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Original

The effect of orally administered ketamine on requirement for anesthetics and postoperative pain in mandibular molar teeth with irreversible pulpitis

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Abstract: Achieving successful anesthesia and pain control in a predictable, efficient manner is a challenge in the endodontic treatment of vital inflamed lower molars. The aim of this study was to evaluate the effect of oral ketamine on the dosage of local anesthetics required and postoperative pain management for irreversibly inflamed mandibular molars. In this randomized double-blind placebo-controlled clinical trial, 36 patients with irreversibly inflamed mandibular molars were randomly divided into two groups of 18. Ten mg of ketamine dissolved in 20 ml of fruit juice was administered orally to patients in the experimental group. The control group was given 20 ml of fruit juice alone as a placebo. After 30 min, inferior alveolar nerve block (IANB) anesthesia was induced using one cartridge of 2% lidocaine and 1:100000 epinephrine. Teeth were tested after 5 to 10 min using an electrical pulp tester. In patients showing a positive response, another IANB injection was applied, and the total number of anesthetic cartridges used was recorded. Postoperative pain was evaluated using a visual analogue scale (VAS). In addition, use of analgesic in the first 24 h after treatment was monitored using a questionnaire. Data were analyzed by *t* test using SPSS software. There were no significant differences in age or gender between the two groups. The number of anesthetic cartridges used in the ketamine group was significantly less than that in the control group ($P = 0.003$). Furthermore, postoperative pain in the ketamine group was significantly lower ($P = 0.019$). Also the number of analgesic tablets taken in the ketamine group was significantly lower ($P = 0.011$). It can be concluded that a low dose of ketamine might be beneficial for enhancing the effect of local anesthetics. (J Oral Sci 53, 461-465, 2011)

Keywords: local anesthesia; endodontics; ketamine; pain.

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Introduction

Prevention and management of pain in dentistry is a crucial part of successful practice. Many patients avoid seeking dental treatment because of the fear of pain, and this is the major reason why more than 50% of adults do not make dental appointments (1).

Furthermore, pain and anxiety impose additional stress

on patients and may cause medical problems such as syncope during dental treatment (2, 3). Unexpected pain may alter the responses of the cardiovascular, respiratory, endocrine and central nervous systems drastically and elicit medical emergencies (1). Evidence from 40,309 dental offices indicates that 75.5% of 30,608 emergency cases over a period of more than 10 years occurred due to stress and fear (1). Many factors can affect pain perception, for example younger, more educated patients are more sensitive to pain than older, less educated ones, and the degree of perceived pain is higher in patients who are agitated (2-5).

Induction of effective anesthesia and successful management of postoperative pain may be especially challenging for endodontic treatment of teeth with pulpitis (5). Walton et al. (6) reported that lower molar teeth were the most difficult for provision of anesthesia in 47% of cases. Malamed (7) performed a similar study at the University of Southern California, and found that sufficient pulpal anesthesia for lower molars was difficult in 91% of cases. In a study by Claffey et al., the success rate for inferior alveolar nerve block with lidocaine and epinephrine was 23% (8). Potocnik and Bajrović (9) reported a failure rate of 30-45% for inferior alveolar nerve block.

Failure to achieve anesthesia for inflamed teeth occurs almost eight times more frequently than for non-inflamed teeth (10). Inability to achieve the desired level of anesthesia for endodontic treatment of inflamed teeth may be related to anatomical, technical and physiological factors (4,5). Pathological pulpal and periapical conditions (inflammation or infection) reduce the pH of tissues surrounding the affected tooth, and this may affect the efficiency of local anesthetics (4,9,11).

A specific group of sodium channels have been observed on C nerve fibers known as tetrodotoxin-resistant (TTXR) receptors. These channels play an important role in sensitizing C fibers and producing hyperalgesia (12). One of the important clinical properties of these channels is their relative resistance to lidocaine, so that after an inferior alveolar nerve block the patient may feel complete anesthesia of the lip and tongue, but may perceive pain upon entrance to the pulp, which indicates insufficient block of these receptors by the anesthetic. In such cases, bupivacaine is more effective for blocking these channels (12).

