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A Comparison of the Postoperative Pain Relief and Clinical Local Anesthetic Efficacy of Levobupivacaine and Articaine for Impacted Lower Third Molar Removal

Gömülü Alt Üçüncü Molar Diş Çekiminde Levobupivakain ve Artikainin Postoperatif Ağrı Giderme ve Lokal Anestezik Etkinliğinin Karşılaştırılması

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ABSTRACT

Objective: A comparison of postoperative pain relief and clinical anesthetic efficacy of 2% articaine and 0.5% levobupivacaine in impacted third molar dental surgery.

Material-Method: Fifty-three patients underwent the removal of symmetrically positioned lower third molars in 2 separate appointments under local anesthesia either with 2% articaine or 0.5% levobupivacaine in a double-blinded, randomized and crossover study. Neither anesthetic agent contained a vasoconstrictor. The time to onset of anesthesia, duration of surgery, intraoperative bleeding, hemodynamic parameters, the duration of postoperative analgesia and anesthesia as well as postoperative visual analogue scale (VAS) scores were evaluated.

Results: The time to onset of anesthesia with articaine (80.28 ± 19.27 seconds) was significantly less compared to levobupivacaine (136.69 ± 33.52 seconds). The average duration of postoperative anesthesia for levobupivacaine and articaine was 8 hours and 3 hours, respectively (p = 0.000). The mean duration of postoperative analgesia for levobupivacaine and articaine was 7-8 hours and 3 hours, respectively (p = 0.000). Additionally, VAS scores with levobupivacaine were significantly lower than articaine up to the 4th postoperative hour. Significantly less bleeding was seen in the surgeries performed with levobupivacaine.

Conclusion: 0.5% Levobupivacaine resulted in a longer period of postoperative anesthesia and analgesia, a longer time to onset of anesthesia, and less postoperative pain compared to 2% articaine.

Keywords: Levobupivacaine, Articaine, Third molar surgery, VAS

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ÖZET

Amaç: Gömülü üçüncü molar diş cerrahisinde %2 artikain ve %0,5 levobupivakainin postoperatif ağrı kesici ve klinik anestezik etkinliğinin karşılaştırılması.

Materyal-Metot: Çalışmaya çift taraflı gömülü üçüncü büyük azı dişleri olan 53 hasta dahil edildi.
Çift kör tekniği ile uygulanan çapraz randomize çalışmada, iki ayrı randevuda bir tarafta levobupivakain (Chirocaine %0.5), diğer tarafta artikain (Ultracaine %2) kullanılarak operasyon gerçekleştirildi. Her iki anestezik ilaç da vazokonstrüktör madde içermedi. anestezik ajanın etkisinin başlama süresi, operasyon süresi, operasyon sırasında kanama miktarı, hemodinamik parametreler, postoperatif analjezi ve anestezi süresi değerlendirildi. Hastadan postoperatif görsel ağrı değerlendirme skalası (VAS) ile ağrı derecesini işaretlemesi istendi.

Bulgular: Articaine ile Anestezinin başlama süresi (80.28 ± 19.27 sn.) levobupivakaine kıyasla (136.69 ± 33.52 sn.) önemli ölçüde daha kısaydı. Levobupivakain ve artikain için ortalama postoperatif anestezi süresi sırasıyla 8 saat ve 3 saat idi ($p = 0.000$). Levobupivakain ve artikain için ortalama postoperatif analjezi süresi sırasıyla 7-8 saat ve 3 saat idi ($p = 0.000$). Ayrıca levobupivakain ile postoperatif görsel ağrı skala skorları postoperatif 4. saate kadar artikainden anlamlı derecede düşüktü. Levobupivakain ile yapılan ameliyatlarda belirgin olarak daha az kanama görüldü.

Sonuç: %0.5 Levobupivakain, %2 artikaine kıyasla daha uzun postoperatif anestezi ve analjezi süresi, daha uzun anestezi başlangıcı ve daha az postoperatif ağrı ile sonuçlandı.

Anahtar Kelimeler: Levobupivacaine, Articaine, Üçüncü molar cerrahisi, VAS

1. Introduction

Post-surgery pain is very common and can emanate from surgical trauma and the release of pain mediators [1]. The pain that occurs after the third molar surgery can cause great discomfort in patients and various studies are being conducted for better pain relief after surgery. Proper pain management with local anesthesia is considered to be the most important factor in facilitating doctor-patient cooperation and management of patient anxiety in an oral surgery procedure [2]. The first hours after the end of third molar surgery is associated with the highest intensity of pain, when the local anesthetic wears off [3]. Although local anesthetics are used for anesthesia and analgesia following surgery or for the management of other acute and chronic pain conditions, they only last a few hours. Postoperative pain is commonly ameliorated with the administration of short-acting local anesthetics or oral analgesics.

Local anesthetics block nerve conduction temporarily and reversibly for a certain period of time. Articaine is a safe anesthetic with fast onset and low side effects. However, theoretically, pain control can be increased by using a longer acting local anesthetic [4,5]. Long-term blocking of nociceptive impulses originating from the surgical site with the use of long-acting local anesthetics has been shown to be a promising strategy for improving postoperative analgesia [6]. Bupivacaine, which provides long-term block anesthesia and long-term postoperative pain control, is a widely used long-acting local anesthetic [7,8]. Levobupivacaine, the pure S (−) enantiomer of bupivacaine, has recently emerged as a safer alternative for regional anesthesia compared to its racemic parental compound. Levobupivacaine is a long acting amide-type local anesthetic. Use of this anesthetic is especially beneficial for use in oral surgeries that entail lengthy procedures or oral surgical extraction that are likely to be associated with postoperative pain and discomfort [9].

