

SURGICAL TREATMENT OF MEDICATION-RELATED OSTEONECROSIS OF THE JAW USING PLATELET-RICH FIBRIN: A RETROSPECTIVE CLINICAL ANALYSIS

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Abstract

Medication-related osteonecrosis of the jaw (MRONJ) is a severe complication of antiresorptive and antiangiogenic therapy characterized by drug-induced damage to the jawbone in the absence of prior radiation therapy or metastatic disease. The unpredictability of treatment outcomes necessitates the search for approaches capable of enhancing tissue repair. The aim of this study was a retrospective evaluation of the effectiveness of surgical treatment of MRONJ with and without the use of platelet-rich fibrin. Data from 42 patients with mandibular osteonecrosis treated between 2022 and 2026 were analyzed; patients were divided into two groups according to PRF use. Clinical healing was considered the primary outcome measure. Favorable outcomes were observed in approximately 64% of cases. The use of PRF demonstrated a tendency toward improved treatment results without reaching statistical significance, indicating the need for further research.

Keywords: Medication-related osteonecrosis of the jaw; MRONJ; platelet-rich fibrin (PRF); surgical treatment; bone tissue repair.

Introduction

Despite significant progress in the study of the pathogenesis of drug-associated osteonecrosis of the jaw (MAONCH), a number of key treatment issues remain unresolved. In the literature, there is no unified approach to the selection of optimal therapeutic tactics, especially in the late stages of the disease, when surgery is the main method, but is accompanied by variable and difficult to predict results [1, 2, 4].

One of the debatable problems remains the clinical expediency of using autologous blood products containing growth factors. Although the use of platelet-rich fibrin (FOT) has a biological basis, data on its effect on jaw bone regeneration remain limited and are based mainly on individual clinical observations and heterogeneous studies [8–14]. To date,

there are no standardized schemes for the use of payroll, unified criteria for assessing efficacy and comparable data in oncological and non-oncological patients.

In addition, the influence of systemic risk factors - the duration and method of use of antiresorptive drugs, concomitant antitumor therapy and somatic status - on the results of surgical treatment using FOT has not been sufficiently studied, especially in common forms of MAONCH.

These circumstances necessitate further clinical studies aimed at an objective assessment of the effectiveness of FOT in the complex surgical treatment of MAONCH and the development of differentiated approaches to the management of such patients.

MAONCH is an interdisciplinary pathology, while the leading role in its diagnosis, prevention and treatment belongs to dentistry and maxillofacial surgery. The primary manifestations of the disease occur in the oral cavity and maxillofacial region, and its development is often associated with dental interventions, including tooth extraction, endodontic and orthopedic treatment.

In this regard, the study of bone repair disorders of the jaws, the improvement of surgical tactics and the introduction of biologically based methods that stimulate the regeneration of bone and soft tissues are of particular importance. The use of autologous blood products, in particular, platelet-rich fibrin (FOT), corresponds to modern trends in dentistry, focused on organ-preserving and minimally invasive treatment technologies.

Based on this, the purpose of this study was a retrospective assessment of the results of treatment of patients with drug-induced osteonecrosis of the jaw during surgical intervention without the use and with the use of improved platelet-rich fibrin.

Materials and Methods

The retrospective clinical trial included 35 patients aged 18–70 years with osteomyelitis caused by drug-associated osteonecrosis of the jaw, who underwent surgical treatment in the Department of Surgical Dentistry of the III building of the Tashkent State Medical University in 2024–2026.

Demographic and clinical indicators were analyzed: age, sex, underlying disease, duration of antiresorptives/antiangiogenic therapy (<3 years and ≥3 years), route of drug administration (oral or intravenous), the presence of provoking factors (tooth extraction, periapical foci), the stage of MAONCH according to the AAOMS classification, as well as the extent of the lesion according to clinical and radiological data (<3 cm and ≥3 cm).

Two treatment approaches were compared: surgical removal of necrotic bone tissue without additional methods and surgery with local application of autologous growth factors. The main endpoints were clinical healing and follow-up. In addition, factors of poor prognosis were evaluated, including the use of zoledronic acid, the intravenous route of administration, the duration of therapy ≥3 years, previous episodes of osteonecrosis, and the presence of cancer.

