Effectiveness of dexamethasone or adrenaline with lignocaine 2% for prolonging inferior alveolar nerve block: a randomized controlled trial

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Abstract (J Korean Assoc Oral Maxillofac Surg 2022;48:21-32)

Objectives: Inferior alveolar nerve block (IANB) is commonly used for mandibular dentoalveolar surgery. The objective of this study was to evaluate and compare the effectiveness of coadministration of dexamethasone (4 mg/mL) or adrenaline (0.01 mg/mL) as an adjuvant with lignocaine 2% in IANB during third molar surgery (TMS).

Patients and Methods: This double-blind, randomized controlled trial was conducted between March and August 2020. The investigators screened patients needing elective TMS under local anesthesia. Based on strict inclusion and exclusion criteria, patients were enrolled in this study. These patients were assigned randomly into two study groups: dexamethasone group (DXN) or adrenaline group (ADN). Outcome variables were postoperative edema, trismus, visual analogue scale (VAS), perioperative analgesia, onset time, and duration of IANB.

Results: Eighty-three patients were enrolled in this study, of whom 23 (27.7%) were eliminated or excluded during follow-up. This study thus included data from 60 samples. Mean age was 32.28±11.74 years, including 28 females (46.7%) in the ADN (16 patients, 57.1%) and DXN (12 patients, 42.9%) groups. The duration of action for DXN (mean±standard deviation [SD], 4:02:07±0:34:01 hours; standard error [SE], 0:06:00 hours; log-rank \( P=0.001 \)) and for ADN (mean±SD, 1:58:34±0:24:52 hours; SE, 0:04:42 hours; log-rank \( P=0.001 \)) were found. Similarly, time at which 1st analgesic consume and total number of nonsteroidal antiinflammatory drugs need to rescue postoperative analgesia was found statistically significant between study groups (\( t(58)=-11.95; \) confidence interval, –2:25:41 to –1:43:53; \( P=0.001 \)). Early-hours VAS was also significantly different between the study groups.

Conclusion: A single injection of dexamethasone prolongs the duration of action of lignocaine 2% IANB. Additionally, it can be used in cases where adrenaline is contraindicated.

Key words: Dexamethasone, Inferior alveolar nerve, Nerve block, Lidocaine, Third molar

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i.e., moderate to severe in intensity. TMS has become the model most frequently used for postoperative acute pain studies. Sufficient numbers of patients available for sample sizes of this particular type of study have attracted researcher attention for clinical trials. Local anesthetic (LA) blocks with long-acting LAa were successful for management of perioperative pain after surgery. Unfortunately, narrow therapeutic margins and higher cardiotoxicity were reported. Therefore, clinicians have been searching for new and safer drugs to manage perioperative pain. Adjuvant drugs have been most commonly investigated with local anaesthesia. Initially, limited only to the fields of anaesthesiology and orthopaedic surgery, dentistry has resulted in an effort to increase sensory nerve block duration with short lived LAa. Epinephrine has been used most extensively in this capacity, while taking its relatively limited efficacy and cautious use into consideration. The most commonly used adjuvant drugs are dexamethasone, α2 agonists (i.e., clonidine and dexmedetomidine), opioids (i.e., buprenorphine), ketamine, midazolam, hyaluronidase, and neostigmine. Dexamethasone has been frequently used as an adjuvant for various nerve blocks, i.e., brachial plexus, femoral, intercostal, and axillary nerve blocks, during limb surgery, but the exact mechanism of prolonged nerve blocks remains unclear. However, the adjuvant use of dexamethasone was not studied with IANB.

The present study was designed to search for better quality perioperative analgesics with a single injection of co-admix dexamethasone and lignocaine in IANB during TMS. The purpose of the present study was to compare the efficacy of two adjuvant drugs, i.e., adrenaline and dexamethasone with lignocaine 2% in IANB, and their effect on postoperative sequelae after TMS. The objective was to compare the effectiveness of coadministration of dexamethasone (4 mg/mL) or adrenaline (0.01 mg/mL) with lignocaine 2% in IANB during TMS. Additionally, this study tested the null hypothesis that the adjuvant drugs, dexamethasone and adrenaline, exhibited equal effects in prolonging IANB with lignocaine 2% during TMS. To the best of our knowledge, no study has compared the efficacy of a freshly prepared mixture of lidocaine with adrenaline to that of lignocaine with dexamethasone.

