

Efficacy of Bromelain versus Aceclofenac on Post-Operative Analgesia following Dental Extractions- A Randomised Controlled Clinical Trail

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Abstract

Aim: The aim of this study is to compare the efficacy of the most commonly used drug aceclofenac against bromelain , a pineapple extract , as a post operative analgesic.

Materials and Methods: A group of 50 patients undergoing extraction were chosen . By randomised control trials , 25 patients each were given aceclofenac and bromelain for twice daily for three days and pain assessment was studied for each day and recorded using a visual analogue scale .

Background: Pain is most commonly associated with Dental extraction and its intensity varies from individual to individual . Post operative analgesics are always prescribed after extractions to eliminate the post operative pain. However , the effect varies from drug to drug . Bromelain is a proteolytic enzyme, particularly effective in the treatment of soft tissue inflammation and trauma, localized inflammations, edematous areas, post operative tissue reaction. It shows anti-inflammatory properties and so can be used for sports injury, trauma, arthritis and other kinds of swelling. Doses of 200 mg have proven to be an efficacious alternative to nonsteroidal anti-inflammatory drugs (NSAIDs).Aceclofenac is a non-steroidal anti-inflammatory drugs (NSAIDs), prescribed for people with painful rheumatic conditions such as osteoarthritis, rheumatoid arthritis and ankylosing spondylitis. Aceclofenac works by blocking the effect of cyclo-oxygenase (COX) enzymes which make chemical prostaglandins at sites of injury or damage, causing pain, swelling and inflammation. It eases pain and reduces inflammation.

Reason: Pain produced post Dental extractions, occurs as a result of inflammation. Thus the use of anti- inflammatory drugs can help , can help reduce the pain.

Key words - post operative analgesics, Bromelain, aceclofenac , 3 day pain analysis, visual analogue scale .

INTRODUCTION

Pain is defined as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[1] After the extraction of the tooth , there will be inflammation along with marked sensitivity to pressure . This is due to the sensitised nociceptor . The decrease of sensitised nociceptor and afferent activity to the dorsal horn will help reduce the sensitivity to pressure .If the inflammatory process and consequent afferent activity is of sufficient intensity and if there has been neuronal damage, a central process is established that increases sensitisation, lowers the threshold of response, and causes ectopic discharges . Additionally, Alpha and delta fibres begin signalling pain, and their inhibitory effect is lost .There is an increased central release of ex- citatory mediators, such as glutamate and nitric oxide production. These changes stimulate the MAP kinase cascades, resulting in messenger RNA-mediated changes that alter the phenotype of nociceptors and mechanoreceptors such that normal cell response becomes genetically changed to a pathologic state. Pain during a tooth extraction is tolerable due to the usage of local anaesthetics and once the local anaesthetic agents' effect disappears, the post extraction pain must be managed by analgesics. Every analgesic agent has its side effects and the efficacy must be compared and weighed against the side effects to decide on the usage of the right analgesic agent for the right patient. Non-steroidal

anti-inflammatory drugs (NSAIDs) are used in treatment of tooth pain for over years. Oral medications that reduce pain, administered pre or post operatively, improve clinical outcomes, making them an integral part of dental practice.Acute dental pain has been well established for the assessment of efficacy of analgesics in various short-term studies.[2] Agents such as non-steroidal anti-inflammatory drugs (NSAIDs), cyclooxygenase (COX)2-selective inhibitors, and opioids are available for the treatment of acute pain[3] .The invention of NSAIDs has significantly improved the management of pain in dentistry.[2] Because of their demonstrated efficacy and safety in relieving moderately severe pain in outpatient setting, dental practitioners now rely completely on NSAID analgesics.[4]An ideal analgesic should alleviate pain with no undesirable side effects.[5] Combining analgesics offers the possibility of increasing effectiveness without increasing dose.[6,7] Aceclofenac is an oral NSAID that is effective in the treatment of painful inflammatory diseases .Aceclofenac appears to be particularly well-tolerated amongst the NSAIDs, with an incidence of gastrointestinal adverse effects.[8] It is the most widely used analgesic and various studies have supported the use of this drug .Pain following dentoalveolar surgery is inflammation related and therefore anti- inflammatory agents are effective in reducing the pain.

Post operative analgesics are always prescribed after Dental extractions . Choosing the right drug for this is highly essential to relieve the patient from unnecessary pain post the extraction. In the case of traumatic extractions , this plays a major role as patient may present with severe pain .

There have been multiple studies comparing various drugs in analgesic relief ,post extractions. However limited research has been done on using bromelain as an analgesic. It was first introduced in medical area in 1957. This proteolytic enzyme from the pineapple extract works by blocking some pro-inflammatory metabolites which accelerate and worsen the inflammatory process. [9] Hence this study aims at comparing the efficacy of the most commonly used drug aceclofenac against bromelain , a pineapple extract , as a post operative analgesic.

MATERIALS AND METHODS

For this study, 50 patients undergoing single or multiple tooth extractions were chosen. Using randomised control trial , 25 patients GROUP A were administered bromelain twice daily for three days and the remaining 25 patients GROUP B were given , aceclofenac twice daily for three days irrespective of the tooth to be extracted . Patients with systemic problems were excluded from the study.

