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ROLE OF SERRAPEPTASE ON TRISMUS AFTER SURGICAL REMOVAL OF MANDIBULAR THIRD MOLAR

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ABSTRACT

Operative removal of submerged teeth represents most often surgical procedure in the field of oral surgery. Etiology of narrow jaw is correlated with continuous reduction of jaw and teeth. Since the teeth, as highly differentiated tissue reduces slower, the result is a disproportion between the size of the teeth and the jaws. Surgical procedure interrupts continuity of soft and bone tissue, resulting with swelling, trismus and pain. Trismus, caused by intramuscular inflammation, represents distressing factor for the patient. Serrapeptase has strong anti-inflammatory, antiedematous and mild analgetic effect and can be used for reducing post-operative reactions.

Materials and Methods: This study was conducted on 100 patients having surgical removal of mandibular third molar. Selected patients were randomly divided into two groups- control group or the serrapeptase group, irrespective of age and sex. Interincisal distance (mouth opening) was measured between the incisal edges of the central incisors using Nonius scale (Vernier calipers). The follow-up was carried out on the 1 st, 2 nd, 5 th and 7 th postoperative days.

Results: Improvement related to trismus has been demonstrated in serrapeptase group compared with control group in 7 days following up postoperative period.

Conclusion: The results in this study showed that serrapeptase was effective in reducing trismus after operative removal of submerged teeth.

Keywords: submerged teeth, trismus, serrapeptase

Introduction

Operative removal of submerged teeth represents most often, surgical procedure in the field of oral surgery. The most common post-operative effects are pain, trismus and facial swelling. Etiology of narrow jaw is correlated with continuous reduction of jaw and teeth. Since the teeth, as highly differentiated tissue reduces slower in comparison to jaws, the result is a dentoalveolar disproportion. Surgical procedures cause a significant amount of tissue injury, followed by the processes of inflammation and subsequently reparation and regeneration of the injured tissues. Operative removal of the third lower molars involves the elevation of a soft tissue flap, adequate bone guttering and odontectomy. These procedures lead to the release of various vasoactive chemical mediators. Though inflammation is a reparative process it causes significant distress due to pain and swelling.

Within 48-72 hours of the surgical procedure swelling usually reaches its maximum. Trismus, caused by intramuscular inflammation, could be an associated distressing factor for the patient. A meticulous surgical technique will not prevent pain, trismus or swelling, but can minimize the sequelae of inflammation [1]. By prescribing corticosteroids it is possible to reduce the intensity of the inflammatory process [2].

The vasoactive amines cause vasodilation resulting in increased blood flow to the inflamed area. The inflammatory process is necessary if healing is to occur, but inflammation also causes edema, pain and trismus [3].

To minimize the unwanted effects of inflammation, it becomes essential to control the process of inflammation. Serrapeptase (proteolytic enzyme from trypsin family) is a protease produced by *Enterobacterium serratia* which has strong anti-inflammatory performance. For the past thirty years serrapeptase is used in Europe and Japan with great success due to anti-inflammatory effect in post-operative period, but also as support for cardiovascular, immunological and respiratory functions in human body.

Recent research shows that Serine protease has a higher affinity for cyclooxygenase, both I and II, which is in tight connection with production of inflammatory mediators like interleukins (IL), prostaglandins (PGs) and thromboxane (TXs) [4].

A prospective study conducted by Al-Khateeb and Nusair after third molar surgery showed significant reduction in swelling achieved with the use of serrapeptase [5]. Authors also suggest anti-sclerotic, fibrinolytic and caseinolytic effects of serrapeptase [6-8].

It is also presented that serrapeptase decreases capillary permeability induced by histamine, bradykinin and serotonin; destroys abnormal exudates and proteins; controls the absorption of decomposed products through blood and lymph [9].

The aim of this study was to determine whether serrapeptase has an effect on the severity of trismus in postoperative recovery of the patient.

Materials and methods

Operative procedure

Operative removal of the third lower molar begins with local anesthesia through inferior alveolar block, lingual and buccal nerve block. Standard Terrence-Wards incision was placed and bone was exposed with mucoperiosteal flap. Using round bur whit adequate saline rinse (using fisiodispenser) bone removal was carried out on buccal and distal side of the tooth. With an elevators and forceps, the tooth was extracted from the socket. After the sharp bony edges were smoothed, the socket was irrigated with saline solution. When full hemostasis was achieved, the wound is closed with 3-0 silk suture.

