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Original Article

Dexamethasone-Enhanced Lignocaine for Mandibular Third Molar Surgery: A Randomized Split-Mouth Clinical Trial

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ABSTRACT

Surgical management of impacted mandibular third molars affects a region rich in blood supply and loose connective tissues, which commonly results in postoperative inflammatory reactions manifested as pain, edema, trismus, and temporary impairment of oral function. Within minor oral surgery, a comprehensive strategy to prolong anaesthetic action and lessen these unavoidable postoperative effects has not yet been thoroughly established. To assess whether incorporating dexamethasone into local anaesthetic solutions enhances the depth and duration of anaesthesia and decreases post-surgical complications following the extraction of impacted third molars. A controlled, randomized, split-mouth, double-blind prospective investigation was undertaken in 35 participants undergoing lower third molar removal. The experimental side (Group I) was administered 8 mg dexamethasone combined with 2 ml of 2% lignocaine with epinephrine, while the comparison side (Group II) received 2 ml sterile water added to 2 ml of 2% lignocaine with epinephrine. Measurements included onset and duration of anaesthesia, followed by assessments of pain, swelling, and mouth opening limitations across 7 postoperative days. Data were analyzed using independent t-tests and repeated-measures ANOVA. The dexamethasone group demonstrated a reduction in anaesthetic onset time by 69 s and an extension of duration by 128.4 min ($p < 0.001$). Pain levels during the initial 24 h (Visual Analogue Scale) were 4.9 versus 7.5 in the test and control groups, respectively ($p < 0.001$). Mean analgesic consumption through day 7 was 12.6 doses in Group I and 18.4 in Group II ($p < 0.001$). Postoperative swelling was markedly reduced in the dexamethasone group, and trismus was also diminished by 1 cm on days 1 and 2 and by 0.2 cm on day 7. Supplementing lignocaine with dexamethasone during nerve blockade accelerates the onset, prolongs anaesthetic duration, and significantly reduces pain, edema, and trismus. Direct incorporation of steroids into the local anaesthetic solution may substantially limit postoperative complications in third molar surgeries while requiring only a single injection.

Keywords: Dexamethasone, Lignocaine, Third Molar, Mandibular, Split-Mouth

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Introduction

Removal of impacted third molars is a common minor oral surgical task carried out with local anaesthesia. Numerous pharmacologic and non-pharmacologic strategies have been proposed to improve postoperative comfort after such procedures [1]. Inadequate depth and short duration of local anaesthesia may result in unnecessary discomfort during minor surgeries [2].

Extraction of third molars frequently leads to pain, swelling, bleeding, infection, trismus, and transient or lasting paraesthesia [3–5]. These postoperative reactions originate from inflammatory pathways, including vasodilation and the release of mediators such as histamine, bradykinin, and prostaglandins [6–8].

Evidence from other surgical fields [9–12] and in vivo experiments has shown that corticosteroids used

alongside local anaesthetics can extend their duration. Perineural dexamethasone as a supplement to peripheral nerve blocks has been linked to faster onset, prolonged anaesthesia/analgesia, reduced postoperative pain, and lower analgesic consumption relative to anaesthetic alone [13–16].

The prolonged analgesia associated with dexamethasone may stem from several mechanisms:

(a) activation of glucocorticoid receptors resulting in vasoconstriction and reduced systemic uptake of the anaesthetic [16];

(b) suppression of C-fibre pain transmission and a direct reduction in neuronal firing [17, 18].

Research specifically addressing the combination of dexamethasone with local anaesthetics in Oral and Maxillofacial Surgery remains limited [19–22]. Lignocaine, an amide-based anaesthetic, allows comfortable execution of minor surgeries without general anaesthesia. When paired with dexamethasone, it creates a formulation worthy of evaluation [23]. Prior work indicates that a lignocaine–dexamethasone mixture remains chemically stable, exhibits a higher pH, enhances comfort during injection, shortens onset time, and prolongs anaesthetic duration [24].

Dexamethasone, a synthetic glucocorticoid without mineralocorticoid activity [25], inhibits vascular dilation, fluid extravasation, and modestly reduces leukocyte migration, accounting for diminished swelling and trismus [26]. It is 25–50 times stronger than hydrocortisone, with a plasma half-life of 100–300 min and a biological half-life of 36–72 h, and is regarded as a highly potent anti-inflammatory agent [27].

At anti-inflammatory doses, it lacks hydrocortisone's sodium-retaining effects and also regulates transcription of anti-inflammatory genes [28–30]. A 4 mg dose produces roughly five times the normal endogenous cortisol output [31]. Its onset is around 1–2 h, allowing adequate time for membrane diffusion [32]. Corticosteroids are most effective within the first 24 h post-procedure, with activity extending up to three days [26].

The primary objective of this investigation was to determine how effectively dexamethasone, when combined with lignocaine and adrenaline, enhances the depth and prolongs the duration of local anaesthesia compared with the use of lignocaine and adrenaline alone. The secondary objective was to assess whether this steroid–anaesthetic formulation lessens postoperative outcomes, including pain, edema, and trismus, as well as to document any adverse reactions associated with administering the dual-agent mixture.

Materials and Methods

A prospective, randomized, split-mouth, double-blind clinical study was conducted at the Department of Oral and Maxillofacial Surgery, Manipal College of Dental Sciences, Mangalore. Individuals reporting to the outpatient clinic for surgical extraction of impacted mandibular third molars between December 2020 and November 2022 were enrolled. Using the specified formula, the required sample size was determined to be 70.

$$n = \frac{2[Z_{1-\frac{a}{2}} + Z_{1} - \beta]^{2}\sigma^{2}}{d^{2}} \quad (1)$$

$Z_{1-\frac{a}{2}}$=1.96 is a standard normal value at 5% level of significance.

$Z_{1}-\beta$=0.84 is a standard normal value at 80% power

σ = combined standard deviation = 2.195

d = clinically significant difference = 1.5

With a 95% confidence interval, the sample size in each bilateral was 35, and the total sample size was 70. After securing approval from the Institutional Ethics Committee (IEC), individuals presenting to the Oral and Maxillofacial Surgery outpatient clinic for management of impacted mandibular third molars were evaluated for study eligibility. Once written informed consent was obtained, 35 ASA II patients aged 18–45 years who required bilateral mandibular third-molar removal in class II position B and showed no evidence of acute inflammation, marked decay, pain, or pathology adjacent to the third molars were recruited. Exclusion criteria included: active infection, a history of peptic ulcer disease, diabetes mellitus, endocrine disturbances, hypertension, renal disorders, bleeding tendencies, obesity, hypersensitivity to any study-related materials, antibiotic use within the previous 2 weeks, NSAID use in the previous 1 week, pregnancy, lactation, or unwillingness to participate.

Screening

Individuals arriving at the Manipal College of Dental Sciences, Mangalore, for the extraction of impacted third molars underwent screening. During the initial consultation, bilateral impactions and adequate gingival coverage permitting flap closure without tension were confirmed clinically. Radiographic evaluation—using either an Orthopantomogram or intraoral periapical view—verified the tooth's position relative to surrounding structures. The medical and dental history, combined with imaging, was reviewed to identify any basis for exclusion. All potential

participants were briefed on the surgery and the nature of the clinical investigation. None displayed pain, trismus, or swelling at the time of extraction.