II. Patients and Methods

1. Study design

The researchers conducted a prospective, double-blind, randomized controlled trial. Written informed consent was obtained from all the study participants. The possible risks and benefits of the procedure were described to all the patients. Subjects willing to participate in the study were scheduled for TMS in the morning. Ethical approval was obtained from the institutional review committee, and trial registration was performed on clinicaltrial.gov (No. NCT04850885).

2. Study setting and population

This quantitative experimental study was conducted in the Department of Oral and Maxillofacial Surgery, National Medical College, Birgunj from March 2020 to August 2020. The study subjects were American Society of Anaesthesiologists (ASA) I-II patients presenting for elective TMS under inferior alveolar block local anaesthesia. The sample size calculation was performed using the formula 2 SD² (Zα/2+Zβ)²/ d², where SD (standard deviation from the previous study), Za/2 (standard normal variance to the level of significance [1% type I error, P<0.01 was 2.58]), (Zβ=standard normal variance for power [for 90% power was 1.28]), d (effect size [the difference between the mean value of the previous study])². The participants were randomly assigned into two groups: 1st, dexamethasone group (DXN) and 2nd, adrenaline group (ADN).

3. Selection criteria

Inclusion criteria were patients above age 18 who required oral surgery under local anaesthesia and could understand and were willing to participate in the study. Non-inclusion criteria were contraindications to dexamethasone (i.e., peptic ulcer, renal insufficiency, pregnancy, or lactating females), allergy to drugs used in this study (lignocaine, dexamethasone, Amoxicillin, or piroxicam), aged younger than 18 years or older than 85 years, ASA physical status >III, TMS needing to be performed under general anaesthesia, patients with any condition precluding the limitation of intraoperative trial drug (lignocaine, adrenaline) administration (i.e., significant coronary artery disease, congestive heart failure), or those receiving any pre-medications (including nonsteroidal anti-inflammatory drugs [NSAIDs], opioids, benzodiazepines, and clonidine, antibiotics, or anti-inflammatory drugs) within two weeks of study entry. In addition, radiographs showing high and bifid mandibular foramen were not included. Exclusion criteria involved subjects who had to consume analgesic drugs other than piroxicam 20 mg, those whose numbness of
the tongue and lip was not achieved up to 15 minutes after injection (failure of a block), and subjects who did not respond on the visual analogue scale (VAS) and did not come for second and seventh postoperative follow-ups.

4. Study variables

Predictor variables were socio-demographic, LA administration time, surgery start time, surgery end time, and operative time. Outcome variables were oedema, trismus, perception of pain in VAS, postoperative analgesia, onset time, and duration of action. The confounding variables were stress and anxiety of the subjects, type and degree of difficulty of the operative procedure, and experience of the surgeon. A single experienced surgeon performed all the surgical procedures following standard operative protocols, allowing for fixed confounding variables.

5. Drug preparation

This study used a freshly prepared mixture of adrenaline or dexamethasone with lignocaine for the groups. The 9 mL solution was discarded, and the remaining 1 mL solution was diluted with 9 mL normal saline (NS). This freshly prepared homogenous mixture contained adrenaline (0.01 mg/mL). From this solution, only 2 mL of solution was transferred to a 5 mL syringe, and 2 mL of lignocaine (20 mg/mL) was added to the same syringe marked as mixture A. Similarly, for Group DXN, 2 mL of dexamethasone (4 mg/mL) was withdrawn in an identical 5 mL syringe, and 2 mL of lignocaine (20 mg/mL) was added to create mixture B.

6. Allocation and randomization of subjects

The non-probability convenience sampling method was used to select the subjects for this study based on availability and willingness to take part. The details of patient recruitment, and follow-ups in this study are shown in Fig. 1. Seventy-three subjects were assigned randomly into one of two groups: DXN or ADN. Group ADN had received 4 mL of mixture A, whereas Group DXN received 4 mL of mixture B. Stratified randomization was performed in a permuted technique. Therefore, each subject would be assigned on a first-come, first basis.

