Comparative evaluation of effect of preoperative alprazolam and diclofenac potassium on the success of inferior alveolar, Vazirani-Akinosi, and Gow-Gates techniques for teeth with irreversible pulpitis: Randomized controlled trial

Pratibha Shetkar, Ganesh Ranganath Jadhav, Priya Mittal, Saikalyan Surapaneni, Dheeraj Kalra, Mohan Sakri, Basavaprabhu A

Departments of Conservative Dentistry and Endodontics and Public Health Dentistry, Sinhgad Dental College and Hospital, Pune, Department of Conservative Dentistry and Endodontics, Rural Dental College, Pravaranagar, Loni, Maharashtra, Department of Conservative Dentistry and Endodontics, Centre for Dental Education and Research, New Delhi, Department of Conservative Dentistry and Endodontics, KIMS Dental College and Hospital, Amalapuram, Andhra Pradesh, Department of Preventive and Pediatric Dentistry, Al-Badar Dental College, Davangere, Karnataka, India

Abstract

Introduction: In teeth with irreversible pulpitis, successful local anesthesia is hard to achieve irrespective of the amount of local anesthesia and technique used. Such cases can be managed by concoction of pre-medications like anxiolytics, analgesics and effective local anesthesia. This double-blind, placebo-controlled study was planned to evaluate the effect of oral administration of alprazolam and diclofenac potassium on the success rate of inferior alveolar nerve block (IANB), Gow-Gates (GG) and Vazirani-Akinosi (VA) techniques for the root canal treatment of mandibular molars with irreversible pulpitis.

Method: 198 emergency patients with symptomatic irreversible pulpitis were randomly divided into three groups as – A, B and C receiving IANB, GG or V-A respectively using 2% lidocaine with 1:100,000 epinephrine. These groups were sub-divided into sub-groups I and II as control and pre-medication groups. Patients who did not react to the stimulus made by an explorer between the canine and first premolar and showing subjective lip and tongue numbness were included in the study.

Result: All sub-groups showed statistically significant reduction in VAS score. However sub-groups V and VI (that is GG with and without pre-medication respectively) showed best improvement in initial severe pain in mandibular molars with irreversible pulpitis. Moreover, all pre-medication sub-groups showed better pain control compared to respective control groups.

Conclusion: It was concluded that use of pre-medications in the form of combination of anxiolytics and analgesics improves the success rate of local anesthesia in teeth with irreversible pulpitis. Use of anxiolytics eases the patient in endodontic emergencies. Also use of GG along with pre-medication is the best method for effective pain management of acute pain in irreversible pulpitis.

Keywords: Analgesics; anxiolytics; Gow-Gates technique; inferior alveolar nerve block; irreversible pulpitis; Vazirani-Akinosi technique

Address for correspondence: Dr. Ganesh Ranganath Jadhav, Department of Conservative Dentistry and Endodontics, Sinhgad Dental College and Hospital, Pune, Maharashtra, India. E-mail: drganesh2009.aims@gmail.com

Date of submission: 05.05.2016
Review completed: 09.07.2016
Date of acceptance: 22.08.2016

Concoction of effective local anesthesia and preanaesthetic

This is an open access article distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as the author is credited and the new creations are licensed under the identical terms.

For reprints contact: reprints@medknow.com

How to cite this article: Shetkar P, Jadhav GR, Mittal P, Surapaneni S, Kalra D, Sakri M, et al. Comparative evaluation of effect of preoperative alprazolam and diclofenac potassium on the success of inferior alveolar, Vazirani-Akinosi, and Gow-Gates techniques for teeth with irreversible pulpitis: Randomized controlled trial. J Conserv Dent 2016;19:390-5.
medication such as anxiolytics, analgesics is decisive for the painless management of endodontic emergencies. Inferior alveolar nerve block (IANB) is commonly used to anesthetize the mandibular molars. However, IANB shows lower success than the other techniques such as Gow-Gates (GG) and Vazirani-Akinosi (V-A) due to various factors such as accessory nerve supply (auriculotemporal, mylohyoid, and cervical cutaneous nerves - C1, C2); bifid alveolar nerve; variable course of inferior alveolar nerve; variation in foramen position. These factors are compensated in high block techniques such as GG and V-A. V-A is a closed mouth technique with mucogingival junction of maxillary second molar used as a landmark and in GG technique, neck of mandibular condyle is used as a target site.