Randomization and blinding procedure

Upon confirming eligibility and obtaining written consent, demographic details (name, age, sex) and clinical variables (contraceptive use in the past month, psychotropic medication use, and smoking quantified as cigarettes per day) were documented. Each participant was assigned a unique identifier, and allocation of the surgical side was determined via simple randomization. Using Microsoft EXCEL, odd numbers were designated on the left side and even numbers on the right. The selected side received 2 ml of 2% lignocaine with 1:200,000 adrenaline plus 2 ml of 8 mg dexamethasone, whereas the alternate side was given 2% lignocaine with 1:200,000 adrenaline plus 2 ml of sterile water.

The opaque envelope technique was used for allocation concealment: each participant's materials were placed inside an opaque container labeled with the injection side and marked with their unique code. Blinding was maintained by having the operator administer injections using syringes prepared beforehand by a co-investigator who handled randomization and envelope management. The 5 ml syringes containing 2 ml of 2% lignocaine with 1:200,000 adrenaline plus 2 ml dexamethasone (8 mg) formed the test mixture, while control syringes contained 2 ml of 2% lignocaine with 1:200,000 adrenaline with 2 ml water. Each surgical side was assigned to one of the two formulations according to the randomization chart.

A single clinician performed all procedures, reducing variability. Prior to surgery, all participants rinsed with 0.12% chlorhexidine for 20 s. The allocated anaesthetic (test or control) was loaded into a 5 ml syringe, and inferior alveolar, lingual, and long buccal nerve blocks were delivered using a 26-gauge, 45 × 38 mm, 1.5-inch needle.

Microsoft EXCEL-generated numbers provided simple randomization for 35 impaction sites in each group, with each patient acting as their own control. Opaque envelopes ensured concealment throughout. Syringes were handed to the operator by the co-investigator, maintaining the allocation system.

The same surgical approach—buccal guttering combined with sectioning—was used for every patient. On the day of treatment, each participant received 1 g of amoxicillin prior to surgery. A single prophylactic dose was considered adequate for perioperative coverage while reducing the potential for adverse reactions and antibiotic resistance. Because extraction procedures did not exceed 3 h, no additional dosing was required. The 1 g dosage was selected since its plasma concentration comfortably exceeds the minimum inhibitory concentration for bacteria commonly implicated in surgical infections [33–36].

Facial measurements were obtained with 2–0 nylon and a millimeter ruler before the procedure and again at 24 h, 48 h, and 1 week post-operatively. Permanent markers were used to designate anatomical landmarks, including the angle of the mandible, tragus, labial commissure, nasal border, lateral canthus, and soft pogonion. The recorded distances were:

D1 – Angle of mandible to tragus
D2 – Angle of mandible to lateral canthus
D3 – Angle of mandible to nasal border
D4 – Angle of mandible to labial commissure
D5 – Angle of mandible to soft-tissue pogonion

Because postoperative edema involves irregular three-dimensional tissue expansion, exact quantification is challenging. The swelling that follows surgical trauma can intensify trismus, which itself arises from multiple contributing mechanisms.

Mouth opening was evaluated by determining the inter-incisal distance with a divider before surgery, and again at 24 h, 48 h, and 1 week after the intervention. All findings were documented on a standardized Proforma. Participants returned after 4 weeks for the extraction of the third molar on the opposite side using the identical workflow.

A total of 4 ml of local anaesthetic—combined with either dexamethasone or sterile injectable water—was delivered to anesthetize the inferior alveolar, lingual, and long buccal nerves, adhering to randomization and blinding procedures. The onset of numbness was noted as the interval from the injection to the point when the patient reported complete absence of pain to a gentle probe in the canine and molar areas, verified every 20 seconds. Removal of the impacted lower third molar was completed under local anaesthesia in an aseptic setting. Anaesthesia duration was defined from the first sensation of mild–moderate discomfort until the individual no longer felt pain to an atraumatic stimulus. All participants were given Paracetamol 650 mg orally as needed and instructed to use Chlorhexidine mouthwash three times daily.

Patients rated their discomfort using a 0–10 VAS scale, where 0 indicated no pain, and 10 represented maximal pain. The effective analgesic period of the nerve block was defined as the interval between the onset of numbness and the point when pain rose to a mild–moderate level.

Pain scores (VAS) and the number of analgesics consumed were recorded every 24 h for 1 week.

Postoperative swelling was assessed from facial linear measurements at 24 h (POD1), 48 h (POD2), and 1 week (POD7).

Trismus was documented by maximal inter-incisal opening at 24 h, 48 h, and 1 week. Subjects were seen again after 4 weeks for treatment of the contralateral side following the same protocol.

Data assessment was performed using IBM SPSS Statistics for Windows, Version 25.0 (Armonk, NY: IBM Corp.).

Quantitative variables—including anaesthetic onset and duration, facial swelling, pain scores, and mouth-opening values—were summarized as means with standard deviations for comparison between experimental and control arms.

Independent t-tests were used to compare the onset and duration of anaesthesia, swelling, pain intensity, and mouth opening between groups. Repeated-measures ANOVA examined changes in swelling and inter-incisal distance from baseline to 24 h, 48 h, and 1 week. A p-value <0.05 was considered statistically meaningful.

Normality testing confirmed that the variables followed a normal distribution, validating the use of t-tests.

The methodology was reported according to CONSORT guidelines [11]. The clinical trial was registered with CTRI (registration number: CTRI/2021/08/035560).

Results and Discussion

Enrolment and random allocation of participants are illustrated in **Figure 1.**

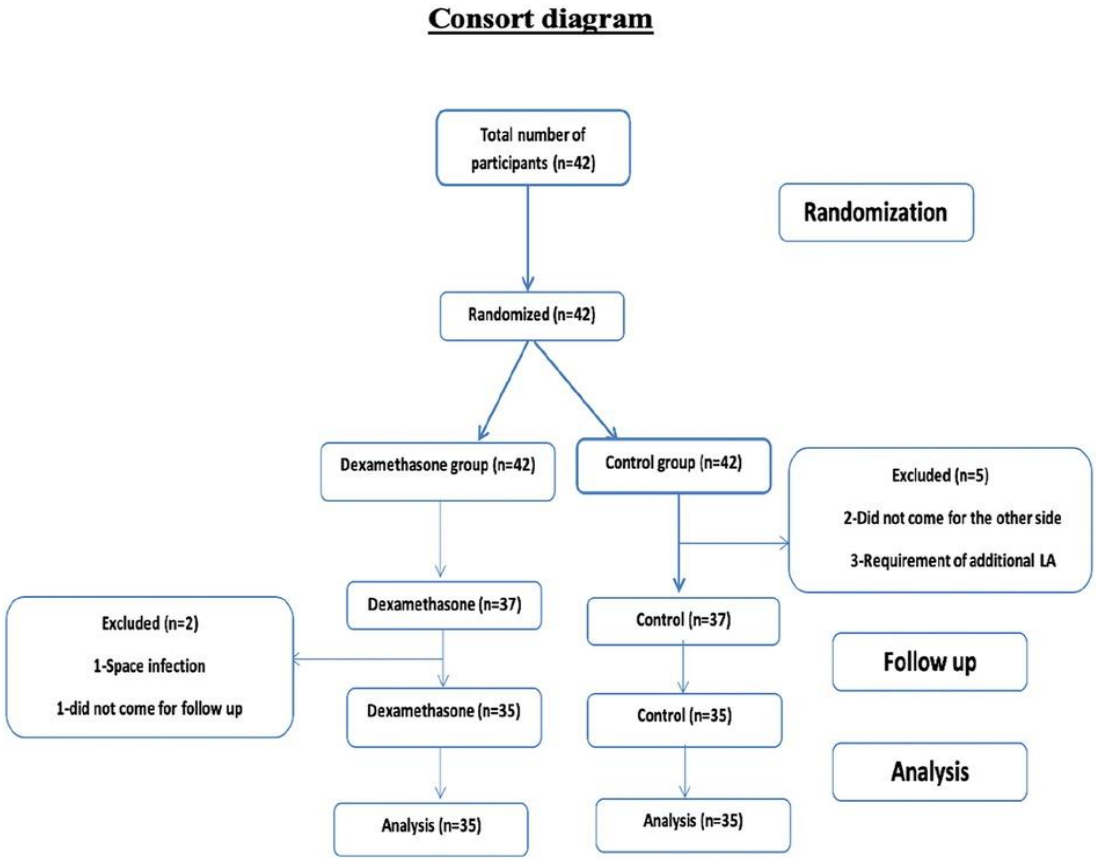

Figure 1. CONSORT diagram illustrating participant flow.

