

The role of oral bromelain on “bad outcome” in mandibular third molar surgery.

A split-mouth comparative study



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The role of oral bromelain on “bad outcome” in mandibular third molar surgery A split-mouth comparative study

AIM: *to evaluate evidence of therapeutic efficacy of 9.6 g bromelain after mandibular third molar surgery.*

MATERIAL OF STUDY: *This study is a prospective split-mouth clinical study of 49 patients, 22 male and 27 female, mean age 25.4 years old (range from 18-30 years). Each patient received two interventions in two different dates with 1 month of distance: the first third molar to be removed was chosen with a coin; at the second date of surgery bromelain was administered, one packet (9.6 g) every 12 hours for seven days. The evaluation of postoperative facial swelling was measured through specific measurements at every date on the side of the surgery.*

RESULTS: *A total of 98 third molars were extracted. No major complications occurred after the surgery. Regarding the comparison between the results of the measurements made after surgery with the use of bromelain a statistically significant difference ($p = 0,0078$) resulted between the interventions that provided the use of bromelain (10.56 average value) and interventions in which bromelain was not provided (12.59 average value).*

CONCLUSIONS: *The usefulness of this clinical trial is to provide a bromelain dosage and reduce the bad outcome after mandibular third molar surgery.*

KEY WORDS: Bromelain, Swelling, Third Molar

Introduction

Third molar removal is one of the most common intervention in oral surgery. The surgical removal of mandibular third molars (M3M) may determine hard and soft tissue trauma and be related to postoperative complications, as swelling, pain and edema¹.

Difficulty of the tooth and experience of the surgeon are

variables that may influence time and recovery after operation: classification of the impaction of the tooth and surgery are reported in (Table I).

In this field the bromelain compound finds its clinical use. Bromelain belongs to a family of proteolytic enzymes derived from the stem of the pineapple plant, *Ananas comosus*. The most remarkable characteristic is the effectiveness in decreasing the inflammation development and also in reduction of swelling. In the specific field of inflammation the mechanisms of action of bromelain appears to be clear, in fact this compound is capable of inhibiting the formation of bradykinin thanks to the depletion of the plasma kallikrein system. Bromelain also seems to reduce leukocyte migration into inflamed areas by removing the CD128 chemokine receptors, and creating a barrier for adhesion of leukocytes to blood vessels at the site of inflammation².

Relatively to M3M surgery, a considerable number of studies aimed to evaluate the possible use of bromelain to reduce postoperative complications:³⁻¹⁰ although most of all authors reported little improvement with its use,

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the clinical indication of bromelain still results not completely defined.

With this paper we present our comparative study in order to evaluate with the benefit of the split-mouth some evidence of therapeutic efficacy of bromelain after M3M surgery.

Patients and Methods

This study is a prospective split-mouth clinical study of 49 patients, 22 male and 27 female, mean age 25.4 years old (range from 18-30 years) in the period between June 2018 and March 2019 at the Department of Dentistry and Prosthodontics, University of Siena.

Inclusion criteria were: presence of both M3M. Exclusion criteria were: diabetes, radiotherapy, chemotherapy, endocarditis, patients with severe maxillo-mandibular and facial asymmetries, patients undergoing antiplatelet agents and anticoagulants and allergy to antibiotic.

All patients signed informed consent. Prophylactic amoxicillin and clavulanate 875 mg + 125mg administration was carried out for each intervention 2 hours before surgery. Patients were instructed to carry out three daily rinses with chlorhexidine (0.12%) from the first day after surgery for two weeks.

Each patient received two interventions in two different dates with 1 month of distance for M3M removal (1 single tooth each time); all interventions were carried out by the same surgeon. In order to reduce recovery variables due to the surgical difficulty (Table I), the first tooth to be removed was determined with a flip coin; at the second date of surgery bromelain was administered, one packet (9.6 g) every 12 hours for seven days. The evaluation of postoperative facial swelling was measured through specific measurements at every date on the side of the surgery: the first measurement was detected taking as reference the distance between the mandibular angle and the wing of the nose (Fig. 1A); the second measurement was performed taking as reference the space between the mandibular angle and the labial commissure angle (Fig. 1B). The mean value of these measurements resulted in the final value. The data were collected before surgery and 7 days after surgery at the suture removal.

