ISSN: 2581-5989
PubMed - National Library of Medicine - ID: 101738774

International Journal of Dental Science and Innovative Research (IJDSIR)

IJDSIR : Dental Publication Service

Available Online at: www.ijdsir.com

Volume – 4, Issue – 3, June - 2021, Page No. : 443 - 451

Comparative evaluation of the effect of dexamethasone and ketorolac tromethamine infiltration on postoperative pain after single visit endodontics in lower molars with irreversible pulpitis: An in vivo study

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Citation of this Article: Dr. Varsha Rani Bangaru, Dr. Ashwija Shetty, Dr. Supritha Atavali, Dr. Srirekha Aswathnarayana, Dr. Champa Chikkamallaiah, Dr. Preetham CN, "Comparative evaluation of the effect of dexamethasone and ketorolac tromethamine infiltration on postoperative pain after single visit endodontics in lower molars with irreversible pulpitis: an in vivo study", IJDSIR- June - 2021, Vol. – 4, Issue - 3, P. No. 443 – 451.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Aim: The aim of the study was to investigate the effect of local infiltration of corticosteroids on postoperative pain in mandibular molar teeth with irreversible pulpitis after single visit endodontic treatment.

Methodology: A total of 70 patients were selected and Inferior alveolar nerve block was administered with 1.5 ml lignocaine, with 1:200,000 epinephrine using a 27-G needle. Single visit endodontic treatment was done with the of gutta-percha and AH26 sealer using the single cone technique. At the end of treatment, the subjects were randomly assigned to 3 groups, namely:

Group 1 (n=30): 0.7 ml dexamethasone; Group 2 (n=30): 0.7 ml ketorolac tromethamine and Group 3 (n=10): 0.7 ml sterile saline as a placebo.

The severity of pain experienced by the subjects was recorded before treatment and were asked to record the severity of pain, using a checklist at 6, 12, 24 and 48 hours postoperative intervals. Postoperative pain severity was determined using a visual analog scale (VAS). Scores were based on self reported measures of symptoms that were recorded with a single handwritten mark.

Results: After 6 and 12 hours, Group 1 and Group 3 had the lowest and highest pain values, respectively (P=0). However, after 24 and 48 hours the difference in the pain was not significant between groups 1 and 2 (P=0.45) but Group 3 had relatively significant higher pain levels (P=0).

Conclusion: Infiltration of dexamethasone and ketorolac tromethamine resulted in decreased postoperative pain experience. Dexamethasone was more effective in alleviating pain within first 12 hr period after treatment. However, infiltration of dexamethasone and ketorolac tromethamine exhibited the same efficacy at 24 and 48 hours.

Keywords: Dexamethasone, Ketorolac tromethamine, glucocorticosteroids, NSAIDS, irreversible pulpitis, postoperative pain, VAS: Visual Analog Scale, VRS: Visual Rating Scale.

Introduction

Today, endodontic treatment is reminiscent of pain in the community.[1] Management of endodontic pain has a positive impact on reducing fear and anxiety in patients undergoing endodontic treatment. However, management of postoperative pain may be important, if not superior. The incidence of postoperative pain following root canal treatment has been reported to be 25% to 69% at 24 hours (Sadaf & Ahmad 2014, Pak & White 2011).[32]

During endodontic treatment there can be release of inflammatory mediators like prostaglandins.[2] Non steroidal anti-inflammatory drugs (NSAIDs) such as ketorolac, a non-selective COX inhibitor that acts by inhibiting the bodily synthesis of prostaglandins.[3,4]

Steroids have been used as intracanal medicaments and systemically as an adjunct to alleviate pain and decrease inflammation in patients undergoing endodontic treatment. Dexamethasone, a potent anti-inflammatory corticoid has the ability to reduce the synthesis of prostaglandins, leukotrienes and decrease the chemotaxis of polymorphonuclear leukocytes (Nogueira et al. 2018). Additionally, it decreases oxygen and nitric oxide free radical production by endothelial cells as well as decreases the proinflammatory cytokines (Nogueira et al. 2018). Studies have shown that dexamethasone is a potent glucocorticoid with anti-inflammatory efficacy and it's infiltration can reduce or even prevent postoperative pain in patients with irreversible pulpitis.[5]

Thus, the aim of this study was to compare the effect of dexamethasone and ketorolac infiltration on postoperative pain after single visit endodontics in lower molars with irreversible pulpitis.