The values for anaesthetic onset and duration in the test versus control conditions are displayed in **Table 1**.

Table 1. Onset and duration of anaesthesia in test and control groups.

Parameter	Test Group Mean	Test Group SD	Control Group Mean	Control Group SD	p-value
Onset (seconds)	118.7	34.7	187.7	52.5	<0.001
Duration (minutes)	240.3	44.3	111.9	24.3	<0.001

Facial swelling, calculated using distances between fixed anatomical landmarks (D1–D5) **(Figures 2–5)**, was significantly lower in the test group ($p < 0.001$) compared with the control arm **(Tables 2–6)**.

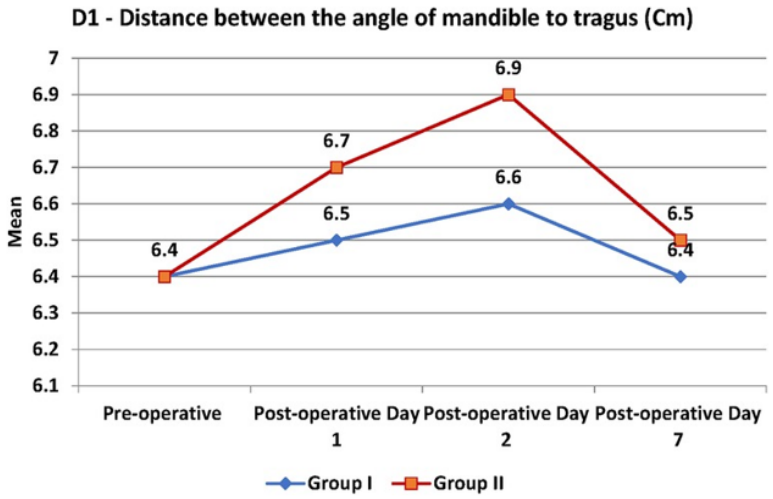

Figure 2. D1—distance from mandibular angle to ear tragus.

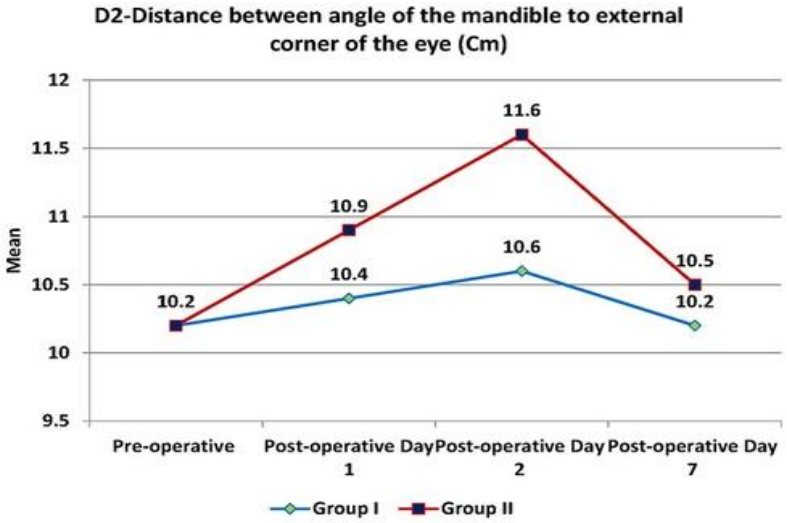

Figure 3. D2—distance from mandibular angle to external canthus.

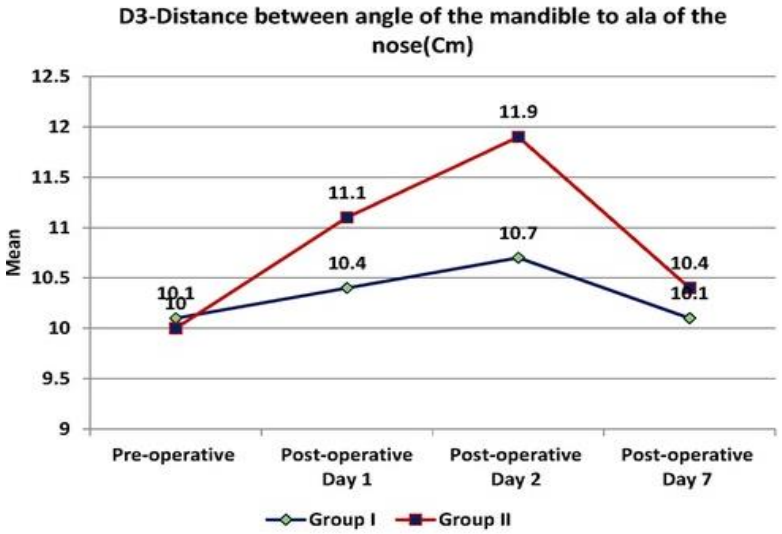

Figure 4. D3—distance from mandibular angle to nasal ala.

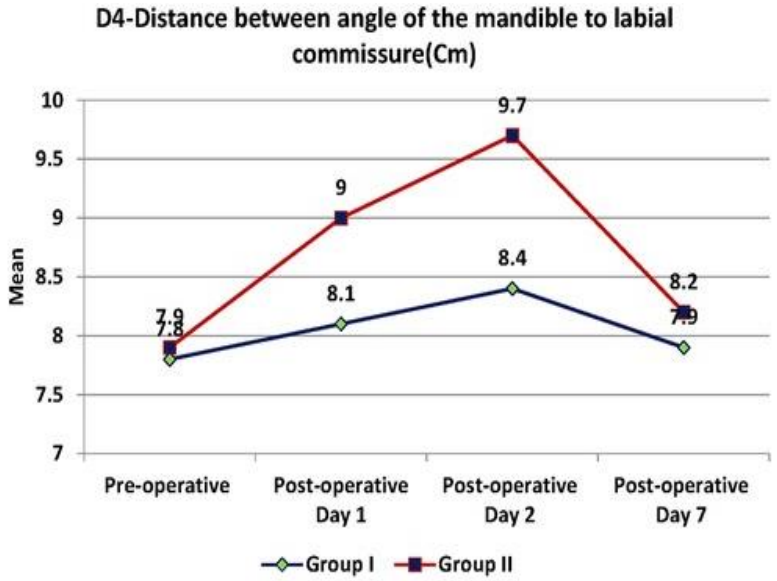

Figure 5. D4—distance from mandibular angle to oral commissure.

Table 2. D1—Mandibular angle to tragus distance.

