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STUDY PROTOCOL

Title

Effect of Preemptive Oral Administration of Naproxen Sodium and Tramadol on Inferior Alveolar Nerve Block Success and Post-Endodontic Pain in Mandibular Molars with Symptomatic Irreversible Pulpitis: A Randomized Triple-Blinded Placebo-Controlled Clinical Trial

Study Design

This study was designed as a prospective, randomized, triple-blinded, placebo-controlled clinical trial conducted to evaluate the effect of preoperative oral analgesics on anesthetic success and postoperative pain following endodontic treatment.

Study Setting

The trial was conducted at the Department of Operative Dentistry/Endodontics, Dow International Dental College, Dow University of Health Sciences, Karachi, Pakistan, between [March 2023–August 2023].

Ethical Approval and Trial Registration

Ethical approval was obtained from the Institutional Review Board of Dow university of health sciences.

The study was registered at ClinicalTrials.gov (Identifier: NCT05982392). Written informed consent was obtained from all participants.

Participants

Inclusion Criteria

- Patients aged 18–60 years
- Mandibular molars diagnosed with symptomatic irreversible pulpitis
- Moderate to severe preoperative pain (VAS ≥ 4)
- Positive response to cold vitality testing
- Ability to understand pain scoring instructions

Exclusion Criteria

- Allergy to study medications or local anesthetics
- Pregnancy or lactation
- Systemic diseases contraindicating NSAIDs or opioids

- Analgesic intake within 12 hours prior to treatment
- Non-restorable teeth or periapical pathology

Sample Size

Sample size was calculated using power analysis based on expected differences in anesthetic success rates, with a significance level of 5% and study power of 80%, resulting in a required sample of 120 participants equally allocated among three groups.

Randomization and Allocation Concealment

Participants were randomly assigned to three groups using a computer-generated randomization sequence created in Microsoft Excel (Microsoft Corp., Redmond, WA, USA). Allocation codes were placed in sealed, opaque, sequentially numbered containers prepared by an independent paramedical staff member not involved in treatment or outcome assessment. Allocation concealment was maintained until completion of data analysis.

Blinding

The study employed triple blinding:

- Participants were unaware of group allocation.
- The operator performing the procedure was blinded.

- Outcome assessors and data analysts were blinded.

Medications were dispensed by trained auxiliary staff according to coded containers.

Intervention Groups

- **Group A (TML):** Tramadol 100 mg orally
- **Group B (NPX):** Naproxen sodium 550 mg orally
- **Group C (PLC):** Placebo capsule

Medication was administered 60 minutes before local anesthesia.

Outcome Measures

Primary Outcome

- Success of inferior alveolar nerve block (IANB), defined as:
 - Presence of soft-tissue anesthesia (lip and tongue numbness)
 - Negative response to cold test
 - No or mild pain during access cavity preparation (VAS 0–4)

Secondary Outcome

- Postoperative pain intensity measured using a Visual Analogue Scale (VAS) at:

- 6, 24, 48, and 72 hours postoperatively.

Anesthesia Protocol

Inferior alveolar nerve block was administered using 2% lidocaine with 1:100,000 epinephrine. Two cartridges (1.8 mL each) were administered following standard clinical protocol. Supplemental intraligamentary or intrapulpal injections were provided in cases of anesthetic failure.

Endodontic Procedure

Access cavity preparation was performed under rubber dam isolation. Working length was established using an electronic apex locator and confirmed radiographically. Canals were prepared using the ProTaper Universal system with irrigation using 3% sodium hypochlorite. Final irrigation with 17% EDTA was performed.

Obturation was completed using a single-cone gutta-percha technique with resin-based sealer. A temporary restoration was placed, and permanent restoration was provided at follow-up.

Postoperative Assessment

Participants recorded pain scores using VAS forms. Telephone reminders were used at scheduled intervals to ensure compliance. Ibuprofen 400 mg was prescribed as rescue medication; patients consuming rescue medication were excluded from postoperative pain analysis.

Statistical Analysis

All statistical analyses were conducted using SPSS version 23. Normality of continuous variables was evaluated with the Shapiro–Wilk test. Since the pain scores were not normally distributed, nonparametric tests were applied. The Kruskal–Wallis test was used to compare the three groups, followed by pairwise Mann–Whitney U tests with Bonferroni correction for multiple comparisons. Changes in pain scores within groups across different time points were analyzed using the Friedman test, with Wilcoxon signed-rank tests and a Bonferroni correction for post hoc analyses. Categorical variables were compared using the chi-square or Fisher’s exact test, as appropriate. A $p\text{-value} < 0.05$ was considered statistically significant, with adjusted significance levels for multiple testing.

Study Timeline

- Recruitment and treatment: March 2023- August 2023
- Follow-up duration: 72 hours
- Data analysis: 2023

Funding

No external funding was received.

Conflict of Interest

The authors declare no conflicts of interest.