RESEARCH PAPER

Effect of Premedication with Meloxicam on Anaesthetic Efficacy of Combination of Mannitol Plus Lidocaine with Epinephrine in Inferior Alveolar Nerve Block: A Randomized Clinical Trial

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ABSTRACT

Introduction: The aim of this study was to assess efficacy of combination of meloxicam premedication, lidocaine formulated with mannitol for IANB success and post-operative pain in the patients diagnosed with symptomatic irreversible pulpitis performed in single-visit root canal treatment.

Methods: this study was a double-blind, randomized controlled trial done on 88 adult patients aged 18 and 65 years old with symptomatic irreversible pulpitis in mandibular molars. They were split into four equal groups. **Group 1:** 2% lidocaine with 1:80,000 epinephrine. **Group 2:** 2% lidocaine with 1:80,000 epinephrine plus 15 mg of oral meloxicam. **Group 3:** 2% lidocaine with 1:80,000 epinephrine mixed with 0.5 mol/L mannitol. **Group 4** got both the meloxicam and the mannitol enhanced lidocaine solution. Anaesthetic success, duration of anaesthesia, postoperative pain (measured using VAS] at 6, 12, 24, and 48 hours), and analgesic usage were recorded. The data was analyzed using ANOVA as well as post hoc tests.

Results: Group 4 showed maximum anesthetic efficacy of (0.95 ± 0.76), and longest duration of pulpal anesthesia (82.2 ± 3.6 mins), with statistically significant reduction in pain ratings and analgesic consumption at all time intervals ($p < 0.001$). Group 1 showed lowest anaesthetic efficacy and shortest period of pulpal anesthesia (61.05 ± 1.9 mins). There was no significant difference in the anaesthetic efficacy or pain ratings among Group 2 and 3.

Conclusion: The combination of meloxicam premedication with mannitol incorporated lidocaine significantly improved anaesthetic efficacy and postoperative effects in patients with symptomatic irreversible pulpitis. This combination represents a promising adjunct to increase the predictability of IANBs in endodontic treatment.

Keywords: IANB, Mannitol, Post -operative pain, Premedication, Single visit RCT

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INTRODUCTION

In patients with symptomatic irreversible pulpitis achieving effective pulpal anesthesia remains a constant problem in endodontic practice[1]. The primary method for mandibular anesthesia is inferior alveolar nerve block, despite its routine usage, the failure rate in symptomatic irreversible pulpitis can reach up to 35-44%. This is associated to the complex interaction of anatomical, biochemical and neurophysiological factors that exhibit failure of the standard local anesthetic technique[2].

The environment around inflamed pulp tissue is rich in inflammatory mediators, like prostaglandins, bradykinin and cytokines. They significantly change the function and threshold of nociceptors which leads to inadequate anesthesia even when clinical signs such as lip numbness are present[3]. Various mechanisms contribute to anesthetic failure in these situations. Inflammation is associated with higher expression of the tetrodotoxin-resistant sodium channels, which is less susceptible to blockade by lidocaine than tetrodotoxin-sensitive channels, thereby contributing to reduced anesthetic efficacy. Moreover, anatomical complexities, such as accessory innervation of nerves and change in position of the mandibular foramen, further inhibit predictable outcomes[4].

To address these all challenges, many adjunctive approaches have been proposed to increase the efficacy of anesthetic solutions. These include modifying the formulation of anesthetic solution or the method/technique of its delivery (e.g., buffering, increasing concentration)[5] using supplemental injections (e.g., intraosseous, intra-ligamentary)[6], and incorporating pharmacologic agents such as NSAIDs and permeability enhancers. Among the

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latter, Meloxicam an NSAID and Mannitol a permeability enhancer have emerged to be as a promising option[7].

Meloxicam 15mg is a COX-2 inhibitor, it reduces synthesis of prostaglandins and helps to decrease the peripheral sensitization of nerves[8,9]. When administered preoperatively, it may decrease pulpal inflammation and improve the success of local anesthetic techniques (Nusstein J et al). Whereas, 0.5mol/L mannitol is a hyperosmolar agent capable of temporarily disrupting the perineurium, thus increasing the permeability of nerves to local anesthetics. Previous studies have shown that mannitol, in combination with lidocaine and epinephrine, can increase the depth and duration of anesthesia (Pathak PK et al.).

