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Research Article

THE EFFECT OF PRE-EMPTIVE DEXAMETHASONE ON POST-OPERATIVE PAIN AND SWELLING AFTER PERIODONTAL FLAP SURGERY

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A B S T R A C T

Background: Pain and swelling after periodontal flap surgery are common occurrences. The aim of this study was to evaluate, the effect of pre-emptive oral 8mg dexamethasone on post-operative pain and swelling after periodontal flap surgery.
Methodology: Total 24 patients with moderate to severe periodontitis who need periodontal flap surgery were randomly selected. Patients were divided into two equal control and test groups. In control group, only periodontal surgery was carried out. In test group, patients were given 8 mg dexamethasone orally 1 hour prior to surgery. Patients were instructed to maintain a pain diary, for first 5 hours, on 2nd, 3rd, 4th day and on the day of suture removal (7th day). Post-operative swelling was evaluated on 3 rd day and 7th day. VAS scale and swelling index were used to assess the pain and swelling respectively.
Results: Compared to control group, mean pain score of test group was statistically significant ($P < 0.05$). Mean swelling score of test group showed no statistical significant difference ($P > 0.05$) compared to control group.
Conclusion: The use of 8mg dexamethasone as pre-emptive steroidal anti-inflammatory drug may be beneficial for post-operative pain management in periodontal flap surgery.

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INTRODUCTION

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Pain after periodontal therapy is a common occurrence. Scaling and root planing is one of the most common procedures in periodontal practice and may promote pain of significant duration and magnitude.[1] Many times, periodontal surgery also generates pain and discomfort with greater intensity than that occasioned by scaling and root planing alone.[2,3] Therefore, patients who are candidates for periodontal flap surgery can be treated with effective pain management. Effective post-operative pain control is achieved by preventing the initial neural cascade which leads to hypersensitivity produced by noxious stimuli and efficient analgesic agent before the onset of the noxious stimulus, to prevent central sensitization and preventing typically painless sensations to be experienced as pain (allodynia). [4-7] Preemptive analgesia has been defined as treatment that starts before surgery, prevents the establishment of central sensitization caused by incisional injury and inflammatory injuries.[8]

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Preemptive analgesia is a protocol that aims to reduce pre and post-operative pain and discomfort. Few trials[9,10] suggested that preoperative administration of different anti-inflammatory drugs reduced postoperative pain intensity and the need for supplementary analgesics.

Dexamethasone is a steroidal anti-inflammatory drug that induces annexin, a protein that, among other actions, is capable of inhibiting phospholipase A2 (i.e., the enzyme responsible for the induction of arachidonic acid).[11] The arachidonic-acid cascade initiation culminates in the expression of prostaglandins, prostacyclins, thromboxanes, and leukotrienes, which are related to pain. The preemptive use of dexamethasone was demonstrated to be effective on pain prevention when used before third-molar extraction surgeries.[12] Thus, the aim of this study was to evaluate, the effect of pre-emptive 8mg dexamethasone on post-operative pain and swelling after periodontal flap surgery.

Objective

To assess the effect of pre-emptive 8mg dexamethasone on post-operative pain and swelling after periodontal flap surgery.

MATERIALS AND METHODS

A total of 24 patients having moderate to severe periodontitis were selected from the out patient department of periodontology and implantology, SMBT dental college and

hospital, Sangamner from January 2018 to March 2018. The age of the patients ranged from 30 to 50 years. A written informed consent was taken from the patients. Patients allergic to any formulations used in the study, patients using analgesic and anti-inflammatory drugs, patients with history of systemic diseases- diabetes mellitus, hypertension or gastric ulcer, pregnant or lactating females, and patients who were at risk for infective endocarditis, osteoporotic patients, patients with infectious diseases like herpes simplex were excluded from study. Patients undergoing periodontal flap surgery were randomly divided by coin toss into 2 equal test and control groups. Control group patients were treated with periodontal flap surgery without any pre-emptive drug, while in test group patients 8mg dexamethasone was given orally 1 hour prior to periodontal flap surgery. For each quadrant, a mucoperiosteal flap was raised under local anesthesia (2% lidocaine with 1:100,000 epinephrine) for complete scaling and root planning. At least a 4-week interval between the appointments was set for adequate healing. Patients were instructed to maintain a pain diary, for first 5 hours, on 2^{nd}, 3^{rd}, 4^{th} day and on the day of suture removal (7^{th} day) and were evaluated for post-operative swelling on 3^{rd} day and 7^{th} day. After surgery periodontal pack (coe-pac) was placed and patients were prescribed Amoxicillin 500mg thrice a day for 3 days and Paracetamol 500mg tablet as and when required. VAS [13, 14] scale (1-10) and swelling score [15] (0-3) were used (0= No swelling (NS), 1=Mild swelling less than 1/2 cm in size, 2=Moderate swelling 1/2 cm and less than 1 cm, 3= Severe swelling of 1 cm or more in size) to assess pain and swelling respectively. All the periodontal flap surgeries were carried out by same person (AM).

