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Original Article

Analgesic effects of gabapentin and ibuprofen on the pain in post therapy of root canal; a randomized double-blind clinical trial

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Abstract

Introduction: Inhibiting the pain which affects both the patients and dentists is an important factor during treating dental patients. The aim of this study was to assess the analgesic effect of two medications ibuprofen and gabapentin on the post-endodontic-therapy pain.

Methods: Forty patients who need root canal therapy with Visual Analog Scale (VAS)>40, participated in this double-blind randomized clinical trial study and randomly divided into two groups. The ibuprofen group received 800 mg ibuprofen 1 hour before the treatment and 400 mg at 6, 12 and 24 hours after the treatment procedure, and the other group received 600 mg gabapentin 1 hour before the treatment and 300 mg at 6, 12 and 24 hours after treatment. Patients recorded the intensity of pain via VAS before treatment and every hour for the first 6 h after taking the medication and then every 6 h thereafter for a total of the 48-hour period. (Two tablets of acetaminophen codeine (325mg/20mg) were given to the patients as a rescue dose.

Results: The analgesic effect of gabapentin was significantly higher than ibuprofen in 12h ($p=0.035$), 24h ($p<0.001$), and 48 h ($p=0.012$) after analgesic intake. It has been also shown that both medicines had analgesic effect significantly. ($p<0.0001$)

Conclusions: Gabapentin had greater analgesic effects on the sample group from 12 h until 48h after taking in comparison with ibuprofen so; it seems that it could be an appropriate option for postoperative pain inhibition.

Keywords: Pulpitis, Root canal therapy, Pain, Ibuprofen, Gabapentin, Visual analogue pain scale

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اثرات ضد دردی گاباپنتین و ایبوپروفن بر درد بعد از درمان ریشه: مطالعه بالینی دوسوکور

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چکیده

مقدمه: کنترل درد یک فاکتور مهم در درمان بیماران دندانپزشکی می باشد که هم بیمار و هم دندانپزشک را تحت تاثیر قرار می دهد. هدف از این مطالعه مقایسه اثر ضد دردی دو داروی گاباپنتین و ایبوپروفن بر درد بعد از درمان کانال ریشه بود.

مواد و روش ها: ۴۰ نفر از بیماران که نیاز به درمان کانال ریشه داشتند با VAS>40 وارد مطالعه شدند و به صورت تصادفی به دو گروه تقسیم شدند. گروه ایبوپروفن 800 mg ایبوپروفن ۱ ساعت قبل و 400 mg ایبوپروفن ۶ ، ۱۲و ۲۴ ساعت بعد از درمان دریافت کردند. گروه دیگر 600 mg گاباپنتین یک ساعت قبل و 300mg گاباپنتین را ۶ ، ۱۲و ۲۴ ساعت بعد از درمان دریافت کردند. بیماران شدت درد خود را بر اساس معیار VAS قبل از شروع درمان و در ۶ ساعت اول بعد از دریافت دارو هر ۱ ساعت تا ۶ ساعت اول و سپس هر ۶ ساعت تا ۴۸ ساعت ثبت کردند. (دو عدد قرص استامینوفن کدئین (325mg/20mg) به عنوان داروی rescue به بیماران داده شد).

یافته ها: اثرات ضد دردی گاباپنتین در ۱۲ ساعت (p=0.035) ، ۲۴ساعت(p< 0.001) و ۴۸ساعت (p=0.012)به طور معنی داری بیشتر از ایبوپروفن بود. همچنین نشان داده شد که هر دو دارو اثرات ضد دردی معنی داری دارند. (p<0.0001)

نتیجه گیری: گاباپنتین اثرات ضد دردی بیشتری نسبت به ایبوپروفن در ۱۲ تا ۴۸ ساعت داشت. بنابراین می تواند یک انتخاب خوب در کاهش دردهای بعد از کار باشد.

