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Dentistry

COMPARISON OF ANTI-INFLAMMATORY EFFECT OF DEXAMETHASONE VS KETOROLAC AS PREEMPTIVE ANALGESIC IN IMPACTED MANDIBULAR THIRD MOLAR SURGERIES

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ABSTRACT **Introduction:** Impacted tooth is a tooth which is completely or partially unerupted and is positioned against another tooth, bone or soft tissue so that its further eruption is unlikely, described according to its anatomic position. Most common complications associated with the removal of the third molar include damage of the pain, sensory nerve leading to paresthesia, dry socket, infection, and hemorrhage. Severe trismus, oro-antral fistula, buccal fat herniations, iatrogenic damage to the adjacent second molar, and iatrogenic mandibular fracture may also occur, though very rarely. **Aim:** This double-blind, and randomized study was aimed to compare the efficacy of dexamethasone and ketorolac tromethamine, through the evaluation of pain, edema, and limitation of mouth opening. **Methodology:** The study group was composed of 20 adult individuals, who were indicated for surgical removal of mandibular third molars with total or partial bone impaction. Group 1 individuals received 1 capsule of 10 mg ketorolac tromethamine 1 h before surger6. Group 2 received 1 capsule of 8 mg dexamethasone 1 h before surgery. **Results:** The values obtained during the study were compared using the t test or Mann Whitney test, depending on the distribution of values. The level of significance was set at 5%. The statistical program SPSS version 26.0 was used. There was no statistically significant difference between the groups for varied pain across time (2, 6, 12, and 24 h). Post-operatively, for the dexamethasone group, mouth opening after 24 hrs, 48 hrs and 72 hrs was 42.20mm, 42.90mm and 43.60mm respectively, which was statistically significantly higher as compared to ketorolac group. Post-operatively, edema after 24 hrs, and 48 hours was lower in the dexamethasone group as compared to the ketorolac group but it was statistically insignificant .**Conclusion:** The results obtained with the use of 8 mg dexamethasone 1 hour prior to the surgical procedure at a single dose and 10 mg of ketorolac 1 hour before the employed distinctly are effective in the control of postoperative inflammation on the pain, edema, and limitation of mouth opening in the extraction of the third inferior molars.

KEYWORDS : Preemptive analgesic, Dexamethasone, NSAIDS, inflammation

INTRODUCTION

The surgical removal of the impacted third molars is one of the most common outpatient procedures performed by Oral and Maxillofacial Surgeons. Typically, an inflammatory process characterized by pain, edema, and limitation of mouth opening follows these surgeries which in turn is responsible for significant functional and aesthetic discomfort during the postoperative period and these complications may compromise quality of life and thus impair the patient's ability to perform their daily activities.[1]

The control of pain and postoperative inflammation are constant concerns of surgeons as well as the welfare of the patient after surgery, and these factors are closely linked to the success of procedures and techniques applied. In these cases, the preemptive use of anti-inflammatory drugs has the potential to reduce the intensity and morbidity of these events by inhibiting the inflammatory response prior to surgical trauma. Two classes of drugs commonly used for this purpose are corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs).

Preemptive analgesia is a concept that has currently aroused much interest, the subject of research in different areas of health. It is defined as an analgesic regimen that begins before nociception, aiming to prevent hyperalgesia and subsequent stimulus that amplifies pain.

Corticosteroids act by increasing lipocortin synthesis. Lipocortin inhibits phospholipase A2 and consequently the formation of arachidonic acid from the phospholipids that originate in cell membranes. This action results in a decreased production of inflammatory mediators such as leukotrienes, prostacyclins, prostaglandins, and thromboxane A2.[2] Dexamethasone is a long-acting corticosteroid, a synthetic analogue of prednisolone, which has a potent anti-inflammatory effect, mainly by promoting the synthesis of regulatory proteins of the inflammatory process, such as lipocortin and vasocortin.