Measurement Time Point	Test Group		Control Group		p-value
	Mean	SD	Mean	SD	
Before surgery	6.4	0.9	6.4	0.9	0.999
First day after surgery	6.5	0.9	6.7	1.0	0.408
Second day after surgery	6.6	1.0	6.9	1.1	0.135
Seventh day after surgery	6.4	0.9	6.5	1.0	0.766
Between-group comparison					0.500
Within-subject change over time					<0.001

Baseline distance was 6.4 cm in both groups. In group I, values were 6.5 cm on POD1, 6.6 cm on POD2, and returned to 6.4 cm by POD7. In group II, the corresponding measurements were 6.7 cm on POD1, 6.9 cm on POD2, and 6.5 cm on POD7. No intergroup differences reached significance ($p > 0.05$), though a significant within-subject change over time was observed ($p < 0.001$).

Table 3. D2—Mandibular angle to external canthus distance.

Measurement Time Point	Test Group		Control Group		p-value
	Mean	SD	Mean	SD	
Before surgery	10.2	1.1	10.2	1.1	0.933
First day after surgery	10.4	1.2	10.9	1.2	0.120
Second day after surgery	10.6	1.2	11.6	1.4	0.004
Seventh day after surgery	10.2	1.1	10.5	1.2	0.362
Between-group comparison					0.149
Within-subject change over time					<0.001

Initial measurement was 10.2 cm in both arms. In the test group, swelling measured 10.4 cm on POD1, 10.6 cm on POD2, and 10.2 cm on POD7. In the control arm, values were 10.9 cm, 11.6 cm, and 10.5 cm for POD1, POD2, and POD7, respectively. There was a statistically significant 1 cm difference on POD2 ($p = 0.004$), favouring the test group. At all other time points, differences were nonsignificant ($p > 0.05$). Significant temporal changes occurred within subjects ($p < 0.001$).

Table 4. D3—Distance from mandibular angle to nasal ala

Measurement Time Point	Test Group		Control Group		p-value
	Mean	SD	Mean	SD	
Before surgery	10.1	1.0	10.0	1.0	0.952
First day after surgery	10.4	0.9	11.1	1.0	0.003
Second day after surgery	10.7	0.9	11.9	0.9	<0.001
Seventh day after surgery	10.1	1.0	10.4	1.0	0.247
Between-group comparison					0.016
Within-subject change over time					<0.001

At baseline, the mandibular angle–to–ala measurement was 10.1 cm in group I and 10 cm in group II. In the test arm, values increased to 10.4 cm on POD1, 10.7 cm on POD2, and returned to 10.1 cm by POD7. The control arm recorded 11.1 cm on POD1, 11.9 cm on POD2, and 10.4 cm on POD7 **(Table 4)**. Intergroup differences of 0.7 cm and 1.2 cm on POD1 and POD2 were statistically meaningful ($p = 0.003$ and $p < 0.001$), favouring the test group. Significant temporal and between-group changes were also detected ($p < 0.001$ and $p = 0.016$).

Table 5. D4—Distance from mandibular angle to oral commissure

Measurement Time Point	Test Group		Control Group		p-value
	Mean	SD	Mean	SD	
Before surgery	7.8	0.9	7.9	0.9	0.939
First day after surgery	8.1	0.9	9.0	1.0	<0.001
Second day after surgery	8.4	1.0	9.7	1.1	<0.001
Seventh day after surgery	7.9	0.9	8.2	0.9	0.184
Between-group comparison					0.007
Within-subject change over time					<0.001

Initial values were 7.8 cm for group I and 7.9 cm for group II. Group I showed postoperative distances of 8.1 cm (POD1), 8.4 cm (POD2), and 7.9 cm (POD7). Group II recorded 9.0 cm on POD1, 9.7 cm on POD2, and 8.2 cm on POD7 **(Table 5).** Differences of 0.9 cm and 1.3 cm on POD1 and POD2 were significant ($p < 0.001$), again indicating lower swelling in the test arm. Both within-subject and between-group effects were significant ($p < 0.001$ and $p = 0.007$).

Table 6. D5—Distance from mandibular angle to soft-tissue pogonion

Measurement Time Point	Test Group		Control Group		p-value
	Mean	SD	Mean	SD	
Before surgery	11.4	0.9	11.4	0.9	0.979
First day after surgery	11.6	0.9	11.9	1.1	0.176
Second day after surgery	11.7	0.9	12.2	1.0	0.046
Seventh day after surgery	11.4	0.9	11.6	1.0	0.524
Between-group comparison					0.290
Within-subject change over time					<0.001

The baseline measurement for both groups was 11.4 cm. In group I, distances were 11.6 cm at POD1, 11.7 cm at POD2, and 11.4 cm at POD7. Group II showed 11.9 cm on POD1, 12.2 cm on POD2, and 11.6 cm on POD7 **(Table 6)**. A significant 0.5 cm difference on POD2 was seen ($p = 0.046$). Temporal variation within subjects was also significant ($p < 0.001$).

Trismus assessment used the maximum inter-incisal distance (MID). The test group demonstrated significantly greater mouth opening than the control group ($p < 0.001$) **(Figure 6)**. MID in the test arm was 4 cm on POD1, 4.1 cm on POD2, and 4.4 cm on POD7

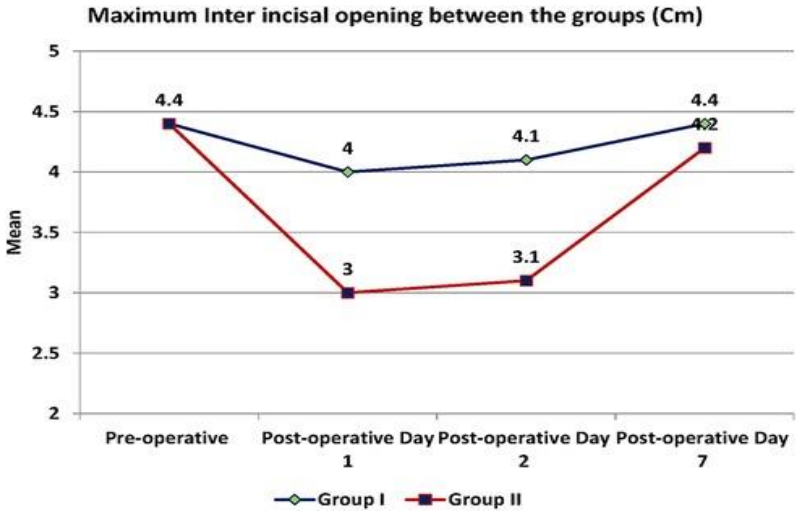

Figure 6. Maximum inter-incisal distance.

The control arm showed 3 cm on POD1, 3.1 cm on POD2, and 4.2 cm on POD7 **(Table 7)**. Pre- and postoperative photographs are shown in **Figure 7.**

Table 7. Maximum inter-incisal distance

Measurement Time Point	Test Group		Control Group		p-value
	Mean	SD	Mean	SD	
Before surgery	4.4	0.4	4.4	0.4	0.976
First day after surgery	4.0	0.4	3.0	0.4	<0.001
Second day after surgery	4.1	0.4	3.1	0.4	<0.001
Seventh day after surgery	4.4	0.4	4.2	0.4	0.013
Between-group comparison					<0.001
Within-subject change over time					<0.001

Baseline MID was 4.4 cm in both groups. Group I had postoperative values of 4 cm (POD1), 4.1 cm (POD2), and 4.4 cm (POD7). Group II recorded 3 cm on POD1, 3.1 cm on POD2, and 4.2 cm on POD7. Significant differences on POD1, POD2, and POD7 were found ($p < 0.05$), with better postoperative opening in the test arm. Between-group and within-subject differences over time were both significant ($p < 0.001$).

