EUROPEAN ENDODONTIC JOURNAL

ORIGINAL ARTICLE

Comparison of Preoperative Analgesics on the Efficacy of Inferior Alveolar Nerve Block with Patients Having Symptomatic Irreversible Pulpitis: A Double-Blinded, Randomized Controlled Trial

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ABSTRACT

Objective: The objective of this study was to evaluate the effectiveness of preoperative analgesics on inferior alveolar nerve blocks (IANB) during root canal treatment in patients with symptomatic irreversible pulpitis of the mandibular molars.

Methods: This study was a randomized, double-blinded, superiority trial with a parallel study design. A total of 120 subjects with symptomatic irreversible pulpitis were randomly assigned to one of four groups: group A (control, Vitamin E, Evion 400 mg), group B (Diclofenac sodium, Voltral SR100 100 mg), group C (Piroxicam, Feldene 20 mg), and group D (Tramadol, Tramal 50 mg). The patients recorded preoperative pain levels, and after administration of local anaesthesia intraoperative pain levels using the Heft-Parker visual analogue scale before and after the oral administration of the analgesics. Statistical analysis was performed using the Kruskal-Wallis test.

Results: All the analgesic groups showed a significant effect on the efficacy of the inferior alveolar nerve block in contrast to the control group ($p<0.05$). However, no significant difference was found between the drug groups on the effectiveness of the inferior alveolar nerve block ($p>0.05$). No side effects were reported in the present study.

Conclusion: Preoperative analgesics significantly increase the effectiveness of inferior alveolar nerve block in patients with symptomatic irreversible pulpitis. Therefore, preoperative analgesics should be considered to increase the effectiveness of inferior alveolar nerve block in patients with symptomatic irreversible pulpitis on the mandibular molars.

Keywords: Inferior alveolar nerve block, local anaesthesia, preoperative analgesics, symptomatic irreversible pulpitis

Please cite this article as: Riaz M, Zafar F, Khalid Z, Sultan T, Wali A, Siddiqui TM. Comparison of Preoperative Analgesics on the Efficacy of Inferior Alveolar Nerve Block with Patients Having Symptomatic Irreversible Pulpitis: A Double-Blinded, Randomized Controlled Trial. Eur Endod J 2023; 8: 246-52

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Received February 27, 2023,
Revised April 08, 2023,
Accepted May 22, 2023

Published online: July 25, 2023
DOI 10.14744/eej.2023.42650

HIGHLIGHTS

- The preoperative analgesic groups show a statistically significant increase in the effectiveness of IANB in contrast to the placebo group.
- Statistically there was no difference between the effectiveness of Piroxicam, Tramadol, and Diclofenac sodium on IANB.
- NSAIDs are generally preferred over opioids due to the fewer reported adverse effects.

INTRODUCTION

Symptomatic irreversible pulpitis (SIP) is an inflamed pulpal tissue that can cause acute pain in response to thermal stimuli. Root canal treatment is the most common treatment for SIP (1), and successful administration of local anaesthe-

sia is essential to manage preoperative pain. Inferior alveolar nerve block is the most frequently used technique to achieve local anaesthesia in mandibular posterior teeth for endodontic treatments (2). However, IANB is a technique-sensitive procedure in contrast to other methods of administering local anaesthesia, making it difficult to eliminate pain effectively (3). Clinical success rates for IANB in non-inflamed tissues are reported to be between 75–90 % (4), this drops substantially to 43–83 % in patients with SIP (5, 6). Consequently, patients undergoing endodontic treatment for SIP often experience intraoperative pain due to ineffective anaesthesia (7).

Numerous studies have suggested that IANB alone is inadequate for managing intraoperative pain in patients with SIP and that supplementation with additional anaesthetic techniques is necessary (8–10). One of the most rudimentary reasons behind the ineffectiveness of IANB in SIP is the release of arachidonic acid (AA) as a consequence of inflammation (11). AA can be metabolized through lipoxygenase or cyclooxygenase (COX) pathways to produce leukotrienes or prostaglandins (PGs), respectively (12). PGs are responsible for impeding the neural response to anaesthesia (13), while leukotrienes significantly decrease patients' pain endurance and increase neutrophil influx (14). Moreover, PGs also cause hyperalgesia and allodynia due to the sensitization of nerves through histamine and bradykinin (14). Other reasons for IANB failure in SIP include anatomic variations, increased vasculature, anaesthesia drainage through dental sinuses, activation of nociceptors, anaesthetic solution resistance to sodium channels, blocked sodium channels due to tetrodotoxin, and localized decreases in pH (15). The underlying cause of IANB failure could also be due to a decrease in the patient's pain threshold as a result of elevated levels of anxiety (5). Additionally, psychological influences can impact the perception of pain and the efficacy of anaesthetic agents (16).