7. Blinding process

Blinding of this clinical study was performed by confi-
Further data collection. Postoperative instructions were provided to all the patients. Amoxicillin 500 mg (Cap. Wynox 500; Pfizer, Mumbai, India) was prescribed to the patients orally three times a day for five days and piroxicam 20 mg (Fc-tab Dolonex DT; Pfizer) orally as required for “rescue” analgesia. They were provided a VAS (no pain, 0-1; mild pain, 2-3; moderate pain, 4-5; severe pain, 6-7; very severe pain, 8-9) and were instructed about the rating scale. The patients were asked to report to the outpatient setting on the second and seventh postoperative days to observe the surgical outcomes and report any adverse drug effects.

9. Outcome measurements

Surgical outcomes of postoperative facial swelling, trismus, and duration of analgesia and adverse drug reactions of nausea/vomiting, bruise, paraesthesia of the lip and tongue, slow wound healing, mood changes, wound infection, and hyperglycaemia were recorded during the follow-ups in the outpatient’s department. Standard and valid tools were used for data collection with the Performa and 10 cm VAS. These tools are reliable and valid and have been increasingly used to evaluate patients’ pain perception. The armamentarium used for this study included a pulse oximeter (SpO₂), thermometer, sphygmomanometer, and stopwatch. Support staff were provided all the above armamentarium and informed on test preparation or control group drugs according to the permuted random table. The staff recorded preoperative, intraoperative, and postoperative data. Pre, intra, and postoperative vitals with non-invasive blood pressure and the respiratory rate were recorded with a pulse SpO₂, allowing for assessment of any adverse effects of the drugs. Wound healing and other local tissue reactions were recorded in the second and seventh postoperative days. IANB was assessed subjectively and objectively. The patients were frequently questioned regarding the numbness of the lip and tongue a few seconds after the administration of the test drugs. Simultaneously, the patients were instructed to palpate the lips and compare sensation or numbness in the upper and lower lips. They were asked to report when lower lip numbness had occurred. Furthermore, the nerve block was assessed objectively by pricking the buccal and lingual gingiva in the canine and first molar areas with a blunt instrument. The block’s success was standardized for profound lip numbness for all the patients. When profound lip numbness was not recorded after 15 minutes, the IANB was considered a failure, and these patients were eliminated from the study.

8. Procedures

The modified IANB technique was used to block the inferior alveolar nerve (IAN) as described by Clark and Homes (1959). The high success rate was the reason to choose this technique. The patients were requested to keep their mouths wide open with their occlusal plane parallel to the floor. Palpation of the anatomical landmarks was correctly performed, and the guide finger was positioned at the retromolar fossa. A 5 mL syringe equipped with a 24-gauge needle with a length of 3.6 cm was used. The needle was advanced into the tissue just above the fingernail until bone was contacted. The body of the syringe was redirected over the lower central incisors and maintained parallel to the molars in the horizontal plane at the same time. The needle was inserted another 2 cm into the tissue, and 3.5 mL of solution X was deposited 1 cm higher than usual after multiple aspirations (90° two planes). Furthermore, 1 mL of solution X was deposited after the needle was withdrawn into the pterygomandibular space. Pre, intra, and postoperative vitals were monitored. Anaesthetic assessments (subjective and objective) were performed as described below. After profound anaesthesia was achieved, the same surgeon performed standard surgical procedures for the third molars. The duration of the operation was recorded as the period between the initial incision to the last suture placed. Details of each procedure were recorded. After completing the surgical procedure, the patients were shifted to the postoperative ward for the next 6 hours for observation and
In the postoperative ward, vitals were recorded for up to 6 postoperative hours. The subjects were instructed to palpate the lower lip and tongue every 20 minutes to determine numbness (no feeling) until normal sensation was regained and asked to note the time. All the events were recorded. The patients were instructed to first consume NSAIDs for postoperative rescue analgesia when moderate pain started and to document the time. The subjects were instructed not to take any other trail analgesic drugs, i.e., piroxicam 20 mg (Fc-tab Dolonex DT; Pfizer).