In teeth with irreversible pulpitis, successful local anesthesia is difficult to achieve irrespective of the amount and technique of local anesthesia used. Endodontic therapy is considered as the most stress-inducing procedure in dentistry and patients in endodontic pain are extremely anxious. Stress affects the patient's adaptive ability to pain and is associated with higher incidence of pain. Preanesthetic medications in the form of psycholeptics such as benzodiazepines (Alprazolam) and analgesics such as nonsteroidal anti-inflammatory drugs (NSAIDs; diclofenac potassium) might improve the efficiency of local anesthesia with reduced chances of interoperative and postoperative endodontic pain.

Exploring from the above information, it can be assumed that combination of alprazolam and diclofenac potassium as a premedication can improve the success of various anesthesia techniques. Hence, this double-blind, placebo-controlled study was planned to evaluate the effect of oral administration of alprazolam and diclofenac potassium on the success rate of IANB, GG, and V-A techniques for the root canal treatment of mandibular molars with irreversible pulpitis.

**MATERIALS AND METHODS**

The Institutional Review Board and Ethical Committee approved the research protocol.

**Inclusion criteria**

The inclusion criteria for the study were patients between the age group of 18 and 50 years, mandibular molars with a clinical diagnosis of symptomatic irreversible pulpitis (severe pain according to Heft-Parker visual analog scale (VAS) in a tooth with prolonged response to cold testing), absence of radiographic evidence of periapical radiolucency with exception of widened periodontal ligament space, vital coronal pulp on access opening; ability to understand and rate the use of anxiety and pain scales.

**Exclusion criteria**

Exclusion criteria included known allergy to benzodiazepines or NSAIDs, history of bleeding disorders, or anticoagulant use within the last month, pregnant or breastfeeding patients, history of known drug abuse, use of analgesics within 12 h before administration of the study drugs, and active pain in more than 1 mandibular posterior tooth. Teeth without pulp exposure following caries excavation and no bleeding (indicating pulp necrosis) following access cavity preparation were also excluded from the study.

**Recruitment of the participants**

Sample size was determined based on the values of mean and standard deviation of the pilot study, using a formula \( n = \left(\frac{2Z_{α/2} σ}{d}\right)^2 \). The minimum sample size per subgroup was obtained to be 29. A total of 210 patients were evaluated for this study. Based on the statistical analysis, inclusion and exclusion criteria, one hundred ninety-eight healthy adult volunteers who reported to the department of conservative dentistry and endodontics were recruited in the study. The risks and complications of the treatment were explained and written informed consent was obtained from each subject. Each patient rated his or her initial pain on a Heft-Parker VAS of 170-mm marked line. It is divided into 4 categories as no pain (0 mm), mild pain (1–54 mm), moderate pain (55–113 mm), and severe pain (114–170 mm). The preoperative anxiety level of each patient was evaluated by Corah dental anxiety scale with 4-item questionnaire about 4 dentally related situations and score is divided into four categories as – no anxiety (4–8), moderate anxiety (9–12), high anxiety (13–14), and severe anxiety (or phobia) (15–20). A registered pharmacist compounded 180 tablets of placebo, 90 are identical with alprazolam (alzolite, alprazolam 0.5 mg, Elite Pharma Pvt Ltd., India) tablets and rest 90 are identical with diclofenac potassium (Voveran D, 50 mg diclofenac potassium, Novartis, India) tablets. All four different tablets are kept in four separate bottles (two for placebos, one for alzolite, and one for Voveran D). A trained dental hygienist assigned 4-digit random number from a random number table to all patients. This master chart of number table was accessible only to dental hygienist to blind the patients and principal investigator. All patients were categorized randomly into six groups as:

- **Group A (n = 66)**
  - Subgroup I \([n = 33] [n_a = 30]\) - patients receiving placebo tablets and IANB
  - Subgroup II \([n = 33] [n_a = 30]\) - patients receiving 0.5 mg alprazolam, 50 mg of diclofenac potassium, and IANB.
- **Group B (n = 66)**
  - Subgroup III \([n = 33] [n_a = 30]\) - patients receiving placebo tablets and V-A block
Subgroup IV (\(n = 33\) \([n_i = 30]\)) - patients receiving 0.5 mg alprazolam, 50 mg of diclofenac potassium, and V-A block.