The statistical analysis was performed using the t-Student statistical method for independent variables and P values <0.05 were considered statistically significant. The software MedCalc version 9.5.2.0 (MedCalcSoftware, Mariakerke, Belgium) was used for statistical analysis.

Results

A total of 98 M3M were extracted. No major complications occurred after the surgery. The results of measurements are reported in (Fig. 1C). Regarding the comparison between the results of the measurements made after surgery with the use of bromelain a statistically significant difference ($p=0.0078$) resulted between the interventions that provided the use of bromelain (10.56 average value) and interventions in which bromelain was not provided (12.59 average value).

Discussion

Surgical removal of impacted M3M can often lead to the onset of pain, swelling, presence of trismus within the first few days after surgery¹¹. These clinical symptoms represent the postoperative “bad” outcome that scares the patients and is the field of relevance of bromelain. This bad outcome of M3M surgery in sometimes associated with surgical difficulty.

The proper mechanism of bromelain still results uncertain: the selective inhibition of the pro-inflammatory prostaglandins biosynthesis from the arachidonic acid degradation probably is the clinically most relevant effect

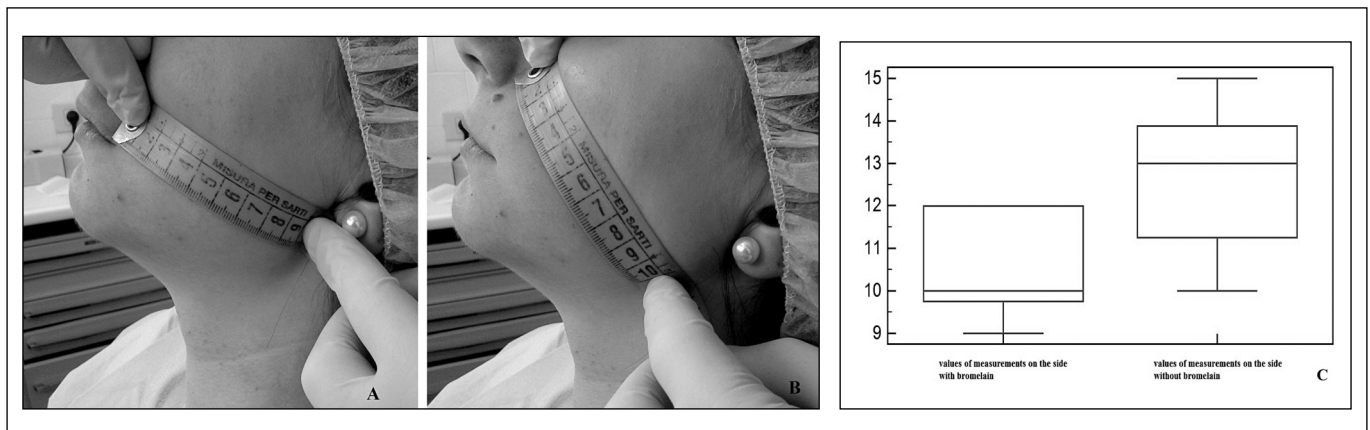


Fig. 1: (A) measurements relative to the distance between the mandibular angle and wing of the nose; (B) measurements relative to the distance between the mandibular angle and labial commissure angle; (C) box-whisker plots of distributions of measurements in bromelain and non bromelain groups.

TABLE I - Classification of third molar impaction and surgical technique.

Figures	Classification	Surgery
	Erupted mandibular third molar	1) Local anesthesia 2) luxation and extraction 3) suture
	Partially impacted mandibular third molar	1) Local anesthesia 2) osteotomy with bur 3) luxation and extraction 4) suture
	Total impacted mandibular third molar	1) Local anesthesia 2) osteotomy with bur 3) odontotomy with high speed bur 4) luxation and extraction 5) suture

¹². This effect differs from the corticosteroid effect that acts on phospholipase A2 and prevents the formation of pro- and anti-inflammatory prostaglandins.

