

Comparison Of Efficacy Of Oral Bromelain and Serratiopeptidase For The Control Of Postoperative Sequelae Following Third Molar Surgery - A Comparative Study

Research Article

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Abstract

Background: Surgical removal of Impacted third molar is widely carried out in dental practice and it is usually associated with postoperative inflammatory sequelae like pain, swelling, and trismus. The objective of the study is to assess and compare the efficacy of Oral Bromelain and Serratiopeptidase for the control of Post - operative sequelae following surgical removal of impacted third molar.

Methods: A randomized, comparative clinical study was conducted on sixty patients who were undergoing impacted third molar teeth surgery, allocated in to two groups each comprising 30 patients. Conventional drugs include Cap Amoxicillin 500mg b.i.d., Tab. Metronidazole 200mg t.i.d, and Tab. Diclofenac sodium 50mg b.i.d. was given to both the groups. Group I was treated with Tab. Bromelain 200mg t.i.d along with conventional treatment for 5 days. Group II received a combination of conventional treatment and Tab. Serratiopeptidase 10 mg b.i.d for 5 days. The parameters such as measurement of pain, facial width and trismus were analysed on postoperative days 1, 2 and 7.

Results: The study comprised of totally 60 otherwise healthy patients. The group of patients who received Bromelain along with Diclofenac sodium seemed to be effective in controlling post-operative sequelae like pain ($p < 0.05$), swelling ($p < 0.05$) but not trismus ($p < 0.05$) when compared to the group who received Serratiopeptidase with Diclofenac sodium.

Conclusion: The intensified anti - inflammatory action of bromelain, possibly by inhibiting the generation of bradykin in and negative action on the prostaglandin pathway. The present study assessed the clinical effect of bromelain and serratiopeptidase on pain, facial swelling and trismus.

Keywords: Bromelain; Oral Bromelain; Serratiopeptidase; Proteolytic Enzyme; Third Molar Surgery.

Background

Impacted third molar removal is usually a chair side procedure performed by oral and maxillofacial surgeons and it is the most common procedure to be performed in dental office [1, 2]. Like any other surgical procedures third molar removal is also associated with several immediate and late complications. Most common complications include pain, swelling, restricted mouth opening, paresthesia etc. The unfavourable effects of the third molar

removal on the quality of life of patients [3, 4] has been recorded to show a threefold increase in patients who experience pain, swelling and trismus alone or in combinations when compared to those who were asymptomatic [5, 6]. So there is a need for pain control, reduction in swelling without restriction of mouth opening in patients undergoing wisdom tooth removal [7].

Prostaglandins and Prostacyclins are responsible for pain and oedema in inflammatory cascade. The mechanism of action of

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Non - steroidal anti - inflammatory drugs is to prevent Prostaglandin and Prostacyclins production thereby reduces the pain and swelling due to inflammation [8]. The use of oral systemic enzyme therapy like bromelain, serratiopeptidase and trypsin provided added benefits for controlling the inflammatory sequelae following impacted third molar removal [9, 10].

Bromelain is a proteolytic enzyme present in tissues of the plant family Bromeliaceae, of which pineapple, is the best known. Bromelain possesses many properties which include anti - inflammatory, [11] antiedemic, anti - tumor and immunomodulatory effects. The mechanism of the anti - inflammatory activity is, it inhibits bradykin generation, proteolytic degradation of circulating immune complexes and interference with the arachidonic acid metabolism [12, 13]. It promotes the absorption of antibiotic drugs topically in the skin debridement of burns. Bromelain has been used as additive agents for anticancer therapy [14, 5].

Serratiopeptidase is also a proteolytic enzyme obtained from silkworms. *Serratia E15* is a microorganism which lives in the gut produces the enzyme. This causes proteolysis of all non - vital tissues including blood clots, tissue plaques and cellular debris and reduces the inflammatory response. The anti - inflammatory activity of serratiopeptidase helps in resolution of postpartum hematomas and breast enlargements, It reduces internal tissue oedema caused at postoperative handling. Serratiopeptidase does not inhibit prostaglandins and so it is safe to the GI system [16].

This study is based on the proposed hypothesis that bromelain can be more efficient in terms of reducing pain and swelling. Co - administration of oral systemic enzyme and NSAID may produce pronounced anti - inflammatory effects without side effects [9, 17]. The rationale of this study is to assess and compare the efficacy of Bromelain and Serratiopeptidase in controlling the postoperative inflammatory sequelae following wisdom tooth removal when given with NSAIDs.