Figure 7. Clinical views before and after surgery.

Pain outcomes were evaluated using VAS scores **(Table 8)** and the total analgesic intake recorded each 24-h period during the first postoperative week **(Figure 8).** The mean number of analgesics taken by each group is illustrated in **Figure 9**. Both metrics showed markedly lower pain in the test arm ($p < 0.001$).

Table 8. VAS pain ratings.

Time Point	Test Group		Control Group		p-value
	Mean	SD	Mean	SD	
First 24 hours after surgery	4.9	0.7	7.6	0.5	<0.001
Post-operative Day 1	4.5	0.7	7.5	0.6	<0.001
Post-operative Day 2	3.9	0.6	6.6	0.9	<0.001
Post-operative Day 3	2.9	0.8	5.9	0.9	<0.001
Post-operative Day 4	1.9	0.8	4.6	1.2	<0.001
Post-operative Day 5	0.7	0.6	3.3	1.2	<0.001
Post-operative Day 6	0.1	0.3	2.3	1.1	<0.001
Post-operative Day 7	0.0	0.2	1.5	1.1	<0.001
Between-group comparison					<0.001
Within-subject change over time					<0.001

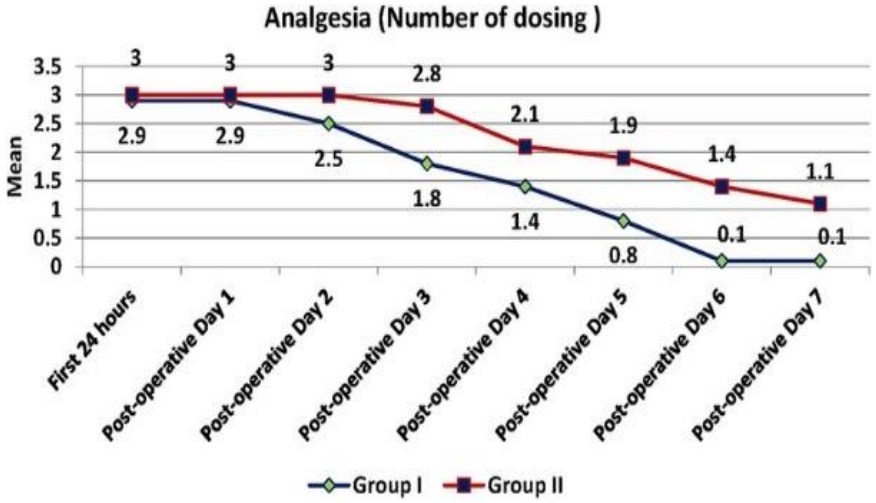

Figure 8. Analgesic dosing patterns during the first 7 postoperative days.

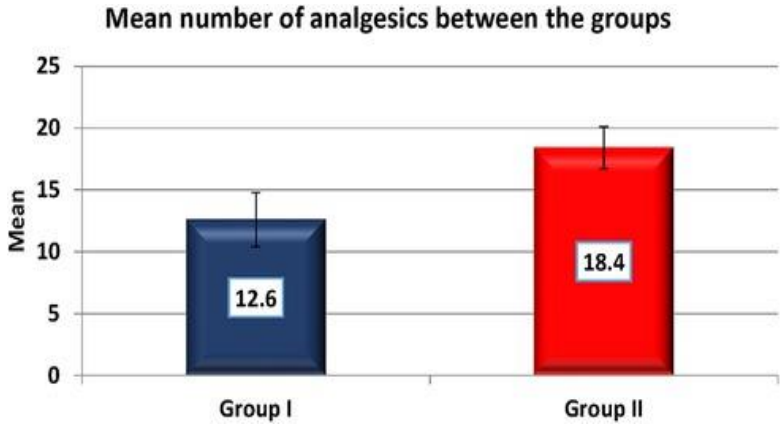

Figure 9. Mean cumulative analgesic intake in each group.

The first analgesic dose occurred 2 h later in the test arm, corresponding to the perceived duration of the nerve block until mild–moderate discomfort appeared; this was statistically significant ($p < 0.001$). Total analgesic consumption across 7 days also differed

significantly: 12.6 doses in the test group vs. 18.4 in the control group ($p < 0.001$).

Dexamethasone, a strong anti-inflammatory agent, is frequently administered to help mitigate surgery-related discomfort. Although various methods of giving dexamethasone have been documented, reports examining its combination with local anaesthetics to lessen postoperative reactions are limited. Operations involving third molars commonly lead to pain, edema, and restricted mouth opening, often impairing daily functioning, particularly during the initial 72 h [37]. Even simple extractions can be unpleasant, but removing an impacted lower third molar is highly technique dependent, involves manipulation of both bone and soft tissues, and carries a considerable infection risk due to its proximity to key fascial spaces of the head and neck [38–40]. The magnitude of these postoperative symptoms is influenced by intraoperative tissue handling, the extent of bone cutting, and the length of the procedure itself. Peak discomfort after third-molar removal is generally noted between 3 and 5 h after surgery [41, 42]. Insufficient pain control during this early interval can lead to mechanical sensitisation of the nerve, producing hyperalgesia [43]. This highlights the importance of pre-emptive analgesia or the need for stronger medication, especially given the relatively brief effect of lignocaine. Bupivacaine may prolong pain relief and reduce additional analgesic use, but its application is restricted due to the possibility of cardiotoxic effects [44]. Thus, combining strategies that extend anaesthetic duration and diminish postoperative inflammation is essential to reduce patient discomfort after removal of impacted mandibular third molars.

In this investigation, 8 mg of Dexamethasone was added to 2% Lignocaine with adrenaline, compared with a control mixture consisting of 2% Lignocaine with adrenaline plus sterile water. Both formulations were used for nerve blocks, and the onset and duration of anaesthesia were assessed. Postoperative variables—swelling, trismus, and pain—were also monitored.

Paracetamol was selected as the rescue drug because it provides moderate analgesia and has minimal anti-inflammatory activity owing to its weak inhibition of COX enzymes [45].

The results of the present work show that supplementing lignocaine with dexamethasone accelerates the onset of numbness and significantly lengthens the anaesthetic effect, allowing patients to better tolerate the peak pain period occurring within the first 3–4 h. Additionally, subjects in the test arm reported lower discomfort during the initial 24 h and across the 7-day period, with fewer analgesics consumed.

Glucocorticoids are believed to extend the duration of anaesthesia by restricting potassium channel-dependent discharge from nociceptive C fibres through glucocorticoid receptor interactions at the ion-channel level [46]. Although this mechanism does not produce anaesthesia by itself, it enhances the effect of local anaesthetics when deposited around nerves by keeping membranes hyperpolarised for a prolonged period [47]. Our observations regarding shorter latency and longer anaesthesia are consistent with previous findings in which dexamethasone administered perineurally extended the duration of bupivacaine-based anaesthesia [48, 49].