Statistical Analysis

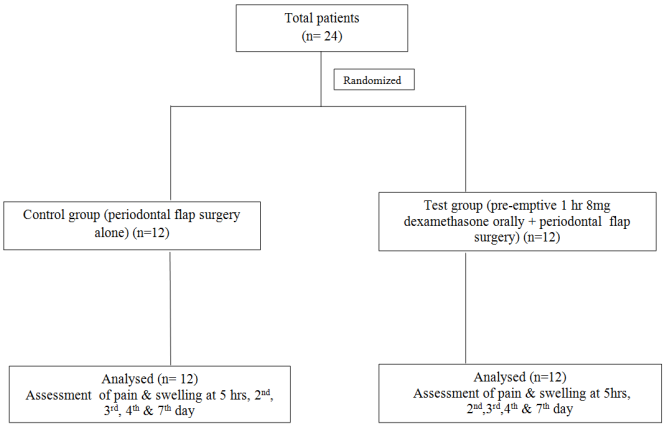
Statistical analysis was performed using Stastistical Product and Service Solution (SPSS) version 16 for Windows (SPSS Inc, Chicago, IL). Descriptive quantitative data will be expressed in mean and standard deviation respectively. Confidence interval is set at 95% and probability of alpha error set at 5%. Power of the study set at 80%.

Data normality was checked using Shapiro- Wilk test. All the data variables were found to be following normality, hence parametric test was used. Intergroup comparison between control and test groups respectively in respect to mean age, mean pain and mean swelling score was done using Student t test.

Intragroup comparison (trend) of mean pain and mean swelling score of control and test groups at two different time interval was done using Paired t test. Chi square test was used for comparison of demographics data like gender ratio between control and test groups.

RESULTS

All 24 patients completed the study (figure 1), and the compliance with the pain diary was 100%. No side effects were reported for any of the medications used.



Postoperative pain and swelling using VAS and swelling index showed that persistent pain and swelling were found to be more in the control group compared with dexamethasone group. Mean age of control group and test group was found to be 42.4 ± 5.2 years and 44.7 ± 6.8 years respectively. There was no statistically significant mean age and gender difference ($p > 0.05$) among control group and test group.

Mean swelling score in control group was 0.47 ± 0.16 and 0.0 at 3^{rd} day and 7^{th} day post -operative respectively. Mean swelling score in test group was 0.33 ± 0.13 and 0.0 at 3^{rd} day and 7th day respectively. Postoperative swelling score showed no significant difference as compared to 3rd day score in control group as well as test group (Table 1).

Table 1 Intra group comparison of mean (mean ± SD) swelling & pain score in control group and test group

Mean swelling score	3^{rd}day postoperative	7th day post operative	t value	'P' value
Control group (n=12)	0.47 ± 0.16	0.0	1.27	0.13
Test group (n=12)	0.33 ± 0.13	0.0	0.94	0.61
Mean pain score	1^{st}hour postoperative	7^{th}day postoperative		
Control group (n=12)	6.75 ± 0.75	0.0	16.48	0.001*
Test group (n=12)	2.58 ± 0.66	0.0	7.49	0.003*

Statistically significant ($p < 0.05^{*}$)

Mean swelling score of control group and test group at 3rd day post-operative was 0.47 ± 0.16 and 0.33 ± 0.13 suggesting that inter group comparison of mean swelling score of control group and test group was not significant (p= 0.083) (Table 2).