This double blinded randomized clinical trial was designed to assess the combined result of meloxicam and mannitol as adjuncts to lidocaine with epinephrine during IANBs in patients with symptomatic irreversible pulpitis. The primary aim was to assess augmentation in anaesthetic efficacy, duration of anesthesia, and postoperative pain control. The study also assessed whether the combination therapy is superior to the use of each agent individually and whether it could be incorporated into standard clinical practice for better patient outcomes.

MATERIALS AND METHODS

Study Design & Population: This randomized, controlled clinical trial conducted at ITS Centre for Dental Studies and Research, Ghaziabad, after obtaining approval from the institutional ethical committee. The protocol of study was listed in the Clinical Trials Registry – India (CTRI) CTRI/2024/11/076797.

Sample Size Calculation:

Sample size estimation was performed using G*Power software version 3.1.9.7 (Heinrich Heine University, Düsseldorf, Germany). Based on findings from previous studies expected standard deviations for Groups 1 and 2 were 50 and 40, respectively, with an anticipated mean difference of 55 between the groups. The calculated effect size was 1.22, yielding an actual study power of 96.86% at an alpha level of 5% ($\alpha = 0.05$). Accordingly, the minimum required sample size was determined to be 20 members per group. Therefore, a total sample size of 80 participants was included across the four study groups.

The study has been written according to the CONSORT 2010 guidelines. The study design is illustrated by a CONSORT flowchart in Figure 1.

Eligible members were healthy people (ASA category $\leq$ II) aged 18–65 years who diagnosed with symptomatic irreversible pulpitis in mandibular molars. The diagnosis was established through scientific history, response to cold testing with the Endo-Ice (1, 1, 1, 2-tetrafluoroethane) [Hygienic Endo ice, Coltene, Switzerland], and electric pulp testing (EPT, API, India), demonstrating a prolonged or lingering response consistent with irreversible pulpitis. Radiographic evaluation ensured no periapical radiolucency and no widening of periodontal ligament.

Inclusion criteria included, mandibular molar with symptoms of lingering, spontaneous, or sharp pain, prolonged response to cold testing, a well as written well-informed consent was taken from every patient.

Exclusion criteria comprised allergy to study drugs, pregnancy or lactation, systemic conditions (ASA II and above), use of interfering medications, and presence of apical pathology. Patients were randomly assigned into one of four study groups (n = 22) the use of computer-generated random numbers by using an impartial researcher. Two participants from each group were lost to follow- up, so a complete of eighty patients had been evaluated. Allocation concealment was ensured using the Sequentially Numbered Opaque Sealed Envelope (SNOSE) approach. Each envelope contained a card indicating the group allocation and was opened after the patient consent[10]. The patients and outcome assessors have been blinded to the study groups.

The treatment groups were as follows:

• Group 1 (Control, n=20): 1.5 mL of 2% lidocaine with 1:80,000 epinephrine (Indoco Remedies Ltd.).

• Group 2 (Meloxicam, n=20): Oral pre-medication with 15 mg meloxicam (Muvera, Sun Pharmaceuticals Ltd.) one hour before administering 1.5 mL of 2% lidocaine with the 1:80,000 epinephrine.

• Group 3 (Mannitol, n=20): 1.5 mL of 2% lidocaine with the 1:80,000 epinephrine mixed with the 0.9 mL of 0.5 mol/L mannitol (Enzymes Pharmaceuticals).

• Group 4 (Combination, n=20): Oral 15 mg meloxicam premedication one hour before administering 1.5 mL of 2% lidocaine with the 1:80,000 epinephrine plus 0.9 mL of 0.5 mol/L mannitol.

Preparation of Anesthetic Solutions: Mannitol used in this study was prepared at a concentration of 0.5 mol/L. commercially available 20% mannitol contains approximately 1.098 mol/L (200 g/L ÷ 182.172 g/mol). To dilute this to 0.5 M, an equal volume of sterile water was added: 1 mL of 20% mannitol + 1 mL sterile water = 0.5 mol/L mannitol. For each patient, a fresh solution was prepared using a 3 mL Leur lock syringe, where:1.5 mL of 2% lidocaine with the 1:80,000 epinephrine was drawn, 0.9 mL of mannitol was added. The solution was gently inverted 20 times to ensure homogeneity before administration. Each mannitol vial was used for a single patient only to maintain sterility and consistency[11].