- Group C (\(n = 66\))
- Subgroup V (\(n = 33\) \([n_i = 30]\)) - patients receiving placebo tablets and GG block
- Subgroup VI (\(n = 33\) \([n_i = 30]\)) - patients receiving 0.5 mg Alprazolam, 50 mg of diclofenac potassium, and GG block.

Moreover, subjects were instructed to rate the pain of needle insertion, needle placement, and anesthetic solution deposition using a 4-point scale as 0 (no pain), 1 (mild pain that was recognizable but not discomforting), 2 (moderate pain that was discomforting but bearable), and 3 (severe pain that caused considerable discomfort and was difficult to bear). Immediately after the nerve block, each subject was asked to rate the pain for each injection phase. Patients completed a Corah dental anxiety scale to rate their level of anxiety. The alprazolam, diclofenac potassium, and compounded tablets were given 1 h before nerve block according to divided groups. Preinjection topical anesthetic gel (20% benzocaine; Patterson Dental Supply, Inc., St Paul, MN, USA) was passively placed at all block injection sites for 60 s using an applicator tip. About 3.6 ml of local anesthesia (2% lidocaine with 1:100,000 epinephrine, LOX 2% Neon Lab, India) was given using 5 ml syringe with 27-gauge 1½-inch long needle.

All patients in Group A received IANB, in Group B received V-A, and in Group C received GG. After 15 min, patients who failed to meet the clinical signs of anesthesia that is tingling in the lower lip and tip of the tongue or those who reacted to the stimulus made by an explorer between the canine and first premolar, were excluded from the statistical analysis. Under rubber dam isolation, access cavities were prepared, and patients were instructed to rate any pain felt during access cavity preparation or initial file placement. If the patient felt pain, the treatment was immediately stopped, and the patient rated the discomfort using Heft-Parker VAS. Furthermore, intraoperative anxiety was rated on Corah dental anxiety scale (Detailed procedure is depicted in CONSORT Flow Chart 1).

**Results**

Of the 210 patients, 12 were excluded from the study and 198 were randomly divided into three groups. There were no differences in age, gender, scores of scales of initial pain, and anxiety between Groups A, B, and C (\(P \leq 0.05\)). The age range was 18–50 years, with an average of 29 ± 8 years. Preoperative values of VAS and Corah anxiety scale for all six subgroups were in the same range (VAS in the range of 116–125 with an average of 120.27 indicating severe pain and CAS in the range of 13–20 with an average of 16.15) [Table 1]. All three injection techniques showed statistically significant reduction in VAS indicating profound pulpal anesthesia can be achieved with above-mentioned injection techniques for teeth with irreversible pulpitis. Furthermore, there were statistically significant differences (\(P \leq 0.05\)) in VAS rating between the control and premedication groups. Although Corah anxiety scale showed statistically significant differences in preoperative and intraoperative ratings in all groups, it did not show any intergroup difference in the level of anxiety (\(P \leq 0.05\)). Subgroup VI (GG technique with premedication) showed a best reduction in intraoperative pain for teeth with irreversible pain. Pain and discomfort ratings for three phases of injection techniques are shown in Table 2. Group A (IANB group) showed the least discomfort in all three phases. There was no significant difference in the age of the patients among the groups (\(P = 0.975\)) [Table 3]. Hence age related bias was automatically eliminated.