10. Statistical analyses

Data analysis was performed using IBM SPSS Statistics software (ver. 11.5; IBM, Armonk, NY, USA). Independent Student's t-test analyses were performed to test the hypothesis, group statistics, and provide a comparison between the groups. Descriptive analysis was performed by calculating the frequency and percentages for categorical data. The mean and standard deviation were calculated for continuous data. The Pearson chi-square test and the t-test were applied to determine the association between the groups. The confidence level was set at 95%. The significance level was set at \( P<0.05 \).

III. Results

The finding of this study was generated from 60 subjects from both study groups. Fig. 1 is a flow chart that describes the final subjects enrolled in this study. The failure rate of IANB was 2.7% in DXN and 11.11% in ADN. (Fig. 1) The mean and standard deviation of the predictor variables were statistically similar in the two groups. (Table 1, 2)

1. Analgesic outcomes

The duration of action (IANB) was longer in DXN (4:02:07±0:34:01 hours) compared to ADN (1:58:34±0:24:52 hours) (t (58)=–15.85; \( P=0.001 \)), whereas the latency periods were similar in DXN (0:04:09±0:02:27 hours) and ADN (0:04:21±0:02:13 hours) (t (58)=0.330; 95% confidence interval [CI], –0:01:01 to 0:01:25; \( P=0.742 \)). (Table 2) Table 3 shows the assessment onset time and duration of action (IANB). The onset time was found in increasing order at different regions, i.e., molar<canine<tongue<lip. (Fig. 2 A) However, the duration of nerve blocks was found in decreas-

### Table 1. Demographic distribution in both study groups

| Characteristic | Overall (n=60) | Group ADN (n=28) | Group DXN (n=32) | \( P \)-value |
|----------------|---------------|-----------------|-----------------|-------------|
| Age (yr)       | 32.28±11.74   | 33.82±11.03     | 30.94±12.35     | 0.915       |
| Sex            |               |                 |                 |             |
| Male           | 32 (53.3)     | 12 (42.9)       | 20 (62.5)       | 0.195       |
| Female         | 28 (46.7)     | 16 (57.1)       | 12 (37.5)       |             |

(ADN: adrenaline, DXN: dexamethasone)

\( *P \leq 0.05 \) is statistically significant.

Values are presented as mean±standard deviation or number (%).

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### Table 2. Comparison duration of perioperative analgesia in different time intervals between the dexamethasone and adrenaline groups

| Characteristic                              | Overall | Group ADN | Group DXN | \( t \)-value | 95% CI (hr:min:s) | \( P \)-value |
|---------------------------------------------|---------|-----------|-----------|--------------|------------------|-------------|
| Time of administration of LA in 24 hours [A]| 10:25:01±0:36:32 | 10:24:21±0:33:39 | 10:25:36±0:39:24 | t (58)=–0.130    | –0:20:19 to 0:17:50 | 0.561       |
| Surgery start time in 24 hours [B]         | 10:29:16±0:36:47 | 10:28:42±0:33:46 | 10:29:45±0:39:46 | t (58)=–0.108    | –0:20:15 to 0:18:11 | 0.914       |
| Latency in hours [B-A]                     | 0:04:14±0:02:20 | 0:04:21±0:02:13 | 0:04:09±0:02:27 | t (58)=0.330     | –0:01:01 to 0:01:25 | 0.742       |
| Surgery end time in 24 hours [C]           | 11:07:12±0:44:40 | 11:08:12±0:45:46 | 11:06:18±0:44:24 | t (58)=0.163     | –0:21:26 to 0:25:14 | 0.871       |
| Operative time in hours [C-B]              | 0:37:56±0:16:01 | 0:39:30±0:17:57 | 0:36:33±0:14:17 | t (58)=0.694     | –0:05:33 to 0:11:25 | 0.484       |
| Exact time 1st analgesic taken after surgery in 24 hours [D] | 13:29:29±1:14:26 | 12:22:55±0:35:23 | 14:27:43±0:44:13 | t (58)=11.95     | –2:25:41 to –1:43:53 | 0.001*      |
| Duration of analgesia in hours [D-A]       | 3:04:28±1:08:57 | 1:58:34±0:24:52 | 4:02:07±0:34:01 | t (58)=–15.85    | –2:18:50 to –1:48:15 | 0.001*      |
| Total No. of analgesics consumed           | 5.98±2.26 | 8.04±1.52 | 4.19±0.78 | t (58)=12.51    | 3.23 to 4.46    | 0.017*      |

