Abstract. – Background and Objective: Bromelain is a proteolytic enzyme, particularly effective in the treatment of soft tissue inflam-
mations and traumas, in localized inflammations, especially in presence of hydropsy and also in postoperative tissue reactions. The aim of
the present study is to assess the efficacy of bromelain in controlling the edema and its relat-
ated pain in the inflamed area after upper third molar exodontia.

Materials and Methods: The effectiveness of our protocol was evaluated by a clinical as-
sessment of the profile of the hemiface corres-
dponding to the treated area: indeed, the linear
values of the trago-pogonion distances were
measured. Algogens were determined by VAS
(Visual Analogue Scale) (Figure 1) with integers
ranging from 1 (no pain) to 8 (maximum pain) up
to a maximum of 10 (paroxysmal and unbear-
able pain).

Results and Conclusions: The obtained re-
sults clearly demonstrate the effectiveness of
bromelain in treating postoperative edema after third molar surgery.

Key Words: Bromelain, Third molar exodontia, Postoperative edema.

Introduction

Bromelain is a proteolytic enzyme, particular-
ly effective in the treatment of soft tissue inflam-
mations and traumas, in localized inflammations, especially in the presence of edema and also in postoperative tissue reactions. It was first introduced in medical area in 1957. It works by blocking some proinflammatory metabolites which accelerate and worsen the inflammatory process. In vitro bromelain decreases migration of neutrophils to sites of acute inflammation and, in vivo, generates almost 50-85% reduction in neutrophil migration. It shows anti-inflammatory properties and so can be used for sports injury, trauma, arthritis and other kinds of swelling. Its main uses are treatment of athletic injuries, digestive problems, phlebitis, sinusitis and aiding healing after surgery. Doses of 200 mg have proven to be an efficacious alternative to non-
steroidal anti-inflammatory drugs (NSAIDs). It has also been proposed for the treatment of arthritis, chronic venous insufficiency, easy bruising, gout, hemorrhoids, menstrual pain, autoimmune disorders and ulcerative colitis. Other studies have shown that bromelain can also be useful in the reduction of platelet clumping and blood clots in the bloodstream, especially in the arteries. Concerning the inflammatory tissue, it has the property to increase capillary permeabi-

ty, to reduce vasodilation, leukocyte migration and local pain by reducing bradykinin and sero-
tonin synthesis also enhancing hemorrhage reab-
sorption, the inflammatory focus drainage and the antibiotics penetration into the infected tis-
sue. If used as anti-inflammatory substance, 40
UI should be employed two to six times a day, al-
though superior dosages resulted without note-
worthy side effects, except for possible minor gastroenteric disorders and/or rare hypersensitiv-
ity reactions. The safety of bromelain, com-
pared to other anti-inflammatory drugs, derives from the difference of its action mechanism: bromelain, in fact, “diverts” COX synthesis, by increasing the production of anti-inflammatory prostaglandins despite the pro-inflammatory ones. In this way, the typical gastrointestinal damage by NSAIDs is avoided and a real phar-
The macological activity is assured. Bromelain absorption, after oral administration, is approximately 40% (half-life of 7-9 hours). Bromelain is contraindicated in patients with severe renal dysfunctions or liver disorders and, more generally, in subjects prone to coagulation disorders.

The aim of the present work is to assess the effectiveness of bromelain in controlling the edema (and the related pain) of the inflamed area after upper third molar surgery.

Materials and Methods

A multicentric study was conducted by including a cohort of 15 patients (Group 1), referred to the Department of Dentistry at Bari General Hospital, together with 21 patients (Group 2) referred to Calabrodental s.r.l., Crotone, Italy, in a Day-Surgery setting and 10 patients (Group 3) referred to the Dept. of Maxillofacial Surgery, “S. Pietro – Fatebenefratelli” Hospital, Rome (Italy). This study was carried out with a “single-blind” method on a total of 46 patients with dysodontiasis, divided into three groups, suitable for exodontia of 3.8 and 4.8; The patients included in the present study had to be without liver or renal diseases, with a normal hematic crasis and with a normal hemocoagulative pattern. Furthermore, smokers and subjects with poor oral hygiene were excluded.

