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CLINICAL EFFECTIVENESS OF THREE ANALGESIC FORMULATIONS ON POST-OPERATIVE ENDODONTIC PAIN: A PILOT STUDY

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ABSTRACT

Introduction: Pulp exposure as a sequel of dental caries continues to be a major cause of odontogenic pain which drives a patient to seek endodontic intervention. However, notable suppression of postoperative endodontic pain still remains an unresolved conundrum.

Aim: To compare the effect of single dose of 100 mg of aceclofenac, 10 mg of ketorolac and a combination of 50 mg tramadol with 75 mg diclofenac, as a pretreatment analgesic for the management of postoperative endodontic pain in patients with symptomatic irreversible pulpitis.

Materials and Methods: Thirty emergency patients with moderate to severe pain, diagnosed with symptomatic irreversible pulpitis were randomly allocated (1:1:1) to any of the three groups; aceclofenac, ketorolac, or tramadol + diclofenac. Medications were administered 30 min before beginning of the endodontic treatment. Patients recorded pain intensity on 10 cm visual analog scale (VAS) after treatment, for upto 24 h.

Results: At 24 h, mean ± standard deviation (SD) of VAS scores (in cm) for aceclofenac, ketorolac, and tramadol + diclofenac were 3.91 ± 0.31, 1.41 ± 0.96, and 1.00 ± 0.94, respectively. Kruskal-Wallis test showed significant difference among the three groups (P = 0.0000).

Conclusion: Single oral dose of 50 mg tramadol with 75 mg diclofenac and 10mg of ketorol as a pretreatment analgesic significantly reduced postoperative endodontic pain in patients with symptomatic irreversible pulpitis when compared to 100 mg of aceclofenac.

Keywords: Aceclofenac; analgesia; diclofenac; ketorolac; postoperative endodontic pain; pretreatment analgesia; tramadol

INTRODUCTION

Defining pain as merely "an unpleasant sensory and emotional experience…"[1] is an understatement when it comes to pain of endodontic origin. It is well known that irreversible pulpitis can cause a significant degree of pain.[2] The International Association for the Study of Pain advocates that the relief of pain should be recognized as a fundamental human right.[3] That's where the art and science of endodontia comes into play. Although root canal therapy ultimately rescues innumerable otherwise doomed teeth every day, postoperative and inter-appointment pain management remains a less than perfect science.[4]

A significant relationship exists between pre- and post-endodontic pain. Up to 80% of patients with preoperative pain continue to report mild to severe pain after endodontic treatment.[5] Thus, prevention and management of postoperative endodontic pain becomes an integral part of endodontic treatment.

The mechanism of action of nonsteroidal anti-inflammatory drugs (NSAIDs) is that they decrease the activity of the enzymes cyclooxygenase (COX) 1 and 2.[6] A variety of NSAIDs have been shown to produce significant reductions in dental pain using

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clinical trials. [6,7-13] Aceclofenac (phenylacetic acid derivative) has anti-inflammatory properties similar to those of diclofenac and of indomethacin. In clinical studies, it has been shown to treat dental pain effectively.[14] Ketorolac has shown high efficacy in inhibiting COX and has analgesic efficacy that is similar to standard dosages of morphine and meperidine.[15]

However, patients having gastrointestinal ulcers, bleeding abnormalities, bronchospasm, and liver function changes are contraindicated to NSAIDs. In these cases, opioids like tramadol have shown to produce significant reductions in dental pain using clinical trials.[16] Tramadol has dual mechanism of action: weak μ-opioid receptor agonism, and norepinephrine and serotonin reuptake inhibition.[17]

Due to a lack of a definitive anti-inflammatory and analgesic protocol to prevent and control the occurrence of postoperative endodontic pain[6,18] it is highly imperative to develop and standardize the best pain management strategy for such cases.

With this purpose in mind the authors designed the present study to evaluate postoperative pain in patients diagnosed with symptomatic irreversible pulpitis, receiving endodontic treatment after pretreatment analgesia with single dose of either 100 mg of aceclofenac, 10 mg of ketorolac, or 50 mg tramadol hydrochloride (IR) with 75 mg diclofenac sodium (SR) combination for the management of postoperative endodontic pain. Null hypothesis tested was that there exists no significant difference among the three groups in postoperative endodontic pain management.

