A Clinical Comparative Study of Two Local Dental Anesthetics: Articaine and Mepivacaine

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บทคัดย่อ

อาติเคนเป็นยาชาแบบเฉพาะที่ชนิดเอไมด์ตัวใหม่ที่มีการนำมาใช้ในประเทศไทย การศึกษานี้มีวัตถุประสงค์ในการเปรียบเทียบความปลอดภัยและประสิทธิภาพของยาชาอาติเคนความเข้มข้นร้อยละ 4 ที่ผสมเอพิเนฟรีนในสัดส่วนหนึ่งต่อแสน และยาชาเมพิวาเคนความเข้มข้นร้อยละ 2 ที่ผสมเอพิเนฟรีนในสัดส่วนหนึ่งต่อแสนซึ่งเป็นยาชาที่นิยมใช้ในทางทันตกรรม การศึกษานี้เป็นการศึกษาโดยสุ่มแบบดับเบิลบลายด์ โดยศึกษาในฟันรากเดียวที่ได้รับการถอนฟันและรักษารากฟัน อาสาสมัครมีอายุระหว่าง 10 ถึง 44 ปีได้รับการฉีดยาชาชนิดใดชนิดหนึ่งโดยการสุ่ม ประสิทธิภาพของยาชาถูกกำหนดโดยใช้วิชวลอะนาลอกสเกลหรือวีเอเอส วิเคราะห์ผลทางสถิติแบบที่มีการกระจายของข้อมูลเป็นแบบไม่ปกติ ผลการศึกษาพบว่าในจำนวนอาสาสมัครทั้งหมด 68 คน ไม่พบความแตกต่างอย่างมีนัยสำคัญทางสถิติเกี่ยวกับสถิติประชากรของอาสาสมัครที่แบ่งออกเป็นสี่กลุ่มในสองการทดลอง ระยะเวลาที่เริ่มชาในแต่ละวิธีการรักษาถูกนำมาเปรียบเทียบกันเมื่อใช้ยาชาต่างชนิดกัน พบว่าไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติในแต่ละกลุ่มการทดลองเมื่อวัดอัตราความเจ็บปวดด้วยมาตรวัดวีเอเอส ($p > 0.05$ ครัสคาล-วาลลิส เทสต์) จากการศึกษาแสดงว่ายาชาอาติเคนความเข้มข้นร้อยละ 4 มีประสิทธิภาพในการลดความเจ็บปวดในทางคลินิกในขณะถอนฟันและรักษารากฟัน และมีระยะเวลาในการเริ่มชาที่เหมาะสมสำหรับการใช้ในทาง

Abstract

Articaine is a new amide local anesthetic in Thailand. This study sought to compare the safety and efficacy of 4 % articaine with epinephrine 1:100,000 and 2 % mepivacaine with epinephrine 1:100,000, which is the most used local anesthetic in dentistry. In two identical randomized double-blinded trials: the single-rooted tooth extraction procedure and the single-root canal treatment procedure, subjects 10 to 44 years of age received either 4 % articaine with epinephrine 1:100,000 or 2 % mepivacaine with epinephrine 1:100,000. In each trial, we randomized the subjects to receive articaine or mepivacaine. Efficacy was determined by subjects using a visual analog scale or VAS. We used a non-parametric analysis to analyze the data. In a total of 68 subjects, we found that there was no significant difference in demographics among four groups in the two trials. The time of onset (or onset time) in each procedure was comparable for both articaine and mepivacaine. We showed no statistical difference between two local anesthetic groups in each trial with respect to subject pain rating, using the VAS ($P>0.05$; Kruskal-Wallis test). Our findings suggest that 4% articaine provided clinically effective pain relief during the

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tooth extraction and the root canal therapy. The time onset of articaine is appropriate for clinical use and comparable to those observed for other commercially available local anesthetics.

