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ENZYMATIC PREPARATIONS – AN ALTERNATIVE ANTI-INFLAMMATORY THERAPY

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ABSTRACT

Tonsillectomy is a common surgical procedure associated with significant post operative pain. It is a challenge for the treating surgeon to manage pain and maintain adequate hydration with minimal adverse effects. The goal of this study is to compare the efficacy and adverse effect of oral enzyme preparation over Diclofenac sodium (NSAID) in treating post operative pain.

Materials and methods: The study was done on 60 patients who underwent tonsillectomy in the age group 18-45 in Department of ENT.30 patients were put on oral Diclofenac for 2 weeks and other 30 patients were put on oral enzymatic preparation for 2 weeks. Patients were reviewed on 3rd, 7th, 14th post op day. Their symptoms were recorded according to the WONG-BAKER FACIAL GRIMACE pain scale.

Results: At the end of two weeks 28 out of 30 patients (93%) on enzymatic preparations were on zero pain scale and 30 out of 30 (100%) on NSAIDS had zero pain scale but adverse drug reactions were seen in 22 out 30 patients (73.3%) with NSAIDS where as only 4 out of 30 (13.3%) with oral enzyme preparations had adverse effects.

Conclusion: Post tonsillectomy pain is one of the difficult things to manage as it interferes with intake of food and hydration. Oral enzyme preparations play a significant role in reducing the pain with very minimal gastrointestinal side effects and can be used as a very effective alternative mode of treatment in such patients.

KEY WORDS: Tonsillectomy, Enzymatic Preparations, Diclofenac sodium, post tonsillectomy pain.

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INTRODUCTION

Tonsillectomy is undoubtedly a painful procedure in adults. Safe and effective analgesia has always been a problem. Improper pain management following tonsillectomy causes poor oral intake, dehydration, vomiting, restlessness and sleep disturbances[1,2]. Various NSAIDs have been administered in managing such pain but each one of them have been associated with various side effects .Non selective NSAIDS inhibit the synthesis of prostaglandin at both the cyclo oxygenase (COX I and COX II)sites causing bleeding in tonsillectomy sites[3]. Enzyme preparations are proteolytic enzymes effective in soft tissue edema and inflammation following surgery there by reducing pain. In this study we tried a combination of two proteolytic enzymes (trypsin and bromelain) and a flavonoid (rutoside) in treating post tonsillectomy patients. Trypsin helps in relieving edema and inflammation by fibrinolysis and regulating cytokine levels thereby alleviating the pain and healing time of the tissue injured. Bromelain has anti edematous, anti inflammatory activity. Rutoside is a member of flavonide class of phytochemicals that acts as a potent anti oxidant and effective anti inflammatory antihistaminic agent. In this study a comparative analysis was done among 60 patients 30 patients were put on diclofenac sodium (NSAID) and 30 were put on these oral enzymatic preparations for 2 weeks.

MATERIALS AND METHODS

A study was conducted among 60 patients who underwent tonsillectomy in age group of 18 – 45years in our ENT department. All patients underwent tonsillectomy by routine Dissection and Snare method after preoperative evaluation and anaesthetic assessment. In all these patients bleeding points were ligated and diathermy was not used. Informed and written consent were obtained from all the patients regarding the study. Out of 60 patients, 30 were randomly selected and put on diclofenac sodium 50 mg twice daily(after food) for two weeks . other 30 patients were put on a combination of trypsin 48 mg, bromelain 90 mg, rutoside 100 mg three times (before food)a day for two weeks. All these patients were put on oral antibiotics for 7 days and explained about the importance of adequate hydration (oral fluid intake). All patients were reviewed on the 3rd, 7th, 14th post op day. Tonsillar fossa, colour of the slough, inflammation of the surrounding structures were all recorded. Grading of pain was recorded using WONG-BAKER FACIAL GRIMACE pain scale. Adverse effects like gastro intestinal disturbances, haematological disturbances, drug hypersensitivity etc., were recorded in both the group of patients.

