

**Original article:**

**A comparative clinical study to evaluate the effect of premedication with Ibuprofen, Tramadol and combination of Ibuprofen and Acetaminophen on success of Inferior Alveolar Nerve Block in patients with Asymptomatic Irreversible Pulpitis.**

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**Abstract**

**Introduction:** Aim of this study was to evaluate the effective of premedication and to determine the difference between non steroidal anti-inflammatory drugs and centrally acting opioids like tramadol on success rate of inferior alveolar nerve block in patients with asymptomatic irreversible pulpitis. **Methods:** This double blind clinical study was conducted on 60 patients with asymptomatic irreversible pulpitis in first or second mandibular molar with normal periapical radiographic findings. Three medications i.e., ibuprofen (600mg), tramadol (50 mg) and combination of ibuprofen (400 mg) + acetaminophen (325) were compared and lactose powder capsules were taken as placebo. All patients received IANB and teeth were examined with a cold pulp test using endofrost. Then, endodontic access cavity preparation was initiated. In case of pain during treatment, patients were asked to rate their pain on the visual analog scale. **Results:** The tramadol group showed significantly higher success rates but ibuprofen and combination of ibuprofen and acetaminophen groups were not significant with placebo (p>05). No Significant differences were there regarding sex of the patients. **Conclusion:** Premedication with tramadol increased the success rate of IANB.

**Keywords:** Endfrost; Ibuprofen; Tramadol; Acetaminophen; Inferior Alveolar Nerve Block; Asymptomatic irreversible pulpitis

Bangladesh Journal of Medical Science Vol. 16 No. 03 July'17. Page : 370-374

**Introduction**

Management of endodontic pain particularly during early phases of endodontic treatment is of paramount importance in reducing fear and anxiety of patient and makes both the dentist and patient confident during the treatment<sup>1</sup>

Inferior alveolar nerve block (IANB) is the standardized injection technique for achieving regional anaesthesia for mandibular molar treatment<sup>2</sup>. IANB is effective in anaesthesia of the tooth with

normal pulp but this technique fails in majority of cases with inflamed pulp<sup>3,4</sup>.

Inferior alveolar nerve block fails in molar having irreversible pulpitis mainly occurs due to inflammation of pulp<sup>5</sup>. Hence, preoperative anti-inflammatory oral drug therapy using NSAIDS can be useful in improving success rate of IANB<sup>6</sup>. As prostaglandins are considered inflammatory mediators, ibuprofen has been suggested to increase the efficacy of the inferior alveolar nerve block by interruption of prostaglandin

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production by inhibiting cyclo-oxygenase enzymes. Amongst drugs, ibuprofen is an interesting choice for analysis because in clinical trials it has yielded significant improvements in efficacy of IANB in patients diagnosed with irreversible pulpitis<sup>7</sup>. Premedication with ibuprofen and indomethacin significantly increased the success rates of inferior alveolar nerve block anesthesia for teeth with irreversible pulpitis<sup>8</sup>.

Ianiro et al. (2007) reported higher success rates in inferior alveolar nerve block anesthesia of mandibular molars with inflamed pulps after premedication with acetaminophen and ibuprofen. Acetaminophen inhibits prostaglandin synthesis, and interacts with both cannabinoid and serotonergic pathways. So, acetaminophen has been considered to have some additional analgesic effect when used in combination with ibuprofen. Acetaminophen has been considered to have some additional analgesic effect on ibuprofen so this might increase the success rate of ibuprofen when used in combination with ibuprofen<sup>10</sup>.

However, nonsteroidal anti-inflammatory drugs suffer from major pharmacodynamic limitations i.e. a ceiling in their dose response curve for analgesia. So, an opioid (tramadol) may be proposed for managing these patients<sup>11</sup>. Several other researchers reported insignificant improvement in success of inferior alveolar nerve block after premedication<sup>12,13</sup>. Tramadol is a cyclohexanol derivative with weak mu-agonist, opioid-like activity. It is centrally acting analgesic that inhibits the reuptake of norepinephrine and promotes the release of serotonin<sup>14</sup>. The synergy of monoaminergic and opioid activity achieves analgesic effects.

So, the aim of this study was to compare 3 kinds of analgesic drugs (Ibuprofen, Tramadol and combination of Ibuprofen and Acetaminophen) in relation to their effects on the success rates of inferior alveolar nerve block for the endodontic treatment of mandibular molars with asymptomatic irreversible pulpitis.

