Full Length Research Paper

The efficacy of premedication with ibuprofen, gelofen and acetaminophen in the depth of anesthesia in mandibular molars with irreversible pulpitis

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Pain control is one of the major aspects in dental practice. Dental pain can usually be controlled using different techniques such as local anesthesia and medications. Acetaminophen is a pain reliever and fever reducer. However, it shows no effect on inflammation. Therefore, non-steroidal anti-inflammatory drugs are currently used to control inflammation and pain. This study sought to compare the efficacy of premedication with ibuprofen, gelofen and acetaminophen in the depth of anesthesia in mandibular molars with irreversible pulpitis. In this double-blind randomized controlled trial, 60 patients with at least one mandibular molar with symptoms of irreversible pulpitis requiring root canal therapy were recruited. Another tooth in the same quadrant was selected as the control. Patients were randomly allocated to one of the following groups: ibuprofen 400 mg, gelofen 400 mg, acetaminophen 325 mg, and placebo 500 mg. The medications were taken 30 min prior to local anesthesia and the cold test and electric pulp test (EPT) were repeated for the test teeth and the control teeth after 10 min with the development symptoms of anesthesia. Access preparation was then initiated and the patients were asked to quantify the level of pain during exposure of the dentin and pulp using a visual analogue scale (VAS). Data was analyzed using analysis of variance (ANOVA), and repeated measure ANOVA, $P < 0.05$ were deemed significant. There were significant differences between the mean baseline VAS score, and the mean VAS score recorded at the time of dentin and pulp exposure however revealed a significant difference in the VAS score only at the time of dentin exposure among the study groups ($P < 0.005$). No significant difference was observed in the mean VAS score at the time of pulp exposure among groups ($P = 0.076$). The EPT was significantly higher after the test compared with the baseline ($P = 0.421$). Premedication with ibuprofen and gelofen have significant effect in the depth of anesthesia in mandibular molars with irreversible pulpitis, and significantly decreased VAS but placebo and acetaminophen are functionally alike and had no significant effect.

Key words: Irreversible pulpitis, pain, root canal therapy.

INTRODUCTION

Pain is one of the most unpleasant feelings that a human being may experience throughout life. Pain control, especially in the early phases of endodontic treatment, is

an important aspect of a successful dental procedure. Optimum pain management results in building up trust and facilitates the entire procedure (Walton et al., 2008).

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Moreover, pain and anxiety is associated with increased stress, which may compromise the patient's health leading to problems such as syncope (Eli, 2003; Maggiri and Locker, 2002). Sudden, severe pain may induce substantial changes in the cardiovascular, respiratory, endocrine and neurogenic systems, resulting in severe medical conditions (Kaviani et al., 2011).

In endodontic therapy, inferior alveolar nerve block (IANB) is the standard method of local anesthesia in the mandibular teeth. Nevertheless, clinical studies have demonstrated a notable range of failure (7 to 77%) for this technique. Moreover, the success rate of anesthesia in teeth with irreversible pulpitis is less than normal pulp (Aggarwal, et al., 2009; Tortamano et al., 2009). According to Hargreaves and Keiser (2002), some of the factors which may account for this failure include: anatomic factors, acute anaphylaxis, the effect of inflammation on the pH of the tissue, the effect of inflammation in blood circulation, the effect of inflammation on central hypersensitivity and its effect on the nociceptors.

Activation of nociceptors in the presence of inflammation is one of the strongest theories explaining the reduced efficacy of anesthesia. Inflammatory mediators reduce the stimulation threshold in nociceptor neurons to a level at which the slightest stimulators induce a severe neurogenic response (Goodis et al., 2006). This inflammatory process occurs as a result of the production of prostaglandins (PGs) as the end point product of the metabolism of arachidonic acid through the cyclooxygenase pathway (COX). PGs then result in increased sensation of pain by increasing the sensitivity of the nerve endings to bradykinin and histamine (Dray, 1995).