In all the cases documented in this study, the surgical phase was performed by the same clinician (Dr. F. I.), not to run into a possible clinician-assistant variability. Exodontia was performed under local anaesthetic (mepivacaine 3%, intraoral injections of 1.8 ml) following by a standardized methodology involving a highly conservative approach on the hard and soft tissues adjacent to the extracted teeth: after plexus anesthesia, syndesmotomy and tooth avulsion were performed; then, the extraction site was cleaned with a curette and an oxidized regenerated cellulose as well as a Polyglactin 910 suture 2/0 were applied. Only in three complex cases odontotomy was performed with a diamond coated cylindrical burr mounted on a turbine. All operations carried out in this study lasted 20±5 minutes and all patients, soon after the surgery, were forced to perform a 6 hours topical treatment.

Each one of the 46 patients, after 3.8 teeth exodontia (left mandibular surgery) (Bromelain Group) was prescribed a therapy with cephazolin sodium, 1 g/12 h/i.m. along 6 days) together with bromelain (40 mg/6 h/os, along 6 days).

Each one of the same 46 patients, after a period of 60 days, were also subjected to 4.8 teeth exodontia (right mandibular surgery) (Ketoprofen Group) and prescribed a therapy with cephazolin sodium, 1 g/12 h/i.m. along 6 days) together with ketoprofen (100 mg/12 h/os, along 6 days). Post-operative pain and oedema were evaluated, at 30
days distance, in both surgery phases (3.8 compared with 4.8) in the same patients detecting the profile of the left hemiface (60 days later treated area) with respect to the right hemiface in the treated area and also assessing follow-up visits at 1-3-5-7 days from each surgical session. The effectiveness of our protocol was evaluated by the same operator into a clinical assessment of the profile of the contralateral hemiface of the same patients who underwent to the first surgery session two months before. Indeed, the linear value of the trago-pogonion distance was measured and then determined the corresponding values by VAS (Visual Analogue Scale) (Figure 1).

At each follow-up visit, patients of the study groups completed the “Algogen Form” giving their personal evaluation through integers ranging from 1 (no pain) to 8 (maximum pain) up to a maximum of 10 (paroxysmal and unbearable pain).

**Statistic evaluation** was performed using a “paired student-t test” comparing the unbiased opinions detected (Visual Analogue Scale = VAS) in the two post-surgical periods (1-3-5-7 days) 30 days far-off.

The obtained VAS mean values (Table I) expressed not significant results between 60 days far-off treatments (n.s.).

**Experimental groups were composed with 46 patients** (bromelain treatment) and the same 46 patients (ketoprofen treatment).

In each T₀, T₁, T₂, T₃, T₄ measures, numeric data were detected and an aritmetic median values were calculated into each of the 2 groups and into each of the 5 measures.

The distance TR-POG is expressed in centimeters. The single measures have been made through the use of a cutaneous marcator with which a visual repere has been detected in trago central part and in the central part of the cutaneous pogonion: the obtained distance between the 2 points was measured with a transparent flexible millimetre device. The measures were detected by the same operator in order to reduce the bias operator-linked. These results lead us to give a not statistically different evaluation for pain and oedema values expressed by the two substances used (bromelain and ketoprofen).

**Results**

Data analysis, performed in all 46 patients coming from three different surgery clinics,
showed similar reduction of the postoperative pain and edema, as a consequence of bromelain or ketoprofen administration.

Data on the effectiveness of the treatment with bromelain, resulting from VAS values detected on all 46 patients during the 4 post-surgical evaluations, allowed us to establish that bromelain group was not statistically different from ketoprofen group, evaluated after the two upmentioned surgical sessions at 60 days distance.

Discussion

Third molar exodontia is a surgical maneuver that nearly always involves a postoperative condition which is extremely uncomfortable for patients, due to a set of symptoms such as localized pain and edema, often associated to functional limitation with reduced mandibular excursion.

The therapeutic protocol proposed in the present work takes in account the effectiveness of bromelain in treating soft tissue inflammations and traumas, through its anti-edematous action performed at the level of peripheral vessels. In addition, this enzyme proved to be particularly effective in reducing leukocyte chemotaxis and release of algogens, by inhibiting the production of cytokines; finally, its action enhances the hemorrhage reabsorption, the drainage of the inflammatory focus and the antibiotics penetration into the infected tissue, by increasing the capillary permeability1-3.

In conclusion, the assessments given in this study clearly demonstrate the effectiveness of bromelain in treating postoperative edema during third molar surgery. A proper antibiotic therapy could be important to grant a rapid post-operative course, without septic complications which are not rare in this type of surgery.

References