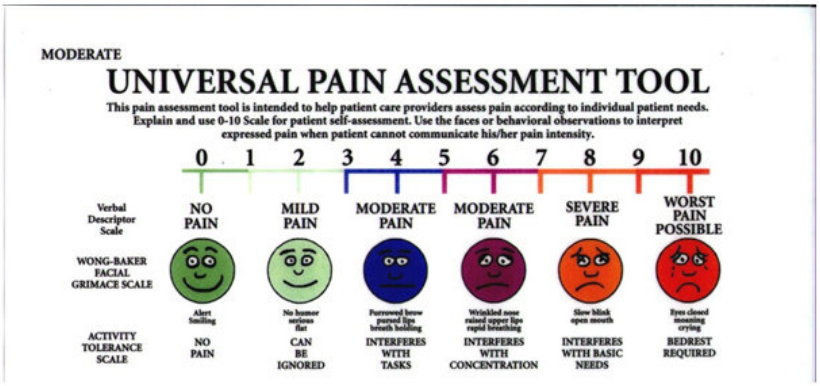
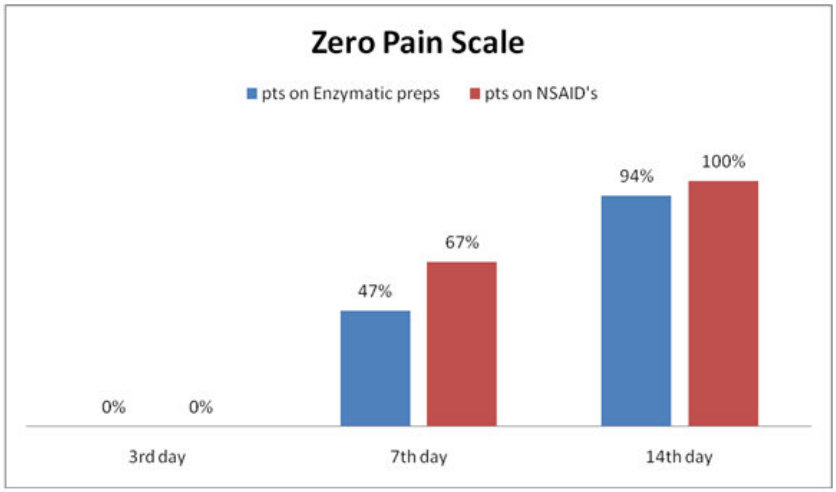


Figure 1
wong baker facial grimace pain scale.

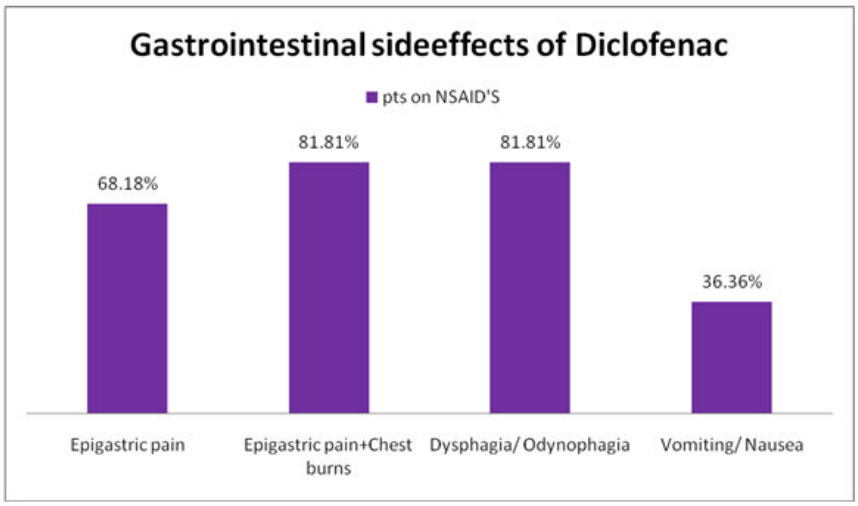
PAIN ASSESSMENT SCALE		
Grading	**Severity of Pain**	**Physical Activity**
0	No Pain	Alert, Smiling
1-2	Mild pain	Can be tolerated
3-4	Moderate pain	Interferes with task
5-6	Moderate severe pain	Interferes with concentration
7-8	Severe pain	Interferes with basic needs
9-10	Worst pain	Bed rest required