To address the shortcomings of IANB in managing pain in patients with SIP, various techniques have been considered, including the use of different anaesthetic agents, topical anaesthetics, and supplementary anaesthetic techniques (17). Moreover, reducing pulp inflammation before local anaesthesia administration can improve efficacy. Thus, the efficacy of different opioid, steroid, and non-steroidal agents has been studied to reduce inflammation and eliminate intraoperative pain (18).

Nonsteroidal anti-inflammatory drugs (NSAIDs) are commonly prescribed by dental practitioners to alleviate mild to moderate pain associated with SIP. The administration of NSAIDs inhibits the production of PGs by blocking the COX pathway, thereby reducing pulpal inflammation and pain (19). Diclofenac sodium and potassium, both derivatives of benzoic acid, are the preferred NSAIDs for moderate to severe pain due to their rapid onset of action, typically within 15–30 minutes (20). Similarly, Piroxicam is an effective NSAID for dental pain as it also inhibits the COX pathway, thereby reducing PG synthesis (21). Tramadol, a widely used opioid-based analgesic, can be used to treat moderate to severe acute pain (22, 23) and has been shown to mimic the effects of local anaesthetic solution. These medications are often used as a single-dose premedication to alleviate discomfort and inflammation associated with SIP and improve the efficacy of IANB.

Some studies have investigated the effects of different analgesics on pain associated with SIP. Oral Diclofenac potassium and Piroxicam were found to be effective, while Tramadol showed inefficacy in managing pain associated with SIP (24, 25). However, no study has compared the effects of orally administered Diclofenac sodium, Piroxicam, and Tramadol on the efficacy of IANB in patients with SIP. Therefore, this double-blinded, randomized controlled trial aims to identify the most effective preoperative drug for improving IANB efficacy in patients with SIP by comparing the effects of these different drug groups. The null hypothesis of the study is that all the preoperative analgesics have the same effect on IANB efficacy in patients with SIP.

MATERIALS AND METHODS

The study was approved by the ethical committee and review board of the dental institute (BDC/ERB/2021/016) and registered on the clinical trial registry (www.clinicaltrials.gov, Identifier: NCT05488925). This study was written in accordance with the PRIRATE 2020 guidelines (26) and all procedures adhered to the Helsinki Declaration.

Sample size was determined based on previous reports (18) with a power of 0.96, effect size of 0.4, and α set at 0.05, resulting in a requirement of 30 subjects per group. Inclusion criteria comprised patients aged 18 to 65, in good systemic health, diagnosed with SIP in mandibular first and second molars with acute moderate to severe pain. Exclusion criteria included were pregnancy or nursing, periapical radiolucency, tenderness to percussion, non-restorable teeth, retreatment, open apex, resorbed roots, grade II and III mobility, intolerance to NSAIDs, and analgesics used in the past 24 hours. Non-probability consecutive sampling was performed, enrolling 120 patients who met the criteria from the outpatient department of endodontics in a private hospital. The study was thoroughly explained to the subjects and informed consent was acquired from the subjects. The treatment was conducted by a single operator with specialized training in endodontics.

The study was a double-blinded, randomized, superiority trial with a parallel design. Both the operating dentist and patients were unaware of the groups of drugs that were used. This anonymity was achieved by marking A, B, C, and D on trans-opaque boxes (Fig. 1) and patients were randomly assigned to one of the four groups using simple randomization. To ensure randomization, patients were given the choice to pick a drug from one of the labelled boxes. A cold sensibility pulp test was performed on the tooth with SIP for 10 seconds (Q-tip sprayed with Endo-Ice by HYGENIC®), and the HP VAS was used to assess pain levels immediately after the test. Pain intensities were categorized on HP VAS scale: no pain (0), mild pain (1–54 mm), moderate pain (55–114 mm), and severe pain (>114 mm). Patients orally ingested a drug from the trans-opaque labelled box: group A (control, vitamin E, Evion 400 mg), group B (Diclofenac sodium, Voltral SR100 100 mg), group C (Piroxicam,