Table 2 Inter group comparison of mean (mean ± SD) swelling score in control group and test group

Swelling score	3rd day post-operative	7th day post –operative
Control group (n =12)	0.47 ± 0.16	0.0
Test group (n=12)	0.33 ± 0.13	0.0
't' value	1.28	0.0
'P' value	0.083	1.0

Mean pain score in control group was 6.75 ± 0.75 and 0.0 at 1^{st} hour and 7^{th} day post -operative respectively. Mean pain score in test group was 2.58 ± 0.66 and 0.0 at 1^{st} hour and 7th day respectively There exists highly significant statistical difference or reduction in mean pain scores in control group. Significant statistical difference or reduction was observed in mean pain score in test group (Table 1).

Mean pain score in control group and test group at 5th hour and 7th day post-operative respectively was found to be 2.83 (for control group at 5^{th} hour) and 0.5 (for test group at 5^{th} hour), which gradually reduced to 0.0 at 7^{th} day for both groups.

Table 3 Inter group comparison of mean (mean ± SD) pain score in control group and test group at 5th hour and 7th day post-operative respectively

Pain score at intervals	Control group (n=12)	Test group (n=12)	't' value	'P'value
1st hour	6.75 ± 0.75	2.58 ± 0.66	14.32	0.001*
2nd hour	6.33 ± 0.77	1.83 ± 0.57	16.08	0.001*
3rd hour	5.08 ± 1.08	1.41 ± 0.51	10.58	0.001*
4th hour	3.75 ± 1.28	1.0 ± 0.6	6.69	0.001*
5th hour	2.83 ± 1.26	0.5 ± 0.52	5.89	0.001*
2nd day	1.33 ± 0.65	0.16 ± 0.38	5.32	0.001*
3rd day	0.33 ± 0.49	0.0	2.34	0.001*
4th day	0.08 ± 0.28	0.0	1.0	0.028*
7th day	0.0	0.0	0.0	0.328

Statistically significant ($p < 0.05^*$)

Thus inter group comparison showed highly significant difference for mean pain score in control group and test group at 5th hour and 7th day post-operative respectively with p value <0.001 (Table 3).

DISCUSSION

Although the surgical extraction of impacted third molars has become the most widely accepted model to compare the efficacy of analgesics and anti-inflammatory drugs, the prevention and control of postoperative pain and swelling after periodontal surgeries are also of great concern for patients and clinicians. Open-flap debridement periodontal surgery is an efficient and widely accepted therapeutic approach for patients who do not respond well to nonsurgical periodontal treatment. However, pain and discomfort are expected after this type of procedure.[3, 16] Several medication protocols were proposed to minimize these effects.[17]

Pre-emptive analgesia is believed to promote improved clinical results for pain prevention than treatment initiated after surgery.[18] Post-operative pain generally lasts for 24 h, with greater intensity at 4-8 h,[19] which justifies the evaluation of an 5-h period on the 1st day of surgery in this study.

Steroidal anti-inflammatory drugs may also be used for pain prevention. Dexamethasone (4 mg) was not an effective reducer of pain inflammatory markers after tissue injury *in vivo* or of pain prevention after open-flap debridement surgeries.[20] In contrast, Baxendale *et al.,*[21] observed significant pain prevention with the use of an 8-mg dose after multiple extractions of third molars. Although a significant amount of the administered glucocorticoid is eliminated from the blood before 24 h, some late anti-inflammatory effects may be observed for up to 3 days, which was the time period evaluated in this study.[22] The time needed for dexamethasone to reach a plasmatic-concentration peak varies from 1 to 2 h, and there were favorable results with its use 1 or 2 h before surgery.[21, 23, 24]

In mucoperiosteal flap surgery for scaling and root planing [25] and in crown lengthening [26], no significant differences for the intensity of pain were demonstrated when both steroidal (SAID) and non-steroidal (NSAID) anti- inflammatories were compared as pre-emptive and post-operative medications. Steffens *et al.*[18] also showed no significant difference for pain between the SAID (8 mg dexamethasone) and NSAID (120 mg etoricoxib) groups; this was also true for mucoperiosteal flap surgery for scaling and root planing, but the medications were administered only in the pre-emptive period. On the other hand, Mehra *et al.*[27]compared different pharmacological regimens using SAIDs and NSAIDs, and demonstrated that the NSAID ibuprofen produced an increased reduction of pain. Patients receiving 600 mg ibuprofen pre-emptive and post-operative for a week reported increased effectiveness in reducing PGE2 level in urine and saliva when compared to dexamethasone alone after the removal of impacted lower third molars. Besides using the same pharmacological protocols, drug administration routes and the surgery of choice in the studies differs, which may influence the morbidity of the surgeries. However, there is a trend towards lower pain levels with the use of dexamethasone.