(LA: local anaesthetic, ADN: adrenaline, DXN: dexamethasone, CI: confidence interval)

\( *P \leq 0.05 \) is statistically significant.

Values are presented as mean±standard deviation.

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ing order at the molar > tongue > canine > lip in both groups. (Fig. 2. B) Similarly, the time at which the first analgesic was consumed and the total number of NSAIDs needed to provide rescue postoperative analgesia were statistically significant between the study groups. (Table 2) The mean VAS was significant between the study groups at the 2nd, 4th, 5th, 6th, 12th, 15th, 18th, and 21st hours as shown in Fig. 3.

2. Benefits versus risks

As shown in Fig. 4, the hemodynamic status including systolic and diastolic blood pressure, pulse rate, respiratory rate and $\text{SPO}_2$ at preoperative, intraoperative, postoperative period after injection showed insignificant differences between the study groups. Postoperative sequelae such as facial oedema, trismus, and pain were observed after every TMS up to the first week postoperatively, but only facial oedema on the 2nd postoperative day was significantly different between the groups. However, the overall measurements were greater in ADN compared to DXN. (Fig. 5) In addition, adverse drug effects were nonsignificant up to the first postoperative week, but intraoperative bleeding was significantly more frequent and nausea and vomiting significantly less frequent in DXN compared to ADN. (Table 4).

### IV. Discussion

This study compared the efficacy of dexamethasone over adrenaline adjuvants with lignocaine 2% in IANB. Past studies used dexamethasone adjuvants in long- to intermediate-acting LAA and found significantly prolonged duration of action in brachial and femoral nerve blocks. Although TMS has been most frequently used for postoperative acute pain studies, there have not been many investigations conducted to determine the effectiveness of dexamethasone adjuvants with lignocaine in IANB. To the best of our knowledge, this study could be the first to use dexamethasone adjuvants with lignocaine in TMS. The null hypothesis was that the mean duration of action of DXN ($\mu_1$) would be equal to that of ADN ($\mu_2$) [H0, $\mu_1=\mu_2$]. Nevertheless, the present study results did not reveal the same mean duration of action in the two study groups. We found a significant difference in the duration of action between the study groups at molar teeth ($P=0.030$), canine teeth ($P=0.030$), tongue ($P=0.016$), and lip regions ($P=0.016$) through use of independent Student’s t-test, Levene’s test, and t-test for equality. (Table 3) Therefore, we rejected the null hypothesis, and an alternative hypothesis

### Table 3: Assessment of inferior alveolar nerve blocks—subjective and objective methods used to assess anaesthesia in different regions between the two study groups