For Groups 3 and 4, 1.5 mL of 2% lidocaine with 1:80,000 epinephrine was combined with 0.9 mL of 0.5 mol/L mannitol immediately before administration, resulting in a total injection volume of 2.4 mL. The resulting solution therefore contained a lower final concentration of lidocaine than the original cartridge solution. This formulation was intentionally adopted based on previously

published studies evaluating mannitol-enhanced local anaesthetic solutions. However, it should be acknowledged that the diluted effect of mannitol may represent a potential confounding factor also should be further assessed in studies.

Clinical Procedure: The study started with the preoperative discomfort levels recorded utilizing the VAS, followed by administration of local anaesthesia, after which the depth of anaesthesia was assessed using EPT at 15-minute intervals. Access cavity preparation followed by root canal instrumentation were performed in a single visit using rotary NiTi files (ProTaper Gold, Dentsply), followed by obturation and placement of a temporary restoration under rubber dam isolation. Post- operative instructions were given, and VAS scores were collected at 6, 12, 24, and 48 hours. After rubber dam isolation, Cases without profound anesthesia were excluded from postoperative pain assessment. The secondary outcomes assessed postoperative pain experience by analysing VAS scores at designated intervals and evaluating the need for rescue analgesics, specifically the consumption of ibuprofen 400 mg taken on an SOS basis, to understand the overall analgesic effectiveness of the interventions[12].

All participants were monitored for adverse events throughout the study period. Patients were specifically questioned regarding gastrointestinal discomfort, nausea, vomiting, dizziness, headache, allergic reactions, swelling, and any other unexpected symptoms at each follow-up assessment. Any adverse event reported by the patient was documented and reviewed by the investigators.

STATISTICAL ANALYSIS

The collected data were entered into Microsoft Excel 2007 (Microsoft Corporation, Redmond, WA, USA) and analyzed using Statistical Package for the Social Sciences (SPSS) software version 23.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as mean and standard deviation (SD).

Data normality was assessed using the Shapiro–Wilk test, homogeneity of variance was evaluated using Levene's test. Intergroup comparisons were performed using one-way analysis of variance (ANOVA) to decide significant differences among the various study groups. Intragroup comparisons among different time durations were done by paired t-test. A p-value of <0.05 was considered statistically significant.

RESULTS

Demographic data of finally analysed 80 patients was comparable among all the four groups. The intergroup comparison of anaesthetic efficacy scores demonstrated statistically significant changes among the four study groups ($p < 0.05$). Group 1 (Control) exhibited the highest mean anaesthetic efficacy score (4.80 ± 1.36), indicating the greatest pain perception during access cavity preparation and consequently the lowest anaesthetic success. Group 2 (Meloxicam) and Group 3 (Mannitol) showed significantly lower mean scores of 2.50 ± 1.17 and 2.35 ± 0.89, respectively, indicating improved anaesthetic efficacy compared with the group 1. The lowest mean values were observed in Group 4 (Meloxicam + Mannitol) (0.95 ± 0.76), reflecting the highest anaesthetic success among all groups.

Post hoc analysis revealed significant differences among Group 1 and all experimental groups (Group 2, Group 3, and Group 4; $p = 0.001$), indicating that both meloxicam premedication and mannitol significantly enhanced anaesthetic efficacy compared with lidocaine alone, suggesting comparable anaesthetic performance of meloxicam premedication and mannitol supplementation. However, Group 4 demonstrated significantly lower values than both Group 2 ($p = 0.001$) and Group 3 ($p = 0.046$), indicating that the combination of meloxicam premedication and mannitol produced superior anaesthetic efficacy compared with either intervention alone.

Overall, the combination of preoperative meloxicam and mannitol with lidocaine–epinephrine achieved the greatest anaesthetic success, followed by mannitol and meloxicam alone, whereas the control group showed the least effective anaesthesia. [Table 1].