#### **Materials and Methods:**

This study was approved by Ethical committee of the Institute (GIDSR-15/EC//1865-68). The present double blind clinical study was conducted on 60 patients (32 male and 28 female) in the Department of Conservative dentistry and Endodontics in Genesis Institute of Dental Sciences and Research, Ferozepur, Punjab (India). Informed consent was taken from patient before his or her participation in the study. Patients having allergies, hypersensitivity, inability to take medicines, allergy to local anesthetics or

sulphites; pregnant and nursing mother; history of epilepsy and subjects below 18 years of age who were not able to give informed consent were excluded from the study. The patients included were between young ages of 18-25 years because as age progresses the incidence of clinical attachment loss increases<sup>(15)</sup>. Patients who had not taken any medicine at least 12 hours before participating in the study were included. Selected patients had a first or second mandibular molar with asymptomatic irreversible pulpitis and normal periapical radiographic findings. The clinical diagnosis of irreversible pulpitis was confirmed by prolonged response to cold testing with the help of Endofrost. (Propane (30-50%), Butane (30-50%) and Isobutane (10-20%) (Roeko, Coltene, Langenau, Germany). Double blinding and randomization was done by making slips of paper with name of the drugs used in each group, written on it. Fifteen slips were made for each group. All the slips were put together in a box. Each patient who came was asked to pick one of the slips and that particular medicine was given by a designated person to the patient.

All patients were divided into 4 groups of 15 each. Group A - Placebo (Lactose powder capsule), Group B- Ibuprofen 600 mg (Brufen 600, Abbott), Group C- Tramadol 50 mg (Tramcros-50, Cross wood), Group D- Acetaminophen 325 mg + Ibuprofen 400 mg (Combiflam, Sanofi).

Cold test was performed by holding the cotton saturated with endofrost on the buccal surface of involved tooth and adjacent tooth. Endo-frost can decrease the temperature upto -50 degree Celsius. The level of pain (moderate/severe) was verified using a 170 mm visual analog scale (VAS). This scale is having readings of no pain, mild, moderate, and severe pain. No pain - 0 mm, mild pain - 0-54 mm, moderate pain >54mm and < 114 mm, severe pain > 114 mm, maximum possible pain upto 170 mm.

After performing the cold pulp test, premedication was given to patients according to group assigned. One hour after oral administration of premedications, standard inferior alveolar nerve block injection was given to patient by using 1.8 mL of 2% lignocaine with 1:200,000 epinephrine (Neon labs limited) using 27 gauge needle. After aspiration, solution was injected at a speed of 1 ml / min.

Lip numbness was checked 15 minutes after administration of block. If complete lip numbness could not be achieved within 15 minutes in particular patient, the block was considered unsuccessful so that patient was excluded from the study. In patients with a successful inferior alveolar nerve block, cold

pulp testing was done again and patient was asked to assess their pain using VAS. If patient gives no response to cold test then after rubber dam application assess cavity preparation was performed on selected tooth. Patient was asked give signal by raising hand if he/she feels pain during the procedure. If pain is encountered, it was rated on VAS after stopping the procedure. The depth of assess cavity preparation and instrumentation was recorded at 3 levels: first “within dentin”, second “within pulpal space” and third “instrumentation of canals”. If there is no pain (VAS score 0) or mild pain (VAS score 54) procedure was considered successful. Any pain more than ‘no pain’ or ‘mild pain’ was considered a failure. In case of failure “alternate mode of anesthesia was considered to provide pain free treatment to patient. Follow up of patient was done for next 48 hours to assess any flare up or discomfort. For statistical analysis chi square test was applied.

**Ethical approval:** This study was approved by the Ethics Committee of genesis institute of Dental sciences & Research, Ferozepur.

### **Results**

Table – 1 shows the difference in success rate among groups, there were higher success rate for tramadol and least success rate for placebo.

Anesthetic success rate was higher for tramadol. There was significant difference when tramadol was compared with placebo as  $p < 0.05$ . Anesthetic success rate for tramadol was 66.7%, chi square test showed no significant difference among ibuprofen, tramadol and combination of ibuprofen and placebo. Table - 2 shows gender distribution among all the groups.

Graph - 1 shows comparison of success and failure rates among four Groups: Group A (Tramadol 50 mg) shows higher success rate among groups followed by Group B (ibuprofen 400 mg and acetaminophen 325 mg), Group C (ibuprofen 600 mg) and placebo.

**Table 1:- Success rate among different groups**

Group	Success (%)	Failure (%)	Total
Group A	5 (33.3%)	10 (66.7%)	15
Group B	7 (46.7%)	8 (53.3%)	15
Group C	9 (6%)	6 (34%)	15
Group D	8 (53.3%)	7 (46.7%)	15

Group A: Control group

Group B: Ibuprofen group

Group C: Tramadol group

Group D: Ibuprofen + Acetaminophen group

**Table 2:- Gender Distribution among groups in percentage**

Sex	Group 1	Group 2	Group 3	Group 4
Men	9 (60 %)	8 (53.3 %)	8 (53.33 %)	7 (46.66 %)
Women	6 (40 %)	7 (46.66 %)	7 (46.66 %)	8 (53.33 %)

### **Discussion**

Asymptomatic irreversible pulpitis is defined as “A clinical diagnosis based on subjective and objective findings indicating that the vital inflamed pulp is incapable of healing”<sup>16</sup>. As Irreversible pulpitis is also defined as a painful response to a cold stimulus that lingers for prolonged time after stimulus was removed. So only patients who gave prolonged response to cold pulp test were included in study. Cold pulp test was used to verify irreversible pulpitis. Cold pulp test is widely regarded as effective for diagnosing pulp vitality in 90% of cases as compared to 83% with the heat test and 84% with the electrical test<sup>9</sup>.