The meta-analysis of Falci et al. regarding corticosteroid injections to reduce the bad outcome after M3M surgery suggested a role with a preemptive modality: the results of this meta-analysis report that dexamethasone (DX) is more effective than methylprednisolone for swelling and trismus, however there is insufficient evidence to conclude that DX is better than other nonsteroidal anti-inflammatories or methylprednisolone as a preemptive analgesic ¹³.

Recently some papers reported update on the use of DX injections to reduce this bad outcome after M3M surgery: Kaewkumnert et al reported better results in trismus on postoperative day 3, with DX submucosal injection compared with intraosseous injection ¹⁴. Atalay et al in their paper reported that combining DX injections with articaine improved the management of discomfort after M3M surgery ¹⁵. Gupta et al recently reported bromelain efficacy comparable to aceclofenac ¹⁶.

With this literature background, bromelain compound may find its space in M3M surgery: de Souza et al. in their systematic review and meta-analysis confirmed the prediction of previous study on the effectiveness of bromelain to control postoperative bad outcome and suggested more research to study the optimal dosage ¹⁷. On the other hand on the same year Liu et al in their

meta-analysis reported that bromelain conferred moderate relief of postoperative discomfort after third molar surgery, alleviated postoperative pain 7 days after surgery but had no apparent effect on early or late trismus ¹⁸. The relevance of our study, compared to randomized studies reported in these meta-analyses, is the split mouth protocol: each patient received M3M surgery without bromelain on one side and with bromelain on the other side, on a second date.

Bromelain was administrated orally to each patient, with a posology of 9.6 g per day for a week, only after the second intervention.

Our results focused on postoperative swelling with precise facial measurements, while all others studies reported mainly different pain scales or scales referred by the patients with questionnaires. We excluded patients with facial asymmetry and used a split-mouth protocol in order to reduce variables between patients that in our opinion may interfere with data collection.

We support the idea that swelling should be considered as postoperative variable capable to interfere in patient's quality of life as pain, but these characteristics of bad outcome are differently influenced by the bromelain: while this compound is capable of controlling postoperative swelling and trismus, this is not the same for postoperative pain ^{17,18}.

With regards to the bromelain dosage, our dosage resulted mainly lower than previous studies: ³⁻¹⁰ however we reported good results in controlling the bad outcome as previous study. Our results let us to answer with the limits of our study to the request of de Souza et al. regarding the dosage ¹⁷.

The split mouth modality of our study let us to report that the dosage was sufficient to reduce the postoperative bad outcome (measured as swelling) significantly. We advocate further research to evaluate the optimal dosage to control postoperative pain: further studies could make use of facial scanner to evaluate tissue swelling.

Conclusion

Bromelain compound 9.6 g reduced significantly the postoperative swelling after M3M surgery. The usefulness of this clinical trial is to provide a bromelain dosage and reduce the bad outcome after M3M surgery. Further studies are advocated to evaluate dosage for postoperative pain reduction, with the aid of facial scanners.

Riassunto

La chirurgia dei terzi molari mandibolari è notoriamente associata ad edema, trisma e tumefazione postoperatoria. Questa condizione che affligge i pazienti rappresenta un grave disagio che deteriora la qualità della vita

sociale e lavorativa, determinando un rinvio non salutare della prestazione chirurgica di estrazione. La letteratura scientifica è uniforme sul dare al composto bromelina una sorta di effetto nel diminuire, in misura variabile, questi sintomi negativi che si verificano dopo la estrazione del terzo molare mandibolare. La difformità in letteratura su tale effetto può essere legata alla variabilità tra i vari pazienti: per questo motivo il presente studio split mouth si inserisce in un contesto scientifico più rigido riducendo le variabili tra pazienti e valutando con misure oggettive sui pazienti le differenze sui due lati del volto, e riportando un ruolo per la bromelina supportato da questa evidenza di rigore scientifico. Ulteriori studi split mouth potranno dare il loro contributo per determinare quale dose può essere efficace per il risultato benefico della bromelina a seguito della estrazione dei terzi molari mandibolari, anche valutando l'uso di scanner facciali.

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