Materials and methodology

A total of 70 patients were screened and selected in the out-patient clinic of the Department of Conservative dentistry and Endodontics, The Oxford Dental College, Bangalore, based on the inclusion and exclusion criteria for the study.

Inclusion criteria

Patients undergoing single visit endodontic treatment with symptomatic irreversible pulpitis in mandibular molars were included. Also, systemically healthy patients with age ranging between 18- 45 years and without gingival recession or existing periodontal disease were included.

Exclusion criteria

Teeth with periapical pathology, abcess, sinus and swelling (non vital teeth) were excluded. Patients who could not interpret the VAS, lactating and pregnant women, immune compromised patients were excluded. Also, patients having history of allergy to local anesthetic solutions and medications that influenced pain threshold, analgesics, steroids in the recent past 24 hours were also excluded.All patients fulfilling the above criteria were explained about the treatment procedure and were asked to sign a consent form. Prior to anesthetizing the treatment area, patients were asked to rate their pain using visual analog scale (VAS).

Procedure

After explanation of the treatment procedure, tooth was anesthetized with the use of 1.5 ml lignocaine, with 1:200,000 epinephrine. Inferior alveolar nerve block was administered using a 27-G needle. The tooth underwent single visit endodontic treatment with the use of gutta-percha and AH26 sealer using the single cone technique. At the end of treatment, the subjects were randomly be assigned to 3 groups, namely:-

Group 1 (n=30): 0.7 ml dexamethasone

Group 2 (n=30): 0.7 ml ketorolac and

Group 3 (n=10): 0.7 ml sterile saline as a placebo.

The severity of pain in the subjects was recorded before treatment and were asked to record their severity of pain using a checklist at 6, 12, 24 and 48 hrs postoperative intervals. Postoperative pain severity was determined using a visual analog scale (VAS). Before dismissal the patients were briefed about filling of the pain questionnaire after 6, 12, 24 and 48 hr and they were also contacted on the due time. Patients were given a non-numeric VAS ruler which had signs and a similar numerated ruler was kept by the operator who had to correlate the VAS pain signs marked by the patient to the corresponding scores from 0 to 170.

The level of pain was scored as follows:

SCORE 0 (mild pain; 0-56),

SCORE 1 (moderate pain; 57-113) and

SCORE 2 (severe pain; 114-170)

Results

Statistical Analysis

SPSS (Statistical Package For Social Sciences) version 20. (IBM SPASS statistics [IBM corp. released 2011] was used to perform the statistical analysis

Data was entered in the excel spread sheet.

Descriptive statistics of the explanatory and outcome variables were calculated by mean, standard deviation, median and IQR (based on data distribution) for quantitative variables, frequency and proportions for qualitative variables.

Inferential statistics like

- Chi-square test was applied for qualitative variables.
- ANOVA/ Kruskal-wallis test (based on normalcy test-Shapiro wilk test) was applied to check the statistical difference of pain intensity among the groups with post hoc Bonferroni / Mann-whitney test (based on normalcy test-Shapiro wilk test) for inter group comparison.
- Repeated measures ANOVA / Friedman test (based on normalcy test-Shapiro wilk test) was applied to check the statistical difference of pain intensity within the groups with post hoc Bonferroni / wilcoxon sign test (based on normalcy test-Shapiro wilk test) for comparison of pain intensity at subsequent time intervals
- The level of significance is set at 5% .

Table 1: Comparison of pain among the groups at different time intervals using kruskal-wallis test

Time intervals	Groups	Minimum	Maximum	Median	IQR	p value
B.T	Dexamethasone	120	170	120	20	0.45
	Ketorol	120	170	120	20	
	Placebo	120	170	130	33	
6 hrs	Dexamethasone	40	50	40	10	0.00*
	Ketorol	50	70	60	0	
	Placebo	80	100	90	20	
12 hrs	Dexamethasone	20	40	30	10	0.00*
	Ketorol	30	50	40	0	
	Placebo	50	60	50	10	
24 hrs	Dexamethasone	10	40	10	10	0.00*
	Ketorol	20	30	20	10	
	Placebo	30	40	30	10	
48 hrs	Dexamethasone	0	10	0	0	0.00*
	Ketorol	0	10	5	10	
	Placebo	10	20	10	0	

*significant

Dexamethasone and Ketorolac tromethamine showed clinically significant relief in pain after 6, 12, 24 and 48 hr compared with the placebo group (P=0). Similarly, there were no significant differences among the groups in terms of preoperative pain levels, but there was a difference in post-operative pain in placebo group.