Key Words: Local anesthetic, Articaine, Mepivacaine

Introduction

Articaine is an amide local anesthetic and has many of the physiochemical properties of the most commonly used local anesthetics (lidocaine, mepivacaine and prilocaine). It effectively penetrates tissue and is highly diffusible. Its plasma protein binding of approximately 95 % is higher than that observed with many local anesthetics[1]. Additionally, the thiophene ring of articaine increases its liposolubility[1], indicating that the efficacy of articaine for penetrating cell membrane is quite high. Several clinical trials reported that articaine with epinephrine is safe and effective to use in clinical dentistry[2-5]. Articaine reversibly inhibits conduction of nerve impulses by blocking sodium and potassium channels during propagation of the nerve action potential through an action mechanism similar to that of other amide local aesthetics used in dental practice, such as lidocaine, prilocaine mepivacaine and bupivacaine. Articaine is a relatively new local anesthetic drug, having been approved for use as a local anesthetic in Thailand in 1998. On the other hand, mepivacaine, other amide local anesthetic drug, has been used in Thailand for more than 15 years and is widely accepted as one of the safest anesthetic drugs. It is very effective in dental treatment, including minor oral surgery. Although the anesthetic activity of articaine with epinephrine combinations in the United States and Europe has been demonstrated to be comparable to that of other anesthetic combinations including lidocaine, mepivacaine, levonordefrin and prilocaine[3,4,6,7], the efficacy of articaine with epinephrine combinations and mepivacaine combinations in Thai clinical dentistry has not been studied. Therefore, the purpose of this study was to compare clinical properties including onset, efficacy, and safety of articaine and mepivacaine in dental procedures.

Materials and Methods

This study was approved by the human ethical committee of the Faculty of Dentistry, Chiang Mai University before initiating the trials. We conducted two identical single-dose, randomized, double-blinded trials to compare the safety and efficacy of 4% articaine with epinephrine 1:100,000 (4% Ubistesin Forte, 3M ESPE) with those of 2% mepivacaine with epinephrine 1:100,000 (2% Scandonest, Septodont). The two trials were identical in all material respects. Subjects 10 to 44 years of age undergoing either the simple, single-rooted premolar extraction procedure or the single-root canal treatment procedure were recruited in this study. Exclusion criteria were a) pregnancy, b) known or suspected allergies or sensitivities to sulfite, amide-type local anesthetics or any ingredients in the anesthetic solutions, c) concomitant cardiac or neurological disease, d) history of severe shock, paroxysmal tachycardia, frequent dysrhythmia, severe untreated hypertension or bronchial asthma, e) concomitant use of monoamine oxidase inhibitors or tricyclic antidepressants, f) subjects who were expected to require general anesthesia and g) subjects who had taken aspirin,

acetaminophen, nonsteriodal anti-inflammatory drugs or other analgesic agents within 24 hours before administration of the study medication. Within each trial, we randomized subjects in a 2:1 ratio to receive articaine or mepivacaine (both formulas contained epinephrine 1:100,000). We used the 2:1 articaine/mepivacaine ratio since the safety and efficacy profile of mepivacaine already is well studied. Subjects received the lowest effective dose of anesthetic, administrated as submucosal infiltration, a nerve block or both. Total dose was not to exceed 7.0 milligrams per kilogram of body weight.

We determined the efficacy on a gross scale immediately after the procedure by having the subject rate the pain experienced during the procedure using a visual analog scale or VAS, ranging from 0 = no pain to 10 = "worst pain imaginable". Since the data were not normality assumptions, a nonparametric test (Kruskal-Wallis test) was used to analyze the VAS data. For other demographic data and procedure onset, one-way ANOVA was used to evaluate. We evaluated safety by assessing adverse events throughout the trials.

Results

Demographics

Of the 68 enrolled patients, 48 (71%) were in treatment group 1 and received a single-rooted premolar extraction procedure and 20 (29%) were in treatment group 2 and received a root canal treatment procedure. Patients in each treatment group were further divided into two different anesthetic therapy groups, receiving respectively 4% articaine with epinephrine 1:100,000 and 2% mepivacaine with epinephrine 1:100,000. The details of patient demographics in each treatment group with articaine and mepivacaine therapy are described in Table 1. The mean ages of patients in the four groups were: 20±1, 21±1, 24±3 and 31±8 years respectively. There were no significant differences between the analyzed groups in age, gender, weight and height (P>0.05, ANOVA, Table 1). Furthermore, no significant correlation was found between painful sensation using VAS as a nociceptive marker following the application of local anesthesia and age or weight or height. Therefore, both articaine and mepivacaine were considered to have a real effect on the VAS variables.