واژگان کلیدی: پالپیت، درمان ریشه، درد، ایبوپروفن، گاباپنتین، VAS

Introduction

Endodontic post-treatment pain is a significant problem facing the dental professions.[1] It has been reported that up to 80% of the patients have complained about the pain after endodontic treatments. It has also been reported that the prevalence of postoperative pain following root canal treatment varied between 3-58%; this report has been diagnosed with pain levels ranging from mild to severe.[1,2] Postoperative pain is most expected to occur within first 24 hours period after root canal treatment. It occurs because of acute inflammation within the peri-radicular tissue in response to an increase in intensity of stimulants from the root canal.[2]

Inhibiting the pain which has effects on both the patients and the clinicians is an important factor during the treatment of dental patients. It seems that the main cause of pain in dental procedure is inflammatory mediators releasing process that activate sensitive nociceptors surrounding the tooth.[3] The efficacy of analgesics differs and depends to the source of the pain. Different classes of drugs have been considered for the control of post endodontic treatment pain.[1] Non-steroidal anti-inflammatory drugs (NSAIDs) are the most analgesics commonly administered to all variates of tooth pain.

Many studies have reported that ibuprofen is very effective on control or reducing the dental pain. Ibuprofen blocks both the cyclooxygenase-1 (COX-1) and-2 (COX-2) enzymes, with a highly effective analgesic and anti-inflammatory role for post endodontic treatment pain.[4]

Another commonly used analgesic medication to control the pain is gabapentin which is a lipophilic medicine that penetrates through the blood-brain barrier; however, its mechanism of action has not been yet fully understood.[5] Gabapentin has an active antinociceptive or antihyperalgesic action for the postoperative pain prevention based on experimental models of neuropathic pain and inflammatory hyperalgesia.[6]

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Because ibuprofen and other NSAIDs have some gastrointestinal side effects and many people don't tolerate it, the purpose of this double-blind prospective clinical pain study was to compare the effect of common analgesic medicine–ibuprofen-against with gabapentin on post endodontic pain**.**

Methods

Over a period of 6 months (from September 2011 to February 2012) 60 patients were screened for the possible criteria. 40 people fulfilled the inclusion criteria and consented to participate in this prospective randomized double-blind clinical trial study (IRCT id: IRCT 201205069564N1), that was approved by the Ethical Committee of Babol University of Medical Sciences.

Participants were selected from patients referred to the root canal therapy sector of Dentistry School of Babol University of Medical Sciences in Babol, Iran. Patients were divided into 2 groups of 20 according to similar clinical study. All patients were in good health as determined by medical history. To this purpose, patients were checked for background systematic diseases.

Then clinical and radiographic examinations were performed. Pulp vitality testing including hot and cold tests and sensitivity to touch and percussion test were also performed. The intensity of preoperative pain was measured by instructing the patients to complete a VAS ranged from 0-100, the figure 0 implied as no pain while the 100 indicated the severest pain.

Those who had irreversible acute pulpitis in their mandibular first molar, with VAS>40 mm were selected according to previous studies.[7] Informed consents were obtained from all the patients and they have expressed their consent to participate in the study. Patients were excluded if they fell into one of the following categories:

- Patients younger than 15 years old
- Pregnant women and breastfeeding mothers
- History of antibiotic intake in the previous week
- Analgesic taken within the last 6 hours
- History of mental illness, seizure-using seizure drugs, systemic diseases such as diabetes, ulcers, kidney diseases, etc.
- History of allergy to NSAIDs, aspirin or local anesthetics

The standardized procedure (done by an undergraduate dental student with supervising an attend) for all participants included local anesthesia (two cartridges of lidocaine 2% and 1:800000 epinephrine (DarouPakhsh, Iran) were used for local anesthesia), rubberdam isolation, standardized access cavity preparation and pulp extirpation.