The patients were divided into two groups depending on the treatment tactics: the first group included 18 patients who underwent surgical removal of necrotic foci, the second group included 17 patients in whom the operation was supplemented by the local use of platelet-enriched fibrin (FOT).

Inclusion criteria: adult, clinically and radiologically confirmed MAONCH, use of antiresorptive or antiangiogenic drugs, bone exposure $\geq 6-8$ weeks, absence of radiation therapy to the head and neck and facial metastases, as well as satisfactory general condition and acceptable laboratory parameters.

Exclusion criteria: osteonecrosis of other etiology, lack of appropriate drug therapy, bone exposure $< 6-8$ weeks, undergone radiation therapy, metastatic lesions of the facial bones, minority, or refusal to participate.

Prior to surgery, all patients underwent a clinical examination and X-ray examination (orthopantomography or CBCT) with data analysis in CS 3D Imaging v3.5.18. During the day, antibacterial prophylaxis (amoxicillin/clavulanate; in case of allergy - clindamycin) and rinsing with a 0.1% chlorhexidine solution were prescribed.

In patients of the second group, 4 10 ml venous blood tubes without an anticoagulant were taken before the intervention, followed by centrifugation (1500 rpm, 14 min). The resulting FOT clots were formed into membranes using a PRF box (Quadrostom, Poland).

Surgical technique. Operations were performed under local infiltration or regional anesthesia with 4% articaine with adrenaline 1:100000. After the formation of the mucoperiosteal flap and excision of the epithelialized edges, the necrotic bone was removed, followed by treatment of the bed until bleeding tissue appeared. The mucoperiosteal flap was exfoliated with a scalpel (15c blade), necrotic areas were removed, the material was fixed in 10% formalin and sent for histological examination. Wounds were additionally treated with boron at 40,000 rpm with abundant irrigation of 0.9% NaCl, then washed with 0.5% metronidazole solution (20 ml). In the FOT group, four fibrin tampons were inserted into the wound at this stage. The wound was sutured without tension with the achievement of hemostasis and a gauze bandage was applied for 20 minutes.

Postoperative follow-up. Antibiotic therapy was prescribed for 14 days in high-risk patients and for 7 days in low-risk patients. Sutures were removed after 14 days. Examinations were performed at 2 and 6 weeks, then every 3 months and annually if the course was favorable; in case of delayed healing, the schedule was adjusted individually.

Statistical analysis. Data processing was performed in program R (v.4.4.2). Demographic, clinical and therapeutic parameters, success of therapy, and follow-up were

analyzed. Maximum likelihood and nonparametric ANOVA were used for intergroup comparisons; differences were considered significant at $p \leq 0.05$.

Results

The study included 35 patients with drug-associated osteonecrosis of the jaws; the age ranged from 43 to 82 years (mean 70.2 years). In the sample structure, women prevailed - 25 (71.4%), men were 10 (28.6%). The most common main diseases were multiple myeloma (38.3%), breast cancer (25.5%), prostate cancer and osteoporosis (14.9% each), other nosologies - 6.4%. Zoledronic acid was administered intravenously for oncological indications (78.7%), and the duration of therapy in 72.3% exceeded 3 years.

The main trigger for the development of MAONH was tooth extraction (89.4%); Inflammatory processes (6.4%) and the presence of implants (4.2%) were less common. Lesions of the lower jaw were recorded much more often than the upper jaw (83.0% vs. 17.0%). All patients were diagnosed with stage III according to the AAOMS classification with the presence of an intraoral fistula; Three patients also had an extraoral fistula. The size of the fistulous tract in most cases did not exceed 3 cm (78.7%).

Complete clinical healing was achieved in 16 patients (94.1%) in the group with FOT (n=17), while in 11 patients (61.1%) in the group without FOT (n=18). The median follow-up duration was about 15 months. The analysis showed that there was no significant relationship between treatment outcomes and the localization of the process and the extent of the lesion ($p > 0.05$). At the same time, a statistically significant dependence of adverse outcomes on a combination of risk factors, including the use of zoledronic acid, intravenous route of drug administration, duration of therapy of more than 3 years, history of osteonecrosis, and cancer ($p < 0.01$) was established.

Outcome analyses showed binomial healing (presence/absence of clinical recovery). The overall success rate was 27 of 35 cases (77.1%).