Researchers have studied different ways to achieve better anesthesia in teeth with pulpitis. Premedication with analgesic agents has been proposed as one of the alternatives with controversial results. Modarresi et al. (2006) and Parirokh et al. (2010) have reported a considerable improvement in the level of anesthesia when patients receive analgesics prior to IANB for the treatment of teeth with irreversible pulpitis. On the other hand, Ianiro et al. (2007) failed to show any significant difference between the case and control groups, although their observations were suggestive of a tendency toward better clinical results in the medication group.

Several other researchers including Aggarwal et al. (2009), Oleson et al. (2010) and Simpson et al. (2011) reported an insignificant improvement in the success of IANB accompanied by premedication with analgesics in treating irreversible pulpitis. Numerous analgesics are used for pain control in endodontics. Non-narcotic analgesics including acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and gelofen are among these drugs. We aimed to compare the efficacy of premedication with three different analgesics (ibuprofen 400 mg, gelofen 400 mg, and acetaminophen 325 mg) in the anesthetic depth of IANB in teeth with irreversible pulpitis.

MATERIALS AND METHODS

This was a double-blind randomized controlled clinical trial. The study population consisted of 60 patients presenting to the Endodontics Department in Babol School of Dentistry, Babol, North Iran. The patients were to have at least one mandibular tooth with symptoms of irreversible pulpitis (spontaneous or nocturnal pain). Patients with history of systemic diseases, consumption of any type of analgesic agent at least 12 h prior to the study, any contraindication towards the use of analgesic agents, hypersensitivity to lidocaine 2% with 1:80000 epinephrine or any of the infiltration techniques, advanced periodontal diseases and periapical radiolucency associated with the study teeth and teeth with extensive restorations or previous endodontic treatments, were excluded from the study. Patients provided informed consent followed by a complete medical and dental history and clinical examination.

The pulp vitality tests including electric pulp test (EPT) and cold test were then performed for each study tooth and a control tooth from the same quadrant. For the EPT, tooth paste was placed between the tip of the pulp tester (COXO Medical Instrument Co, LTD) and the tooth. The tip of the pulp tester was placed on an area of sound enamel at the incisal third of the tooth where there was no contact with the gingiva, restoration or any cracks in the enamel. As soon as the patient reacted to the stimulus (feeling of heat or tinkling), the test was over. The EPT and cold test results were recorded for each study tooth and the respective control tooth. The patients were asked to determine their level of pain before and after taking the medications based on a visual analogue scale (VAS: 0 cm = no pain, 0 to 3: mild pain (patient can feel the pain, however does not become uncomfortable), 3 to 6: moderate pain (the pain is irritating but tolerable), 6 to 10: severe pain (the pain is intolerable) (Ianiro et al., 2007), > 10: very severe pain).

The medications included acetaminophen 325 mg (Kharazmi, Iran), ibuprofen 400 mg (Rooodaru, Iran), gelofen 400 mg (Zakaria, Iran), and placebo (capsule of 500 mg glucose). All medications were prepared identically with similar sizes and shapes in the Department of Pharmacology, Babol University of Medical Sciences and were presented to the patients as blue gelatinous capsules. The capsules were placed in identical envelopes and coded, yielding a total of 60 envelopes (four groups of 15 each).

The patients were randomly divided into four groups of 15 and were asked to take one capsule of the same drug group. The patients and the operator were blind to this procedure. After 30 min, one cartridge (1.8 mm) of 2% lidocaine, with 1:80000 epinephrine (Pharmaceutical Mfg. Co. Daroupakhsh, Iran), was injected using the IANB technique. Patients who failed to meet the clinical signs of anesthesia after 10 min, that is tingling in the lower lip and the tip of the tongue, or those who reacted to the stimulus made by an explorer between the lateral incisor and the canine, were excluded. With the advent of signs of anesthesia, EPT and cold test recordings were repeated for the test and study teeth. Access preparation was then initiated and the quality and quantity of pain during dentin and pulp exposure were recorded using the VAS.

Data were submitted to the statistical package for social sciences (SPSS) software version 18, and analysis was performed using the following tests: Analysis of variance (ANOVA) and repeated measure ANOVA. $P < 0.05$ was considered as significant.

RESULTS

This double blind clinical study included 60 patients (30 men and 30 women), with ages ranging between 14 to 55 years (25.69 ± 9.50 years). Table 1 summarizes patients' age and sex as well as their pain level prior to treatment. Statistical tests failed to show any significant difference in

Table 1. Comparison between the groups in terms of age, sex and pain at baseline.