The canals were prepared by using step back technique and rotary instruments (Mtwo) (VDW, Germany), 30.5% for mesial canal and 35.4 % for distal canal, the canals were thoroughly rinsed during and after instrumentation with sodium hypochlorite 2.5%, then obturated by using lateral compaction technique with gutta-percha and AH26 sealer (Dentsply, Germany). The teeth access cavity were sealed with cavit (3M ESPE) and the patients were scheduled for the next appointment.

A licensed pharmacist prepared the following drug groups: 400 mg ibuprofen and 300 mg gabapentin, then they were placed in clear, unmarked, indistinguishable, gelatin capsules (which were similar in shape and size for blindness) with added lactose to take up the remaining space in the capsules.

Following the root canal therapy, each patient was randomly assigned to either of two groups. The ibuprofen group was received2 capsules of the ibuprofen (800 mg), 1 hour before the root canal treatment and 400 mg at 6, 12 and 24 hours after the treatment procedure.

And the another experimental group was taken 600 mg of gabapentin 1 hour before the treatment and 300 mg of gabapentin at 6, 12 and 24 hours after treatment. Patients received a VAS to record the intensity of pain before treatment, every hour for the first 6 h after taking the medications and then every 6 h thereafter for a total of the 48-hour period (The treatment procedure was clearly explained for each patient before and after the treatment and each patient was monitored via phone calling). (Two tablets of acetaminophen codeine (325mg/20mg) were given to the patients as a rescue dose)

At the end of the 48 h, treated patients have recorded the efficacy of the treatment scaling from 0-100. The patients have also expressed the side effects of the drugs such as diarrhea, stomachache, bellyache, bloat, drowsiness, dizziness, tinnitus and etc .Because the distribution of the data was non- normal, the non-parametric tests like the Mann-Whitney U and

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Friedman tests with SPSS V.18 and EXCELL 2013 software were used to analyze the data.

Results

In this study there were 14 male and 26 female and all the patients returned the diaries (table 1). As illustrated in table 2 the analgesic effect of gabapentin was significantly higher than ibuprofen in 12 (p=0.035), 24 (p<0.001), and 48 h (p=0.012) after analgesic intake. It has been observed that the analgesic effect of ibuprofen was higher at 3 hours postoperatively. A significant difference was observed within the groups for both ibuprofen and gabapentin (p<0.0001) users.

According to the figure 1 the efficacy of gabapentin was higher than ibuprofen. However until 6h, there was no significant difference between 2 groups and there was a significant difference at, 12 (p=0.035), 24 (p=0.000) and 48 hours (p=0.012), which indicates that gabapentin had a better long-term analgesic effect than ibuprofen.

Table1. Demographic and clinical features of patient

Variables	Ibuprofen (N=20)	Gabapentin (N=20)
Age, y (mean±SD)	30.25±9.92	32.70±9.97
Male	7 (35)	7 (35)
Female	13 (65)	13 (65)
Baseline pain, VAS (mean±SD)	74±12.31	72±11.47

Table2. The VAS mean in two groups with concerning the time of taking the analgesics

	Time, h									
	0	1	2	3	4	5	6	12	24	48
Ibuprofen	74±12.31	12.5±15.85	13.5±14.96	10.5±13.17	13±12.18	12.5±12.51	13.5±15.31	13±14.18	16±14.65	12±13.99
Gabapentin	72±11.47	9.5±12.34	12±10.56	11.5±11.37	8.5±10.89	7±9.23	5±10.51	3.5±8.13	1.5±4.89	1±4.47
P-Value	0.733	0.738	0.968	0.640	0.221	0.174	0.49	0.035	0.0001	0.012

