



# An *in vivo* study comparing efficacy of 0.25% and 0.5% bupivacaine in infraorbital nerve block for postoperative analgesia

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**Background:** Pain is an unpleasant sensation ranging from mild localized discomfort to agony and is one of the most commonly experienced symptoms in oral surgery. Usually, local anesthetic agents and analgesics are used for pain control in oral surgical procedures. Local anesthetic agents including lignocaine and bupivacaine are routinely used in varying concentrations. The present study was designed to evaluate and compare the efficacy of 0.25% and 0.5% bupivacaine for postoperative analgesia in infraorbital nerve block.

**Methods:** Forty-one patients undergoing bilateral maxillary orthodontic extraction received 0.5% bupivacaine (n = 41) on one side and 0.25% bupivacaine (n = 41) on the other side at an interval of 7 d. The parameters evaluated for both the bupivacaine concentrations were onset of action, pain during procedure (visual analog scale score [VAS]), and duration of action. The results were noted, tabulated, and analyzed using the Wilcoxon signed rank test.

**Results:** The onset of action of 0.5% bupivacaine was quicker than that of 0.25% bupivacaine, but the difference was not statistically significant (P = 0.306). No significant difference was found between the solutions for VAS scores (P = 0.221) scores and duration of action (P = 0.662).

**Conclusion:** There was no significant difference between 0.25% bupivacaine and 0.5% bupivacaine in terms of onset of action, pain during procedure, and duration of action. The use of 0.25% bupivacaine is recommended.

**Keywords:** Bupivacaine; Local Anesthesia; Postoperative Pain; Tooth Extraction.

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## INTRODUCTION

It is rightly said that pain is inevitable, but it can be reduced if intercepted correctly. Pain is an unpleasant sensation that ranges from mild localized discomfort to agony and is one of the most commonly experienced symptoms in oral surgery. Usually, local anesthetic agents and analgesics are used for pain control in oral surgical procedures.

In the late 1800s, the introduction of local anesthetic

agents was a major milestone in the history of medicine that facilitated pain-free procedures and better patient compliance. Since then, formulations of various classes of anesthetic drugs are commercially available for use in different concentrations. Lignocaine, first synthesized by Nils Lofgren and Bengt Lundquist in 1946, is the most commonly used anesthetic drug and is still considered as the gold standard [1].

Lignocaine (N-diethylaminoacetyl-2, 6-xylidide) is an intermediate-acting amide-type local anesthetic drug with minimal side effects; however, there is a need for re-

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administration of local anesthesia while performing complicated oral surgical procedures or additional requirement of post-operative analgesics to reduce the anticipated pain due to its short duration of action.

Bupivacaine (1-butyl-2', 6'-pipecoloxylidide) was first formulated by Bo af Ekenstam et al. in 1957 [2]. It is a long-acting amide-type local anesthetic that was introduced for clinical use in 1963 [1,3]. Bupivacaine has a longer duration of action than lignocaine because of its higher lipid solubility and higher protein-binding ability. The onset of action of bupivacaine is 1–10 min, duration of action is about 2–9 h, and half-life in adults is 2.7 h [4]. The potency of bupivacaine is four times that of lignocaine at equivalent doses [5]. The onset of action of bupivacaine is slightly longer than that of lignocaine in case of block anesthesia, but it is similar in case of infiltration anesthesia. The major advantage of bupivacaine is that after the return of sensation, an analgesic period follows that reduces the need for analgesics postoperatively [6]. Although 0.5% bupivacaine is widely used, anesthesia can be achieved even with concentrations as low as 0.25% [5].

The split-mouth study design was selected to minimize research bias by avoiding psychological and physiological differences between tested patients. Orthodontic extractions were considered in this study because they are usually bilateral and present in the same anatomical position, thereby showing similar amount of difficulty in extraction [7]. The present study was designed to evaluate the effectiveness of two different concentrations of bupivacaine (0.25% and 0.5%) used to reduce post-operative pain after bilateral infraorbital nerve block for maxillary orthodontic extractions.