Group		Placebo	Acetaminophen	Ibuprofen	Gelofen	Total	P-value
Age (mean±SD)		22.80±8.53	24.53±7.44	26.47±10.58	28.80±10.91	25.65±9.50	0.353
Gender	Female	7	6	10	7	30	0.494
	Male	8	9	5	8	30	
Pain at baseline (mean±SD)		7.52±2.01	8.18±1.89	6.16±2.40	6.52±1.46	7.09±2.08	0.027*

SD = Standard deviation, *Significant.

Figure 1. Comparison between baseline VAS scores and VAS scores at the time of dentin and pulp exposure.

any of these factors between the groups. ANOVA revealed a significant difference in the mean VAS scores at baseline and during access preparation (dentin and pulp exposure) between the groups. However, accordingly, this marked difference was only seen at the time of dentin exposure ($P = 0.005$) and not pulp exposure ($P = 0.076$).

In the acetaminophen group, the mean VAS score showed a reduction rate of 70.4 and 54.52% at the time of dentin and pulp exposure, respectively compared with the baseline. In the ibuprofen group, the reduction rate at the time of dentin and pulp exposure was 100 and 82.14%, respectively; and in the gelofen group, this reduction rate was 100% at the time of dentin exposure and 70.39% at the time of pulp exposure. The reduction rate in the placebo group at the time of dentin exposure was 92.95% and at the time of pulp exposure was 55.85% compared to the baseline (Figure 1).

The success rate of anesthesia was defined by complete elimination of pain or slight pain during the

endodontic treatment. The success rate among the placebo, acetaminophen, ibuprofen and gelofen groups was 20, 13.33, 66.66, and 46.66%, respectively. Table 2 presents the success and failure rates of IANB at the time of dentin and pulp exposure among the study groups. The mean EPT values increased in all groups after taking the test medications and the injection, however, according to the ANOVA and repeated measure ANOVA, this increase was not deemed significant ($P = 0.421$) (Figure 2).

DISCUSSION

The present study investigated the effect of premedication with 325 mg dose of acetaminophen, 400 mg dose of gelofen and 400 mg dose of ibuprofen in the depth of anesthesia in mandibular molars with irreversible pulpitis. EPT and cold test were used to evaluate the sensitivity of

Table 2. The success and failure rates of IANB at the time of dentin and pulp exposure among the study groups.

Group	Success (%)	Failure (%)	
		Dentin exposure	Pulp exposure
Placebo	3 (20)	1 (6.66)	11 (73.33)
Acetaminophen	2 (13.33)	5 (33.33)	8 (53.33)
Ibuprofen	10 (66.66)	0	5 (33.33)
Gelofen	7 (46.66)	0	8 (53.33)

Figure 2. Mean EPT values in all groups after taking the test medications and the infiltration.

teeth at base line and after the intervention. Cold test is a common method to evaluate pulp vitality. Petersson et al. (1999) reported 90% sensitivity for an accurate cold test compared to heat test (83%) and electric pulp test (84%).

Certosimo and Archer (1996) demonstrated that EPT is a valuable tool in diagnosing the potential problems associated with local anesthesia in endodontic and restorative procedures. The present findings confirmed this conclusion.

Belonging to the category of fast-acting analgesics with minimal adverse effects, acetaminophen, gelofen and ibuprofen were chosen to be evaluated in the present study. Researchers have studied the analgesic effects of a wide range of dosages for different medications. Bjornsson et al. (2003a,b) revealed that compared to 500 mg naproxen, premedication with 1000 mg acetaminophen shows a significant reduction in pain up to 1 h post third molar surgical extraction. They further demonstrated that premedication with 600 mg ibuprofen and 1000 mg acetaminophen have similar effects in pain reduction

after third molar surgical extraction. Mehlich (2002) stated that in cases of mild to moderate pain, acetaminophen remains the most appropriate medication of choice. Seymour et al., (1996) studied the efficacy of three doses of ibuprofen (200, 400 and 600 mg) in reducing post surgical pain. Their findings suggested that the 600 mg dose renders more successful pain reduction.