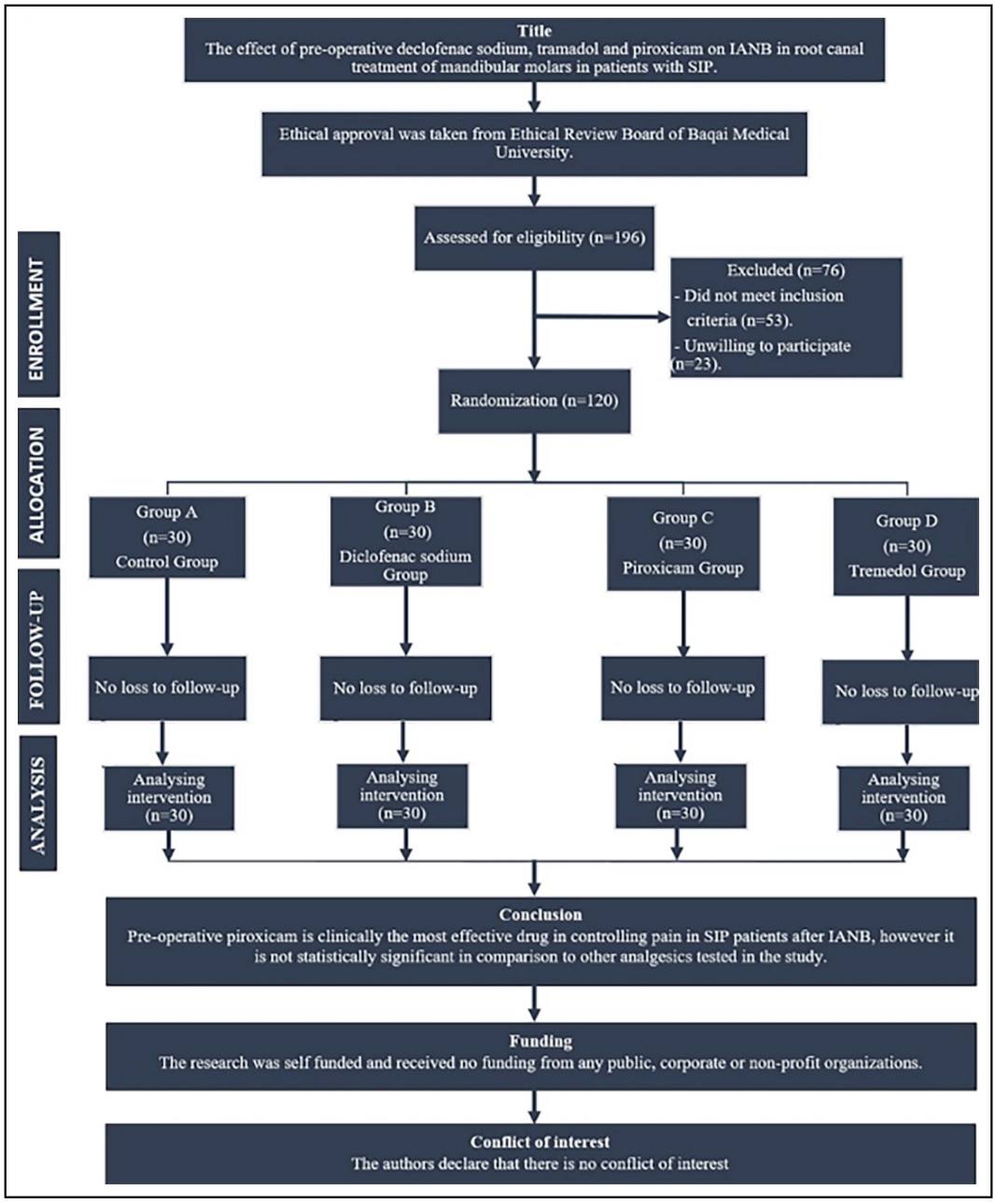

Figure 1. PRIRATE flowchart of the randomized control trial

Feldene 20 mg), and group D (Tramadol, Tramal, 50 mg). After 1 hour, a conventional IANB was slowly administered with Medicaine 1.8 ml of 2 % lidocaine with 1:100000 epinephrine (Huons Co. Ltd., Seongnam, South Korea) using a non-aspirating syringe (DentArt instruments Mfg. Co., Sialkot, Pakistan) through H-Dent long needle of 27-Gauge (Hakusui Trading Co. Ltd, Tokyo, Japan) at the rate of 2.0 ml/min. Standard root canal treatment was initiated 15 minutes after the lip numbness was achieved, and pain levels were reassessed by HP VAS during the initial filing. Patients reporting discomfort and pain during the treatment were intervened appropriately with additional local anaesthesia through local infiltration, intra-ligamentry, and/or intra-pulpal techniques. Patients who did not achieve numbness of the lips were excluded from the study. Preoperative analgesic effectiveness was determined by the difference in preoperative and intraoperative HP VAS scores.

Statistical Analysis

The statistical analysis was performed using SPSS Statistics version 25 (IBM Corp., Armonk, NY, USA). The Significance level (α) was set at 0.05 with a confidence interval of 95%. Normality was assessed using Shapiro Wilk test. Since the data did not meet parametric assumptions, Kruskal–Wallis test with post-hoc analysis was employed. The Pearson Chi-square test was used to examine the relationship between gender and drug groups in relation to IANB efficacy.

RESULTS

Patient recruitment began in July 2021, and the study was conducted over a 9-months period. Of the randomly included patients, 53.3% were female and 46.7% were male. The overall effectiveness of the preoperative drug in improving IANB efficacy was observed in 69.2% of patients, with the remaining

30.8% reporting pain during the root canal procedure (Table 1). Pearson Chi-squared test revealed a significant relationship between the preoperative analgesics and IANB effectiveness (p<0.001). However, gender had no significant effect on IANB efficacy (p=0.616) (Table 2).