A regular follow up was done , to asses the pain of these patients on each day , since the start of the medication. The assessment was done using a visual analogue scale . Patients were asked to rate their level of pain on a scale from 1 to 10 and the study was performed. Patients graded pain as 0 (no pain), 3 (mild pain) , 5 moderate pain , 10 (severe pain). The patients using bromelain , the rescue drug was prescribed when pain was not relieved. The rescued drug used was paracetamol.

From the table 1.1, the statistical data shows that the rate of pain was significantly high on day 1 for both drugs . However Mild pain is seen with regard to Group A patients on Bromelain medicine. But there is drastic reduction of pain on day 2 . It can be inferred from this data that the drug appears to be more effective on the second day of administration when compared with the aceclofenac . The standard drug used, aceclofenac showed a very consistent action . It's action was gradual and reduced the pain significantly on all three days . The Figure 1.1 depicts the gradual decrease of pain with the use of analgesics on all three days . But day 2 shows that Group A patients using Bromelain had reduced pain when compared to those on aceclofenac . However the pain was higher for Group A patients on day 1 with a Mean value of 5.12.

RESULTS

	Group	N	Mean	Std. Deviation	Std. Error Mean
Rate of Pain - Day 1	Group A	25	5.12	3.219	.644
	Group B	25	4.72	3.208	.642
Rate of Pain - Day 2	Group A	25	1.84	2.911	.582
	Group B	25	2.40	2.858	.572
Rate of Pain - Day 3	Group A	25	1.00	2.236	.447
	Group B	25	1.16	1.972	.394

Table 1.1 Group Statistics

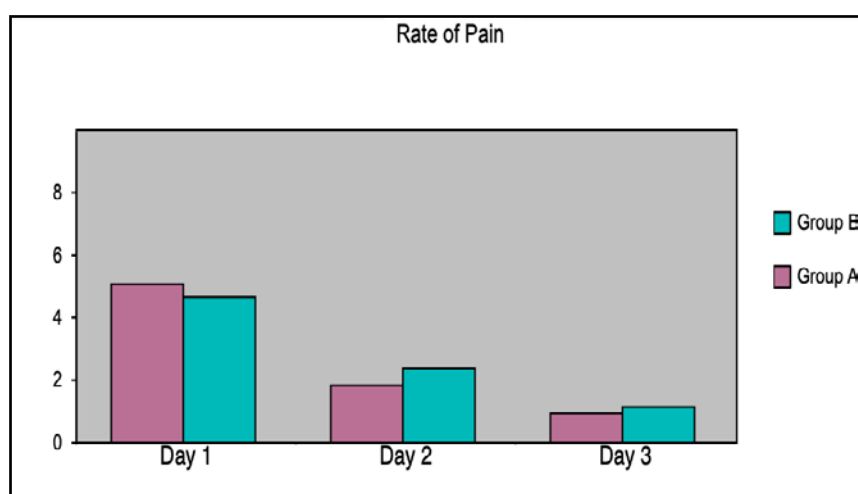


Fig 1.1 Comparison of pain all three days

Paired Samples Test							
		Paired Differences			t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean			
Pair 1	Rate of Pain - Day 1 - Rate of Pain - Day 2	3.280	3.494	.699	4.693	24	.000
Pair 2	Rate of Pain - Day 1 - Rate of Pain - Day 3	4.120	3.734	.747	5.517	24	.000
Pair 3	Rate of Pain - Day 2 Rate of Pain - Day 3	.840	2.593	.519	1.620	24	.118

Table 1.2 Comparison of pain on all three days with Bromelain

Paired Samples Test							
		Paired Differences			t	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean			
Pair 1	Rate of Pain - Day 1 - Rate of Pain - Day 2	2.320	3.119	.624	3.719	24	.001
Pair 2	Rate of Pain - Day 1 - Rate of Pain - Day 3	3.560	2.931	.586	6.073	24	.000
Pair 3	Rate of Pain - Day 2 - Rate of Pain - Day 3	1.240	2.278	.456	2.721	24	.012

Table 1.3 Comparison of pain on all three days with Aceclofenac

The significant P values obtained from the paired T test showed that on comparing pain for day 1 and 3, they have a high pain mean of 4.120 showing a value (p) of 0.000 which is ideally below 0.05 making it significant. It had a similar result when pain was compared for pain on day 1 and 2. However the pain assessed for day 2 and 3 showed no significant value (0.118). Thus the use of the drug, bromelain has proven to be more efficient in action on day 1 and day 2.

Table 1.3 shows that pain when compared to each other on all three days showed p values that were highly significant proving their standard efficacy. Thus the drug, aceclofenac, is efficient and reduces pain effectively on all days.

It is thereby proved that Bromelain is highly efficient when compared with aceclofenac. Aceclofenac being the standard and most preferred drug of choice as a post operative analgesic drug, Bromelain can also be used widely to treat the same cause. The only advantage of Bromelain is that, its action is more on the second day of administration. But slight pain is felt on the first day of administration.