Sample of respondents

This study was conducted on 100 patients who had surgical removal of mandibular third molar. Selected patients were divided into two groups - control group and the serrapeptase group, irrespective of age and sex.

Inclusion criteria was healthy patients, undergoing impacted third lower molar removal for the

indications of deep caries with pulpitis, pericoronitis and orthodontic reasons.

Exclusion criteria was patients with systemic diseases.

All patients were given full information about purpose of the study and effects of the drugs used and all patients signed a consent form to participate in the research.

In one group, patients were given 500 mg amoxicillin every 8th hours for 7 days and ibuprofen 400 mg postoperatively.

In the other group, patients were given amoxicillin 500 mg every 8th hours for 7 days, ibuprofen 400 mg postoperatively and serrapeptase 60000 i.u. one daily.

The follow-up was carried out on the 1st, 2nd, 5th and 7th postoperative days. Interincisal distance (mouth opening) was measured between the incisal edges of the central incisors using Nonius scale (Vernier calipers).

Results

The results are presented by table and graphs. Data analysis was carried out by Microsoft Excel 2016. Table 1 and graphs 1 and 2 present more pro-

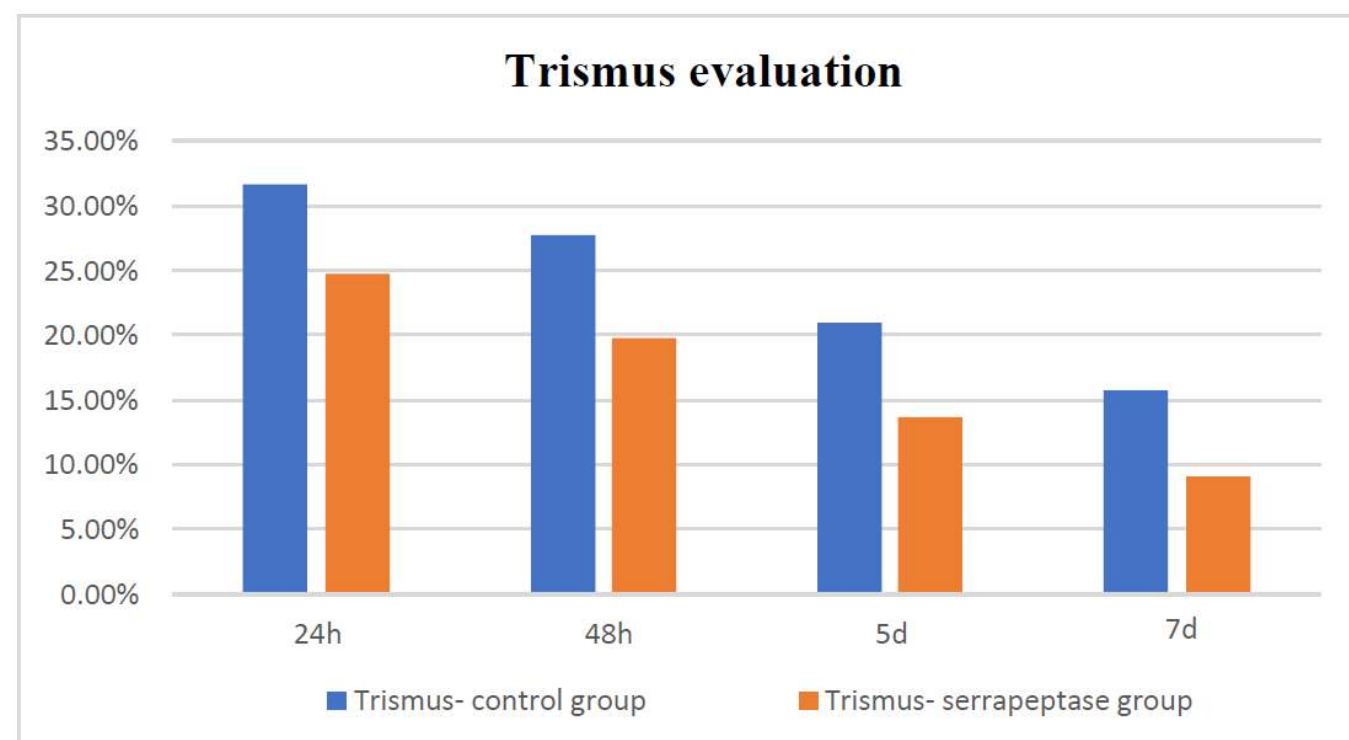


Table 4. Trismus evaluation

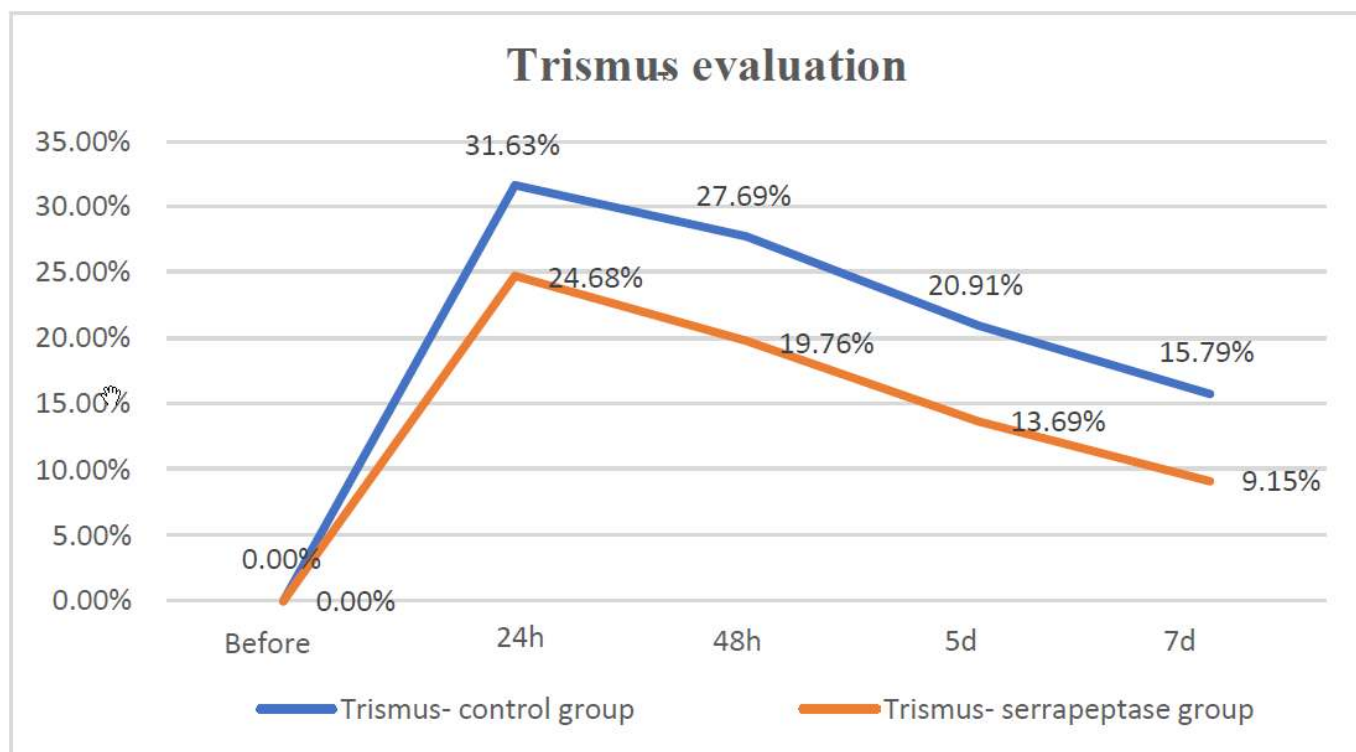
	Postoperative period	Trismus - control group	Trismus - serrapeptase group
1.	24 h	31.63%	24.68%
2.	48 h	27.69%	19.76%
3.	5 days	20.91%	13.69%
4.	7 days	15.79%	9.15%

nounced trismus in the control group of patients in all measurements. The most pronounced difference between the control group and the serrapeptase group is the second day of surgery.

On day 7 there is still insignificant trismus (6,64% higher in control group), suggesting that these drugs are not completely effective in relieving trismus on 7th postoperative days.

Discussion

Serrapeptase is a proteolytic enzyme being used for effective relief from pain and swelling



alone or in combination with steroids and NSAID's [10]. During chronic inflammation use of NSAID's have many limitations and side effects. Inflammation causes edema, pain and trismus but the inflammatory process is necessary for healing [1].