**Discussion**

The present prospective, placebo-controlled, double-blind study was conducted to compare and evaluate the effect of preoperative anxiolytic and analgesic drugs on success of inferior alveolar, GG, and V-A techniques for teeth with irreversible pulpitis. The patients’ age, gender, initial pain, anxiety level, and type of tooth were not significantly different between all six groups [Table 1], and thus, effect of these variables on the study outcome would be minimized. Heft-Parker VAS has been selected as the method of assessing pain because it is reliable, reproducible, and scientifically valid. In the present study, patients who met this criterion of a mean initial severe pain (114–170 mm) on the VAS and painful response to the cold stimulus that lingers for several minutes after the stimulus is removed were selected. The Corah dental anxiety scale is the most commonly used dental anxiety scale and is easy to administer [8,9]. The mean score of anxiety scale in all groups was in the range of 13–14 - that would indicate high anxiety that would be expected in patients with symptomatic irreversible pulpitis.

Conventional IANB is most commonly used technique for anesthetizing mandibular molars. However, its failure rate reported to be as high as 30% in teeth with irreversible pulpitis. Thus, a continuing need exists to improve its success.
CONSORT (Consolidated Standards of Reporting Trials) flow chart of patients through each stage

Assessed for eligibility
(n = 210)

- Excluded (n = 12)
  - known allergy to benzodiazipines or NSAIDs,
  - history of bleeding disorders or anticoagulant use within the last month,
  - pregnant or breast-feeding patients,
  - history of known or suspected drug abuse,
  - patients who had taken analgesics within 12 hours before administration of the study drugs

- active pain in more than 1 mandibular posterior tooth

Included (n = 198)
- patients between the age group of 18 to 50 years,
- mandibular molars with a clinical diagnosis of symptomatic irreversible pulpitis [severe pain in a tooth with prolonged response to cold testing],
- absence of radiographic evidence of periapical radiolucency with exception of widened periodontal ligament space,
- vital coronal pulp on access opening;
- ability to understand the use of anxiety and pain scales

VAS, CDA scale were taken and patients were randomly categorized (n = 198)

Group A (n = 66) IANB

- Group I Control (n = 33) [n₁ = 1; n₂ = 2] (nᵢ = 30)
- Group II Alprazolam + diclofenac potassium (n = 33) [n₁ = 2; n₂ = 1] (nᵢ = 30)

Group B (n = 66) GG

- Group III Control (n = 33) [n₁ = 2; n₂ = 1] (nᵢ = 30)
- Group IV Alprazolam + diclofenac potassium (n = 33) [n₁ = 3; n₂ = 0] (nᵢ = 30)

Group C (n = 66) V-A

- Group V Control (n = 33) [n₁ = 3; n₂ = 0] (nᵢ = 30)
- Group VI Alprazolam + diclofenac potassium (n = 33) [n₁ = 3; n₂ = 0] (nᵢ = 30)

Patients instructed to rate pain felt during access cavity preparation or initial file placement on VAS

Post-operative anxiety rated on CDA scale

Statistical analyses were carried out to
1. Rate and compare pain of NI, NP and SD in all three techniques;
2. Compare the effect of pre-operative alprazolam and diclofenac potassium on the success of all three techniques for teeth with irreversible pulpitis

NSAIDs – non-steroidal anti-inflammatory drugs; VAS - Heft-Parker visual analogue scale; CDA - Corah Dental Anxiety Scale IANB - inferior alveolar nerve block; GG - Gow-Gates V-A - Vazirani-Akinosi NI – needle injection; NP – needle placement; SD – solution deposition

n₁ - patients eliminated due to unsuccessful anesthesia;

n₂ - patients eliminated for statistical ease;

nᵢ - patients recruited finally in study

Flow chart 1: CONSORT flow chart
Table 1: Comparative evaluation of variables of inferior alveolar nerve block, Gow-Gates, and Vazirani-Akinosi technique