Since achieving adequate anesthesia is essential before proceeding with endodontic treatment, adjunctive methods for enhancing anesthesia should be considered. Most dentists use supplemental injection techniques, either intrapulpal or intraosseous, according to their experience, both of which may be associated with potential problems or side effects. Alternatively, oral administration of certain drugs to enhance local anesthesia remains an appealing option.

Modaresi et al. studied the effect of premedication with oral ibuprofen and acetaminophen codeine on the depth of anesthesia in inflamed teeth, and found that premedication one hour before treatment increased the depth of anesthesia (13). Berthold et al. showed that pretreatment with sedative drugs reduced pain sensation (10).

Ketamine is one drug that may reduce pain sensation. It is a derivative of phencyclidine, which causes dissociative anesthesia. Ketamine interacts with N-methyl D-aspartate (NMDA) receptors, opioid receptors, monoaminergic receptors, muscarinic receptors and calcium and sodium ion channels, and may cause nerve block like local anesthetics (14-18). Higher doses of ketamine have a general anesthetic effect, while lower doses exert sedative and analgesic effects (14,15). Ketamine is more often administered intravenously or intramuscularly; however, for chronic pain, ketamine is most often prescribed orally (14,15). Friedman et al. (17) studied the effect of ketamine on acute pain, and found that oral administration reduced the doses of opioids required for pain control. It has been revealed that a combination of ketamine and local anesthesia enhances the quality of local anesthesia and reduces postoperative pain (19). Heidari et al. (20) showed that oral ketamine was as effective as other analgesics for reducing pain after orthopedic surgery.

The aim of the present study was to determine the effect of low-dose oral ketamine on the amount of local anesthetic required for endodontic treatment of vital inflamed lower molar teeth, and postoperative pain management.

Materials and Methods

In this double-blind placebo-controlled randomized clinical trial, 36 patients aged 15-45 years were randomly selected from among patients attending the Department of Endodontics at Isfahan Faculty of Dentistry. Selection criteria included informed consent to take part in the study, absence of systemic disease, and planned endodontic treatment for a vital inflamed first or second lower molar. Preoperative instructions to the subjects included being accompanied by another person, and being banned from driving for 24 h after treatment. Also postoperative instructions on how to use the visual analogue scale (VAS) and fill up the questionnaire were given. On the day of treatment, patients were randomly assigned to either an experimental or a control group. Half an hour before the treatment, patients in the experi-

Table 1 Means and standard deviations of the number of ibuprofen tablets in the case and control groups

Properties	Group	Mean	Std. Deviation	*P* value
Age	Ketamine	28.27	7.20	0.72
	Control	29.22	8.41	
Number of local anesthetic cartridges	Ketamine	1.41	0.60	0.003
	Control	2.27	0.95	
Pain score	Ketamine	0.61	1.09	0.019
	Control	1.61	1.33	
Number of analgesic tablets used	Ketamine	0.83	1.33	0.011
	Control	2.17	1.61	

mental group were given 20 ml of cherry juice containing 10 mg of ketamine, and patients in the control group were given 20 ml of cherry juice alone (placebo) orally. In order to minimize side effects and complications, only low-dose ketamine was used. During and after treatment, patients were monitored for ketamine side effects such as hallucination.

All containers were previously coded by an operator, and neither the patients nor the practitioners were informed about their content.