DISCUSSION

Pineapples are a tropical fruit that present with a wide array of health benefits. They are not only valued for its sweet taste, but has been used for centuries to treat

digestion problems and inflammation. Bromelain present in pineapples can reduce swelling, bruising, healing time, and pain associated with injury and surgical intervention. Bromelain is currently being used to treat and reduce inflammation from tendinitis, sprains, strains, and other minor muscle injuries as well as swelling related to ear, nose and throat surgeries or trauma.[10]

In vitro bromelain has the tendency to reduce the migration of neutrophils to the areas of acute inflammation and in vivo, it reduces the neutrophil migration by 50 to 85%[11]. Due to its anti-inflammatory properties, it is widely used to treat any injury, trauma, arthritis and other types 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 nonsteroidal anti-inflammatory drugs (NSAIDS). It has also been proposed for the treatment of arthritis[12], chronic venous insufficiency, easy bruising, gout, hemorrhoids, menstrual pain, autoimmune disorders and ulcerative colitis. It is also found to be effective in preventing platelet clumping and blood clots, particularly 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 haemorrhage reabsorption, the inflammatory focus drainage[11]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[12-13]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 despite the pro-inflammatory ones. 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 disorder. Bromelain content is found in maximum quantity within the stem of the plant. Making it an inexpensive product.[14]the average consumption of bromelain a day is 12 gm.. and it has no side affects . [13]. Bromelain is absorbed from the gastrointestinal tract in a functionally intact form making it more effective.

Non-steroidal anti-inflammatory drugs (NSAIDs) form a heterogeneous group of organic acids which have analgesic, antipyretic, anti-inflammatory and platelet inhibitory actions. [15] The usual dosage of Aceclofenac in adult patients with arthritic disorders or moderate to severe pain is 100 mg orally twice daily [16,17] Due to short half- life, it is necessary to be administered frequently in order to maintain the desired concentration [17]. Therefore, Aceclofenac is an ideal candidate for sustained release formulation, resulting in more reproducible drug absorption compared to single dosage forms [17, 18].Aceclofenac should not be administered to patients with peptic ulcers or GI bleeding, moderate or severe renal impairment, sensitivity to aceclofenac or other NSAIDs. The drug is not recommended in pregnant or breast-feeding women [16]

Aceclofenac is eliminated mainly via the renal route, with a plasma elimination half-life of approximately 4 hours [17]. Approximately 70% of the drug is excreted in urine as glucuronide of Aceclofenac and diclofenac and 20% in feces [16]. Aceclofenac is also more than 99% bound to plasma proteins.

Aceclofenac has not only been used as a post operative analgesic drug but has also been used as a pre- operative analgesic . A study showed that ,this drug gave significant pain relief when administered 1 hour prior to Dental extractions .[18]

In a study conducted by Pavithra.P et al, the efficacy of ibuprofen and Aceclofenac was used to assess Dental pain. After oral administration of the drug , pain was assessed at intervals of 15, 30 and 45 minutes ,using a visual analogue scale. The results from the study showed that Aceclofenac is very efficient when compared to ibuprofen in reliving the pain as the pain scores with aceclofenac had a gradual decrease in value when compared to ibuprofen . [19]

A similar study showed the comparison between two NSAIDs , aceclofenac and ketorolac. Pain was recorded with VAS score at 3 hours, 8 hours and 19 hours from the time of extraction of the tooth. The results from this study

proved that aceclofenac and ketorolac aren't that different and have similar action with regard to decreasing pain. [20]

From all these studies we can infer that, aceclofenac has excellent analgesic and anti-inflammatory properties.

A multi centric study was conducted at “S. Pietro – Fatebenefratelli” Hospital, Rome (Italy) with 46 patients to asses their post operative pain . The operation lasted for 20 mins and after 6 hours of surgery, the patients were asked to apply topical. After undergoing extraction of 38, the patients were prescribed a therapy with cephazolin sodium, 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 48 extraction followed by post operative medication with cephazolin sodium, 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 in the same patients detecting the profile of the left side (60 days later treated area) with respect to the right side in the treated area and also assessing follow-up visits at 1-3-5-7 days from each surgical session. Data on the effectiveness of the treatment with bromelain, resulting from VAS values detected on all 46 patients during the 4 post-surgical evaluations, showed that bromelain group was not statistically different from ketoprofen group. [21]

Though there have been a few studies on bromelain's anti inflammatory and analgesic properties , this is a highly effective drug of choice in the treatment of osteoarthritis. In clinical trials, bromelain-based formulations were more effective than an NSAID drug in relieving arthritis pain. Supplementing with bromelain-based formulations after injury or surgery also speeds healing and reduces pain. It's action is enhanced when used along with diclofenac.[22].

CONCLUSION

Bromelain has a wide range of therapeutic benefits, but the mode of its action is not properly understood. It is proved that bromelain is well absorbed in body after oral administration and it has no major side effects, even after prolonged use. From this study ,it has been proved that bromelain has analgesic property.

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