Methods

A randomized, clinical study was conducted on a total of 60 patients requiring surgical removal of impacted third molar teeth. Sample size was calculated using G power based on the mean and SD of a study done by NK Tiwari et al [30]. The recruitment period of the study was 3 months (November 2019 - February 2020). Saveetha Dental College and Hospitals, SIMATS, Chennai. The study protocols were approved by the Institutional ethical committee. Consent was taken prior to the surgery and the procedures were adhered to the ethical guidelines of the Declaration of Helsinki.

The inclusion criteria between the age group of 20 - 40 years, both genders, patients willing to give informed consent, patients willing to adhere to the study protocol, patients with no history

of oral surgical interventions during the past 3 weeks, patients with free of pain and other inflammatory symptoms that included swelling and decreases mouth opening at the time of surgery.

Exclusion criteria were pregnant and lactating women, patients with cardiac, renal or hepatic disease, and patients with previous or present gastric ulcers, known hypersensitivities, allergies, or idiosyncratic reactions to any study medications, patients who had taken anti - inflammatory drugs within 2 days before surgery, patients not willing to give informed consent.

Sixty patients who fulfilled inclusion and exclusion criteria were included in the study and they were randomly allocated in to two groups following simple randomisation. SNOSE method was followed and each group comprising 30 patients received the respective study medication orally for 5 days. Conventional drugs include Cap Amoxicillin 500mg b.i.d., Tab. Metronidazole 200mg t.i.d., and Tab. Diclofenac sodium 50 mg b.i.d. was given to both the groups. Group I was treated with Tab. Bromelain 200mg TID along with conventional treatment for 5 days. Group II received a combination of conventional treatment and Tab. Serratiopeptidase 10 mg BD for 5 days.

The first dose of the study medication was administered to the respective group of patients 30 minutes prior to the surgery. The proper postoperative care instructions and medication direction were given to all the participants. The following study parameters were recorded on 1st, 2nd and 7th postoperative days.

Pain Measurement

Preoperative pain was assessed using a Visual Analogue Scale (VAS). Accordingly, pain was recorded as: 0 - No pain, 1 - 3 Mild pain, 3 - 5 Less moderate pain, 5 - 7 Intense moderate pain and 7 - 9 Severe pain 10 - Worst pain possible. For each patient, the appropriate score was recorded by the investigator at pre - operative, postoperative days 1, 2 and 7. Before leaving the clinic, the investigator ensured that all patients were thoroughly instructed how and when to take medications.

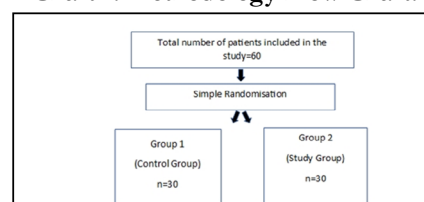
Measurement Of Facial Width

As there is no published method that satisfies all criteria to assess facial swelling, we used a measuring tape to measure facial width and swelling in one - dimension only. The reference points were the tip of the tragus of right and left ears, with the gonion in between. The measurements were carried out (in mm) just before the surgery and at 1st, 2nd and 7th postoperative days.

Measurement Of Mouth Opening

A Caliper was used to measure maximum interincisal mouth - opening at the commencement of the procedure with maximum

Chart 1. Methodology Flow Chart.



mouth opening. The measurements were made in millimeters (mm). The measurement was carried out just before the surgery and at 1st, 2nd and 7th postoperative days.

Statistical Analysis

Statistical analyses were performed using SPSS for Windows, version 20 (IBM Corp, Armonk, NY. Student t test was used for Visual Analogue Scale, interincisal opening and facial swelling. The level of significance was set at P < 0.05.

Results

A total of 60 patients distributed into Groups 1 (n 30), II (n 30) who completed the study were included in the analysis. The anti-inflammatory effect of Bromelain and Serratiopeptidase as an add on therapy with conventional treatment (diclofenac) following surgical removal of impacted mandibular third molar were compared.

Table 2 and Figure 3 represents Comparison of mean Post-operative pain on day 1, 2 and 7 and the Bromelain group has con-

Figure 1. Types of Impactions - Bromelain group.

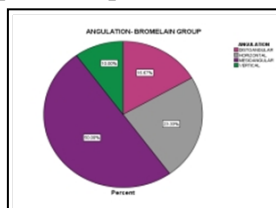


Figure 2. Types Of Impactions - Serratiopeptidase Group.

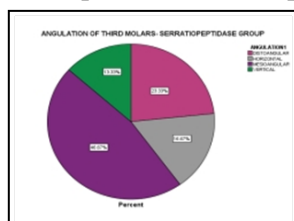


Figure 3. Measurement of Pain.