MATERIALS AND METHODS

Clearance was obtained from the Institutional Ethical Committee prior to the commencement of the study. Patients reporting to the emergency wing of the endodontic clinic were randomly enrolled and allotted to three groups in to the study after obtaining a written informed consent. Subjects in all three groups were age and sex matched. Thorough history was recorded followed by clinical examinations including thermal (cold) and electrical pulp testing as well as radiographic examination.

Thirty patients diagnosed with symptomatic irreversible pulpitis in multirooted teeth with baseline pain scores greater than 6 cm on visual analog scale (VAS) were included in the study. Exclusion criteria were any drugs taken within the last 8 h; patients under any currently acting analgesics; patients with any systemic or mental illness, pregnant or lactating mothers; patients with acute endodontic abscess, periodontal diseases, and retreatment cases; and any known allergy or sensitivity to the study groups.

The selected patients were randomly assigned to any of the three study groups:

Group 1- 100 mg Aceclofenac (Zerodol – IPCA Laboratories Ltd)

Group 2- 10 mg Ketorolac (Ketorol DT - Dr Reddy Laboratories Ltd)

Group 3- 50 mg Tramadol hydrochloride (IR), 75 mg Diclofenac sodium (SR) (Durapain – Abbott Healthcare Pvt Ltd)

Single oral dose of medication was provided 30 min before the initiation of endodontic therapy. Food intake was with held for next 3 h and patients were allowed only drinking water, to prevent injury to the oral tissues by biting on the anesthetized areas.

Patients were anesthetized with 2 ml of Lignocaine (2%) with adrenaline (Xylocaine-AstraZeneca, India) followed by rubber dam isolation and access cavity preparation. Working length was determined radiographically. Cleaning and shaping was done using passive step-back technique to enlarge the canal to a minimum apical size of #30 file or larger depending on the size of the canal. Warm sodium hypochlorite (2.5%) and normal saline were used for intracanal irrigation. Finally, canals were dried with paper points and the access cavities were restored temporarily with Cavit (3M ESPE, St Paul, MN, USA). Endodontic therapy in all patients was instituted by the same operator (RK).

Each patient was provided with a postoperative pain questionnaire having VAS. Patients were encouraged to make initial preoperative pain measurement (Ti) in order to ensure patient understanding of the pain questionnaire. Patients were instructed to complete the questionnaire immediately postoperatively (T0), and after 12 (T12) and 24 h (T24). Pain intensity was recorded using VAS, which consisted of a 10-cm line anchored by two extremes, "no pain" and "worst possible, unbearable, excruciating pain". For situations when the patient could not report personally to the clinic, readings were obtained telephonically.

All the statistical calculations were made through the Statistical Package for Social Science (SPSS) version 20. The three test groups were compared for VAS score of preoperative pain and pain at T0, T12 and T24 using Kruskal-Wallis (K-W) test. Statistical significance was set at P = 0.05.

RESULTS

The analysis was carried out on the VAS scores of 30 fully compliant patients.

Table 1 : Shows the comparison of mean and standard deviations of VAS scores.

Time Intervals (hours)	Group 1 Aceclofenac N = 10	Group 2 Ketorolac N = 10	Group 3 Tramadol + Diclofenac (TD) N = 10	P value	Kruskal Wallis Test (H)	Remark
Ti	7.9±0.56	8.0±0.81	7.70 ±0.67	0.75	0.576	Not Significant
T0	4.9± 0.87	3.3 ±1.15	2.51 ± 0.76	0.0001	16.05	Significant
T12	3.41±0.84	2.21±0.42	1.71±1.25	0.0002	11.91	Significant
T24	3.91±0.31	1.41±0.96	1.00±0.94	0.0000	21.63	Significant

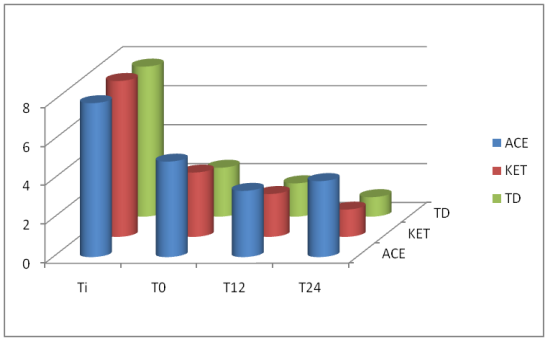

Figure 1: Mean VAS scores for the three groups (ACE- Aceclofenac, KET- Ketorol, TD- Tramadol + Diclofenac)