## MATERIALS AND METHODS

This prospective, randomized, in vivo, split-mouth clinical study was conducted at the Department of Oral and Maxillofacial Surgery after receiving approval from the Ethics committee at the Dr. D. Y. Patil Dental College and Hospital, Pimpri, Pune (institutional review board number DPU/R&R(D)/971(18)/16) in accordance with the Ethical Principles for Medical Research Involving Human Subjects outlined in the Helsinki Declaration. This study included 41 patients (28 females and 13 males). Each patient underwent two extractions on two different occasions, where 0.5% bupivacaine was administered on one side (site A) and 0.25% bupivacaine on the other (site B). Both the solutions were evaluated for onset of action, pain during procedure, and duration of action. The results were noted, tabulated, and analyzed (Table 1).

### 1. Inclusion criteria

- i. Patients requiring maxillary bilateral orthodontic extractions
- ii. Patients willing to be a part of the study

### 2. Exclusion criteria

- Traumatic extractions
- i. Patients consumed analgesics in last 24 h
  - ii. Patients requiring unilateral orthodontic extraction

### 3. Preoperative patient assessment

A detailed and thorough case history of the patient was recorded, followed by meticulous clinical examination.

**Table 1.** Distribution and comparison of onset of action, duration of action, VAS score of local anesthesia with two different concentrations of bupivacaine

	0.5% Bupivacaine	0.25% Bupivacaine	P-value
Sex ratio M:F (n, %)	13:28 (31.7%:68.3%)		
Age (y)	16.6 ± 3.6 (12–24)		
Onset of action (min)	3.88 ± 1.3	4.24 ± 1.241	0.306
Duration of action (h)	5.71 ± 1.45	5.74 ± 1.26	0.662
VAS score	1.22 (1–5)	1.32 (1–4)	0.221

Values are represented as mean ± standard deviation (range), or number of patients (%); VAS: Visual analog scale; Wilcoxon signed rank test

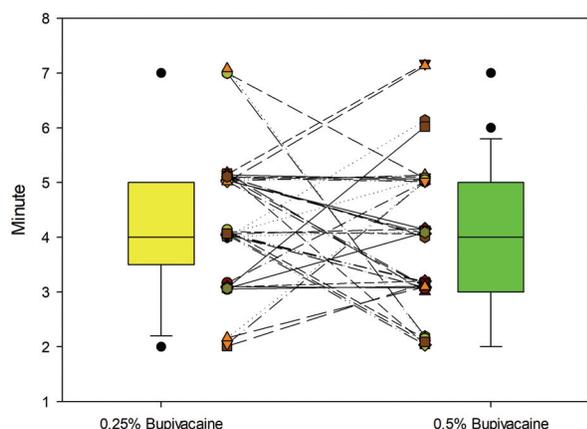


Fig. 1. Distribution and comparison of onset of action of local anesthesia for two different concentrations of bupivacaine

Valid written informed consent for the surgical procedure was obtained from each patient.

#### 4. Investigations

- 1) Hemogram
- 2) Bleeding time
- 3) Clotting time

#### 5. Methodology

Patients fulfilling the aforementioned criteria were included in the study. Detailed case histories of all patients was taken, and all patients underwent clinical examinations. A valid written informed consent was obtained from the patients. Infraorbital nerve block was administered using either 1.2 ml 0.25% bupivacaine (site A) or 1.2 ml 0.5% bupivacaine (site B) and 0.5 ml of the same solution was used for palatal infiltration as per the Sequentially Numbered Opaque Sealed Envelopes method. The time of administration of the injection and onset of action was noted. Extraction was carried out using appropriate armamentarium. Patients were asked to mark the intensity of pain on the visual analog scale (VAS) for comfort during the procedure. Patients were asked to note the time when the pain started and prescribed one tablet of a combination of ibuprofen (400 mg) and paracetamol (325 mg) [Tab. Combiflam<sup>®</sup> (SANOFI INDIA LIMITED, India)] for pain relief. Similar procedure was carried out on the contralateral side