The normality of the data was assessed and found not normally distributed (Shapiro-Wilk: p<0.001). Therefore, a non-parametric Kruskal-Wallis test was performed with post hoc analysis. The Kruskal-Wallis test revealed a significant difference in pain levels due to drug intervention between the groups (p<0.001). The post hoc analysis indicated that registered pain levels differed significantly between the control group and the active drug groups (p<0.001). Clinically, Piroxicam was found to show slightly higher effectiveness on IANB with SIP (Table 3); however, there was no statistically significant difference in the IANB efficacy between Diclofenac sodium, Piroxicam, and Tramadol groups (p=0.906) (Fig. 2).

TABLE 1. IANB effectiveness of different drug group (p<0.001)

Groups	Effective		Ineffective	
	Frequency	%	Frequency	%
A (Control)	9	30.0	21	70.0
B (Diclofenac sodium)	20	66.6	10	33.3
C (Piroxicam)	28	93.3	2	6.7
D (Tramadol)	26	86.6	4	13.3

IANB: Inferior alveolar nerve blocks

TABLE 2. IANB effectiveness on gender (p=0.616)

Groups	Effective		Ineffective	
	Frequency	%	Frequency	%
Male	40	71.4	16	28.6
Female	43	67.2	21	32.8

IANB: Inferior alveolar nerve blocks

DISCUSSION

The study incorporated simple randomization to ensure regularity and balance among the subjects of the experimental groups. Blinding of both participants and the operator was also implemented to eliminate any potential bias. While the number of male and female subjects was not balanced, the results of the Pearson Chi-squared test revealed no significant relationship between gender and the effectiveness of preoperative analgesics on IANB. Therefore, balancing gender in the study groups was deemed unnecessary.

The dosages of 100 mg Diclofenac sodium, 20 mg Piroxicam, and 50 mg Tramadol were used in accordance with earlier literature (27). Vitamin E was used as a control, given its safety as a dietary supplement and lack of reported effect on local anaesthesia effectiveness. In fact, vitamin E has been reported to reduce the systemic adverse effects of lidocaine (28). HP VAS was utilized as a tool to register because of its reliability in endodontic studies. Patients were instructed to use the vas before recording their pain scores to increase consistency and minimize bias.