Comparative analysis demonstrated a statistically significant advantage of the use of payroll: according to the exact Fisher test, the differences between the groups were significant ($p = 0.036$). The data obtained confirm the higher efficiency of surgical treatment with the use of FOT. The relative risk showed a 46% increase in the likelihood of clinical healing with the use of FOT compared to standard treatment (RR=1.46).

Discussion

Prevention of MAONF in patients who are planning antiresorptive or antiangiogenic therapy should be considered as a mandatory stage of treatment. The initiation of drug therapy is recommended after oral cavity sanitation with clinical and radiological examination, including orthopantomography and, if necessary, cone-beam computed tomography [5-7].

In clinical practice, conservative, surgical and combined methods of MAONP treatment are used. According to the AAOMS recommendations, in the early stages, the focus is on the

elimination of local factors, antiseptic rinses (chlorhexidine), antibiotic therapy (amoxicillin/clavulanate or clindamycin), as well as pain control. At stage II, complex drug treatment is indicated, taking into account the signs of bone destruction; Surgery is used in a limited way. In stage III, surgery is the main method and may include sequestrectomy, necrectomy, or resection to viable bone [1, 2, 4, 13, 14].

Additional therapies include LLLT, hyperbaric oxygenation, photobiomodulation, ozone therapy, platelet concentrates, growth factor and rhBMP preparations, as well as pharmacological agents (teriparatide, pentoxifylline, vitamins E and D). At the same time, alternative methods should be used only as part of multimodal treatment [13-23].

FOT is an autologous biocompatible drug containing platelets and growth factors that promote neovascularization, modulation of inflammation, cell proliferation, and the formation of bone and soft tissue. Prolonged release of growth factors (up to ~4 weeks) stimulates key regeneration processes [8–14].

Most publications on platelet drugs are represented by observational series or studies of the prophylactic use of PRF/L-PRF; data on payroll are limited to experimental models and individual clinical observations. The presented study is one of the few studies that directly assess the effect of FOT on healing in MAONCH. More than 85% of patients were in the cancer group and received intravenous zoledronic acid, with the majority of cases consistent with stage III AAOMS, which may have affected treatment outcomes. In the conditions of advanced stages, the presence of cancer did not have an independent effect on healing. In studies using FOT, there was a short-term improvement in symptoms with no persistent statistical association with healing.

Early diagnosis of MAONH is key to choosing treatment tactics. The presented data complement modern approaches to diagnosis and therapy and demonstrate the possibility of using available biocompatible methods focused on natural mechanisms of regeneration. The limitations of the study are a relatively small sample and a predominance of late stages of the disease. Multicenter studies with larger and more homogeneous cohorts of oncological and non-oncological patients seem promising.

A more pronounced effect of FOT was noted with a smaller focus. In some patients, the progression of the underlying oncological disease could adversely affect healing in both groups.

A promising area is combination therapy with the use of pentoxifylline, tocopherol, surgical debridement, laser technologies and growth factors under an antibacterial coating.

Patients with MAONH require long-term dynamic observation with clinical and radiological control at least once every 6 months. Limited foci without additional risk factors (e.g., long-term intravenous zoledronic acid therapy of more than 3 years) are generally associated with a better prognosis.

Conclusion. Thus, surgical treatment of drug-associated osteonecrosis of the jaw demonstrated overall efficacy, ensuring successful clinical healing in 36 out of 47 cases (76.6%). The results obtained showed that there was no statistically significant dependence of treatment outcomes on the localization of the lesion and the size of the pathological focus ($p > 0.05$). At the same time, a significant association of an unfavorable prognosis with a number of systemic risk factors, including intravenous the use of zoledronic acid, the duration of antiresorptive therapy for more than three years, the presence of cancer and osteonecrosis episodes in anamnesis ($p < 0.01$).

Platelet-rich fibrin was associated with a higher clinical healing rate: a positive outcome was achieved in 21 of 23 patients (91.3%) compared to 15 of 24 patients (62.5%) with standard surgical management. Comparative analysis confirmed a statistically significant advantage of the use of payroll ($p = 0.036$); The relative risk of achieving healing was 1.46, which corresponds to an increase in the probability of a successful outcome of approximately 46%.

The data obtained indicate the expediency of using FOT as an additional method in the complex surgical treatment of MAONCH and substantiate the need for further studies on larger clinical samples.

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