Movafegh *et al.* also reported that adding dexamethasone to lidocaine markedly extended sensory blockade of the axillary brachial plexus by 144 min, with a p-value <0.001 [50]. Corticosteroids stimulate the formation of intracellular proteins that prevent phospholipase A2 activation, thereby limiting the formation of arachidonic acid and subsequently reducing prostaglandins, leukotrienes, and other mediators linked to inflammation and pain. Unlike NSAIDs, corticosteroids intervene at the earliest point of the inflammatory pathway and demonstrate greater benefit when administered prior to the procedure [51]. Dexamethasone additionally produces mild to moderate vasoconstriction, helping retain the anaesthetic solution around the nerve for a longer period, which contributes to extended numbness [52]. The marked reduction in swelling and restricted mouth opening in the test group is likewise explained by the established anti-inflammatory properties of corticosteroids. The biochemical basis for the faster onset associated with dexamethasone remains uncertain, although clinical data consistently support its presence. Further investigation is needed to clarify this aspect.

The incorporation of corticosteroids has become increasingly common in oral and maxillofacial surgical practice, yet the optimal mode of delivery remains debated. Various systemic and local options—including intramuscular, intravenous, oral, submucosal, and endo-alveolar powder applications—have been described in the literature [53]. In this study, combining a steroid with a local anaesthetic in a single injection provided four distinct advantages while requiring only one needle penetration.

Drug uptake is strongly influenced by the vascular characteristics of the target site. The pterygomandibular space, which is routinely accessed during inferior alveolar nerve block administration,

contains abundant vasculature and loose connective tissue with minimal fibrous resistance. These anatomical features support rapid dispersion and absorption of injected agents as well as minimal needle deviation [54].

Structurally, the mandible consists of a dense cortical layer surrounding a thick cancellous centre, and areas such as the ramus and condyle retain hematopoietic marrow into adulthood—including beyond age 25 years [55]. This marrow hosts a capillary–venous network with discontinuous endothelial linings, enabling swift exchange between circulating blood and substances deposited into the surrounding tissue [1, 55]. Consequently, intra-osseous injection in this region may permit enhanced anaesthetic diffusion.

Applying steroids locally may offer distinct advantages, as the drug directly modulates eicosanoid release at injury sites, subsequently suppressing inflammatory cascades [56, 57]. Eicosanoids—derived from 20-carbon polyunsaturated fatty acids, particularly arachidonic acid—are central mediators of immune and inflammatory activity and include prostaglandins, thromboxanes, leukotrienes, and lipoxins [57–59].

Although perioperative steroids show clear clinical value, their routine integration into oral and maxillofacial surgery protocols remains inconsistent. Based on our findings, the steroid–anaesthetic combination appears to reduce predictable postoperative discomfort without producing any adverse reactions.

Dexamethasone demonstrates an anti-inflammatory potency approximately 20–30 times greater than cortisol and possesses a biological t1/2 of 36–54 h, making it well suited as a single-dose agent for mitigating postoperative sequelae associated with third molar removal [60, 61].

Our results parallel those of Shivanagi *et al.*, who reported superior intra- and postoperative comfort in test groups receiving similar mixtures, although their formulation utilised bupivacaine and ropivacaine as the local anaesthetic components [62].

Only a limited number of investigations have explored whether adding dexamethasone to local anaesthetic solutions accelerates the onset or extends the duration. Broader clinical trials are necessary to confirm the efficacy of steroid–anaesthetic blends, establish pharmacokinetic profiles across delivery routes, determine whether they reliably enhance anaesthetic quality, and assess their impact on analgesic requirements. Standardisation of dexamethasone dosing remains another critical unmet need.

Clinically, lignocaine combined with dexamethasone demonstrated favourable outcomes in this study, reducing postoperative pain, trismus, and swelling in patients undergoing impacted mandibular third molar surgery. However, the chemical stability of the combined agents over time was not evaluated and warrants future investigation, along with studies focused on formulation, storage, latent effects, and shelf life for practical clinical use.

The strengths of this investigation include a consistent methodology, complete follow-up, and procedures completed by a single surgeon, thereby minimising operator-related variability. The split-mouth approach also reduced discrepancies in individual pain perception.

Postoperative swelling is influenced by numerous local factors—including tooth angulation, bone removal technique, haemostatic approach, suture tension, and tissue handling—as well as systemic considerations such as age, bleeding profile, diet, medications, and diabetes [63]. A limitation of the study is that these diverse variables make it challenging to determine whether dexamethasone affects all contributors to postoperative inflammation. The split-mouth design helped reduce some confounders, yet the larger injection volume compared with conventional 2 ml administration may cause momentary discomfort, particularly in anxious individuals. Additional work with expanded sample sizes and plasma-level monitoring of dexamethasone following injection is advised.

Conclusion

This study indicates that incorporating dexamethasone into lignocaine with adrenaline shortens the onset time and prolongs the anaesthetic effect, allowing patients to better tolerate periods of peak postoperative pain. Pain reduction was reflected in lower scores during the first 24 h and throughout the subsequent 7-day period, along with decreased overall analgesic intake. The mixture also diminished secondary postoperative effects, such as swelling and trismus.

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requirements. Written informed consent for participation in this study was provided by the participants' legal guardians/next of kin. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

References

1. Kaewkumnert S, Phithaksinsuk K, Changpoo C, Nochit N, Muensaiyat Y, Wilaipornsawai S, et al. Comparison of intraosseous and submucosal dexamethasone injection in mandibular third molar surgery: a split-mouth randomized clinical trial. Int J Oral Maxillofac Surg. 2020;49(4):529–35. doi:10.1016/j.ijom.2019.10.006
2. Yamaguchi A, Sano K. Effectiveness of preemptive analgesia on postoperative pain following third molar surgery: review of literatures. Jpn Dent Sci Rev. 2013;49(4):131–8. doi:10.1016/j.jdsr.2013.07.002
3. Valmeseda-Castellon E, Berini-Aytes L, Gay-Escoda C. Lingual nerve damage after third molar extraction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2000;90:567–73. doi:10.1067/moe.2000.110034
4. Contar CM, de Oliveira P, Kanegusuku K, Berticelli RD, Azevedo-Alanis LR, Machado MA. Complications in third molar removal: a retrospective study of 588 patients. Med Oral Patol Oral Cir Bucal. 2010;15:e74–8. doi:10.4317/medoral.15.e74
5. Loescher AR, Smith KG, Robinson PP. Nerve damage and third molar removal. Dent Update. 2003;30:375–82. doi:10.12968/denu.2003.30.7.375
6. Cheung LK, Leung YY, Chow LK, Wong MC, Chan EK, Fok YH. Incidence of neurosensory deficits and recovery after lower third molar surgery: a prospective clinical study of 4338 cases. Int J Oral Maxillofac Surg. 2010;39:320–6. doi:10.1016/j.ijom.2009.11.010
7. Kang F, Sah MK, Fei G. Determining the risk relationship associated with inferior alveolar nerve injury following removal of mandibular third molar teeth: a systematic review. J Stomatol Oral Maxillofac Surg. 2020;121(1):63–9. doi:10.1016/j.jormas. 2019.06.010
8. Sreesha S, Ummar M, Sooraj S, Aslam S, Roshni A, Jabir K. Postoperative pain, edema and trismus following third molar surgery–A comparitive study between submucosal and intravenous dexamethasone. J Family Med Prim Care. 2020;9(5):2454. doi:10.4103/jfmpc.jfmpc_188_20
9. Biradar PA, Kaimar P, Gopalakrishna K. Effect of dexamethasone added to lidocaine in supraclavicular brachial plexus block: a prospective, randomised, double- blind study. Indian J Anaesth. 2013;57(2):180–4. doi:10.4103/0019-5049.111850
10. Hwang H, Park J, Lee WK, Lee WH, Leigh JH, Lee JJ, et al. Crystallization of local anesthetics when mixed with corticosteroid solutions. Ann Rehabil Med. 2016;40(1):21–7. doi:10.5535/arm.2016.40.1.21
11. Castillo J, Curley J, Hotz J, Uezono M, Tigner J, Chasin M, et al. Glucocorticoids prolong rat sciatic nerve blockade in vivo from bupivacaine microspheres. Anesthesiology. 1996;85(5):1157–66. doi:10.1097/00000542-199611000-00025
12. Dräger C, Benziger D, Gao F, Berde CB. Prolonged intercostal nerve blockade in sheep using controlled-release of bupivacaine and dexamethasone from polymer microspheres. Anesthesiology. 1998;89(4):969–79. doi:10.1097/00000542-199810000-00022
13. Kawanishi R, Yamamoto K, Tobetto Y, Nomura K, Kato M, Go R, et al. Perineural but not systemic low-dose dexamethasone prolongs the duration of interscalene block with ropivacaine: a prospective randomized trial. Local Reg Anesth. 2014;7:5–9. doi:10.2147/lra.s59158
14. Kim YJ, Lee GY, Kim DY, Kim CH, Baik HJ, Heo S. Dexamethasone added to levobupivacaine improves postoperative analgesia in ultrasound guided interscalene brachial plexus blockade for arthroscopic shoulder surgery. Korean J Anesthesiol. 2012;62(2):130–4. doi:10.4097/kjae.2012.62.2.130
15. Kumar S, Palaria U, Sinha AK, Punera DC, Pandey V. Comparative evaluation of ropivacaine and ropivacaine with dexamethasone in supraclavicular brachial plexus block for postoperative analgesia. Anesth: Essays Res. 2014;8(2):202–8. doi:10.4103/0259-1162.134506
16. Pehora C, Pearson AM, Kaushal A, Crawford MW, Johnston B. Dexamethasone as an adjuvant to peripheral nerve block. Cochrane Database Syst Rev. 2017;11. doi:10.1002/14651858.CD011770.pub2
17. Singh NP, Makkar JK, Chawla JK, Sondekoppam RV, Singh PM. Prophylactic dexamethasone for rebound pain after peripheral nerve block in adult surgical patients: systematic review, meta-analysis, and trial sequential analysis of