For the purpose of achieving IANB, lidocaine was chosen as the local anaesthetic solution in this study due to its ease of availability. Although alternative agents such as articaine, mepivacaine, and prilocaine are available, their effectiveness in comparison to lidocaine is reported to be statistically insignificant (29). Local anaesthesia was administered using the IANB technique one hour after the premedication was given to ensure peak plasma concentrations of the drug in the patients (30). Additional anaesthetic techniques were administered to patients who did not achieve effective anaesthesia, which is in line with previous reports of the effectiveness of such supplementation in SIP patients (31). However, the present study did not evaluate the effectiveness of additional anaesthesia since it was beyond the scope of the study.

Preoperative pain was disregarded as a confounding factor as there was no significant difference in pain levels among the test groups. While electric pulp testing and cold sensibility testing have been used in previous studies to analyse the efficacy of IANB, these techniques are not reliable during root canal treatments and were therefore not used in this study (32, 33). Instead, the clinical endodontic pulp extirpation method was implemented to test the effectiveness of preoperative analgesics on IANB.

The results of this study supported the alternate hypothesis and demonstrated that preoperative analgesics significantly improved the clinical and statistical success rate of IANB compared to the control group. The anti-inflammatory effect of the analgesic drugs used in this study might be the reason for a significant anaesthetic efficacy, as these drugs act by inhibiting the formation of AA, COX, and lipoxygenase pathways, and/or PGs and leukotrienes (34). While there is a strong division among researchers regarding whether Tramadol has anti-inflammatory potential or not (35–38), a study suggests that Tramadol helps to achieve effective analgesia irrespective of the presence of inflammation (39).

The Kruskal-Wallis results of the present study were in harmony with previous research, which found no significant difference in the effectiveness of IANB between Piroxicam, Tramadol, and Diclofenac sodium (40). Similarly, the clinical findings of the present study showed that Piroxicam was the most effective preoperative analgesic (93.3 %), followed by Tramadol (83.3 %) and Diclofenac sodium (60 %). These results align with the previous studies reporting the efficacy of Piroxicam at 90 %, Tramadol at 60 %, and Diclofenac sodium at 56–64 % on IANB (24,25,34). However, some studies did not support our findings. For instance, one study reported Diclofenac potassium's success rate of up to 75 %, which does not coincide with our results for Diclofenac sodium (24). This could possibly mean that Diclofenac potassium is more effective in comparison to Diclofenac sodium. Similarly, another study revealed that the Tramadol group do not have any statistically significant difference from the control group (41). These variations could be due to differences in the location of the included subjects or the manufacturers of the analgesics used.

TABLE 3. Comparison of drug efficacy on IANB

Groups	Age			Min-max	Gender		Tooth		Preoperative pain			Intraoperative pain			Difference in pain (Preoperative pain-Intraoperative pain)		
	Median	95% CI			Male	Female	First molar	Second molar	Median	95% CI		Median	95% CI		Median	95% CI	
		LB	UB							LB	UB		LB	UB		LB	UB
A (Control)	39.5	31.0	47.0	18-64	15	15	17	13	85.0	85.0	85.0	54.0	36.0	54.0	18.0	0.0	31.0
B (Diclofenac Sodium)	38.0	31.0	48.0	20-65	11	19	16	14	85.0	85.0	85.0	23.0	0.0	36.0	58.0	49.0	62.0
C (Piroxicam)	42.5	35.0	48.0	19-65	14	16	19	11	85.0	85.0	85.0	0.0	0.0	0.0	70.0	54.0	85.0
D (Tramadol)	44.5	34.0	52.0	18-65	16	14	18	12	85.0	85.0	85.0	0.0	0.0	23.0	62.0	62.0	85.0

IANB: Inferior alveolar nerve blocks, CI: Confidence interval, LB: Lower bound, UB: Upper bound

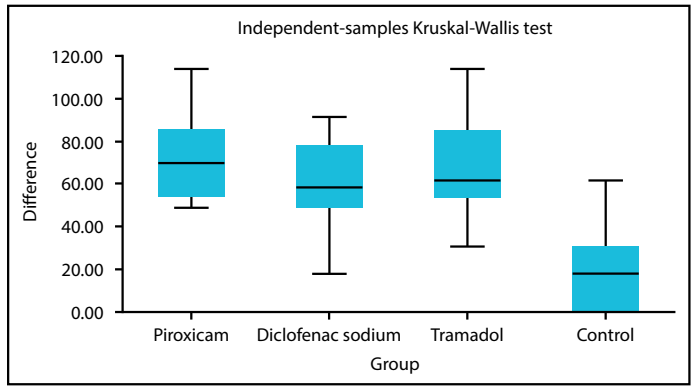

Figure 2. *Post-hoc* test of Kruskal-Wallis reveals a statistically significant difference in intraoperative pain between the control group and the active drug groups ($p<0.001$). The box plots depict the interquartile range (IQR) for each group, with the line inside the box indicating the median. The whiskers extend to the minimum and maximum values