Idea of using enzymes, as extremely potent substances, as a therapy for inflammation is attractive. It is usually administered orally, absorbed through the intestine and directly transported into the bloodstream. However, due to its peptide nature, there is greater tendency to undergo enzymatic degradation in the gastrointestinal tract, leading to poor bioavailability. Researchers have demonstrated that enzyme possesses the unique ability to dissolve the dead and damaged tissue without harming living tissues, although the exact molecular mechanism of serrapeptase is not known completely. One of the anti-inflammatory activities of serrapeptase is increasing the viscosity of accumulated fluid facilitating drainage. [11]

Bhagat et al. in systematic review on serrapeptase compiled the findings of various randomized controlled trials in medical and dental practice. In

our study, descriptive statistical methods showed the difference in the expression of trismus in the postoperative period between the control and serrapeptase groups. For all measurements in the postoperative period, there is less pronounced trismus in the serrapeptase group. On the seventh postoperative day, patients still have mild trismus, but less pronounced in the serrapeptase group [8].

Concerning the safety of use, there are not any published studies on some serious adverse drug reactions to serrapeptase, although as possible reactions are mentioned muscle and joint pain, anorexia, nausea, skin reactions and coagulation disturbances.

Researchers suggests that serrapeptase could significantly enhance the effectiveness of antibiotics (including ampicillin, cyclacillin, cephalexin, minocycline and cefotiam) against biofilm and can inhibit biofilm formation. A statistically significant improvement in trismus has been presented in comparison with steroids and NSAID's [12, 13].

Conclusion

The results in this study showed that serrapeptase was more effective in reduction of trismus after operative removal of submerged teeth compared to standard protocols. Administration of serrapeptase can accelerate recovery from trismus and can bring benefits for patients. Studies conducted on this topic can serve as an argument for introducing serrapeptase in standard postoperative protocol, along with antibiotics and pain reliever for reducing postoperative complications.

Declaration of interest

The authors declare no conflict of interest.

References

- 1) Hupp JR. Prevention and Management of Surgical Complications. Contemporary Oral and Maxillofacial Surgery. 5th ed. St. Louis: Mosby Elsevier; 2008. 185-200.
- 2) Sisk AL, Bonnington GJ. Evaluation of methylprednisolone and flurbiprofen for inhibition of the postoperative inflammatory response. Oral Surg Oral Med Oral Pathol 1985;60:137-45.
- 3) Gersema L, Baker K. Use of corticosteroids in oral surgery. J Oral Maxillofac Surg 1992;50:270-7.
- 4) Tiwari M., The role of serratiopeptidase in the resolution of inflammation. Asian journal of pharmaceutical sciences. 2017; 12: 209-215
- 5) Al-Khateeb TH, Nusair Y. Effect of the proteolytic enzyme serrapeptase on swelling, pain and trismus after surgical extraction of mandibular third molars. Int J Oral Maxillofac Surg 2008;37:264-8.
- 6) Seymour RA, Blair GS, Wyatt FA. Post-operative dental pain and analgesic efficacy. Part I. *Br J Oral Surg*. 1983;21:290-297.
- 7) Joshi KK, Nerurkar RP. Anti-inflammatory effect of the serratiopeptidase—rationale or fashionable: a study in rat paw oedema model induced by the carrageenan. *Indian J Physiol Pharmacol*. 2012;56:367-374.
- 8) Bhagat S, Agarwal M, Roy V. Serratiopeptidase: a systematic review of the existing evidence. *Int J Surg*. 2013;11:209-217.
- 9) Flower R.J. , Blackwell G.J. Anti-inflammatory steroids induce biosynthesis of a phospholipase A2 inhibitor which prevents prostaglandin generation. *Nature*. 1979; 29:278
- 10) Selan L, Papa R, Tilotta M, et al. Serratiopeptidase: a well-known metalloprotease with a new non-proteolytic activity against *S. aureus* biofilm. *BMC Microbiol*. 2015;15:207.
- 11) Ishihara Y, Kitamura S, Takaku F. Experimental studies on distribution of cefotiam, a new betalactam antibiotic, in the lung and trachea of rabbits. II. Combined effects with serratiopeptidase, *Jpn J Antibiot*; 1983; 36 (10):2665-2670
- 12) Murugesan K, Sreekumar K, Sabapathy B - Indian J Dent Res, Comparison of the roles of serratiopeptidase and dexamethasone in the control of inflammation and trismus following impacted third molar surgery. 2012; 23(6):709-13
13. A. Panagariya, A.K. Sharma A preliminary trial of serratiopeptidase in patients with carpal tunnel syndrome, *J Assoc Physicians India*. 1999; 47 (12), 1170-1172