

Effect of Bromelain, Rutoside and Trypsin Combination on Postoperative Pain, Swelling and Trismus After Surgical Third Molar Extraction

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ABSTRACT

Introduction: Surgical removal of mandibular third molar is one of the common minor surgical procedures in dentistry. Local inflammatory response due to the procedure results in severe postoperative complications such as pain, swelling and trismus in the patients. A prospective, intraindividual, randomized, double-blind, crossover study was done to evaluate role of bromelain 180 mg + rutoside 200mg + trypsin 96 mg (BRT) along with routine medicine in reducing such postoperative complications.

Material & Method: A total of 20 patients, age ranged from 20 to 35 years, requiring surgical extraction of both the mandibular third molars with a similar degree of difficulty were included in the study. Extraction of one quadrant followed the opposite quadrant in a gap of 4 to 6 weeks; BRT was added to standard medicine regime in the latter after extraction. Swelling, pain and trismus were evaluated on 3rd, 5th and 7th postoperative days.

Result: There was a statistically significant reduction in the extent of cheek swelling and mean pain intensity in VAS (visual analogue scale) in the BRT group when compared to the control group ($p < 0.05$). No significant reduction in trismus was observed for both the groups postoperatively ($p > 0.05$).

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Conclusion: Amount of postoperative complications differ from patient to patient due to their unique body response to injury. BRT has shown significant results in reducing postoperative pain and swelling but efficiency in reducing trismus can't be confirmed.

Key words: Bromoline; Impaction; Inflammation; Rutoside; Trypsin.

INTRODUCTION

Surgical third molar extraction causes severe local inflammatory response leading to pain, swelling and trismus. Inflammation is a local response due to tissue injury. It was first documented by Celsus during the 1st century AD. The tissue response to injury was anticipated to give rise to rubor (redness, due to hyperemia), tumor (swelling, caused by increased permeability of the microvasculature and leakage of protein into the interstitial space), calor (heat, associated with increased blood flow and metabolic activity of the cellular mediators of inflammation), and dolor (pain, in part due to changes in the perivasculature and associated nerve endings). Rudolf Virchow in the 1850s added *Functio laesa* (loss of function) as a fifth characteristic of inflammation.¹

Non-specific injury in the body, including any operating procedures, causes inflammation. Surgical third molar extraction is the most common minor oral surgical procedure with inflammatory response quite apparent in it. Patients who undergo surgical third molar extraction usually have some degree of facial swelling, pain and difficulty during mastication post-operatively. Oral and maxillofacial surgeons are well aware of such impediments during recovery and have tried and tested different extraction techniques and various combinations of medication to reduce such complications. Drugs such as steroids, xanthine derivative, antiepileptic drugs, high dose of antibiotics, proteolytic enzyme etc, had been tried in the past, few of them had shown some favourable results.^{1,2}

Literature reveals certain studies have been performed to evaluate the role of proteolytic enzymes like serratiopeptidase, trypsin-chymotrypsin in assessing their advantage after surgical extraction. Recently a new combination of proteolytic enzyme bromelain 180mg + rutoside 200mg + trypsin 96mg (BRT) in combination is introduced and claims to have anti-oedematous activity and also increase vascularity in inflammatory areas. Trypsin is produced in the pancreas in the form of the inactive zymogen trypsinogen, bromelain is a crude extract from the pineapple and rutoside is a natural flavone derivative.² With the above background, the present study was performed to explore the role of BRT to reduce postoperative pain, swelling and trismus after surgical third molar extraction.

MATERIALS & METHOD

A prospective, intra-individual, randomized, double-blind, crossover study was performed after approval from the institutional ethical committee. Twenty patients with bilateral impacted mandibular third molars undergoing surgical removal, from the department of oral and maxillofacial surgery were recruited for the study. Two patients who failed to come up for follow-up and with a history of drug allergy were excluded from the study. Out of these remaining 18 patients, 7 were male and 11 were female with age range of 20 to 35 years.

A proper case history and informed consent was taken from all the patients. Preoperative intraoral periapical (IOPA) and orthopantomographic radiographs were obtained. WAR (White, amber, red line) and

WHARFE analysis was done accordingly to determine difficulty during surgical extraction [Figure 1]. The six criteria for WHARFE assessment are:

- Winters classification
- Height of the mandible
- Angulation of the 2nd molar
- Root shape & morphology
- Follicle development
- Path of Exit of the tooth during removal.