NSAIDs are drugs which inhibit the Cyclooxygenase (COX) enzyme involved in the synthesis of chemical mediators of inflammation. NSAIDs are effective in the treatment of acute inflammatory conditions and are employed to decrease postoperative swelling and trismus, delay the onset and reduce the intensity of pain following oral surgery, with fewer undesirable adverse effects.[2] Ketorolac tromethamine is a non- selective COX inhibitor and has important analgesic, anti-inflammatory and antipyretic properties.

Thus, the objective of this study was to compare via clinical parameters the anti-inflammatory effect of 8mg dexamethasone orally and 10mg ketorolac tromethamine orally when administered prior to impacted mandibular third molars surgery. The specific aim of this study was to determine the differences in pain level, swelling and mouth opening limitation (trismus) between the two anti-inflammatory drugs.

MATERIALS AND METHODS

STUDY DESIGN

A randomized, prospective, double-blind, clinical trial was carried out, for a period of 4 months. This study was submitted and approved by the Ethics Committee of Saveetha Dental College and hospital Chennai , India. All subjects received the information regarding the research, in the form of informed consent, the objectives and rationale of the study and the benefits and the risks associated were explained to each patient. The study design was in compliance with the CONSORT (Consolidated Standards of Reporting Trials) guidelines for clinical trials.

STUDY GROUP

The study group was composed of 20 adult individuals, divided into Group 1 and Group 2 who were indicated for surgical removal of mandibular third molars with total or partial bone impaction. The inclusion criteria of the study were: Males and Females aging between 18 and 35 years. Each case was classified according to Pell and Gregory classification of impacted Mandibular third molar. To reduce the risk of classification bias, the assessment of tooth position was performed by a single subject expert in Oral and Maxillofacial Surgery in digital panoramic radiographs.

Considering its influence on the surgical procedure and/or on the evaluated outcome variables, the exclusion criteria for the study included: those individuals who were allergic to any of the drugs used in the study; who presented a disease or systemic condition that contraindicated the procedure; who were in gestation or lactation period; who used chronic medications or other substances that influence the inflammatory response; Patients whose surgical procedure lasted for equal to or greater than 40 minutes; who refused to adopt the drug regimen proposed by the study; or who refused to participate in the data collection steps.

SURGICAL PROCEDURE

According to the radiograph available, WHARFE assessment was done for the impacted teeth. Muccoperiosteal flap elevation and bone guttering was done, surgical removal of impacted teeth were performed followed by suturing using 3-0 silk.

Post operative management: Following surgery, patients were instructed to follow a liquid, pasty, cold, and high-protein diet for the first 48 postoperative hours in addition to regular general care, avoid strenuous activity and sun exposure, and refrain from using any mouthwash for the first 24 hours. The patient would be treated and removed from the study if they experienced any postoperative complications.

Every 24 hours following surgery, a new visit was planned within 24 hours (1 day), 48 hours (2 days), 72 hours (3 days), and eventually after 168 hours (7 days) to watch the research patients and submit them to the measurement of edema and mouth opening limitation. The patient would also be eliminated from the study if they, perhaps, skipped postoperative examinations, just underwent one therapeutic intervention, or used other medications that weren't indicated in the survey.

The research participants received a bottle containing 180 ml of chlorhexidine gluconate 0.12% 24 hours (1 day) after the surgery so they may use 15 ml of it every 12 hours for 6 days as mouthwash. Seven days later, suture removal was done.

Method of pain assessment—visual scale of 11 points in box: A visual scale, the Box Scale (BS-11), with a maximum possible score of 11, was employed to evaluate the presence and severity of postoperative pain. The BS-11 is a line with 11 identical boxes whose squares reflect the extreme boundaries of pain, from nonexistent to severe. Subjects were directed to record the existence and degree of pain within the first 24 hours following surgery in this line. The option that best reflected the degree of pain the patients were experiencing at that specific time was to be marked with a BX in one of the boxes of the visual BS-11, according to instructions given to the patients. The scale had 11 boxes, and it was decided that the left edge end (box 0), which was annotated as "no pain," and the opposite end, which was annotated as "worst conceivable pain" (insufferable pain), were best understood by the patient. In the next 2, 6, 12, and 24 postoperative hours, the research patients were given a visual 11-point Box Scale assessment. At the conclusion of each surgical procedure, patients were given a pain assessment protocol with scales so they may note any painful episodes and, if necessary, use analgesics. In this study, pain was only evaluated for the first 24 postoperative hours because, according to several authors, moderate to severe pain in impacted third molar surgery typically occurs during the first 12 h after surgery, reaching its peak intensity after about 6 h when a conventional local anaesthetic is used.