Similarly, the duration of anesthesia followed this pattern, Group 4 exhibited the longest duration (82.2 ± 3.61 minutes), significantly exceeding Group 3 (66.7 ± 1.95), 2 (64.85 ± 1.90), and 1 (61.05 ± 1.99) ($p < 0.05$). At 6 hours, Group 4 had a mean VAS of 1.65 compared to 4.5 (Group 2), 4.3 (Group 3), and 8.15 (Group 1). By 48 hours, Group 4 reported near-complete pain relief (VAS 0.05), while Group 1 remained at 3.45[Table 2].

Analgesic consumption over 48 hours supported these findings: Group 4 required the least doses (0.55), while Group 1 needed the most (2.3). Groups 2 and 3 had moderate use at 1.45 and 1.435, respectively [Table 3]. Altogether, these findings show that the meloxicam as well as mannitol combination enhances anesthetic effectiveness, extends anesthesia, lowers postoperative pain, and moreover cuts down on analgesic use more than the individual agents. Mild transient gastrointestinal discomfort was reported by 4 participants receiving meloxicam; however, no participant required discontinuation of treatment. No allergic reactions, dizziness, nausea requiring intervention, or other clinically significant complications were observed.

DISCUSSION

The findings of this randomized clinical trial show that premedication with 15mg Meloxicam NSAID, 0.5mol/L mannitol incorporated in anesthetic solution significantly improved anaesthetic efficacy and postoperative pain outcomes in participants with the symptomatic irreversible pulpitis undergoing endodontic treatment. There was no significant difference among the demographic data ($P > .05$). Among the four groups evaluated, the highest efficacy(0.95 ± 0.76), and the longest duration of anesthesia (mean: 82.2 minutes) were achieved in Group 4, where patients received both meloxicam premedication and formulation of 0.5mol/L mannitol in conjunction with lidocaine and epinephrine for the IANB.

These results support previous literature highlighting the potential of both NSAIDs and hyperosmolar additives in improving local anesthetic efficacy[13,14]. The selective COX-2 inhibitor meloxicam has been previously shown to recover IANB success in inflamed pulp. A previous randomized double-blind trial was shown by Davoudi et al in which preoperative meloxicam showed significantly better anesthetic outcomes in patients with the irreversible pulpitis, reducing the need for supplemental injections. Similarly, improved efficacy and decreased pain perception with meloxicam compared with placebo in patients receiving IANBs for inflamed teeth were stated by Modaresi et al. and Shahi et al.

The literature supports these findings, Prostaglandins, particularly PGE2, play an important role in sensitizing nociceptors and increasing the tetrodotoxin-resistant (TTX-r) expression sodium channels which are less susceptible to inhibition by local anesthetics like lidocaine15. By inhibiting COX-2 and reducing PGE2 production, meloxicam lowers nociceptor excitability, therefore enhancing nerve responsiveness to local anesthetics[15,16].

Mannitol, an inert sugar alcohol with hyperosmolar properties, has also shown significant potential in improving the efficacy of the local anesthetics. In a clinical study evaluating 3% mepivacaine with 0.5 mol/L mannitol, improved anesthetic success in patients with the symptomatic irreversible pulpitis was reported. The study concluded that mannitol temporarily disrupts the perineural sheath and opens paracellular pathways, thereby allowing better dispersal of anesthetic to nerve trunk[17,18]. A study further validated this hypothesis in an animal model, demonstrating that hyperosmolar mannitol enhanced the permeability of the perineurium without eliciting inflammatory cell infiltration[19].

In our study, while both meloxicam (Group 2) and mannitol (Group 3) individually improved outcomes over the control group, the combination group (Group 4) provided the most pronounced outcome. This suggests that the permeability enhancing and anti-inflammatory activity of mannitol and meloxicam respectively are superior. Although ketorolac was not evaluated in the present study, the anesthetic efficacy observed with meloxicam and mannitol were comparable to those reported by Aggarwal et al. for ketorolac premedication. Furthermore, Aggarwal et al. observed no significant difference in anesthetic success between ketorolac and ibuprofen in a similar affected patient population, supporting the notion that various premedication regimens may yield comparable anesthetic outcomes[20].