randomised controlled trials. Br J Anaesth. 2024;132(5):1112-21. doi:10.1016/j.bja.2023.09.022

18. Madhoon HW, Al-Kafarna M, Ayyad NJ, Gbreel MI, Zaazouee MS. The efficacy of methylprednisolone versus dexamethasone in reducing postoperative sequelae after third molar surgery: a systematic review and meta-analysis. J Oral Maxillofac Surg Med Pathol. 2022;34(4):365–74. doi:10.1016/j.ajoms.2021.12.004
19. Giri KY, Joshi A, Rastogi S, Dandriyal R, Indra B Prasad N, Singh HP, et al. Efficacy of intravenous dexamethasone administered preoperatively and postoperatively on pain, swelling, and trismus following third molar surgery. A comparative study. Oral Surg. 2019;12(2):110–7. doi:10.1111/ors.12399
20. Gozali P, Boonsiriseth K, Kiattavorncharean S, Khanijou M, Wongsirichat N. Decreased post-operative pain using a sublingual injection of dexamethasone (8 mg) in lower third molar surgery. J Dent Anesth Pain Med. 2017;17(1):47. doi:10.17245/jdapm.2017.17.1.47
21. Deo SP. Role of addition of dexamethasone to lignocaine 2% with adrenaline in dental nerve blocks for third molar surgery: a prospective randomized control trial. Ann Maxillofac Surg. 2016;6(2):260. doi:10.4103/2231-0746.200341
22. Atalay B, Şitilci AT, Onur ÖD. Analgesic and anti-inflammatory effects of articaine and perineural dexamethasone for mandibular third molar surgery: a randomized, double-blind study. J Oral Maxillofac Surg. 2020;78(4):507–14. doi:10.1016/j.joms.2019.10.024
23. Hwang H, Park J, Lee WK, Lee WH, Leigh JH, Lee JJ, et al. Crystallization of local anaesthetics when mixed with corticosteroid solutions. Ann Rehabil Med. 2016;40(1):21–7. doi:10.5535/arm.2016.40.1.21
24. Movafegh A, Razazian M, Hajimaohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs brachial plexus blockade. Anesth Analg. 2006;102(1):263–7. doi:10.1213/01.ane.0000189055.06729.0a
25. Antunes AA, Avelar RL, Martins Neto EC, Frota R, Dias E. Effect of two routes of administration of dexamethasone on pain, edema, and trismus in impacted lower third molar surgery. Oral Maxillofac Surg. 2011;15:217–23. doi:10.1007/s10006- 011-0290-9
26. Herrera-Briones FJ, Sánchez EP, Botella CR, Capilla MV. Update on the use of corticosteroids in third molar surgery: systematic review of the literature. Oral Surg Oral Med Oral Pathol Oral Radiol. 2013;116:e342–51. doi:10.1016/j.oooo.2012.02. 027
27. Selvido DI, Bhattarai BP, Niyomtham N, Riddhabhaya A, Vongsawan K, Pairuchvej V, et al. Review of dexamethasone administration for management of complications in postoperative third molar surgery. J Korean Assoc Oral Maxillofac Surg. 2021;47(5):341–50. doi:10.5125/jkaoms.2021.47.5.341
28. Messer EJ, Keller JJ. The use of intraoral dexamethasone after extraction of mandibular third molars. Oral Surg Oral Med Oral Pathol. 1975;40:594–8. doi:10.1016/0030-4220(75)90369-2
29. Barnes PJ. Mechanisms and resistance in glucocorticoid control of inflammation. J Steroid Biochem Mol Biol. 2010;120:76–85. doi:10.1016/j.jsbmb. 2010.02.018
30. Simone JL, Jorge WA, Horliana AC, Canaval TG, Tortamano IP. Comparative analysis of preemptive analgesic effect of dexamethasone and diclofenac following third molar surgery. Braz Oral Res. 2013;27:266–71. doi:10.1590/S1806-83242013005000012
31. Neupert EA III, Lee JW, Philput CB, Gordon JR. Evaluation of dexamethasone for reduction of postsurgical sequelae of third molar removal. J Oral Maxillofac Surg. 1992;50(11):1177–82. doi:10.1016/0278-2391(92)90149-T
32. Waldron NH, Jones CA, Gan TJ, Allen TK, Habib AS. Impact of perioperative dexamethasone on postoperative analgesia and side-effects: systematic review and meta-analysis. Br J Anaesth. 2013;110:191–200. doi:10.1093/bja/aes431
33. Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med. 1992;326(5):281–6. doi:10.1056/NEJM199201303260501
34. Aravena PC, Oyarzún CP, Arias MF, Monardes H, Jerez A, Benso B. Single-Dose bioavailability for prophylactic coverage in patients undergoing dental implant surgery. Int J Oral Maxillofac Implants. 2018;33(2). doi:10.11607/jomi.5943
35. Iglesias-Martín F, García-Perla-García A, Yañez-Vico R, Rosa E, Arjona- Gerveno E, González-Padilla JD, et al. Comparative trial between the use of amoxicillin and amoxicillin clavulanate in the removal of third molars. Medicina Oral Patología