Table 1 *Patients demographic and baseline characteristics*

	Premolar extraction		Root canal treatment	
	Articaine	Mepivacaine	Articaine	Mepivacaine
Women, n (%)	18 (27%)	14 (21%)	7 (10%)	3 (4%)
Men, n (%)	7 (10%)	9 (14%)	7 (10%)	3 (4%)
Age (years) mean±SE	20±1	21±1	24±3	31±8
Weight (kg) mean±SE	48±2	51±2	52±3	55±7
Height (cm) mean±SE	155±5	159±2	161±2	161±5

Procedure onset

Mean onset times of articaine and mepivacaine in the single-rooted premolar extraction treatment were 57.2±4.7 and 55.5±4.0 sec respectively. In the single-root canal treatment they were 50.7±4.7 and 45.0±8.7 sec respectively (Figure 1). In both treatment groups, the onset times of articaine and mepivacaine were not significantly different (P=0.6, ANOVA for the single-rooted premolar extraction treatment and P=0.6, ANOVA for the single-root canal treatment).

Pain rating or Efficacy of anesthetics

We included in the efficacy analyses all patients who received a study drug and had a VAS evaluation performed. On average, the patients participating in the single-rooted premolar extraction treatment and the single-root canal treatment had no significant differences of subject rating pain using the VAS scoring system between 4 % articaine and 2 % mepivacaine as

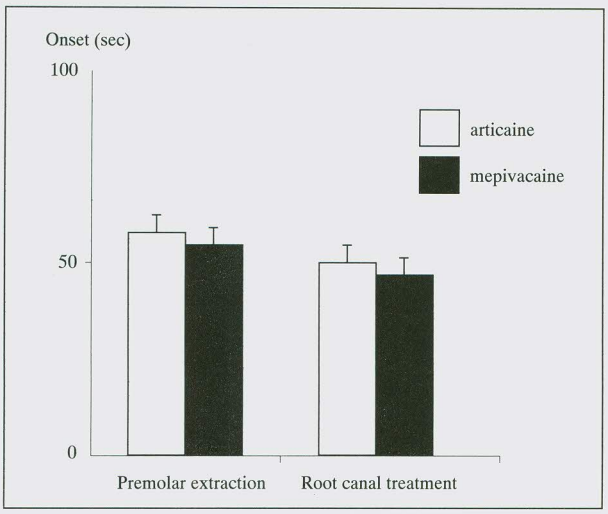

Figure 1 : The onset times of the anesthetis drugs 4% with epinephnine 1:100,000 articaine and mepivacaine before the premolar extraction treatment and the single-root canal treatment. Data is equal mean±SE.

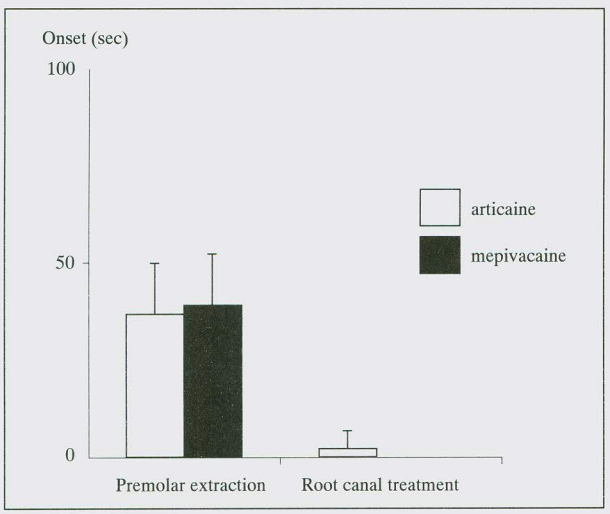

Figure 2 : Intensity of pain (VAS) during the single-rooted premolar extraction treatment and the single-root canal treatment following the use of articaine and mepivacaine as the anesthetics. Data is equal mean±SE.

shown in Figure 2 (P=0.7; *Kruskal-Wallis test* for the single-rooted premolar extraction and P=0.9; *Kruskal-Wallis test* for the single-root canal treatment). Our findings suggest that the anesthetic efficacy of articaine is similar to that of mepivacaine. For both groups tested, mean pain scores determined by patients were less than 1.0.