Table 2: Inter- group comparison of pain at different time Intervals using post-hoc mann-whitney test

Groups	**B.T**	**6 hrs**	**12 hrs**	**24 hrs**	**48 hrs**
Dexamethasone Vs Placebo	0.23	0.00*	0.00*	0.00*	0.00*
Ketorol Vs Placebo	0.42	0.00*	0.00*	0.00*	0.00*

*p value set significant at 0.05/3=0.016

The above table shows that there is statistically significant difference in postoperative pain between the experimental groups and the placebo group at 6, 12, 24 and 48 hrs intervals (P=0.016). Also, after 24 and 48 hrs the difference in the pain was not significant between dexamethasone and ketorolac tromethamine group.

Discussion

Post-treatment pain after RCT is a common problem, particularly for the patients exhibiting pre-operative pain. It has been reported that up to 80% of these patients may experience post-operative pain and the more severe the pre-operative pain, more severe will be the post-operative pain.[8,9]

Postoperative pain is usually mild and rarely lasts longer than three days. However, some patients will suffer from a moderate to severe pain that persists for several days even after appropriate endodontic treatment. The persistent pain is often attributed to the release of inflammatory mediators such as prostaglandins, leukotrienes, bradykinin and serotonin. Consequently, peripheral and central hyperalgesia are resulted from the activation and sensitization of nociceptors by these released mediators, especially prostaglandins.[22]

Post-operative pain develops when the integrity of the periapical tissues is compromised. This can occur during endodontic treatment due to mechanical irritants such as hand instruments and obturation materials protruding beyond the minor foramen. Chemical irritation can occur if any of the solution extrudes beyond the apex. Sealers used in obturation are often both mechanical and chemical irritants since many commercially available sealers are cytotoxic.[18] In response to the tissue irritation, an inflammatory response is initiated, leading to an influx of inflammatory cells and mediators as described above, ultimately resulting in post operative pain.[20]

Disruption of the inflammatory cycle has long been the focus of pain research. The primary target sites for pharmacological approaches have been two classes of enzymes, namely: phospholipase, which synthesizes arachidonic acid from phospholipids, and cyclooxygenase, which synthesizes prostaglandins. Steroidal anti-inflammatory drugs (SAID), also known as glucosteroids, are a class of drugs that function by inhibiting phospholipase A2, thus reducing the production and concentrations of prostaglandins and leukotrienes. Non-steroidal anti-inflammatory drugs (NSAIDS), are a class of drugs that function by inhibiting cyclooxygenase enzymes, which reduces prostaglandins but does not affect leukotriene production.[7,23]

The present study was conducted to assess the effectiveness of buccal infiltration of dexamethasone (glucocorticosteroid) and ketorolac tromethamine (NSAID) on postoperative pain after single visit endodontics in lower molars with irreversible pulpitis. Pain levels were recorded at 6 hours, 12 hours, 24 hours and 48 hours postoperatively. Patients in the experimental groups had significantly lower pain levels post-operatively compared to the placebo group. Dexamethasone provided statistically significant pain relief at 6 hours and 12 hours compared to placebo, but the difference between dexamethasone and ketorolac tromethamine at 24 and 48 hours was not significant statistically.

We focused on single visit treatment due to increasing prevalence amongst endodontists of treatment completed in one visit, particularly while treating cases with irreversible pulpitis. Single visit treatments have become more common due to advancements in dental materials, namely the development of nickel titanium files rotary files. Unlike traditional hand instrumentation, rotary instrumentation removes significant amount of debris away from the apex towards the access cavity, reducing the amount of debris that is extruded from the apical foramen into the periapical tissues.[19] Nickel-titanium rotary files, as well as improved understanding of irrigation have made single appointment treatment much more accessible. Other advantages include greater patient acceptance and cost effectiveness.[29]

This study sought to evaluate post-operative pain up to forty-eight hours post treatment. Liesinger et al (1993) showed that the greatest level of post-operative pain occurred within the first twenty-four hours following treatment.[33] Their study also showed that the greatest therapeutic effects of dexamethasone were observed during this time period. By implementing a 48 hour post-

treatment observation period it became possible to fully document the post-operative pain cycle.