| Anaesthetic assessment regions | Administration time (A) | Sensation lost (B) | Sensation regained (C-A) | Duration of action (C-A) | t-value | 95% CI (hr:min:s) | P-value |
|------------------------------|-------------------------|-------------------|--------------------------|--------------------------|---------|------------------|---------|
| Lower 1st molar              | ADN                     | 10:24:21±0:33:39  | 10:26:55±0:33:26         | 12:24:55±0:35:07         | 154     | –2:25:14 to –1:58:44 | 0.000*  |
|                             | DXN                     | 10:25:36±0:39:24  | 10:28:15±0:39:29         | 14:34:50±0:47:34         | 99      | –2:21:47 to –1:50:47 | 0.030*  |
| Lower canine                 | ADN                     | 10:24:21±0:33:39  | 10:28:34±0:33:34         | 12:17:42±0:35:41         | 232     | –2:21:47 to –1:50:47 | 0.030*  |
|                             | DXN                     | 10:25:36±0:39:24  | 10:29:26±0:39:29         | 14:24:50±0:46:34         | 161     | –2:23:20 to –1:51:16 | 0.016*  |
| Tongue                      | ADN                     | 10:24:21±0:33:39  | 10:27:02±0:34:03         | 12:17:34±0:30:24         | 168     | –2:23:43 to –1:52:15 | 0.016*  |
|                             | DXN                     | 10:25:36±0:39:24  | 10:28:24±0:39:29         | 14:26:15±0:47:01         | 349     | –2:23:43 to –1:52:15 | 0.016*  |
| Lower lip                   | ADN                     | 10:24:21±0:33:39  | 10:30:10±0:33:23         | 12:13:45±0:32:20         | 430     | –2:23:43 to –1:52:15 | 0.016*  |
|                             | DXN                     | 10:25:36±0:39:24  | 10:30:45±0:39:34         | 14:20:03±0:47:44         | 309     | –2:23:43 to –1:52:15 | 0.016*  |

(ADN: adrenaline, DXN: dexamethasone, CI: confidence interval)

*P ≤ 0.05 is statistically significant.

Values are presented as mean±standard deviation.
(H1) was formed that the mean duration of analgesia should not be equal between the study groups [H1, $\mu_1 \neq \mu_2$]. Similarly, this study found a significant difference in the mean duration of perioperative analgesia between the two study groups ($t = 15.85$; 95% CI, $-2.18.50$ to $-1.48.15$; $P = 0.001$). (Table 2) A meta-analysis by Choi et al. found prolongation of nerve block duration to be in the range from 168 to 343 minutes (mean, 175 minutes; 95% CI, 73 to 277) with intermediate-acting LAa. Accurate comparison with the above studies
is not justified because the present study used dexamethasone
adjuvants in the trigeminal nerve branches, i.e., IAN for
TMS is composed of only small, rapid-firing sensory fibres.
However, the above studies used dexamethasone in larger
diameter a-delta fibres. Smaller fibres are generally more sus-
ceptible to LAa because a given volume of LA solution can
more readily block the requisite number of sodium channels
for impulse transmission to be entirely interrupted. Moreover,
several previous studies had reported a statistically significant
increase in the mean duration of soft tissue anaesthesia rang-
ing from 197 to 301 minutes (P≤0.05) when dexamethasone
was administered locally into the pterygomandibular space
after IANB with lignocaine 2% with adrenaline10,55. Unfor-
fortunately, those studies did not assess perioperative analgesia
and VAS and were not well-documented. To the best of our
knowledge, the current study could be the first that used co-
admix dexamethasone adjuvants with short-acting LAa, i.e.,
lignocaine 2%. Therefore, this is a unique study because of
its design, drugs, volume, and assessment tools compared
to previous studies. Nevertheless, this study used single-
injection techniques, offering many advantages over dual-
injection techniques used in previous studies.

The present study compared the anaesthetic properties of
study drugs through both subjective (patient perspective)
and objective assessment methods. The patient perspective,
i.e., VAS and total number of NSAIDs consumed for rescue
postoperative analgesia, depended on the patient᾽s decision
about the level of pain. Objective assessment by pricking the
first molar, canine teeth, lower lip, and tongue every 20 min-
utes was used until normal sensation was regained. We found
immediate postoperative VAS, i.e., VAS-2, VAS-4, VAS-5,
VAS-6, VAS-12, VAS-15, VAS-18, and VAS-21, to exhibit
statistically significant differences between the study groups.
(Fig. 3) Similarly, past studies found a significant reduction
in VAS in the early postoperative hours19-25. Fig. 3 shows the
step ladder pattern of VAS in both study groups. The first step
in the graph is due to reversal of the anaesthetic effect of the
study drugs. A significant difference between the study groups
was shown at hour 2 for ADN and at hour 4 for DXN.(Fig.
3) These anaesthetic properties of the study drugs are consid-
ered the duration of action. The 2nd and 3rd steps in the VAS
d graph could be due to clearance of the NSAIDs36. VAS-4 and
VAS-15 were lower in ADN and was statistically significant
between the study groups. The step-in graph could have oc-
curred by inhibiting β-endorphins from entering the anterior
pituitary by dexamethasone, which might have increased
pain37. The systemic anti-inflammatory effect of dexametha-

