Official Title: Local Submucosal Dexamethasone versus Methylprednisolone for Pain and Three-Dimensional Facial Edema After Impacted Mandibular Third Molar Surgery: A Randomized Controlled Trial

NCT Number: NCT Number: Pending (To be assigned upon release)

Document Date: February 27, 2026

CLINICAL STUDY PROTOCOL AND STATISTICAL ANALYSIS PLAN

1. Introduction and Objectives

The extraction of fully bone-impacted mandibular third molars routinely induces significant inflammatory sequelae, including pain and edema, which substantially impair patient quality of life. Suppressing the formation of inflammatory mediators via local pharmacological adjuncts is a well-established approach to minimize postoperative discomfort. This prospective, randomized, controlled, parallel-group clinical trial aims to compare the anti-inflammatory efficacy of local submucosal injections of dexamethasone versus methylprednisolone following impacted lower third molar surgery.

2. Study Design and Blinding

- **Study Design:** Prospective, randomized, controlled, parallel-group, single-blind clinical trial.
- **Allocation:** Computer-based randomization at a 1:1:1 ratio using consecutively numbered, opaque, sealed envelopes.
- **Blinding:** Single-blind design. Complete patient and surgeon blinding could not be achieved due to the absence of a placebo injection in the control group. However, the outcomes assessor responsible for analyzing the three-dimensional digital facial scanning data was completely blinded to group allocations.

3. Participant Eligibility Criteria

- **Inclusion Criteria:** Systemically healthy individuals (ASA I); aged 18 to 35 years; presenting with an indication for unilateral extraction of a fully bone-impacted mandibular third molar; classified as Class II–III and Position B–C according to the Pell–Gregory system; mesioangular or vertical angulation based on Winter's classification; and a moderate difficulty level (score 5–7) according to the Pederson difficulty index.
- **Exclusion Criteria:** Systemic diseases contraindicating corticosteroid use; pregnancy or lactation; use of antibiotics, systemic steroids, or anti-inflammatory drugs within the past month; history of regular daily smoking within the past six months.

4. Interventions and Arms

- **Group 1: Control Group (n = 20):** Standardized surgical extraction performed under local anesthesia. No local submucosal injection or pharmacological adjunct is administered post-extraction.

- **Group 2: Methylprednisolone Group (n = 20):** Following extraction and debridement, a local submucosal injection of 40 mg methylprednisolone sodium succinate (reconstituted to a final volume of 2 mL) is slowly delivered into the adjacent mucobuccal fold prior to primary closure.
- **Group 3: Dexamethasone Group (n = 20):** Following extraction and debridement, a local submucosal injection of 8 mg/2 mL dexamethasone sodium phosphate is slowly delivered into the adjacent mucobuccal fold in its ready-to-use form prior to primary closure.

5. Surgical and Postoperative Protocols

All surgical procedures are performed by a single experienced surgeon to ensure technical standardization. Local anesthesia is achieved using 2% articaine with 1:100,000 epinephrine. After structural flap elevation, conservative osteotomy is completed with rotary instruments under continuous sterile saline irrigation.

Postoperatively, all patients receive a standardized pharmacological protocol: amoxicillin/clavulanic acid (1000 mg, twice daily for 5–7 days), an oral rinse (0.12% chlorhexidine digluconate + 0.15% benzydamine hydrochloride), and 500 mg paracetamol every 8 hours during the first 48 hours. For severe breakthrough pain, 25 mg dexketoprofen trometamol is prescribed as a rescue analgesic.

6. Outcome Measures

- **Primary Outcome:** Change in three-dimensional facial edema from baseline to postoperative day 3. Volumetric soft tissue swelling is quantified in cubic millimeters (mm^3) via digital superimposition and surface alignment of Qlone mobile 3D scans in CloudCompare software using the root mean square (RMS) method.
- **Secondary Outcomes:** Change in three-dimensional facial edema from baseline to day 7 and day 3 to day 7; patient-reported pain intensity scored on a 10-cm horizontal Visual Analog Scale (VAS, where 0 indicates no pain and 10 indicates unbearable pain) recorded on postoperative days 1, 3, and 7; and the total consumption of rescue analgesic tablets.

7. Statistical Analysis Plan (SAP)

Statistical analyses are executed using the R programming language (v4.5.0). The sample size was calculated using G*Power software (v3.1.9.7), determining that a total of 60 participants (20 per arm) achieves 90% power ($\mathit{f} = 0.40$, $\alpha = 0.05$, $\beta = 0.10$).

- **Normality and Descriptive Statistics:** The normality of continuous distributions is verified via the Shapiro–Wilk test. Descriptive metrics are reported as Mean ± Standard Deviation (SD) or Median (Minimum–Maximum) where applicable.
- **Intergroup Comparisons:** Comparisons among the three independent parallel arms are conducted using the non-parametric Kruskal–Wallis test. For variables demonstrating statistical significance, pairwise post-hoc evaluations are executed using the Dunn test with Bonferroni adjustment. Comparisons between two independent subgroups are analyzed using the Mann–Whitney U test.

- **Correlation Analysis:** The relationships between continuous surgical variables (e.g., operation time, age, difficulty index) and clinical outcomes (VAS scores, volumetric edema) are assessed via Spearman's rank correlation analysis.
- **Interaction Assessment:** To evaluate the main effects of sex, group allocation, and the potential group × sex interaction without relying on parametric assumptions, the Aligned Rank Transform (ART) method is applied as a non-parametric two-way analysis approach. Statistical significance across all investigative domains is defined at a threshold of $\mathit{p} < 0.05$.