Studies have [23, 28] showed that the use of SAID as a pre-emptive medication was effective in preventing pain after removal of third molars surgeries, despite the surgery performed and drug dosage showing a better efficacy of dexamethasone; this can be explained by the mechanism of action of this drug, since corticosteroids inhibit the phospholipase A2 enzyme reducing the release of arachidonic acid into leukotrienes and inflammatory cells. Additionally, a lower accumulation of neutrophils may justify, at least in part, the power of SAIDs[29]. On the other hand, the NSAIDs act by blocking the cyclooxygenase pathway, producing effects on arachidonic acid metabolism and inhibition of the synthesis of certain metabolites such as prostaglandins (PGs) [24]. Apart from pain, the morbidity of a surgery also takes into account the intensity of edema experienced during the late postoperative period, which showed that the group receiving dexamethasone as pre-emptive and post-operative medication demonstrated lower edema rates when compared to ibuprofen. Alcantara *et al.*[30], using linear measurements, demonstrated that dexamethasone controlled edema better than methylprednisolone at all post-operative evaluations. According to Peres *et al.*[26], the intensity of edema was similar between the COX-2 inhibitor and SAID groups, which is in accordance with Emery.[31] Although the crown lengthening surgeries performed by Peres *et al.*[26] showed low edema, their follow-up was 4, 8, 12 and 24 h after surgery, which is different from the current study where the patients were analysed hourly for the first 5 h after surgery and on 3rd day and the seventh day. The NSAID, ibuprofen, is responsible for inhibiting COX-1 and COX-2 as well, which leads to changes in the gastric mucosa and renal toxicity. The clinical use of dexamethasone has the advantage that it does not act on the COX pathway, thus not promoting changes at the gastric and renal level, but its use should be moderate and rational, for a limited time and dose, which justifies the single dose of 8mg.[32]

The findings of the present study are correlated to the previous studies in which the adoption of a pre-emptive medication protocol using either etorocoxib or dexamethasone may be considered effective for pain and discomfort prevention after open flap debridement surgeries.[18]

Studies investigating the clinical pharmacokinetics of dexamethasone have demonstrated that after an 8-mg dose of dexamethasone, t1/2 and Vd (volume of distribution) are~ 3 hours and 1.0 liter × kg^{-1}, respectively.[33] Higher Vd and t1/2 values result in a greater distribution of the drug through the tissues and a slower elimination, which results in a prolonged therapeutic effect. The low pre-operative dose of dexamethasone used in the study (4mg) just 1 hour before the surgery may in part explain the fact that pain intensity did not statistically differ from the placebo group, except at the 3-hour period. In another study with multiple third-molar surgeries, Baxendale *et al.*[21] demonstrated a significant reduction in severe swelling and pain 4 hours postoperatively with the use

of 8mg dexamethasone. Therefore, a sufficient time to reach t max and higher doses may be necessary for SAIDs to reduce arachidonic acid metabolites and also suppress many proinflammatory cytokines (IL-1-b, TNF-b, IL-6, IL-8, IL-12, and IL-18) and free oxygen radicals.

Steroids undoubtedly decreased post operative swelling [34], though several studies have shown the efficacy of steroid in the reduction of post operative swelling following third molar surgery, but the selection of appropriate drug, its proper dosage and route of administration is still discussable.[35,36] Corticosteroid also reduced edema by decreasing permeability of capillary endothelium and therefore reduced the amount of fluid, protein, macrophages and other inflammatory cells entering areas of tissue injury.[37]

CONCLUSION

Within the limit of present study the use of 8mg dexamethasone as pre-emptive steroidal anti-inflammatory drug may be beneficial for post-operative pain control in patient's undergoing periodontal flap surgery. However additional studies should be carried out to clearly indicate the potential of dexamethasone drug in periodontal surgical therapy.

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