Dexamethasone has a biological half-life between 36-72 hours and has been classified as a long acting corticosteroid.[33] In the present study, dexamethasone was effective in decreasing the severity of pain during the first postoperative hours; in this context, even during the first 6-hour period after treatment, despite the effects of anesthetic agents, the pain in the dexamethasone group was significantly less severe than that in the other groups and this significant decrease in pain severity continued for 24 hours after treatment. The pain at the 48-hour interval was significantly less severe than that in the placebo group and similar to that in the ketorolac tromethamine group.

Ketorolac tromethamine is a member of the pyrrolo-pyrrole group, and its primary mode of action is the inhibition of the cyclo-oxygenase pathway that metabolizes arachidonic acid to prostaglandins and thromboxanes. It has been shown to be extremely effective for pain reduction from a variety of etiologies, such as oral surgery, cancer and migraine headaches. Prostaglandins play a role in the induction of inflammation, lowering the pain threshold and sensitizing nociceptors to other pain mediators, such as histamine and bradykinin. Ketorolac tromethamine acts by inhibiting the production of prostaglandins through the inhibition of cyclo-oxygenase. This provides the rationale for the efficacy of ketorolac tromethamine as an analgesic for the relief of post endodontic pain.[10, 26, 28]

Given the fact that in the present study corticosteroids were injected after the injection of lidocaine with epinephrine, which resulted in a decrease in local circulation in the area and a severe decrease in the systemic absorption of the medication, it appears that local administration of a small amount of corticosteroids will not cause any problems for patients. Therefore, short-term administration of corticosteroids in patients in which measurement of pain is more important than the complications of corticosteroids might be considered a solution for this problem.

Pain intensity is influenced by various factors, including environmental, previous experience, mental health and attitude making it a challenge to measure. Numerous scales have been used for pain intensity evaluation. Of these, the numerical rating scale (NRS), which is a scale with end points of the extremes of no pain and as bad as it could be or the worst pain. There is also the visual rating scale (VRS), which is made up of a list of descriptors that represent the level of pain intensity. It is subjective and its association with disease may be indirect; however, it is a personal qualitative judgment of patients' perception of pain strength. In this study were used the visual analogue scale (VAS) that is a 10-cm line arrangement that relates to verbal parameters.[4]

The use of dexamethasone infiltration provided statistically significant pain relief at 6 hr and 12 hr time period, compared with placebo. Ketorolac tromethamine also provided statistically significant pain relief at the 24 hr and 48 hr time period, compared with placebo. In addition, no significant differences were demonstrated between dexamethasone and ketorolac at 24 hr and 48 hr time period.

It could therefore be assumed that glucocorticoids have greater anti-inflammatory and analgesic effects than NSAIDs while considering the fact that multiple inflammatory mediators are released or produced during pulpal inflammation. Thus systemic administration of corticosteroid as an alternative strategy to decrease endodontic post-treatment pain might be suggested just in those patients who present with moderate/severe pain with irreversible pulpitis. [5,8]

According to Nobuhara et al. the average number of PMNs in the apical and middle regions of the PDL space significantly decreased following buccal infiltration of dexamethasone, but not until 48 hr postoperatively. However, this study indicated the immediate analgesic effect of dexamethasone after 6 and 12 hr. Moreover it is important to note that endodontic treatment per se has a major effect on reducing post endodontic pain regardless of analgesic intervention.[8]

Conclusion

- Root canal therapy for three groups had a statistically significant reduction in post-operative pain, demonstrating the effectiveness of root canal therapy.
- Also, infiltration of dexamethasone and ketorolac tromethamine resulted in decreased postoperative pain experience. Dexamethasone was more effective in alleviating pain within first 6 and 12 hour period after treatment.
- However, infiltration of dexamethasone and ketorolac tromethamine exhibited the same efficacy at 24 and 48 hours.

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