Postoperative pain management remained a significant concern in all groups except Group 4. Whereas, mean VAS rankings in the combination group were significantly lower at all time points on the postoperative period (6, 12, 24 and 48 hrs) compared to the other groups. These findings and conclusions are similar to those of Soltaninia et al. who demonstrated that mannitol could enhance anesthesia during surgery and have anti-inflammatory and antioxidant properties which help to reduce postoperative pain. Andre et al. suggested that mannitol may have free-radical scavenging properties, which could contribute to the modulation of inflammatory pathways and reduction of nociceptive activity associated with tissue inflammation[21]. In a similar manner, Mehrvarzfar et al[22] have found and Mahajan et al. support the use of meloxicam in endodontic pain control, which displays long lasting pain alleviating results and lessened the need for rescue drug after root canal procedures.

The results are further supported by the data on analgesics consumption. Significant fewer doses of rescue analgesics were required by patients in the formulation (Group 4) compared to other groups indicating more effective pain control in this group[23].

This design also allowed a uniform evaluation of the anesthetic activity during all points of the treatment, canal instrumentation, access preparation, and obturation, providing a full evaluation of the anesthetic activity throughout the procedure. As highlighted by Jespersen et al. and Sun et al., single-visit protocols are effective in minimizing inter-appointment pain and are ideal for evaluating immediate treatment outcomes.

The strength of present study is that it is the first study to adopt an approach including premedication with meloxicam and the use of mannitol-enhanced anaesthesia offers a promising path toward overcoming the limitations of traditional anaesthetic techniques and optimizing pain control in endodontic treatment.

The present study has several boundaries. First, it was a single centre examines with low sample size, which may limit external validity. Second, only mandibular molars diagnosed with symptomatic irreversible pulpitis have been evaluated; therefore, the findings might not be generalizable to different tooth or pulpal conditions. Third, incorporation of mannitol altered the final concentration and volume of the anaesthetic solution, introducing a potential confounding factor. Fourth, long term safety outcomes were not comprehensively evaluated. Finally, multicentre randomized medical trials with larger sample sizes are required to verify these findings and establish clinical recommendations.

CONCLUSION

Within the limits of this single-centre double blinded randomized clinical trial, the combination of meloxicam premedication and mannitol-enhanced lidocaine showed improved anaesthetic efficacy, prolonged pulpal anaesthesia and decreased rescue analgesic consumption in patients with symptomatic irreversible pulpitis. Although these findings are promising, larger multicentre studies with long-term safety assessment are required before routine clinical implementation can be recommended.

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Conflict of Interests - The authors have noted that there is no conflict of interest.