Only those patients who had identical WHARFE scores (score difference less than 3) on both sides were included [Figure 2]. Surgical extraction of teeth was done in one quadrant followed by the opposite quadrant in the gap of 4 to 6 weeks by the same oral surgeon. A standard technique was followed. After inferior alveolar, lingual and buccal nerve anaesthesia with 2% lignocaine hydrochloride and epinephrine 1:100000, a standard WARD's incision was placed and a triangular full-thickness mucoperiosteal flap was elevated. Crown of the tooth was exposed with buccal osteotomy and guttering of bone was done with 702 straight fissure bur. The tooth was sectioned wherever necessary and was gently elevated. The socket was irrigated with normal saline and flap sutured with interrupted 3-0 silk

sutures. [Figure 3] During extraction of first tooth, amoxicillin 500 mg TDS for 5 days and aceclofenac 100 mg + paracetamol 325 mg TDS for 5 days was prescribed. During removal of the opposite mandibular third molar, amoxicillin 500 mg TDS for 5 days, aceclofenac 100 mg + paracetamol 325 mg TDS and enzyme bromelain 180 mg + rutoside 200mg + trypsin 96 mg (BRT) BD for 5 days were prescribed.

Post-operative evaluation: Pain, swelling and maximum mouth opening was observed on the third, fifth and seventh post-operative day. The pain was evaluated via visual analogue scale (1 to 10). The maximum mouth opening was determined using a divider by measuring the interincisal distance. Facial swelling was measured through a measuring tape as shown in Figure 4. The horizontal measurement corresponds to the distance between the corners of the mouth to the attachment of the ear lobe following the bulge of the cheek. The vertical measurement corresponds to the distance between the outer canthus of the eye to the angle of the mandible.

The percentage of facial swelling was obtained from the below formula:

(Postoperative value - preoperative value) / Preoperative value × 100 = % of facial swelling

All the data obtained were recorded in a proforma specially designed for the study and