| Variables                  | Sub-group I | Sub-group II | Sub-group III | Sub-group IV | Sub-group V | Sub-group VI | P   |
|----------------------------|-------------|--------------|---------------|--------------|-------------|--------------|-----|
| Total subjects             | 30          | 30           | 30            | 30           | 30          | 30           | 0.975 |
| Age (years)                | 18-50       | 18-50        | 18-50         | 18-50        | 18-50       | 18-50        |     |
| Gender                     |             |              |               |              |             |              |     |
| Male                       | 17          | 17           | 16            | 16           | 15          | 15           |     |
| Female                     | 13          | 13           | 14            | 14           | 15          | 15           |     |
| Visual analog scale -preoperative pain (average) | 120.45 | 120.74 | 120.26 | 120.16 | 119.77 | 120.26 | 0.832 |
| Intraoperative pain (average) | 79.32 | 69.16 | 58.61 | 50.26 | 35 | 23.19 | 0.000 |
| P                          | 0.000       | 0.000        | 0.000         | 0.000        | 0.000       | 0.000        |     |
| Corah anxiety scale - preoperative rating (average) | 16.17 | 16.37 | 16.53 | 15.93 | 15.80 | 16.07 | 0.732 |
| Intraoperative ratings (average) | 10.37 | 10.47 | 10.47 | 10.27 | 10.23 | 10.30 | 0.936 |
| P                          | 0.000       | 0.000        | 0.000         | 0.000        | 0.000       | 0.000        |     |
| Tooth                      |             |              |               |              |             |              |     |
| First molar                | 23          | 22           | 22            | 21           | 20          | 20           |     |
| Second molar               | 5           | 6            | 5             | 7            | 8           | 9            |     |
| Third molar                | 2           | 2            | 3             | 2            | 2           | 1            |     |

Table 2: Comparison of pain ratings for each injection phase of inferior alveolar nerve block, Gow-Gates, and Vazirani-Akinosi technique

| Groups | Needle insertion | Needle placement | Anesthetic solution deposition | P value of Kruskal-wallis ANOVA |
|--------|------------------|------------------|--------------------------------|-------------------------------|
| I      | 1                | 1                | 1                              | 0.000                         |
| II     | 2                | 2                | 2                              | 0.000                         |
| III    | 2                | 2                | 2.5666                         | 0.000                         |

Table 3: Statistical analysis to that there is no significant difference in the age of the patients among the groups

| n | Mean | SD   | SE   | P value of ANOVA |
|---|------|------|------|------------------|
| 1 | 30   | 33.23| 8.800| 1.581            |
| 2 | 30   | 34.71| 9.126| 1.639            |
| 3 | 30   | 33.81| 8.588| 1.543            |
| 4 | 30   | 34.82| 9.510| 1.797            |
| 5 | 30   | 33.60| 8.536| 1.559            |
| 6 | 30   | 33.50| 8.815| 1.609            |
| Total | 180 | 33.93| 8.791| 0.653            |

SD: Standard deviation, SE: Standard error

Benzodiazepines stimulate GABA<sub>A</sub> receptors in dorsal horn of spinal cord. It shows antihyperalgesic effect by reducing the pain-induced anxiety, stimulating the release of endogenous opioids such as enkephalins in central nervous system areas involved in pain processing. Approximately, 90% of peak benefits are achieved within the first hour after use, and hence, it was given 1 h before procedure. A single dose of alprazolam has minimal side effects for the patient. It was theorized that premedication with alprazolam reduces anxiety level of patients, decreasing pain reaction, and increasing the success of anesthesia techniques. However, according to Lindeman et al. and Khademi et al., preoperative oral or sublingual administration of benzodiazepines did not improve success of IANB in mandibular molars with irreversible pulpitis. In the inflammation, NSAIDs such as diclofenac potassium blocks, the cyclooxygenase pathway produced prostaglandins that are responsible for pain and tenderness. Prasanna et al. and Wali et al. stated that diclofenac increases the effectiveness of IANB as a premedication. In this study, alprazolam and diclofenac potassium were given in combination orally 1 h before the treatment. This was the reason for higher reduction in VAS scores in groups taking these premedications compared to corresponding groups.

**CONCLUSION**

We concluded that administration of inferior alveolar nerve block technique shows least pain and discomfort compared to GG and V-A techniques. Use of premedications in the form of combination of anxiolytics (alprazolam) and analgesics (diclofenac potassium) improves the success of anesthesia techniques in mandibular molars with irreversible pulpitis. In irreversible pulpitis, all three injection techniques are effective in achieving profound pulpal anesthesia; however, use of GG nerve block along with premedication is the best method for effective pain management of acute pain in irreversible pulpitis.
Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