After 30 min, inferior alveolar nerve block was elicited using a cartridge of 2% lidocaine with 1/100000 epinephrine on the side of the tooth being treated. The tooth was tested by a pulp tester after 5-10 min. If a positive response was elicited, another cartridge of lidocaine was injected. In cases of a negative response, the treatment was started and if the patient experienced pain during the procedure, supplemental injections were applied. Intraoperative pain was assessed immediately after the treatment, using the VAS. Ten tablets of 400 mg ibuprofen were prescribed for each patient, and he/she was instructed to use analgesics if pain was experienced, taking two tablets each time, with an interval between no shorter than 4 h. Each patient completed the questionnaire for the first 24 h after treatment, indicating the number of ibuprofen tablets taken. At most, four local anesthetic capsules per patient were administered. Although low-dose oral ketamine does not induce serious complications, each patient was monitored for allergic reactions, hallucinations and drowsiness before, during and after treatment. Data were analyzed using *t* test with the SPSS software package version 16.

Results

Mean age (mean ± SD) was 28.27 ± 7.20 yr in the experimental (ketamine) group and 29.22 ± 8.41 yr in the control group. There was no statistically significant age difference between the groups (*t* test, $P = 0.72$).

The mean number of cartridges used in the experimental group (1.41 ± 0.60) was significantly lower than that in the control group (2.27 ± 0.95) (*t* test, $P = 0.003$).

The mean VAS score for intraoperative pain in the experimental group (0.61 ± 1.09) was significantly lower than that in the control group (1.61 ± 1.33) (*t* test, $P = 0.019$).

The mean number of ibuprofen tablets used in the first 24 h after treatment was significantly lower in the experimental group (0.83 ± 1.33) than in the control group (2.17 ± 1.61) (*t* test, $P = 0.011$) (Table 1).

Discussion

The high failure rate of inferior alveolar nerve (IAN) block in patients with irreversible pulpitis necessitates further investigations of alternative options for anesthesia (9,11,13). In the present study, preoperative administration of oral ketamine significantly decreased the amount of local anesthetic required to provide anesthesia, along with reduction of postoperative pain.

Various mechanisms have been hypothesized to explain the analgesic action of ketamine (15,16,21). Ketamine interacts with sodium channels as a local anesthetic and shares a binding site with commonly used local anesthetics, enhancing their anesthetic effect (15). In a study by Tverskoy et al. (21) ulcers were infiltrated with a solution of 0.5% bupivacaine and 0.3% ketamine after herniorrhaphy, and an increased level of anesthesia was demonstrated. In addition they found that subcutaneous infiltration with 0.3% ketamine produced a local anesthetic effect (21). They concluded that ketamine acts via a peripheral mechanism and enhances the anesthetic and analgesic actions of local anesthetics profoundly (21). It has been suggested that ketamine, as an NMDA receptor antagonist, blocks the action potential of nerve fibers by affecting the sodium and potassium channels in their membranes. Ketamine may also play an important role in the management of postoperative acute pain when

used alone or as an adjunct to local anesthetics (16).

In a study by Heidari at al. (20), oral ketamine was found to be effective in reducing postoperative pain as well as the amount of analgesics required after orthopedic surgery, which is in agreement to our present findings. In another study, Nikolajsen et al. (22) used oral ketamine to manage post-amputation pain and found that it was effective for neuropathic pain management. Jage et al. (23) recommended oral ketamine as a new approach for managing postoperative pain.

Contrary to the studies mentioned above, some other studies (24-26) have shown that ketamine had no effect in reducing postoperative pain after surgical procedures conducted under general anesthesia, in contrast to the present findings. However, because general anesthesia was not used in the present study, this contradiction was not strict.

In the above studies, ketamine was used in multiple doses and in higher amounts than in the present study. Considering the safety of low-dose ketamine and its simple clinical use, the present study showed that oral ketamine was effective for enhancing the anesthetic effect of lidocaine and epinephrine. This is especially important for patients with irreversible pulpitis of mandibular molars. However, because of the limited clinical trials performed in this field, and disagreements among existing reports, more clinical studies are required to evaluate the efficacy of prophylactic administration of systemic ketamine for successful management of patients with irreversible pulpitis.

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