REFERENCES

1. Hargreaves KM, Keiser K. Local anesthetic failure in endodontics: Mechanisms and Management. EndodTopics. 2002; 1:26–39.
2. Abarna SJ, Chakravarthy D, Raja SV, Venkatapathi A, Soundarya S, Prasad SH. Effect of laser-assisted articaine local anesthesia in single-visit root canal treatment for mandibular molars with symptomatic irreversible pulpitis: a randomized clinical trial. *J Conserv Dent Endod*. 2026;29:430-434.
3. Karunakar P, Solomon RV, Kumar BS, Reddy SS. Evaluating the pain at site, onset of action, duration and anesthetic efficacy of conventional, buffered lidocaine, and precooled lidocaine with intraoral cryotherapy application in patients with symptomatic irreversible pulpitis: a clinical study. *J Conserv Dent Endod*. 2024;27:1228-1233. doi:10.4103/JCDE.JCDE_117_24
4. Modaresi J, Davoudi A, Badrian H, Sabzian R. Irreversible pulpitis and achieving profound anesthesia: complexities and management. Anesth Essays Res. 2016;10:3-6.
5. Singhal A, Taksande K. Role of adjuvants in enhancing the efficacy and duration of anesthesia blocks: a comprehensive review. *Cureus*. 2024;16:e69880. doi:10.7759/cureus.69880
6. Jose J, Teja K, Palanivelu A, Khandelwal A, Siddique R. Analgesic efficacy of corticosteroids and nonsteroidal anti-inflammatory drugs through oral route in the reduction of postendodontic pain: a systematic review. *J Conserv Dent*. 2022;25:9-18.
7. Pathak P, Singh A, Agrawal S, Singh D, Mali D, Kumar U. Role of 0.5 M mannitol as an adjuvant with lidocaine with or without epinephrine for inferior alveolar nerve block: a randomized controlled trial. *J Clin Exp Dent*. 2019;11:e500-e506. doi:10.4317/jced.55582.
8. Karapinar-Kazandag M, Tanalp J, Ersev H. Effect of premedication on the success of inferior alveolar nerve block in patients with irreversible pulpitis: a systematic review of the literature. Biomed Res Int. 2019;2019:6318382. doi:10.1155/2019/6318382
9. Cohen H, Reader A, Drum M, Nusstein J, Beck M. Anesthetic efficacy of a combination of 0.9 M mannitol plus 68.8 mg of lidocaine with 50 μg epinephrine in inferior alveolar nerve blocks: a prospective randomized, single-blind study. *Anesth Prog*. 2013;60:145-152. doi:10.2344/0003-3006-60.4.145.
10. Kreimer T, Kiser R, Reader A, Nusstein J, Drum M, Beck M. Anesthetic efficacy of combinations of 0.5 mol/L mannitol and lidocaine with epinephrine for inferior alveolar nerve blocks in patients with symptomatic irreversible pulpitis. *J Endod*. 2012;38:598-603. doi:10.1016/j.joen.2012.01.021.
11. Aggarwal V, Singla M, Kabi D. Comparative evaluation of effect of preoperative oral medication of ibuprofen and ketorolac on anesthetic efficacy of inferior alveolar nerve block with lidocaine in patients with irreversible pulpitis: a prospective, double-blind, randomized clinical trial. J Endod. 2010;36:375-8.
12. Soltaninia O, Shojaee M. Mannitol reduces pain and trismus after impacted mandibular third molar surgery. *J Oral Maxillofac Surg*. 2024;82:572-580. doi:10.1016/j.joms.2024.01.021
13. André P, Villain F. Free radical scavenging properties of mannitol and its role as a constituent of hyaluronic acid fillers: a literature review. *Int J Cosmet Sci*. 2017;39:355-360. doi:10.1111/ics.12382.
14. Santini M, Da Rosa RA, Ferreira MB, Barletta FB, Weissheimer T, Só MVR, et al. Medications used for prevention and treatment of postoperative endodontic pain: a systematic review. *Eur Endod J*. 2021;6:15-24. doi:10.14744/eej.2020.42787
15. Shahi S, Mokhtari H, Rahimi S, Yavari HR, Narimani S, Abdolrahimi M, et al. The effect of premedication with meloxicam on the success of inferior alveolar nerve block in patients with irreversible pulpitis. *J Endod*. 2010;36:730-733. doi:10.1016/j.joen.2010.01.015
16. Singla M, Gugnani M, Grewal MS, Kumar U, Aggarwal V. Does the presence and amount of epinephrine in 2% lidocaine affect its anesthetic efficacy in the management of symptomatic maxillary molars with irreversible pulpitis? J Dent Anesth Pain Med. 2022;22:39.
17. Kumar A, Khanna R, Srivastava RK, Ali I, Wadhwani P. Mannitol: an adjuvant in local anaesthetic solution—recent concept and changing trends. *J Clin Diagn Res*. 2014;8:ZE08-ZE11. doi:10.7860/JCDR/2014/9634.5114.
18. Gupta A, Singh TK, Gill S, Kulshrestha A, Dalai S. Comparative evaluation of supplemental buccal infiltration adjuncts for enhancing inferior alveolar nerve block in symptomatic irreversible pulpitis: a randomized double-blind clinical study. *J Conserv Dent Endod*. 2026;29:72-79.
19. Pulikkotil SJ, Nagendrababu V, Veettil SK, Jinatongthai P, Setzer FC. Effect of oral premedication on the anaesthetic efficacy of inferior alveolar nerve block in patients with irreversible pulpitis: a systematic review and network meta-analysis of randomized controlled trials. *Int Endod J*. 2018;51:989-1004. doi:10.1111/iej.12907

20. Smith S, Reader A, Drum M, Nusstein J, Beck M. Anesthetic efficacy of a combination of 0.5 M mannitol plus 127.2 mg of lidocaine with 50 μg epinephrine in inferior alveolar nerve blocks: a prospective randomized, single-blind study. *Anesth Prog*. 2013;60:3-10. doi:10.2344/0003-3006-60.1.3.