Based on the doses used in the literature and the doses available in the pharmaceutical market in Iran, we provided each patient with one capsule of 325 mg acetaminophen, 400 mg ibuprofen and 400 mg gelofen. Lidocaine 2% with 1:80000 epinephrine is one of the most common local anesthetic agents used in dentistry as well as many other studies (Modaresi et al., 2006; Ianiro et al., 2007; Mikesell et al., 2005; Claffey et al., 2004). Therefore, one cartridge (1.8 ml) of this agent was used. Mikesell et al. (2005) and Claffey et al. (2004) showed no significant difference in the success of IANB using lidocaine and articaine.

In another study by Ianiro et al. (2007), there was no

significant difference in the success of IANB between the group taking 1000 mg acetaminophen and their counterparts taking 1000 mg acetaminophen + 600 mg ibuprofen.

Oleson et al. (2010) and Aggarwal et al. (2009) failed to show a significant difference in the success rate of IANB when the anesthesia was accompanied by premedication with two different doses of ibuprofen (600 and 800 mg). Likewise, Simpson et al. (2011) concluded that premedication with 800 mg ibuprofen + 1000 mg acetaminophen has no significant effect in the success of IANB in patients with symptomatic irreversible pulpitis.

Oleson et al. (2010) further stated that while Ibuprofen can inhibit the production of new prostaglandins, early production of other inflammatory mediators and the effects of pre-activated nociceptors are likely responsible for the high failure rate of anesthesia even after taking the analgesic agent.

On the other hand, Parirokh et al. (2010) and colleagues compared the efficacy of premedication with 600 mg ibuprofen, 75 mg indomethacin and placebo in 150 patients with irreversible pulpitis. Their findings showed that premedication with the test drugs significantly increased the success of IANB compared to the placebo group ($P < 0.01$). According to Parirokh et al. (2010), the severity of pulpal inflammation at the time of treatment may also account for the differences in the results. In their study, only patients with asymptomatic irreversible pulpitis (patients with delayed response to cold test and absence of spontaneous pain) were included in the study. In the present study, however, the study population consisted of patients with spontaneous pain who were referred to the endodontics clinic.

The mean EPT readings at baseline were 32.87 and 40.46 in the case and control teeth, respectively. These readings increased to 53.22 and 57.37 in teeth with irreversible pulpitis and healthy teeth. These changes may explain why inflammation affects the depth of anesthesia. After taking the placebo agent and the IANB, the mean EPT readings in the control teeth and inflamed teeth was 62.07 and 51.47, respectively. This increase was solely attributed to the anesthetic agent, and the readings in the inflamed teeth marked the failure of local anesthetic agent in inducing a deep anesthesia in the presence of inflammation.

The increase in EPT readings in all groups after taking the premedication is indicative of the effect of premedication in increasing the depth of anesthesia. This increase was observed in all groups including the placebo group, with no significant difference. Modarresi et al. (2006) evaluated the effectiveness of premedication with 400 mg ibuprofen in comparison with acetaminophen codeine (600 mg acetaminophen + 40 mg codeine) 1 h prior to local anesthesia in treating irreversible pulpitis using EPT. They revealed that both medications increased the depth of anesthesia, with no significant difference.

Our findings resembled those of Modarresi et al. (2006). Although the difference between the groups was

deemed insignificant, our observations were suggestive of a greater reduction in pain in the ibuprofen and gelofen group. Seven patients in the acetaminophen group, four in the ibuprofen group, seven in the gelofen group, and nine patients in the placebo group received intrapulpal infiltration because of the pain during pulp exposure.

Conclusion

Premedication with ibuprofen 400 mg and gelofen 400 mg have significant effect in the depth of anesthesia in mandibular molars with irreversible pulpitis, and significantly decreased VAS, but placebo and acetaminophen 325 are functionally alike and had no significantly effect.

ABBREVIATIONS

ANOVA, Analysis of variance; **EPT**, electric pulp test; **IANB**, inferior alveolar nerve block; **PGs**, prostaglandins; **COX**, cyclooxygenase; **NSAIDs**, non-steroidal anti-inflammatory drugs; **VAS**, visual analogue scale.

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