Method for assessment of postoperative edema: The patient's facial contour was assessed prior to surgery using the method outlined by Markovick and Todorovic. In this method, the bottom margin of the ear lobe is measured in centimetres from the tip of the chin, which corresponds to the interincisal mandibular midline (between the dental components 41 and 31). Before surgery (pre-operative) and 24, 48, 72, and 168 hours after surgery, these measurements were noted on individual recording devices (7 days). All measurements were repeated three times for operator calibration in order to validate the validity of the approach in maximum intercuspal and with the lips at rest. Small marks with Bhenna-type ink (Henafix® - Brazil) were created at the previously mentioned points (lower border of the ear lobe and interincisal midline of the tip of the chin) to assure the precision of the measurements such that the bullet points remained until 7 days postoperatively.

Evaluation of limitation of mouth opening

A caliper was used to measure the maximum mouth opening preoperatively, 24, 48, 72, and 168 hours (7 days) after surgery between the incisal edges of the maxillary central incisors and mandibular central incisors on the right side (interincisal opening). The difference between each maximal mouth opening in the postoperative period, as well as the clinical interpretation of the limitation of mouth, were taken into consideration, as well as the maximum mouth opening of the preoperative period. The mouth opening after 7 days was measured after removing the suture.

Statistical treatment of data

The values obtained during the study were compared using the t test or Mann Whitney test, depending on the distribution of values. The level of significance was set at 5%. The statistical program SPSS version 26.0 was used.

RESULTS

The total sample size for our study consisted of 20 people who took part in all phases of the research (7 women and 23 males, mean age 20.8 years, standard deviation 1.80 years). The examination of 20 participants formed the basis for the findings. There were no instances of surgical complications or negative medication reactions. The average surgery time was the same across all groups, and this uniformity in the amount of time needed for surgery in each session indicated that the degree of difficulty for extractions was also comparable. The dexamethasone group took 16.8 (±11.45) min and the ketorolac group 15.0 (±6.88) min.

According to Pell- Gregory's classification, this study found that there were 7 patients (2B), 6 patients (2C), and 2 patients (1C), meaning that 15 patients (or 75%) needed bone removal, tooth sectioning, or both, while only 5 patients (1A) (25%) needed an elevator and a mucoperiosteal flap (with intrasulcular incision without relief incision).

There was no statistically significant difference between the groups for varied pain across time (2, 6, 12, and 24 h), and Table 1 shows the comparison of pain intensity between dexamethasone and ketorolac groups. Post-operatively, there was no difference in pain intensity after 2 hrs, 6 hrs, 12 hrs and 24 hrs between two groups. It may be noted that for both groups, the greater mean pain score was presented after 6 h of surgery.

Table 2, shows the comparison of mouth opening between dexamethasone and ketorolac group. The average preoperative mouth opening the dexamethasone group was 48.20 ± 2.10 while that of the ketorolac group was 49.70± 2.06. Post-operatively, for the dexamethasone group, mouth opening after 24 hrs, 48 hrs and 72 hrs was 42.20mm, 42.90mm and 43.60mm respectively, which was statistically significantly higher as compared to ketorolac group. Again after 7 days, there was no difference in mouth opening between two groups.

For facial edema, table 3 shows the comparison of edema (in cms) between dexamethasone and ketorolac group. The average facial contour measurement preoperatively for dexamethasone group and ketorolac group was 13.20cms and 13.20cms respectively. Post-operatively, edema after 24 hrs, and 48 hours was lower in the dexamethasone group as compared to the ketorolac group but it was statistically insignificant . Again after 7 days, there was no difference in edema between two groups.