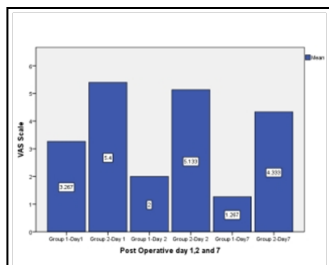


Figure 4. Post-operative Swelling of two groups.

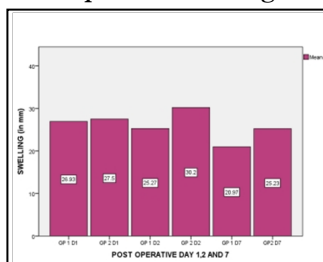
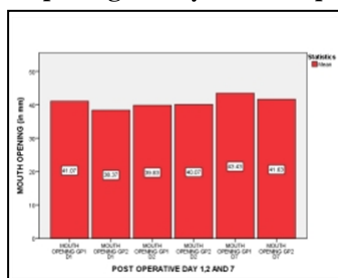


Figure 5. Mouth opening on day 1,2 and 7 post-operatively.



siderably less pain compared to the serratiopeptidase group.

Table 3 and Figure 4 represents comparison of Mean of post-operative swelling on day 1, 2 and 7, bromelain decreases postoperative swelling compared to serratiopeptidase group.

Table 4 and Figure 5 represents Comparison of mean of mouth opening on postoperative day 1, 2 and 7 and there is no significant improvement in mouth opening in both the groups.

Discussion

Prostaglandins (PG) play a major role in initiation of inflammation [18]. The mechanism of action of NSAIDs is to inhibit COX pathway and thereby lowers the production of prostaglandins [19]. Preoperative administration of non-steroidal anti-inflammatory drugs are reported to be efficient in minimising pain and other sequelae of inflammation [20]. Like COX pathway NSAIDs are known to block arachidonic acid pathway also.

The rationale behind administration of NSAIDs before surgery is, the drug is widely absorbed and distributed in the tissues before any surgical insult happens. So the prostaglandin synthesis is also reduced before initiating any trauma [21] and thereby the inflammatory sequelae. If the inflammatory sequelae is prevented before the trauma, then there will be reduction of pain and swelling. Many drugs are shown to be effective in controlling the above said sequelae. One among those is Diclofenac sodium which had both analgesic and anti-inflammatory properties [22].

To reduce the postoperative inflammation we can administer oral systemic enzymes. Bromelain / serratiopeptidase have the ability to interfere with inflammation cascade and, thus reduces pain, swelling [23, 24]. Studies also stated that administration of bromelain / serratiopeptidase lowers the bradykinin production [16].

The enhanced anti-inflammatory action of bromelain, possibly by inhibiting the generation of bradykinin, negative action on the prostaglandin pathway [25]. As known, pain and enhanced vascular permeability is caused by kinins namely bradykinin and kallikrein. Both kinins may act alone as well as together. Due to its anti-inflammatory effects, the administration of oral systemic enzymes reduce inflammatory cascades like pain and swelling [26]. So when given with NSAIDs these enzymes may lower the kinin levels.

This study analysed the clinical efficacy of bromelain and serratiopeptidase on pain, facial swelling and trismus. There is a significant difference in terms of pain in Bromelain group when compared to serratiopeptidase group ($p < 0.05$). This is in accordance with previous literatures [27-29].

Post-operative facial edema is difficult to quantify accurately. Many methods are there to objectively measure the swelling. In this study we have measured from tip of the tragus to gonion to the contralateral tragus. A single measurement was taken. The bromelain group showed reduction in swelling post-operatively. This result shows that bromelain effectively decreases postoperative facial swelling than serratiopeptidase. This is in accordance with previous literatures [30].

The mean pain scores in day 1 in group I were significantly lower than that of group II. This result shows that addition of bromelain enhances the control of postoperative pain on day 1. The mean pain score in day two in group I was also significantly lower than that of group II. This result shows that patients who received bromelain and diclofenac have greater control of postoperative pain than other groups. The result is in accordance with previous literatures. However there is no significant reduction in trismus in both the groups ($p > 0.05$).

Conclusion

The present study concludes that anti-inflammatory effects of bromelain on post-operative pain, facial swelling were enhanced compared to the serratiopeptidase group following impacted third molar removal. However there was no significant improvement in trismus (mouth opening) between Bromelain and Serratiopeptidase group. Thus this study helped us to understand the importance of oral proteolytic enzymes and proved to have a beneficial role in co-administration with conventional therapy in the management of pain and inflammation.

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