REFERENCES

1. Goldberg S, Reader A, Drum M, Nusstein J, Beck M. Comparison of the anesthetic efficacy of the conventional inferior alveolar, Gow-Gates, and Vazirani-Akinosi techniques. J Endod 2008;34:1306-11.
2. Hargreaves KM, Keiser K. Local anesthetic failure in endodontics: Mechanisms and management. Endod Topics 2002;1:26-39.
3. Aggarwal V, Jain A, Debipada K. Anesthetic efficacy of supplemental buccal and lingual infiltrations of articaine and lidocaine following an inferior alveolar nerve block in patients with irreversible pulpitis. J Endod 2009;35:925-9.
4. Perez B, Moshonov J. Dental anxiety among patients undergoing endodontic treatment. J Endod 1998;24:435-7.
5. Torabinejad M, Cymerman JJ, Frankson M, Lemon RR, Maggio JD, Schilder H. Effectiveness of various medications on postoperative pain following complete instrumentation. J Endod 1994;20:345-54.
6. Heft MW, Parker SR. An experimental basis for revising the graphic rating scale for pain. Pain 1984;19:153-61.
7. Corah NL, Gale EN, Illig SJ. Assessment of a dental anxiety scale. J Am Dent Assoc 1978;97:816-9.
8. Stanley W, Drum M, Nusstein J, Reader A, Beck M. Effect of nitrous oxide on the efficacy of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis. J Endod 2012;38:565-9.
9. Fullmer S, Drum M, Reader A, Nusstein J, Beck M. Effect of preoperative acetaminophen/hydrocodone on the efficacy of the inferior alveolar nerve block in patients with symptomatic irreversible pulpitis: A prospective, randomized, double-blind, placebo-controlled study. J Endod 2014;40:1-5.
10. Aggarwal V, Singla M, Kabi D. Comparative evaluation of anesthetic efficacy of Gow-Gates mandibular conduction anesthesia, Vazirani-Akinosi technique, buccal-plus-lingual infiltrations, and conventional inferior alveolar nerve anaesthesia in patients with irreversible pulpitis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2010;109:303-8.
11. Wilson S, Johns P, Fuller PM. The inferior alveolar and mylohyoid nerves: An anatomic study and relationship to local anesthesia of the anterior mandibular teeth. J Am Dent Assoc 1984;108:350-2.
12. Heasman PA, Beynon AD. Clinical anatomy of regional analgesia: An approach to failure. Dent Update 1986;13:469-76.
13. Meechan JG. How to overcome failed local anaesthesia. Br Dent J 1999;186:15-20.
14. Knabi J, Zeilhofer UB, Crestani F, Rudolph U, Zeilhofer HU. Genuine antihyperalgesia by systemic diazepam revealed by experiments in GABAA receptor point-mutated mice. Pain 2009;141:233-8.
15. Greenblatt DJ, Wright CE. Clinical pharmacokinetics of alprazolam. Therapeutic implications. Clin Pharmacokinet 1993;24:453-71.
16. Kaplan GB, Greenblatt DJ, Ehrenberg BL, Goddard JE, Harmatz JS, Shader RI. Single-dose pharmacokinetics and pharmacodynamics of alprazolam in elderly and young subjects. J Clin Pharmacol 1998;38:14-21.
17. Lindemann M, Reader A, Nusstein J, Drum M, Beck M. Effect of sublingual triazolam on the success of inferior alveolar nerve block in patients with irreversible pulpitis. J Endod 2008;34:1167-70.
18. Khademi AA, Saatchi M, Minaiyan M, Rostamizadeh N, Sharafi F. Effect of preoperative alprazolam on the success of inferior alveolar nerve block for teeth with irreversible pulpitis. J Endod 2012;38:1337-9.
19. Prasanna N, Subbarao CV, Gutmann JL. The efficacy of pre-operative oral medication of lornoxicam and diclofenac potassium on the success of inferior alveolar nerve block in patients with irreversible pulpitis: A double-blind, randomised controlled clinical trial. Int Endod J 2011;44:330-6.
20. Wali A, Siddiqui TM, Qamar N, Khan R, Jawaid N. Effectiveness of premedication with analgesics vs placebo for success of inferior alveolar nerve block in irreversible pulpitis. Int J Prosthodont Restor Dent 2012;2:5-9.