![Fig. 5. Postoperative recovery from third molar surgery sequelae; left side, 2nd and 7th day reduction of facial contour from baseline in mm and right side, 2nd and 7th day reduced IIO from normal mouth opening in mm. Postoperative swelling was statistically significantly reduced in 2nd postoperative day in dexamethasone (DXN). *P≤0.05 is statistically significant. (ADN: adrenaline, POD: postoperative day).](image)

Table 4. Adverse outcomes found between the study groups

| Characteristic            | Overall (n=60) | Group ADN (n=28) | Group DXN (n=32) | P-value |
|---------------------------|---------------|-----------------|-----------------|--------|
| Intraoperative bleeding   | 17 (28.3)     | 3 (10.7)        | 14 (43.8)       | 0.001* |
| Slow wound healing        | 9 (15.0)      | 3 (10.7)        | 6 (18.8)        | 0.482  |
| Bruise                    | 11 (18.3)     | 7 (25.0)        | 4 (12.5)        | 0.318  |
| Paraeesthesia/nerve palsy | 1 (1.7)       | 1 (3.6)         | 0 (0)           | 0.475  |
| Nausea and vomiting       | 16 (26.7)     | 14 (50.0)       | 2 (6.3)         | 0.001* |
| Mood changes              | 4 (6.7)       | 0 (0)           | 4 (12.5)        | 0.116  |
| Wound infection           | 5 (8.3)       | 2 (7.1)         | 3 (9.4)         | >0.999 |

(ADN: adrenaline, DXN: dexamethasone, CI: confidence interval)

*P≤0.05 is statistically significant.

Values are presented as number (%).
sone could probably be the reason for statistically significant VAS-12, VAS-18, and VAS-21 between the two study groups. Furthermore, the prolonged durations of action in DXN were confirmed at 2 hours for ADN and 4 hours for DXN (t (58)=–11.95; 95% CI, –2:25:41 to –1:43:53; P=0.001). Again, we found that DXN patients consumed a smaller number of NSAIDs. Therefore, NSAID-associated adverse drug reactions could be minimized using single-dose dexamethasone.

Subjective and objective anaesthesia assessments in different regions36 (first molar, canine, lip, and tongue) represented loss and regain of normal sensation. (Table 3) Onset time is the latency period between LA administration to the beginning of numbness/loss of sensation. The duration of action is the beginning of numbness/loss of sensation to the return of sensation. The onset of numbness first began at the first molar, then tongue, canine, and finally the lip. (Fig. 2. A) In comparison between the study groups, onset time was not statistically significant. However, DXN exhibited an earlier onset time compared to ADN, possibly because of dexamethasone fastening the diffusion of the LA solution into the nerve sheath. The duration of action in all four regions was statistically significant between the study groups. (Table 3) As patients recovered from anaesthesia, they first regained sensation at the lip, then the tongue, and finally at the canine and first molar. (Fig. 2. B)

In Fig. 2, onset time and duration of action exhibited reverse patterns. Clinicians, especially dentists who perform IANBs, should be aware of these differential onset times and durations of action at different regions. This phenomenon could occur because the trigeminal nerve branches are composed of only tiny, rapid-firing sensory fibres. The neuroanatomy of IAN fibres has been described in anatomy textbooks, where a nerve encloses a cable-like bundle of axons (neurons) called fibres, surrounded by endoneurium. The axons are bundled together into groups called fascicles. The perineurium wraps each fascicle, and the entire nerve is wrapped with epineurium. (Fig. 6) The fibres near the surface of the nerve are called mental fibres and tend to innervate more proximal regions, i.e., the molar area, whereas fibres in the centre are called core bundles and innervate the more distal regions, i.e., incisors and canines. LA solution deposited onto the surface of the nerve sheath slowly diffuses from the mental fibres to the core fibres of IAN over time. Early diffusion into the mental fibres provided early onset in the molar region (99 seconds vs 154 seconds), and late diffusion into the core fibres resulted in delayed onset time (309 seconds vs 349 seconds) between DXN and ADN. Similarly, the lowest duration of block (6,429 seconds vs 14,067 seconds) and longest onset time (309 seconds vs 349 seconds) were observed in the lip between DXN and ADN. (Fig. 2) Therefore, reversal of local analgesia occurs in an inverse manner to onset. LA solution in mental fibres washes out earlier than that in core fibres, which is the probable mechanism by which we found the highest nerve block duration in the molar region and the lowest in the lip region. As a result, the lipid-binding capacity of dexamethasone could delay the recovery of local anaesthesia, leading to prolongation of nerve blocks in DXN.