DISCUSSION

The purpose of this study was to assess the anti-inflammatory efficacy of a single dose of 8mg dexamethasone orally when compared to a single dose of 10mg ketorolac tromethamine orally when administered one hour prior to impacted third molar surgery.

Studies of the effectiveness and safety of anti-inflammatory drugs in treating postoperative oral surgery pain have historically been based on the use of single doses of research drawings [10]. However, patients typically need analgesics and/or NSAIDs for 2 or 3 days after the surgical procedure [1].

In order to achieve postoperative analgesia, Joshi et al. [6] noted that standard single dosages, whether administered prophylactically or not, are not very efficient; as a result, the anti-nociceptive medication should also be continued throughout the recovery phase.

The length of time that patients are exposed to unpleasant stimuli should be completely covered by treatment. This study's use of 650 mg of paracetamol every eight hours for three days was another contributing factor.

Many researchers have lately attempted to alter the single-dose trials of doses for many projects, but the technique and sensitivity testing employing multiple doses of analgesics and/or NSAIDs have not been effectively standardized [4].

In their investigation, Mehra et al. [7] found that a single dosage of

dexamethasone had a considerable improvement when compared to a single dose of ibuprofen (for seven days), but that improvement was significantly more pronounced when compared to a single dose of dexamethasone.

The available research shows that ketorolac tromethamine is effective at reducing moderate to severe pain during the initial postoperative hours. However, none of these studies examined their ability to relieve pain for longer than 12 hours with a single dose (8). The findings of Ong et al. (8) for this medication point to a brief action with a modest long-term impact, which may be justified by its brief half-life of about 5 hours . When you take into account the 8-hour gap between the immediate postoperative period and the second pain evaluation, this element may help to explain why it performed less well in the current study.

While many articles address the evaluation of postoperative pain using ketorolac tromethamine in a variety of dosages and administration methods (8), few studies have also examined the development of swelling and trismus during this time , whereas the impact of dexamethasone and other corticosteroids in these outcomes is better documented.

Markiewicz et al. [5]; in a meta-analysis concluded that use of corticosteroids pre-operatively was able to reduce signs and postoperative inflammatory symptoms; it has also been observed by other authors; the use of corticosteroids pre-operatively is a widely accepted option in the literature to reduce edema, limitation of mouth opening, and pain after removal of impacted third molars.

NSAIDs are less efficient than corticosteroids at reducing edema.(3)This is probably because lipocortin promotion, which inhibits Phospholipase A2, and vasocortin, a histamine release inhibitor, work together to decrease inflammation more broadly while also preventing the synthesis of eicosanoids.

In contrast to earlier research [10], which showed a significant reduction in facial edema when corticosteroids were taken alone or in conjunction with NSAID, this study found no statistically significant difference between the ketorolac group and the dexamethasone group.

When compared to NSAIDs, corticosteroids with an intermediate duration of action did not significantly reduce swelling [12]. When compared to methylprednisolone, dexamethasone, which has a longer-lasting effect, significantly reduces swelling [11]. In light of swelling's delayed onset during acute inflammation, the long-term anti-inflammatory activity appears to be crucial in the management of swelling in this sense.

In their investigation, Mehra et al. [7] found that a single dosage of dexamethasone had a considerable improvement when compared to a single dose of ibuprofen (for seven days), but that improvement was significantly more pronounced when compared to a single dose of dexamethasone.

This methodology, which was applied in numerous research [7], involved measuring the distance between the interincisal maximum mouth opening using a calliper at various postoperative intervals.

For this research, regarding the limitation of mouth opening, it was observed that there were significant differences among treatments in the periods of 24 h , 48 hrs and 72 hrs postoperatively between the dexamethasone and ketorolac tromethamine groups, and the dexamethasone group showed a lower limit of mouth opening for these periods. Corroborating the findings, Markiewicz et al. [5] and Chopra et al. [4] also found less limitation of mouth opening in the groups that used corticoids when compared to groups that used NSAID.