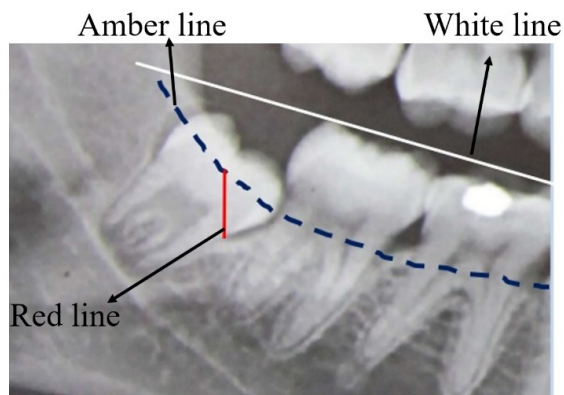


Figure 1 : WAR line assessment



Figure 2 : Preoperative OPG

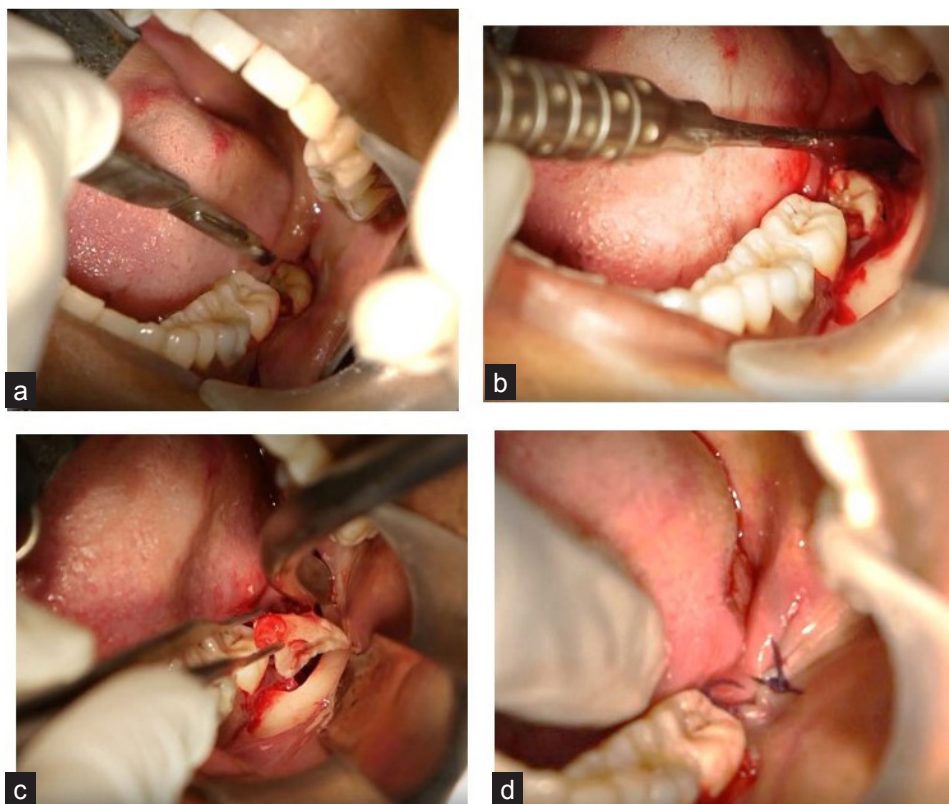


Figure 3 : Surgical procedure

subjected to statistical analysis. Student's t-test was performed for evaluation of swelling and mouth opening. The pain was analysed using the Wilcoxon test and mouth opening was evaluated using Student's unpaired t-test with the help of SPSS version 16.01 (statistical package for social sciences) software. Statistical significance was considered at p value > 0.05 .

RESULTS

A total of 18 patients (7 males and 11 females) with mean age of 27.5 years were selected for the study. Surgical extraction of teeth was done in one quadrant followed by the opposite quadrant in the gap of 4 to 6 weeks followed by postoperative evaluation of pain, swelling and maximum mouth opening on the third, fifth and seventh postoperative day.

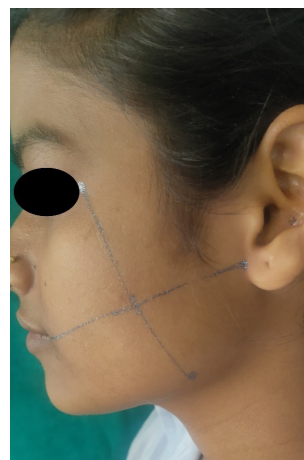


Figure 4 : Measurement of facial swelling

Swelling

The comparison of preoperative and postoperative measurements showed a sizable amount of swelling on both sides of

extraction in the post-operative period. The maximum swelling was observed on the 3rd post-operative day in both the groups. There was a statistically significant reduction in the extent of cheek swelling in the BRT group at the 3rd, 5th and 7th postoperative days ($p < 0.05$) as compared to the control group. [Table 1]

Pain (VAS assessment)

There was a significant reduction in mean pain intensity in VAS in the BRT group when compared to the control group. At the 3rd ($p < 0.05$), 5th ($p < 0.05$) and 7th

($p < 0.05$) post-operative days was noted. [Table 2]

Mouth Opening Interincisal difference

Analysis of the data showed no significant reduction in the interincisal distance for both the groups post-operatively compared to pre-operative values ($p > 0.05$). [Table 3]

DISCUSSION

Third molar impaction is one of the common minor oral surgical procedures performed

Table 1 : Comparative evaluation of maximum mouth opening preoperatively, 3rd, 5th and 7th day

Maximum mouth opening	Surgical extraction with BRT		Control group	
	Mean	SD	Mean	SD
Pre-operative	39.16	4.78	39.16	4.78
Day 3	31.18	5.15	29.45	4.12
Day 5	34.76	5.41	33.45	4.88
Day 7	36.82	4.65	36.01	3.20

Table 2 : Comparative evaluation of swelling preoperatively, 3rd, 5th and 7th day

Swelling	Surgical extraction with BRT		Control group	
	Mean	SD	Mean	SD
Pre-operative	0	0		
Day 3	2.85	0.76	5.39	1.54
Day 5	4.34	0.67	7.65	1.86
Day 7	1.68	0.64	2.00	1.73

Table 3 : Comparative evaluation of pain preoperatively, 3rd, 5th and 7th day

Pain	Surgical extraction with BRT		Control group	
	Mean	SD	Mean	SD
Pre-operative	0	0	0	0
Day 3	3.42	0.76	3.71	0.83
Day 5	2.48	0.75	2.24	0.67
Day 7	0.16	0.55	0.65	0.61

under local anaesthesia on an out-patient basis, but may result in unwanted distress in patients. The patients usually belong to young age groups and are particularly concerned about their facial aesthetic as well as post-operative discomfort. Extent of post-operative complications varies from patient to patient due to their unique body response to injury, skill of the oral surgeon and technique used by him. It also depends on patient's motivation and how well he/she is following the postoperative instruction given by the surgeon. Study done by Yashua et al.(2004) elucidated that the short-term sequel following wisdom tooth removal are influenced by factors such as the difficulty of the surgical procedure involved, age and gender of the patient, and experience of the surgeon.⁴

