical oxidation of blood, discrete plasmapheresis, both in isolation and in combination with each other. Indications for the use of these methods were determined on the basis of laboratory data and the following clinical indicators: progressive intoxication, generalization of infection, ineffectiveness of drug therapy, slowing down the purification of a purulent wound, a marked slowdown in the rejection of necrotic tissues, and a decrease in the repair processes in the wound, a marked slowdown in the rejection of necrotic tissues, and a decrease in repair processes in the wound. Improving the general condition, normalizing body temperature, a satisfactory level of glucose in the blood first determine a decrease in the number of injected solutions and the frequency of procedures, and then their cancellation. In cases of severe inflammation of the tissue of the maxillofacial area, when, despite adequate therapy, the general condition of the patient and the local development of the inflammatory process do not change for the better, double and triple blood transfusions are given. Due to impaired liver function and protein metabolism during a prolonged course of the inflammatory process, it becomes necessary to alternate the transfusion of contained blood with transfusion of blood substitutes. In order to normalize the metabolic processes and vascular disorders in patients with diabetes mellitus, the appointment of vitamins, antioxidants, antihypoxants, angioprotectors, and hypersensitizing things are shown in the complex treatment. It should be borne in

mind that the treatment regimens for patients with diabetes in recent years have been revised from the perspective of evidence-based medicine and brought into line with international standards traditionally established in our country. The modern approach to the treatment of diabetes is aimed not only at eliminating the development of decompensation of carbohydrate metabolism, but also at preventing the development of late complications of the disease [4-6]. Odontogenic purulent-inflammatory processes of the maxillofacial area in patients with diabetes proceed against the background of noticeable changes in the immune status. Moreover, the course of odontogenic purulent-inflammatory processes and the state of immunological status are directly related to the severity and form of diabetes. With IDDM, odontogenic purulent-inflammatory processes proceed more severely than with NIDDM. Secondary immunological deficiency, developing in diabetes, required drug and non-drug correction of immunity [7-9]. An analysis of the results of a comprehensive rehabilitation treatment of inflammatory and destructive periodontal diseases using plasmolifting indicates a significant improvement in periodontal conditions. The method is considered simple, safe and effective [17].

5. Conclusions

Treatment of purulent wounds in the background of diabetes should be carried out with the participation of an endocrinologist under the control of criteria reflecting objectively the course of the wound process: cytological examination of wound prints, morphological examination of wound tissues, determination of tissue homeostasis in the lesion, quantitative and qualitative microbiological analysis. The use of the above methods, as well as the volume and direction of the therapy in each case, are considered the prerogative of the attending physician. Our study showed that the treatment of odontogenic infection with autothrombocyte mass makes it possible to stop the purulent foci and reduce the healing time of the purulent wound due to the stimulating effect of platelet growth factors on bone and collagen metabolism, proliferation of vascular endothelial cells, and reduces the risk of complications.

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