DISCUSSION

Notable suppression of postoperative endodontic pain remains an unresolved conundrum till date. Incidence and severity of post-operative pain has been shown to be highest after root canal filling amongst various dental procedures.[19] Instrumentation itself can be held responsible for postoperative pain in many cases.[4] Furthermore, postoperative pain is more likely to occur within the first 24 h following endodontic treatment.[20]

As postoperative endodontic pain has multiple etiologies, a multipronged approach is needed to counter the hyperalgesia with both proper endodontic technique as well as efficacious pharmacological therapy.

Since endodontic therapy was instituted by a single operator, bias was eliminated and the study focused on the pharmacology variable.

Although numerous studies have been conducted on reduction in postoperative endodontic pain after pretreatment analgesia with NSAIDs[6], few have utilized aceclofenac. Ketorolac seems to be the favorite of many authors with many studies being conducted with it.[6,11] Ketorolac peripherally inhibits prostaglandin synthesis resulting in a decreased amount of prostaglandin to sensitize pain receptors. In one study, oral formulation of 10 and 20 mg ketorolac as postoperative doses provided the same analgesia as 400 mg ibuprofen, and significantly better analgesia than acetaminophen and acetaminophen codeine combinations.[21]

Tramadol is a synthetic, centrally acting analgesic that is thought to relieve pain through synergistic monoaminergic and μ-opioid mechanisms of action.[22] It is widely used for the treatment of acute and chronic pain, but has low abuse potential[23], and unlike pure opioids, clinically relevant effects on respiratory or cardiovascular parameters are rare at recommended doses for postoperative pain.[24] Recent 2014 meta-analysis[25] suggests that tramadol provides slightly better pain management than tapentadol.

For grading the subjective parameter of pain, a single pain scale was utilized instead of multiple ones as Attar et al[18] suggested the rationale after

comparing three different pain scales for a similar study using different drugs.

Results of the present study clearly demonstrate that pain reduction was maximum in Group 3 i.e. with 50 mg Tramadol hydrochloride (IR) with 75 mg Diclofenac sodium (SR) followed by Group 2 i.e. 10 mg of ketorol and the least in Group 3 i.e. 100 mg of aceclofenac.

This is the sole study comparing these three analgesic formulations to the best of the authors' knowledge. Furthermore, this study evaluated dispersible form of ketorol versus simple tablets for other drugs. The combination of immediate and sustained release drugs in Group 3 further elucidates the potential of these in context of endodontic pain which can spiral from acute to chronic variety. These attributes make the study one of a kind.

Further studies with larger sample sizes are warranted to validate the findings of the present one. Multivariate analysis needs to be done in these to identify the role of sex, demographics, genotype etc.

SUMMARY AND CONCLUSION

Under the conditions of this study, pretreatment analgesia with single oral dose of 50 mg tramadol with 75 mg diclofenac and 10 mg of ketorol when given 30 minutes before endodontic intervention showed statistically significant reduction in postoperative pain as compared to 100 mg of aceclofenac.

The authors therefore recommend a protocol of using combination of 50 mg Tramadol hydrochloride (IR) with 75 mg Diclofenac sodium (SR) or 10 mg Ketorol preoperatively for endodontic management of moderate to severe pain which is in accordance with the WHO analgesic ladder.

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REFERENCES

1. Bonica JJ. The need of a taxonomy. Pain. 1979 Jun;6(3):247-8.

2. Matthews R, Drum M, Reader A, Nusstein J, Beck M. Articaine for supplemental buccal mandibular infiltration anesthesia in patients with irreversible pulpitis when the inferior alveolar nerve block fails. J Endod. 2009;35:343–6.

3. Delegates to the International Pain Summit of the International Association for the Study of Pain (2010). "Declaration of Montreal". International Association for Study of Pain. Available from: http://www.iasp-pain.org/DeclarationofMontreal [Last accessed on 2015 Jul 13].

4. Siqueira JF, Barnett F. Interappointment pain: Mechanisms, diagnosis, and treatment. Endod Topics 2004;7:93-109.

5. van Wijk AJ, Hoogstraten J. Reducing fear of pain associated with endodontic therapy. Int Endod J 2006;39:384-8.