One other factor which can determine the post-operative outcome is proper planning. WAR line and WHARFE assessment should be done in all the cases preoperative with the help of orthopantomogram and IOPA before the surgery. Recently with the growing use of Cone-beam computed tomography (CBCT) in dentistry, Matzen et al. (2015) has shown that CBCT can also be used as an efficient diagnostic tool before third molar surgeries.⁵ All these imaging techniques and assessments give a visual blueprint about the difficulty which can be encountered and also help the surgeon to do surgical extraction uneventfully. One of the key considerations is whether to do sectioning of the teeth or not. Jain et al. (2016) concluded that sectioning reduces the arc of rotation of the tooth while preserving sound bone and adjacent anatomical structures. If surrounding structures are preserved and judicious amount of surrounding bone is removed then post-operative inflammation is certain to be less and thus reducing the intensity of complications.⁶

Numerous drugs e.g. steroids like dexamethasone and methylprednisolone,

opioids, antiepileptics like lamotrigine, xanthine derivatives like oxyphenbutazone and pentoxifylline also proteolytic enzymes like serratiopeptidase and trypsin-chymotrypsin have been tried to reduce such post-operative complications.^{7,8,9,10,11,12} Dexamethasone, methylprednisolone and oxyphenbutazone were useful but also had their side effects. Opioids and lamotrigine were of no benefits.

The concept of using proteolytic enzyme is not new as postoperative medication, serratiopeptidase and trypsin-chymotrypsin has also proven their advantageous effect.⁷ In our study, we used bromelain, trypsin and rutoside in a fixed-dose for analysing the benefits after third molar surgeries. The combination of both serine and cysteine proteases (bromelain, trypsin) is logical as the different enzymes do have different substrate specificities. The mechanism of action of enzymes is not fully understood, but there is a variety of effects that are thought to contribute to their clinical efficacy such as anti-oedematous effects and effects on antiproteinases and α_2 macroglobulin.¹³ BRT combination has no known gastric side effects. Kerkhoffs et al. (2004) rated gastric tolerability of bromelain, trypsin, and rutoside as very good.¹⁴

We designed this study in a simple but effectual way and the armamentarium used were non-invasive. The surgical procedure used in the study is a model for trial of different drugs after surgical extraction of third molar, inflammation and pain, and has a high predictability of the development.¹⁵ Data obtained from our study showed that surgical extraction followed by BRT administration had a significant reduction in pain and swelling compared to the control group extracted without the use of BRT. The reduction of swelling with BRT was evident on the 5th and 7th day. It was greater when compared to a study done by al-Khateeb et al. (2008) in which he used serratiopeptidase

as proteolytic enzyme after extraction of impacted third molar.¹¹ In our study, it was noted that on the 3rd day, swelling was less in BRT group compared to the control group. Use of methylprednisolone in a study done by Essen et al. (1999) showed that the swelling was evident on the second postoperative day, regardless of whether corticosteroids are administered or not.⁸

Postoperative pain was also less in the BRT group when compared to the control group during all the three days of postoperative evaluation. Although aceclofenac and paracetamol were given to all the patients for pain control in our study, BRT along with standard analgesics had shown synergistic effect. Post-operative pain can be best controlled with opioids. Tompach et al. (2019) suggested that acute pain and other opioid related complications can be effectively controlled if opioid prescribing protocol is followed.¹⁰

There was a slight improvement in the interincisal distance in the extraction group with BRT compared with the control group but the results were not significant. The muscles responsible for mouth closure, namely the masseter, temporalis and medial pterygoid exert a force 10 times greater than exerted by the muscles that open the mouth, which include the lateral pterygoid, digastric and hyoid. While the inciting insult may be unilateral, the reflex activated is bilateral.¹⁶ Chau et al. (2001) proved drugs like pentoxifylline have shown a remarkable effect in patients with post-radiation induced trismus.¹⁷

CONCLUSION

This article aims to create a general awareness among the dentists regarding the use of proteolytic enzymes and their anti-inflammatory implication after a routine impacted third molar extraction. Use of postoperative bromoline, trypsin, and rutoside addition to routine regime of

medication is advisable after third molar extraction. In our study, BRT have helped in reducing postoperative swelling and pain but not reducing trismus.

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Abbreviations:

BRT – Bromoline, trypsin and rutoside

WAR – White, red, amber lines

VAS – Visual analogue scale

IOPA – Intraoral periapical

CBCT – Cone beam computed tomography