21. Nekoofar MH, Sadeghipanah M, Dehpour AR. Evaluation of meloxicam (a COX-2 inhibitor) for management of postoperative endodontic pain: a double-blind placebo-controlled study. *J Endod*. 2003;29:634-637. doi:10.1097/00004770-200310000-00004.

22. Alagappan B, Sundar S, Velmurugan N. Comparative evaluation of the effect of various transdermal patches and oral nonsteroidal anti-inflammatory drugs on postoperative endodontic pain and quality of life: a placebo-controlled randomized clinical trial. *J Conserv Dent Endod*. 2025;28:1102-1108. doi:10.4103/JCDE.JCDE_179_24.

23. Mergoni G, Ganim M, Lodi G, Figini L, Gagliani M, Manfredi M. Single versus multiple visits for endodontic treatment of permanent teeth. *Cochrane Database Syst Rev*. 2023;1:CD005296. doi:10.1002/14651858.CD005296.pub4

INTERGROUP COMPARISON OF ANAESTHETIC EFFICACY AND DURATION OF ANAESTHESIA

Table 1 Intergroup comparison of anaesthetic efficacy and duration of anaesthesia

Group	N	Anaesthetic Efficacy Mean ± SD (Range)	Duration of Anaesthesia Mean ± SD (Range, min)
Group 1 (Control)	20	4.80 ± 1.36 (1.00–7.00) [123]	61.05 ± 1.99 (57–64) [123]
Group 2 (Meloxicam)	20	2.50 ± 1.17 (0.00–4.00) [145]	64.85 ± 1.90 (62–68) [145]
Group 3 (Mannitol)	20	2.35 ± 0.89 (0.00–3.00) [246]	66.70 ± 1.95 (65–74) [246]
Group 4 (Combination)	20	0.95 ± 0.76 (0.00–2.00) [356]	82.20 ± 3.61 (75–88) [356]

Post Hoc Significance Key:

1. Group 1 (Control) vs Group 2 (Meloxicam): **Highly significant** ($p = 0.001$)
2. Group 1 (Control) vs Group 3 (Mannitol): **Highly significant** ($p = 0.001$)
3. Group 1 (Control) vs Group 4 (Combination): **Highly significant** ($p = 0.001$)
4. Group 2 (Meloxicam) vs Group 3 (Mannitol): **Not significant** ($p > 0.05$)
5. Group 2 (Meloxicam) vs Group 4 (Combination): **Highly significant** ($p = 0.001$)
6. Group 3 (Mannitol) vs Group 4 (Combination): **Significant**

INTERGROUP COMPARISON OF MEAN PAIN SCORES

Table 2 Intergroup comparison of mean pain scores

Time	Group	Mean ± SD	Post Hoc Significance[1]
Pre-op	Group 1 (Control)	8.55 ± 0.61	ns (no significant differences)
	Group 2 (Meloxicam)	8.85 ± 1.23	ns
	Group 3 (Mannitol)	8.80 ± 0.95	ns
	Group 4 (Combination)	8.65 ± 1.32	ns
6 Hours	Group 1	8.15 ± 0.67	*** (significantly higher than Groups 2,3,4)
	Group 2	4.50 ± 0.85	*, ** (vs Group 4); ns (vs Group 3)
	Group 3	4.30 ± 1.21	* (vs Group 4); ns (vs Group 2)
	Group 4	1.65 ± 0.93	–
12 Hours	Group 1	7.45 ± 0.61	*** (higher than Groups 2,3,4)
	Group 2	3.20 ± 0.95	*** (vs Group 4); ns (vs Group 3)
	Group 3	2.95 ± 0.85	*** (vs Group 4); ns (vs Group 2)
	Group 4	0.45 ± 0.51	–
24 Hours	Group 1	6.50 ± 0.89	*** (higher than Groups 2,3,4)
	Group 2	1.85 ± 0.81	*** (vs Group 4); ns (vs Group 3)
	Group 3	1.75 ± 0.79	*** (vs Group 4); ns (vs Group 2)

	Group 4	0.15 ± 0.37	–
48 Hours	Group 1	3.45 ± 1.40	*** (higher than Groups 2,3,4)
	Group 2	1.40 ± 1.08	** (vs Group 4); ns (vs Group 3)
	Group 3	1.25 ± 0.95	* (vs Group 4); ns (vs Group 2)
	Group 4	0.05 ± 0.22	–