To ensure the standardization of the study and to eliminate confounders that would affect the outcome of the study, many parameters such i.e. inclusion and exclusion criteria were controlled; which resulted in causing a few limitations. For instance, the results may not be generalizable to individuals outside the age range of 18–65 years. Another evident limitation of the study was the provision of a single technique to achieve anaesthesia which may not reflect realistic clinical scenarios where supplemental anaesthesia is often necessary to eliminate pain effectively. However, administering anaesthesia through a single technique eliminated possible confounders and enabled accurate evaluation of preoperative analgesic efficacy. Although Tramadol is clinically effective, it has been associated with more adverse effects than NSAIDs, particularly nausea and vomiting, limiting its frequent use (42, 43). In contrast, NSAIDs have been reported to be less harmful and clinically more effective than opioids. The present study found that Piroxicam was clinically superior to Diclofenac sodium with fewer adverse effects (25). The side effects of either of these NSAIDs were expected to be negligible due to a single preoperative dosage form. However, no adverse effects were reported by the patients, but these effects were considered a limitation of the study. Additionally, the small sample size limited our results' interpretation, which could be improved by increasing the sample size. The duration of the present study was adequate for the recruitment of the desired sample size. Further studies may examine other factors such as age, ethnicity, or weight that could affect the effectiveness of preoperative analgesics.

The present study has several strengths that contribute to the rigor and reliability of its results. Firstly, ethical guidelines approved by the board were strictly adhered to, and the trial was registered for transparency and accountability. The study also followed the PRIRATE 2020 guidelines for accurate reporting (26). In addition, sample size calculation was performed to ensure adequate power for detecting a meaningful effect size. Other methodological features that enhance the study's robustness include a single operator performing the procedure, double-blinding of both patients and the operating dentist, randomization of patients, and the use of validated outcome measures such as the HP VAS to assess pain levels. Appropriate statistical analyses were also employed to ensure the validity of the results.

The rigorous methodology employed in this study increases the credibility of its findings and contributes to the advancement of the field. Specifically, the results could help clinicians select the most effective preoperative analgesic for patients with SIP, leading to better pain management and increased patient satisfaction. Furthermore, the study's findings may contribute to improving the overall quality of care for patients undergoing root canal treatment.

CONCLUSION

The present study demonstrated that Piroxicam (93.3%) was more clinically effective than Tramadol (83.3%) and Diclofenac sodium (60%) in achieving IANB in patients with SIP of the mandibular molars, although without any statistical significance (p=0.906). Therefore, while Piroxicam cannot be statistically considered superior to Tramadol or Diclofenac sodium, it may be preferred as a preoperative analgesic to enhance the efficacy of IANB in this patient population. However, further research is needed to confirm these results and evaluate the clinical applicability of Piroxicam as an analgesic adjunct to IANB in patients with SIP of the mandibular molars.

Disclosures

Acknowledgments: The authors would like to express their gratitude to the department of endodontics of a private hospital for their cooperation in data collection for this study.

Conflict of interest: The authors deny any conflict of interest.

Ethics Committee Approval: This study was approved by The Baqai Dental College Ethics Committee (Date: 15/06/2021, Number: BDC/ERB/2021/016).

Peer-review: Externally peer-reviewed.

Financial Disclosure: This study did not receive any financial support.

Authorship contributions: Concept – A.W., M.R., T.M.S.; Design – A.W., F.Z., T.M.S.; Supervision – T.M.S., A.W.; Funding - F.Z.; Materials - M.R., Z.K.; Data collection and/or processing – M.R., Z.K.; Analysis and/or interpretation – F.Z., M.R., Z.K.; Literature search – F.Z., M.R., Z.K.; Writing – F.Z., M.R., T.S.; Critical Review – T.S.

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