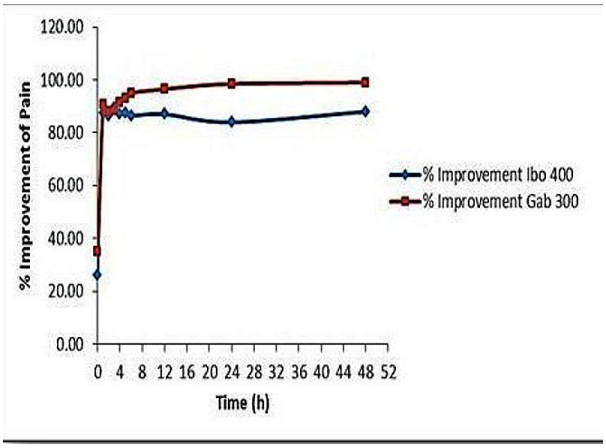


Figure1. The percentage of pain relieving based on the type of painkiller

The patients also recorded any adverse effects during the 42 h following treatment. From the five of 40 participants, a total of 5 reported adverse side effects. Drowsiness was the most commonly reported side effect. In the ibuprofen group, 2 out of 20 suffered from drowsiness and 1 patient complained about stomachache, while in the gabapentin group 1 participant out of 20 suffered from drowsiness and 1 suffered from stomachache. In both ibuprofen and gabapentin groups 3 out of 20 patients (3 in each group) were taken rescue medication and no significant difference was observed (p=0.000).

Discussion

The present study revealed that gabapentin had more analgesic effect after root canal treatment compared to ibuprofen. Postoperative pain after root canal therapy is a disaster occurrence for patients and it is due to stimulation of mechanisms of hyperalgesia by

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inflammatory mediators.[8] The usual painkillers for the postoperative pains are non steroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and several studies have compared it with other medications.[9, 10]

According to some previous studies, the use of painkiller before root canal therapy had a considerable effect on reducing the pain in patients.[11, 12] Therefore, in the present study patients received analgesics before therapy. According to Srivastava and et al's study, the preoperative gabapentin can cause a significant reduction in a postoperative pain in open cholecystectomy.[13]

In the current this study, gabapentin showed no significant analgesic effect at the first hours after root canal therapy. Maybe, it was due to the mechanism of up taking and action of the drug. However, at 6, 12, 24 and 48 h it showed a higher effect than ibuprofen and it was found that gabapentin had a considerable effect in long term. The long-term effect of gabapentin was due to its longer half-life in comparison to ibuprofen (respectively, 5-9 hours and 2 hour).[14, 15]

According to many studies, ibuprofen is an effective painkiller for root canal treatment. The result of Arsalan and et al's study showed that ibuprofen had more analgesic effect a more effective analgesic in comparison to tenoxicam.[7]

In Parirokh and et al's study on patients with irreversible pulpitis, the analgesic effect of ibuprofen was significantly higher than indomethacin.[16] Ibuprofen reduces pain by blocking the cyclooxygenase 2 enzymes which release in the case of tissue injury and inflammation.[16]

The present study indicated that there was no difference in the side effects of both gabapentin and ibuprofen. The common side effects of gabapentin are drowsiness, dizziness, weight gain, peripheral edema and fatigue but these may happen in high doses and after a long-time usage. In the studies of Eckhardt and Bartholdy and et al, there were no significant difference between the side effects of gabapentin group and placebo group.[17, 18]

Although in this study ibuprofen did not show any significant side effects, its long-term use may lead to some common side effects such as headache, nausea, dyspepsia, gastrointestinal bleeding, raised liver enzymes, dizziness, hypertension and its too unusual side effects include cardiovascular diseases, kidney diseases, and pulmonary disorders.[19]

Comparison of these two drugs with each other together in root canal therapy for the first time is the power of this study and the small sample size is the weak point of it. The authors suggest repeating this study with wider sample size and doing it in comparison with placebo to detect the analgesic effect of these drugs lonely and together.

Conclusions

In conclusion, the current study has shown that gabapentin has more analgesic effect in comparison with ibuprofen. Although NSAIDs such as ibuprofen are common analgesics in root canal therapy, gabapentin due to its higher ability in reducing the pain and its fewer side effects can consider as a good option for postoperative pain in root canal treatment.

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Conflict of interest: We declare that there is no conflict of interest.

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