Oral y Cirugía Bucal. 2014;19(6):e612. doi:10.4317/medoral.19778

36. Sathish R, Anil A. Single dose preoperative intravenous antibiotic versus 5 days postoperative per oral antibiotic therapy in third molar surgery-A randomised clinical trial. J Clin Diagnostic Res. 2021;15(10). doi:10.7860/JCDR/2021/50068.15517
37. Hallab L, Azzouzi A, Chami B. Quality of life after extraction of mandibular wisdom teeth: a systematic review. Ann Med Surg. 2022;81:104387. doi:10.1016/j.amsu.2022.104387
38. Hupp JR, Ferneini EM. Head, Neck, and Orofacial Infections: An Interdisciplinary Approach. St. Louis, Missouri: Elsevier Health Sciences; 2015.
39. Shetty S, Uchil S. Systemic conditions and oral health. J Calif Dent Assoc. 2017;45(5):219. doi:10.1080/19424396.2017.12222443
40. Boynton TT, Ferneini EM, Goldberg MH. Odontogenic infections of the fascial spaces. In: Hupp JR, Ferneini EM, editors. Head, Neck and Orofacial Infections: An Interdisciplinary Approach E-Book. St. Louis, Missouri: Elsevier Health Sciences; 2015. p. 203.
41. Fisher SE, Frame JW, Rout PG, McEntegart DJ. Factors affecting the onset and severity of pain following the surgical removal of unilateral impacted mandibular third molar teeth. Br Dent J. 1988;164(11):351–4. doi:10.1038/sj.bdj.4806453
42. Hyrkas T, Ylipaavalniemi P, Oikarinen VJ, Paakkari I. Effective postoperative pain prevention through administration of bupivacaine and diclofenac. Anesth Prog. 1994;41(1):6–10.
43. World Health Organization. WHO Guidelines for the Pharmacological and Radiotherapeutic Management of Cancer Pain in Adults and Adolescents. Geneva: World Health Organization; 2018. ISBN-13: 978-92-4-155039-0.
44. Tijanic M, Buric N. A randomized anesthethic potency comparison between ropivacaine and bupivacaine on the perioperative regional anesthesia in lower third molar surgery. J Craniomaxillofac Surg. 2019;47(10):1652–60. doi:10.1016/j.jcms. 2019.07.019
45. Ohashi N, Kohno T. Analgesic effect of Acetaminophen: a review of known and novel mechanisms of action. Front Pharmacol. 2020;11:1916. doi:10.3389/fphar. 2020.580289
46. McCartney CJ. Analgesic adjuvants in the peripheral nervous system. NYSORA; 2020. p. 147–54 (cited December 22, 2022).
47. Desai N, Kirkham KR, Albrecht E. Local anaesthetic adjuncts for peripheral regional anaesthesia: a narrative review. Anaesthesia. 2021;76(S1):100–9. doi:10. 1111/anae.15245
48. Tan ES, Tan YR, Liu CW. Efficacy of perineural versus intravenous dexamethasone in prolonging the duration of analgesia when administered with peripheral nerve blocks: a systematic review and meta-analysis. Korean J Anesthesiol. 2022;75(3):255–65. doi:10.4097/kja.21390
49. Heesen M, Klimek M, Imberger G, Hoeks SE, Rossaint R, Straube S. Co- administration of dexamethasone with peripheral nerve block: intravenous vs perineural application: systematic review, meta-analysis, meta-regression and trial-sequential analysis. Br J Anaesth. 2018;120(2):212–27. doi:10.1016/j.bja.2017.11.062
50. Movafegh A, Razazian M, Hajimaohamadi F, Meysamie A. Dexamethasone added to lidocaine prolongs axillary brachial plexus blockade. Anesth Analg. 2006;102(1):263–7. doi:10.1213/01.ane.0000189055.06729.0a
51. Bhandage SG, Kurki MS, Sachdeva G, Shetty N, Kundu M, Yadav AB. Evaluación de la eficacia de la administración peri-operatoria de hidrocortisona y dexametasona para prevenir las complicaciones postoperatorias de la cirugía oral y maxilofacial. Revista Española de Cirugía Oral y Maxilofacial. 2018;40(4):163–8. doi:10.1016/j.maxilo.2018.01.001
52. Choi S, Rodseth R, McCartney CJ. Effects of dexamethasone as a local anaesthetic adjuvant for brachial plexus block: a systematic review and meta-analysis of randomized trials. Br J Anaesth. 2014;112(3):427–39. doi:10.1093/bja/aet417
53. Majid OW, Mahmood WK. Use of dexamethasone to minimise post-operative sequelae after third molar surgery: comparison of five different routes of administration. Oral Surg. 2013;6(4):200–8. doi:10.1111/ors.12049
54. Khoury JN, Mihailidis S, Ghabriel M, Townsend G. Applied anatomy of the pterygomandibular space: improving the success of inferior alveolar nerve blocks. Aust Dent J. 2011;56(2):112–21. doi:10.1111/j.1834-7819.2011.01312.x
55. Yamada M, Matsuzaka T, Uetani M, Hayashi K, Tsuji Y, Nakamura T. Normal age-related conversion of bone marrow in the mandible: mR imaging findings. AJR Am J Roentgenol. 1995;165(5):1223–8. doi:10.2214/ajr.165.5. 7572508

56. McMillan RM, Foster SJ, Shaw JS, editors. Approaches to novel anti-arthritic drugs by modulation of the arachidonic acid cascade. In: Mechanisms and Models in Rheumatoid Arthritis. Cambridge, MA: Academic Press; 1995. p. 283–300.
57. Naray-Fejes-Tóth A, Rosenkranz B, Frölich JC, Fejes-Tóth G. Glucocorticoid effect on arachidonic acid metabolism in vivo. J Steroid Biochem. 1988;30(1-6):155–9. doi:10.1016/0022-4731(88)90088-X
58. Barnes PJ. How corticosteroids control inflammation: quintiles prize lecture 2005. Br J Pharmacol. 2006;148(3):245–54. doi:10.1038/sj.bjp.0706736
59. dos Santos Canellas JV, Ritto FG, Tiwana P. Comparative efficacy and safety of different corticosteroids to reduce inflammatory complications after mandibular third molar surgery: a systematic review and network meta-analysis. Br J Oral Maxillofac Surg. 2022;60(8):1035–43. doi:10.1016/j.bjoms.2022.05.003
60. Bhargava D, Deshpande A, Thomas S, Sharma Y, Khare P, Sahu SK, et al. High performance liquid chromatography determination of dexamethasone in plasma to evaluate its systemic absorption following intra-space pterygomandibular injection of twin-mix (mixture of 2% lignocaine with 1: 200,000 epinephrine and 4 mg dexamethasone): randomized control trial. Oral Maxillofac Surg. 2016;20:259–64. doi:10.1007/s10006-016-0564-3
61. Ngeow WC, Lim D. Do corticosteroids still have a role in the management of third molar surgery? Adv Ther. 2016;33:1105–39. doi:10.1007/s12325-016-0357-y
62. Gaur S, Marimuthu M, Wahab A, Krishnan N, Ramasubbu S. Twin mixed local anesthesia in third molar surgery-randomized controlled trial. J Oral Maxillofac Surg. 2022;80(1):63–9. doi:10.1016/j.joms.2021.07.013
63. Chaudhary PD, Rastogi S, Gupta P, Niranjanaprasad Indra B, Thomas R, Choudhury R. Pre-emptive effect of dexamethasone injection and consumption on post-operative swelling, pain, and trismus after third molar surgery. A prospective, double blind and randomized study. J Oral Biol Craniofac Res. 2015;5(1):21–7. doi:10.1016/j.jobcr.2015.02.00