Safety

No serious adverse events related to the study medication occurred. Minor adverse events, including post-procedural pain and headache, occurred with equal frequency in the 4 % articaine and 2 % mepivacaine groups.

Discussion

The efficacy of 4% articaine with epinephrine 1:100,000 vs. that of 2% mepivacaine with epinephrine 1:100,000 was demonstrated on a gross level in two well controlled, randomized double-blind trials. A total of 68 subjects was treated in these groups, 48 of whom received 4% articaine with epinephrine 1:100,000 and 20 of whom received 2% mepivacaine with epinephrine 1:100,000. VAS assessment of pain provides a gross, but validated and meaningful, measure of anesthetic efficacy. Articaine's anesthetic efficacy was demonstrated by the low mean pain scores in both procedures. We found no significant differences in VAS pain scores between subjects receiving the 4% articaine with epinephrine and those receiving the 2% mepivacaine with epinephrine regardless of the treatment group. We ensured the number of subjects treated were sufficient to justify statistical comparisons of efficacy. The use of a 10-centimeter VAS scoring system was expected to reveal any gross difference existing between the two anesthetics. In addition, the demograph between 4% articaine with epinephrine 1:100,000 and 2% mepivacaine with epinephrine 1:100,000 was no different when measuring efficacy was on a gross scale. In previous studies, articaine with epinephrine has been shown to be comparable with other local anesthetics including 4% prilocaine with epinephrine 1:200,000 or 2% lidocaine with epinephrine 1:100,000 with respect to anesthetic efficacy during dental procedures[3,4,6,8-10]. All of those studies reported that time of onset, duration of anesthesia and

the efficacy of articaine with epinephrine were no significantly different compared to other similar agents.

In this study, the average onset times of the articaine and the mepivacaine in the single-rooted premolar extraction procedures were 57.2 seconds and 55.5 seconds. The average onset times of the articaine and the mepivacaine in single-root canal treatment were 50.7 seconds and 45.0 seconds. These times were consistent with previous studies[2-4,11].

For routine dental treatment, including simple tooth extraction and pulpal extirpation, there are no significant differences of efficacy between articaine and mepivacaine. Both local anesthetics have enough profound potency for patients to undergo the dental treatment. The mean pain rating score for each local anesthetic in the tooth extraction group was lower than 1, but that score in the root canal treatment group was close to 0. These scores suggest that subjects who received either 4% articaine with epinephrine1: 100,000 or 2% mepivacaine with epinephrine 1:100,000 were nearly pain-free during both procedures. Although the inclusion criterion for the single-root canal treatment was tooth diagnosed as the irreversible pulpitis or hot tooth syndrome, which those teeth were hard to anesthetize with any the anesthetic drugs. Using 4% articaine and 2% mepivacaine in this study, we found no complications following the procedures. Allergy to local anesthetics is very rare; most of the cases represent allergy to the preservative contained in the cartridge. The new generation of local anesthetics, such as articaine, contains no preservative substance. Thus, articaine is a safe and effective local anesthetic for use in clinical dentistry. This finding is consistent with previous studies[3,4,7,12,13].

Conclusions

In this clinical investigation, articaine provided clinically effective pain relief during tooth extraction and root canal treatment. Furthermore, we observed no significant difference in pain relief between subjects in the 4% articaine with epinephrine 1: 100,000 groups and those in the 2% mepivacaine with epinephrine 1:100,000 groups. For 4 % articaine with epinephrine, time to onset of anesthesia is appropriate for clinical use and is comparable to those observed for other commercially available local anesthetics.

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