6. Sethi P, Agarwal M, Chourasia HR, Singh MP. Effect of single dose pretreatment analgesia with three different analgesics on postoperative endodontic pain: A randomized clinical trial. J Conserv Dent 2014;17(6):517-521.

7. Dionne RA, Campbell RA, Cooper SA, Hall DL, Buckingham B. Suppression of postoperative pain by preoperative administration of ibuprofen in comparison to placebo, acetaminophen, and acetaminophen plus codeine. J Clin Pharmacol. 1983;23:37–43.

8. Gopikrishna V, Parameswaran A. Effectiveness of prophylactic use of rofecoxib in comparison with ibuprofen on postendodontic pain. J Endod. 2003;29:62–4.

9. Holstein A, Hargreaves KM, Niederman R. Evaluation of NSAIDs for treating post-endodontic pain. Endod Topics. 2002;3:3–13.

10. Doroschak AM, Bowles WR, Hargreaves KM. Evaluation of the combination of flurbiprofen and tramadol for management of endodontic pain. J Endod. 1999;25:660–3.

11. Penniston SG, Hargreaves KM. Evaluation of periapical injection of Ketorolac for management of endodontic pain. J Endod. 1996;22:55–9.

12. Mehrvarzfar P, Abbott PV, Saghiri MA, Delvarani A, Asgar K, Lotfi M, et al. Effects of three oral analgesics on postoperative pain following root canal preparation: A controlled clinical trial. Int Endod J. 2012;45:76–82.

13. Comfort MB, Tse AS, Tsang AC, McGrath C. A study of the comparative efficacy of three common analgesics in the control of pain after third molar surgery under local anaesthesia. Aust Dent J. 2002;47:327–30.

14. Presser Lima P, Fontanella V. Analgesic efficacy of aceclofenac after surgical extraction of impacted lower third molars. Int J Oral Maxillofac Surg. 2006;35:518–21.

15. Gillis JC, Brogden RN. Ketorolac. A reappraisal of its pharmacodynamic and pharmacokinetic properties and therapeutic use in pain management. Drugs 1997;53:139-88

16. Doroschak AM, Bowles WR, Hargreaves KM. Evaluation of the combination of flurbiprofen and tramadol for management of endodontic pain. J Endod 1999;25:660-3.

17. Grond S, Sablotzki A. Clinical pharmacology of tramadol. Clin Pharmacokinet. 2004;43(13):879-923.

18. Attar S, Bowles WR, Baisden MK, Hodges JS, McClanahan SB. Evaluation of pretreatment analgesia and endodontic treatment for postoperative endodontic pain. J Endod. 2008;34:652–5.

19. Levin L, Amit A, Ashkenazi M. Post-operative pain and use of analgesic agents following various dental procedures. Am J Dent 2006;19:245-7.

20. Menhinick KA, Gutmann JL, Regan JD, Taylor SE, Buschang PH. The efficacy of pain control following nonsurgical root canal treatment using ibuprofen or a combination of ibuprofen and acetaminophen in a randomized, double-blind, placebo-controlled study. Int Endod J 2004;37:531-41.

21. Forbes JA, Kehm CJ, Grodin CD, Beaver WT. Evaluation of ketorolac, ibuprofen, acetominophen, and an acetominophencodeine combination in postoperative oral surgery pain. Pharmacotherapy 1990;10:94-105.

22. Desmeules JA, Piguet V, Collart L, Dayer P. Contribution of monoaminergic modulation to the analgesic effect of tramadol. Br J Clin Pharmacol 1996; 41(1):7-12.

23. Cicero TJ, Adams EH, Geller A, Inciardi JA, Munoz A, Schnoll SH, et al. A postmarketing surveillance program to monitor Ultram (tramadol hydrochloride) abuse in the United States. Drug Alcohol Depend 1999; 57(1):7-22.

24. Moore RA, McQuay HJ. Single-patient data metaanalysis of 3453 postoperative patients: oral tramadol versus placebo ,codeine and combination analgesics. Pain 1997; 69(3):287-94.

25. Mercier F, Claret L, Prins K, Bruno R. A Model-Based Meta-analysis to Compare Efficacy and Tolerability of Tramadol and Tapentadol for the Treatment of Chronic Non-Malignant Pain. Pain Ther. 2014 Jun;3(1):31-44.