DISCUSSION

NSAIDS have been associated with higher incidence of adverse effects particularly when associated with reduced intake as in cases of post tonsillectomy pain. Ultra structural damage to the gastric epithelium occurs within minutes and severe endoscopically detectable haemorrhages and erosion of lining epithelium occurs within hours after taking NSAIDs[4]. Two studies compared blood loss following pre operative administration of rectal diclofenac 0.65-1.0 mg kg^{-1} and paracetamol showed greater blood loss, longer duration of surgery[5], additional measures to obtain haemostasis. Aspirin and ibuprofen has shown to disrupt sleep by increasing the number of awakenings and decreasing sleep efficiency[6]. Paracetamol has been proved to be safe and effective in managing pain. Over dosage can lead to irreversible liver injury which can be life threatening[7]. Paracetamol exerts weaker inhibition of prostaglandin synthesis though it produces effects on sodium and water excretion , it doesn't affect renal blood flow and glomerular filtration rates even in stressed kidneys[8].Though NSAID can be combined with paracetomol in reducing the pain , further studies are required for a special focus on potential increase in side effects in their combined use. Opioides provide effective analgesia[9] but are often associated with respiratory depression which can be lethal to the patient with obstructive airway disease. One study revealed no significant analgesic effect in using specific COX_2 inhibitor (refecoxib 0.625mg/kg) in relieving post operative pain[10]. Our drug combinations of trypsin, bromelain and rutoside have inflammation inhibiting properties as well as positive effects on edema and an effective analgesic effect[11]. A number of studies have shown that the full treatment effect occurs only after a latency period probably one week [11]. Diclofenac is a NSAID which can be given orally, IM or rectally. It has a short half limit, no dose adjustment is required in elderly, and in patients with hepatic / renal insufficiency. Its anti inflammatory is related to its initiation of synthesis of Prostoglandin,prostacyclin and thromboxane products. It is administered orally 75 to 150 mg daily in 2-3 divided doses. In our study we gave 50 mg BD orally.



Enzyme preparations are one of the most useful nutritional supplements and a safe alternative to NSAIDs for treating pain and inflammation. All enzymatic preparations are derived from microbial, plant and animal sources for example bromelain from pinapple stem,trypsin from pancreatic juice of animals[12]. Trypsin is proteolytic enzyme (endopeptidase) that alters the permeability of cell membrane and inner cell structures and shows immuno modulatory activity. Bromelain selectively decrease the thromboxane generation and the changes thromboxane /prostacyclin ratio. This reduces the venous strain, facilitates drainage, increase permeability and restores the biological activity. It is an effective fibrinolytic agent limiting the spread of coagulation reaction by degrading fibrin. It increases the vascular permeability and absorption of oedematous fluid by tissues. Rutin is a bio flavonoid which inhibits both enzymes and other mediators of inflammatory process like CRP or adhesive molecules. This inhibits synthesis of leukotriene (LTB4) and PGE_2. It is also known to provide many health benefits by scavenging the O_2 free radicals. The combination of these three is that each enzyme compliments the other resulting in the synergism of the final therapeutic efficacy. Further these combinations are known to increase the resorption of individual protease by the intestinal mucous membrane. There are some contra indications for one these enzyme preparations. These drugs should be avoided in pregnancy, lactation. It should not be administered in patients with bleeding disorder, liver damage, and patients on warfarin therapy. There can be sudden fall of Blood Pressure in hypertensive patients on medication. They can cause certain side effects like change in consistency, colour of stool which is harmless and flatulence and fullness due to over dosage. Occasional allergic reactions can occur which will subside on discontinuing the medication.



RESULTS

Out of the 60 patients selected in our study 36 were male and 24 were female.18 male and 12 female were selected in each group. All were informed regarding the study and meticulous follow up was done .All criteria were followed and tabulated. None of the patients were on zero pain scale in both study grouping the 3rd post operative day many of them were in mild and moderate pain scale. They were all reassured and advised on good hydration. Only 7(23.3%) patients put on oral enzyme preparation were on severe and very severe pain scale on the 3rd post op day. They were started on oral Paracetamol 500mg four times daily for two days.28 patients on (93%) on enzymes came to zero pain scale at the end of two weeks. Though 100% of the patients on diclofenac became painless by the end of 2 weeks, 22 patients(73.3%) had gastro intestinal side effects including epigastric pain, chest burns, dysphagia and vomiting..Only 4 patients (13.3%) on enzymes had side effects like change in colour and consistent of stools and flatulence. These were totally harmless and was clearly explained to the patient.2 out

of 30 patients (7%) on diclofenac had drug hypersensitivity and were changed to other NSAIDS. None of the patients on enzymes developed hypersensitivity. The enzyme preparations were active in a broad pH range and are safe and well tolerated. They have fibrinolytic activity, activate endogenous proteases (plasmin) and remove necrotic tissue. They also help in wound healing by allowing healthy tissue to grow.

CONCLUSION

Post tonsillectomy pain is one of the commonest problem encountered in ENT OP. Inspite of adequate pre op counselling patients are taken by surprise by the severity of pain. Reduced oral intake and dehydration adds on to the pain. Various analgesic drugs have been in use with adverse effects of varying degrees including high risk of secondary haemorrhage. Modification in surgical method of removing tonsils have been attempted to reduce pain but surgeon should be aware of the potential drawback of such modification. Our study of using Oral Enzyme Preparation with adequate emphasis on rehydration has been very effective in reducing pain. Though the initial improvement is delayed due to latency period of the enzymes the overall pain relief at the end of two weeks was very appreciable with minimal side effects.

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