Two percent lignocaine with 1: 200,000 epinephrine was chosen in this study because it is considered as standard and common anesthetic solution in dental practice<sup>9</sup>. It is suggested that solutions of 2% lignocaine with different doses of epinephrine (1: 50,000; 1: 80,000; 1: 100,000) are equivalent in IANB of 50 minute duration<sup>17</sup>.

Visual analog scale has achieved wide acceptance in the experimental field, having important attributes of simple conversions to numbers. The scale is a reliable tool for evaluating IANB and is easily managed by patients<sup>18</sup>. Transient receptor potential vanilloid channels (TRPV) have been strongly implicated in pain signaling. TRPV plays an important role in hyperalgesia in both peripheral sensory transduction and central nervous system<sup>19</sup>. TRPV channel is sensitized by prostaglandins. Therefore, it appears logical that if one could decrease the amount of prostaglandins, it might lead to increased efficacy of anesthetics. Ibuprofen acts as analgesic by blocking continued production of prostaglandins. So there might be increase in effectiveness of inferior alveolar nerve block.

However, modest success rate of 46.7% in present study for ibuprofen group does not support this hypothesis. The less success rate could be due to several factors. There are vast array of inflammatory mediators those increase the Nav 1.9 current and excitability in nociceptors upregulation of sodium

channel isoforms was seen. So synergistic action of multiple inflammatory mediators like prostaglandins, serotonin and histamine is seen. Therefore removal of single inflammatory mediator might not be enough to overcome the effects of other inflammatory mediators.

Ibuprofen can increase the efficacy of inferior alveolar nerve block by interruption of prostaglandin production. Success rate of current study for ibuprofen is comparable to range as reported in previous studies<sup>4,13,20, 21,22</sup>.

Acetaminophen inhibits both isoforms of cyclooxygenase (COX): the constitutive COX-1 and inducible COX-2. COX enzyme is highly active when it is appropriately oxidized. Acetaminophen reduces the oxidized form of the COX enzyme to the resting form, preventing it from forming pro-inflammatory chemicals. Acetaminophen is also considered selective for COX-2<sup>23</sup>. The mechanism of acetaminophen described are partially different from and perhaps complementary to ibuprofen's mechanism of action<sup>(10)</sup>. Theoretically there might be some potential for a combination of preoperative ibuprofen and acetaminophen to increase the effectiveness of the inferior alveolar nerve block despite ibuprofen inability to do so alone.

In the present study the success rate of combination of acetaminophen (325 mg) and ibuprofen (400 mg) is 53.3%. Present study contradicts the study done by Ianiro et al. (2007)<sup>9</sup>. There was higher success rate for combination of ibuprofen and acetaminophen for IANB in irreversible pulpitis with statistically

significant difference from control group. Reason might be different dosage of acetaminophen taken.

Tramadol is potent analgesic with effect of analgesia beginning within first hour of oral dosing and peaks in four to six hours<sup>24</sup>. As tramadol is an opioid, drug is indicated in moderate to severe pain of any type. Tramadol lowers the seizure threshold, so patients with history of epilepsy were excluded from the study. Also, tramadol is considered as atypical opioid as it acts independently on opioid and non opioid components. Due to both of these actions it shows high analgesic effect<sup>25</sup>. So being an opioid with combined actions of central nervous system and peripheral nervous system, the success rate of tramadol is slightly higher when compared to ibuprofen and combination of ibuprofen with acetaminophen. The success rate for tramadol on inferior alveolar nerve block with asymptomatic irreversible pulpitis in this study is 66.6%, which shows significant effect on success rate of inferior alveolar nerve block in asymptomatic irreversible pulpitis as compared to placebo but the results are non-significant among three groups that is tramadol, ibuprofen and combination of ibuprofen and acetaminophen.

**Conclusions:** Tramadol is centrally acting opioid analgesic with potent analgesic effect that's why it showed higher success rate effect than ibuprofen and combination of ibuprofen and acetaminophen.

So tramadol is considered as most effective measure for pain control in patients with inferior alveolar nerve block when compared to non-steroidal anti-inflammatory drugs.

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