*** : $p \leq 0.001$ (highly significant), ** : $p \leq 0.01$ (significant, * $p \leq 0.05$ (significant) ns : not significant

All Intragroup comparison are statistically significant

LEGENDS

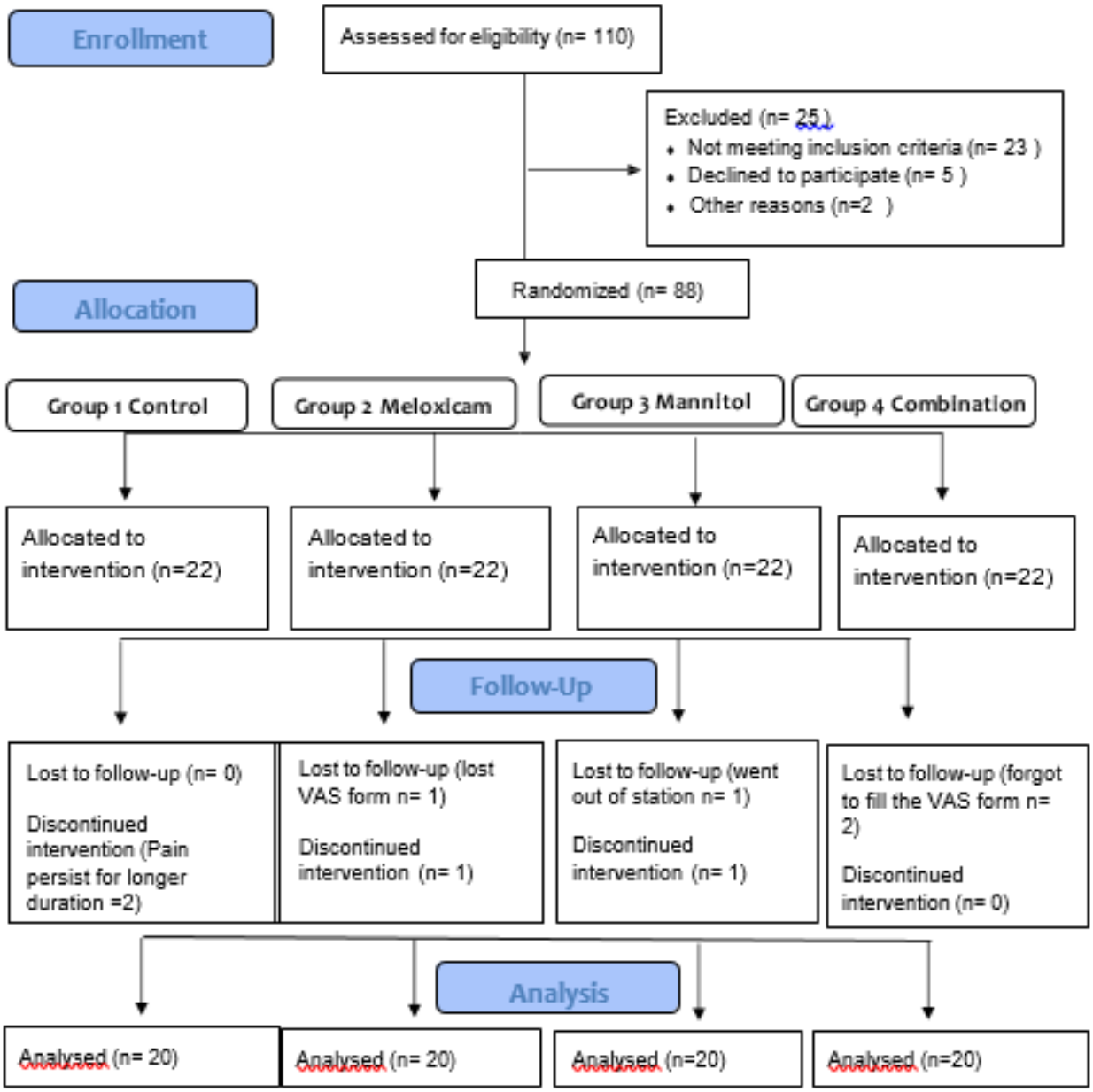

Figure 1 CONSORT Flowchart