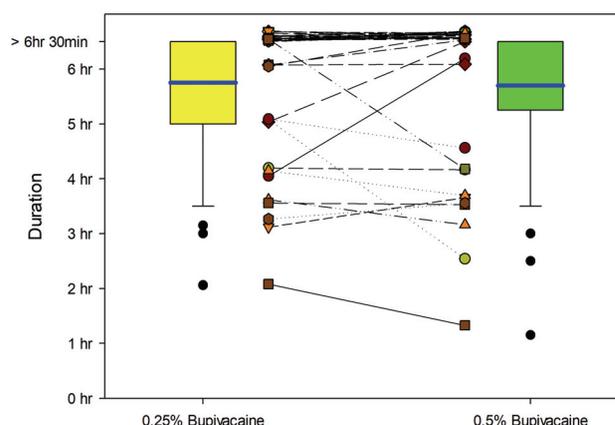


Fig. 2. Distribution and comparison of duration of action of local anesthesia for two different concentrations of bupivacaine

using the other solution after one week. The obtained values were recorded, tabulated, and statistically evaluated. Data obtained were compiled on MS Office Excel Sheet (2010 version) and subjected to statistical analysis using the Statistical package for Social Sciences (SPSS version 22.0, IBM). The Wilcoxon signed rank test was used to compare the paired data.

## RESULTS

Distribution and comparison of onset of action, duration of action, and VAS scores for the two different concentrations of bupivacaine (0.5% and 0.25%) showed no statistically significant differences ( $P = 0.306$ ;  $P = 0.662$ ;  $P = 0.221$ , respectively). For 0.5% and 0.25% bupivacaine concentrations, the mean values of onset of action were  $3.88 \pm 1.345$  min and  $4.24 \pm 1.241$  min (Fig. 1), those of duration of action were  $5.71 \pm 1.45$  h and  $5.74 \pm 1.26$  h (Fig. 2), and those of VAS scores were 1.22 (range 1 - 5) and 1.32 (range 1 - 4), respectively.

## DISCUSSION

Pain has always been one of the most distressing of all emotions, and modern surgery has been a blessing for patients with seemingly unending pain. Postoperative care

is as important as addressing the patient's complaint perioperatively. Since pain is one of the most common complaints of patients after any surgical procedure, attempts should be made to reduce it.

No matter how skilled the surgeon or atraumatic the procedure, patients always make their judgment based on the level of discomfort they experience postoperatively. Pain after various dental procedures such as extractions, endodontic treatment, and crown preparations is very common.

Commonly, local anesthetics and oral analgesics are effective in reducing postoperative pain. Lignocaine (lidocaine), which is considered the gold standard, is universally used as a local anesthetic. However, it may require re-administration for lengthy procedures including placement of multiple implants or removal of deeply impacted third molars.

Presumably, pain control can be maximized by using long-acting local anesthetics [8]. Therefore, bupivacaine, a long-acting water-soluble amide is pertinent for extended procedures. In the field of oral surgery, the first clinical trial of bupivacaine was performed in 1966 [3]. After being used extensively in obstetrics and general surgery, it was insinuated into dentistry in 1972 [9]. Bupivacaine is most commonly preferred in oral and maxillofacial surgery for prolonged postoperative analgesia because of its longer duration of action [1], thus reducing undue usage of oral analgesics.

Bupivacaine can be used with or without epinephrine. In adults, maximum dosage without epinephrine should not exceed 200 mg, while 250 mg can be safely administered with epinephrine [5]. Major advantage of bupivacaine is its longer duration of action and extended residual analgesia [10] due to high lipid-solubility and high protein-binding ability [1,8].

Malamed [4] stated that the onset of action of lignocaine was 2–3 min, while that of bupivacaine was 6–10 min, which could be due to the 8.1 and 7.7 pKa of bupivacaine and lignocaine, respectively. Consequently, at a tissue pH of 7.4, lesser number of molecules will be accessible in free base form to permeate the nerve

membrane, thus resulting in slower onset [11,12].

A study conducted by Vilchez-Pérez et al. [10] showed that 70% of pulpal anesthesia was achieved in 5 min with bupivacaine, while the success of infiltration of bupivacaine solution was 78% according to Gross et al. [11]. The protein binding co-efficient of bupivacaine is 96%, which is much higher than that of lignocaine (64%) [13].

Bupivacaine can be used in combination with lignocaine in cases where adrenaline is contraindicated [14]. If the success rate of local anesthesia is analyzed in dentistry, according to the meta-analysis published by Su et al. [9], 0.5% bupivacaine is superior to 2% lidocaine in cases of inflamed pulp, whereas 2% lidocaine is better than 0.5% bupivacaine in cases of vital pulp. With respect to adverse effects, bupivacaine toxicity was one-fourth times lower than that of lidocaine [9]. The therapeutic ratio of bupivacaine is higher than that of lignocaine, as established by De Jong and Bovin [15].