Nevertheless, regarding the limitation of mouth opening, López-Carriches et al. [9] when comparing 50 mg diclofenac sodium and 4 mg methylprednisolone, found no statistically significant differences in the 24 h and 7 days postoperatively.

Lopez-Carriches et al. [9]. In the analysis of 7-day postoperative period suggested that there was a significant reduction in mouth opening between the groups and the ketorolac group showed greater limitation of mouth opening , these findings are confronted with the results of this study which reveals that there was no statistical difference in mouth opening between two groups at 7 days post-operatively.

CONCLUSION

In conclusion, the results obtained with the use of 8 mg dexamethasone 1 hour prior to the surgical procedure at a single dose and 10 mg of ketorolac 1 hour before the procedure employed distinctly are effective in the control of postoperative inflammation on the pain, edema, and limitation of mouth opening in the extraction of the third inferior molars. However, after analyzing the results and verifying the similarity and difference of the same, the choice for one of the pharmacological treatments employed should take into consideration other factors such as the cost. Pharmacological treatment with dexamethasone was approximately four times lower than with ketorolac tromethamine. Due to the higher margin of safety, lower adverse effects reported in the literature and lower mouth opening limitation observed at 24 hour and 7 days postoperative in this study, the use of dexamethasone as a single dose is a viable alternative for use in routine surgical extractions of third molars.

Table 1: Comparison of pain intensity between dexamethasone and ketorolac group

Interval	Dexamethasone		Ketorolac		p value
	Mean	SD	Mean	SD	
2hrs	1.20	1.03	1.70	1.16	0.322 (NS)
6hrs	2.10	0.99	2.70	0.95	0.184 (NS)
12hrs	1.10	0.74	1.90	1.10	0.089 (NS)
24hrs	0.90	0.74	1.20	0.42	0.284 (NS)

Independent t test; Mann Whitney test; NS: Non-significant difference

Table 2: Comparison of mouth opening between dexamethasone and ketorolac group

Interval	Dexamethasone		Ketorolac		p value
	Mean	SD	Mean	SD	
Pre-op	48.20	2.10	49.70	2.06	0.124 (NS)
24hrs	42.20	1.31	40.50	1.84	0.029*
48hrs	42.90	0.99	41.10	1.29	0.008*
72hrs	43.60	1.51	42.10	0.74	0.006*
7days	46.10	1.97	46.40	3.31	0.808 (NS)

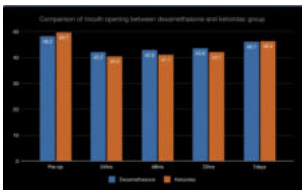
Independent t test; Mann Whitney test; * indicates significant difference at p≤0.05; NS: Non-significant difference

Table 3: Comparison of edema (in cms) between dexamethasone and ketorolac group

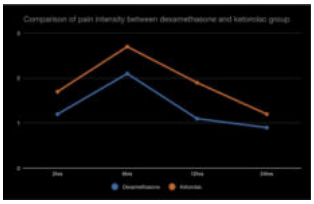
Interval	Dexamethasone		Ketorolac		p value
	Mean	SD	Mean	SD	
Pre-op	13.20	1.14	13.20	1.03	1.000 (NS)
24hrs	13.70	0.68	14.80	0.92	0.010*
48hrs	14.60	0.52	15.50	0.71	0.007*
72hrs	14.20	0.42	14.90	0.74	0.022*
7days	13.80	0.79	14.40	0.70	0.123 (NS)

Mann Whitney test; * indicates significant difference at p≤0.05; NS: Non-significant difference

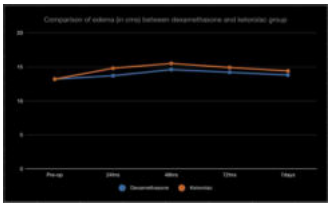
Graph 1



Graph 2



Graph 3



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