Presently, there is no literature predicting the interaction of dexamethasone with lignocaine in vivo or in vitro. However, the safety profile of dexamethasone’s perineural use is well-established, and no trial has reported neurotoxicity attributable to dexamethasone. In this study, patients were hemodynamically stable in both study groups when we recorded vitals up to 6 hours postoperatively. (Fig. 4) Pain, trismus, and facial swelling are the most common postoperative sequelae after TMS and have been described frequently in the literature. These are an effect of local inflammatory mediator release immediately after surgical trauma40,41. In this study, postoperative recovery in the 2nd postoperative day exhibited significantly reduced swelling and perioperative analgesia in DXN compared with ADN. (Fig. 5) Similarly, many past studies found significant recovery of postoperative sequelae after TMS with administration of a single dose of dexamethasone.

**Fig. 6.** Neuro-anatomy of inferior alveolar nerve; cable wire network of neurons surrounds by the endoneurium in central (core) and periphery (mental) fibers, wrapped into the perineurium and epineurium diffusion of local anaesthetic solution from the mantle to core fibers.

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through different routes, i.e., per-oral, intravenous, intramus-
cular, local (intra-alveolar or submucosal), and perineural. 
Therefore, the anti-inflammatory action of dexamethasone is 
the primary mechanism of action for the reduction of these 
sequelae on the second postoperative day. As a result, this 
finding has improved the immediate postoperative quality of
life of patients. Other adverse outcomes such as slow wound
healing, bruising, paraesthesia of the lip, mood changes, and 
wound infection were studied for one week after TMS and 
were not statistically significant between the study groups.
However, intraoperative bleeding was significantly more
frequent in ADN and nausea and vomiting significantly less
frequent in DXN. (Table 4)

Intraoperative bleeding could be a disadvantage of using
dexamethasone. This injection technique has offered many
advantages over the dual-injection technique of dexametha-
sone, such as one short injection, better patient compliance,
exact anatomical deposition, and fast onset time resulting
in improved success rates. The benefit is that this technique
allows for patients to return to work earlier, avoid hospital
admissions, and reduces postoperative morbidity after TMS.
Dexamethasone adjuvants could be used in conditions like
hypertension, cardiovascular disease, and hyperthyroid dis-
ease. Unfortunately, the use of dexamethasone is discouraged
in patients on anti-depressant medications where adrenaline
is contraindicated. In addition, dexamethasone should not be
used in patients with diabetes mellitus, peptic ulcers, renal
insufficiencies, and in pregnant women or lactating females.
A limitation to the present study is the lack of assessment of
the depth of anaesthesia and the inability to perform triple
blinding. More studies are required to evaluate perineural
dexamethasone’s practical benefits and clinical safety as an
LA adjunct in IANB.

V. Conclusion

Single-injection techniques have produced profound peri-
operative analgesia using adjuvant dexamethasone with
lignocaine, which prolongs the duration of IANBs. An ad-
titional benefit of adjuvant dexamethasone with lignocaine
was an improvement in postoperative sequelae such as tris-
mus, swelling, nausea, vomiting, and perioperative analge-
sia. Therefore, a simple one-step single injection technique
improves the overall surgical outcome and the patient’s
postoperative quality of life. Therefore, we recommend dexa-
methasone for all routine third molar surgeries except where
it is contraindicated.
Effectiveness of DXN or ADN with lignocaine 2% for prolonging IANB

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