Off-print:

2010; 14:

European Review for Medical and Pharmacological Sciences

Editors:
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Verduci Publisher
Via Gregorio VII, 186 - 00165 Rome (ITALY) - Tel. +39-06.393.75.224 (a.r.)
Fax: +39-06.63.85.672 - E-mail: Info@verduci.it
http://www.europeanreview.org

European Review for Medical and Pharmacological Sciences 2010; 14: 771-774

Clinical trial with bromelain in third molar exodontia

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Abstract. – *Background and Objective:* Bromelain is a proteolytic enzyme, particularly effective in the treatment of soft tissue inflammations 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 related pain in the inflamed area after upper third molar exodontia.

***Materials and Methods:* The effectiveness of our protocol was evaluated by a clinical assessment of the profile of the hemiface corresponding 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 unbearable pain).**

***Results and Conclusions:* The obtained results 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, particularly effective in the treatment of soft tissue inflammations and traumas[1], in localized inflammations, especially in the presence of edema and also in postoperative tissue reactions[2]. 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[3]. 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[5], 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 permeability, to reduce vasodilation, leukocyte migration and local pain by reducing bradykinin and serotonin synthesis also enhancing hemorrhage reabsorption, the inflammatory focus drainage[3] and the antibiotics penetration into the infected tissue. If used as anti-inflammatory substance, 40 UI should be employed two to six times a day, although superior dosages resulted without noteworthy side effects, except for possible minor gastroenteric disorders and/or rare hypersensitivity reactions[4-5]. The safety of bromelain, compared 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 despites the pro-inflammatory ones. In this way, the typical gastrointestinal damage by NSAIDs is avoided and a real phar-

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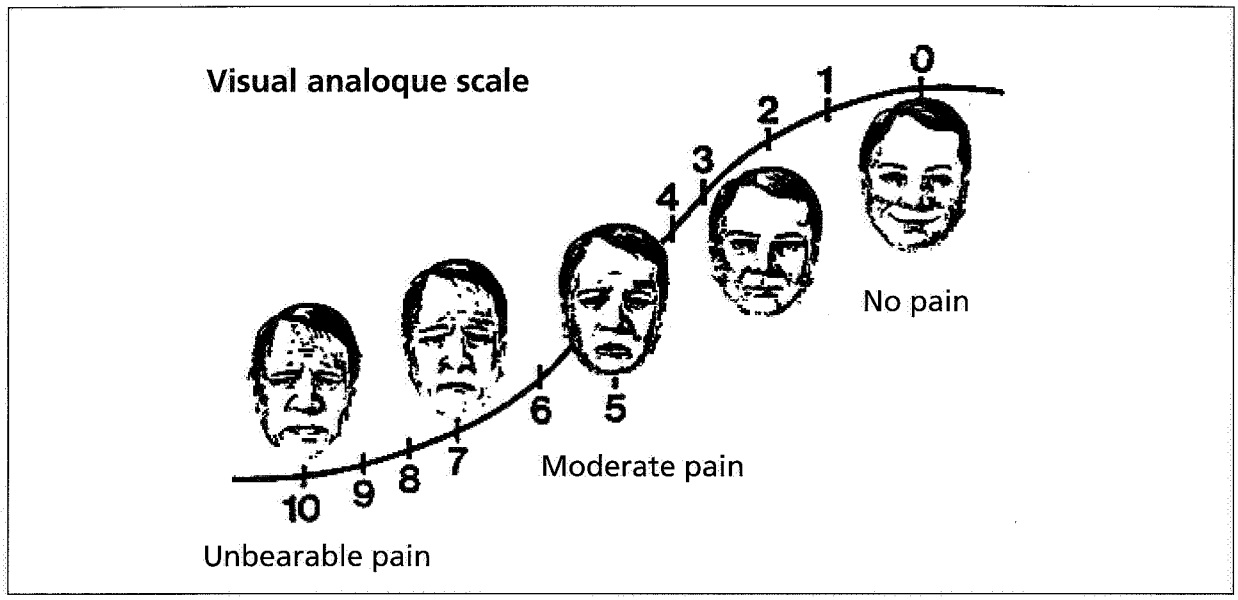

Figure 1. Intuitive prospect of the Visual Analogue Scale.

macological activity is assured[6]. 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 topic-ice 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). Postoperative 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 controlateral 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 unbiassed 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 T_0, T_1, T_2, T_3, T_4 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,

Table I. Results overview.

	Bromelain group	Ketoprofene group
Algia reduction (VAS)	7 patients	5 patients
Lack of algia reduction (VAS)	39 patients	41 patients

Into "Algia reduction" box we calculated only patients referring sintomatology with VAS scale values less than 2 points with respect to the algogen values detected during contralateral sintomatology comparison. Example: Mario Rossi patient declares VAS value = 5 after exodontia of 4.8 (with ketoprofen treatment) while VAS value = 2 after exodontia of 3.8 (with bromelain treatment).

	Bromelain group	Ketoprofene group
Normal post-surgical mouth opening	3 patients	0 patients
Reduced post-surgical mouth opening	43 patients	46 patients

Taking in account the reduced "physiologic" mouth opening after exodontia and evaluating as 5 mm the BIAS consequent to the antalgic posture assumed by the patient in post-surgical mandibular opening, it is evaluated as normal the opening included in a cut-off between 30 and 40 mm.

Trago-pogonion distance	Median value at T_0 Pre-Surgery	Median value at T_1 24 hours after	Median value at T_2 3 days after	Median value at T_3 5 days after	Median value at T_4 7 days after
Bromelain group	13.89	14.38	14.06	13.92	13.81
Ketoprofen group	13.87	14.51	13.95	13.85	13.77