Laskin [16] concluded that in oral surgery, 0.5% bupivacaine with 1:200000 epinephrine is the quintessential concentration; however, anesthesia can be achieved with 0.25% bupivacaine. Nespeca et al. [14] found that postoperative pain and use of analgesics were less in the bupivacaine group than that in the lidocaine group, while the difference between 0.5% bupivacaine and 0.25% bupivacaine was not significant.

Bupivacaine can be used as a primary block or as supplemental injection towards the end of the procedure for additional pain-free period, but the study by De Souza et al. [17] revealed that other than better patient acceptance, there was no apparent value of the second injection in terms of analgesic use and pain.

Fox and Patrie [18] showed that 0.5% bupivacaine offered more pain relief than 0.25% bupivacaine, but the difference was not statistically significant. Similarly, Iamaroon et al. [19] reported that compared with 0.25% bupivacaine, 0.5% bupivacaine rendered longer time for first analgesic dose and reduced the narcotic requirements after patellar tendon graft in anterior cruciate ligament reconstruction.

Palma et al. [20] advocated the use of 0.25%

bupivacaine for pain control in pediatric patients undergoing cardiac catheterization. Souza et al. [21] reported that femoral nerve block using 0.25% bupivacaine or 0.25% ropivacaine was efficacious in postoperative analgesia after total knee replacement or anterior cruciate ligament reconstruction. Similarly, Mulroy et al. [22] reported that both 0.25% and 0.5% bupivacaine provided adequate analgesia following femoral nerve block after arthroscopic anterior cruciate ligament repair.

Brajkovic et al. [13] conducted a study to evaluate the quality of analgesia after mandibular third molar extraction and concluded that both 0.5% bupivacaine and 0.5% levobupivacaine provided profound analgesia postoperatively, as opposed to 2% lidocaine with epinephrine, thus confirming that using bupivacaine leads to lesser postoperative intake of analgesics [23].

Nielsen et al. [24] reported that both plain 0.5% bupivacaine and plain 0.25% bupivacaine showed similarities with respect to time of onset, credibility of motor blockade, and duration of analgesia, when used for spinal analgesia.

Reduction of concentration of any drug helps in reducing systemic toxicity. Use of lower concentrations of a drug in higher volumes is better than using higher concentration of the same drug in lower volumes. This was confirmed in a study by Lyons et al. [25], where the level of analgesia produced by 0.125% (weight/volume) bupivacaine was analogous to that produced by 0.5% bupivacaine.

A study conducted by Dhanrajani et al. [26] compared the analgesic efficacy of 0.5% bupivacaine and 0.25% bupivacaine in third molar extraction, but the procedure was performed under general anesthesia. Hence, the effect of anesthesia (bupivacaine), providing pain relief, is questionable because the patients were already under the influence of sedatives and opioid analgesics such as fentanyl.

Our study included patients requiring bilateral maxillary orthodontic extractions. We followed the split-mouth study as it diminishes research bias and each patient acts as his/her own control, thereby eliminating any disparity

in inflammatory response and subjective response to pain [7,17]. As most of our patients were children, management of postoperative pain was essential not only for medical reasons, but also for ethical reasons [27].

We found that the onset of action of 0.5% bupivacaine was faster than that of 0.25% bupivacaine, but the difference was not statistically significant. Duration of action of both the solutions was found to be similar, and no significant difference was found in their VAS scores. Thus, we concluded that there was no significant difference between 0.25% bupivacaine and 0.5% bupivacaine in terms of onset of action, pain during procedure, and duration of action, and we recommend the use of 0.25% bupivacaine.

Bupivacaine is a routinely used long-acting amide local anesthetic that is very effective in the management of postoperative pain. Many studies have been published comparing various concentrations of bupivacaine with lignocaine and articaine, but no comparative split-mouth study has been conducted that compared 0.5% bupivacaine and 0.25% bupivacaine during intra-alveolar extractions.

A further long-term prospective, randomized controlled trial should be undertaken to compare the efficacy of both the concentrations of bupivacaine.

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