Although numerous studies comparing the clinical efficacy of articaine and lidocaine have been reported in the literature, the number of studies comparing articaine and levobupivacaine is very few. Therefore, the aim of this work was to assess the clinical efficacy of 2% articaine or 0.5% levobupivacaine for the surgical removal of symmetrically positioned lower third molars. Neither anesthetic agent contained a vasoconstrictor.

2. Material and Method

The protocol and the informed consent document of this study was approved by the institutional Ethics Committee (Gulhane Medical Academy Command Pharmaceutical Research Local Ethics Committee, 17.04.2009; 1491-64209/15399). All patients provided written informed consent during the pretreatment screening period and before any study procedures were performed. This study was conducted in accordance with the tenets of the Declaration of Helsinki. The study population included 53 adult patients, with similarly positioned lower third molars, as observed in panoramic radiographies. All the subjects were generally healthy; none of the participants were taking any medication that was likely to alter pain perception, as established by self-report and written health history. The current study had a double-blind design, that is, neither the surgeon nor the patients were aware of the local anesthetic being used at the two different appointments. The same surgeon performed all 106 surgeries and postoperative evaluations.

The patients recruited to the study underwent removal of symmetrically positioned lower third molars in 2 separate appointments at least 2 weeks apart, under local anesthesia either with articaine or levobupivacaine. The study was designed as a double-blind, randomized, and crossover study. The patients received a regional anesthetic blockade with 2 mL of the anesthetic solution at three locations: lingual, buccal, and inferior alveolar nerves. When anesthesia of inferior lip was achieved (approximately five minutes after the initial injection), an additional 1 mL of the same anesthetic was injected into the mucosa. This was carried out to guarantee hemostasis and anesthesia of the site. The removal of lower third molars followed a standard surgical technique. Postoperative pain control was established with oral once daily piroxicam for 4 days. Additional painkillers such as paracetamol was available to the patients as and when needed. The amount of bleeding during the operation was evaluated with a three-category scale; 1- a small amount of bleeding, 2- moderate bleeding, 3- a large amount of bleeding.

Time to the onset of anesthesia, duration of postoperative anesthesia and postoperative analgesia, intraoperative bleeding, hemodynamic parameters, total amount of rescue medication and postoperative visual analogue scale (VAS) scores were evaluated. The duration (in hours) between the end of surgery and ingestion of the first piroxicam for pain relief was considered as the duration of postoperative analgesia.

Subjective pain evaluation was carried out with the aid of a 10 cm length VAS with 0 anchored by “no pain” and 10 anchored by “worst pain imaginable.” The study participants recorded their postoperative pain intensity at 15-minute intervals for the first 60 minutes after surgery and at the 2nd, 4th, 8th, 24th and 48th hours afterwards.

Statistical Method

The data were evaluated using the SPSS for Windows V.15.0. Descriptive statistics are shown as number (%) for intermittent variables and mean ± standard deviation for continuous variables. The normal distribution of data of the groups was established using the Kolmogorov Smirnov Test. Mann Whitney U test was used for comparison between groups, Wilcoxon test was used for comparison of the sides to which levobupivacaine and articaine were applied. Pearson and Spearman correlation coefficients were used to evaluate the relationship between variables. Statistical significance was determined as 5%.

3. Results

The average age of the 53 patients who participated in the study was 22.2 ± 3.6 years. The cohort consisted of 33 women and 20 men. Osteotomy was performed in 30 patients while 23 patients did not require osteotomy. Surgeries requiring osteotomy, regardless of the local anesthetic used, are

considered to be more difficult, more traumatic and generally take longer than surgeries that do not require osteotomy.

Time to the onset of anesthesia was 80.28 ± 19.27 seconds for articaine and 136.69 ± 33.52 seconds for levobupivacaine; this difference was statistically significant (p=0.00) (Table 1). The mean duration of postoperative anesthesia in patients who underwent osteotomy was 3.01 ± 0.94 hours for articaine and 7.85 ± 2.49 hours for levobupivacaine. The same for patients who did not undergo osteotomy was 3.10 ± 1.02 hours for articaine and 8.22 ± 2.25 hours for levobupivacaine. The duration of postoperative anesthesia with levobupivacaine was significantly longer than that with articaine (p =0.000) (Table 2). The mean duration of postoperative analgesia in osteotomy patients was 3.07 ± 1.26 hours for articaine and 7.10 ± 2.88 hours for levobupivacaine. The same in patients without osteotomy was 2.58 ± 1.14 hours for articaine and 8.01 ± 2.04 hours for levobupivacaine. Levobupivacaine provided significantly longer duration of postoperative analgesia compared to articaine (p =0.000) (Table 2).

Table 1: Time of anesthesia onset of articaine and levobupivacaine

	Articaine	**Levobupivacaine**	**p**
Time of anesthesia onset, seconds	80.28± 19.27	136.69±33.52	**0,00**

Table 2: Comparison of articaine and levobupivacaine in operations with and without osteotomy

	Surgeries With Osteotomy (n=30)			**Surgeries Without Osteotomy**		
	Articaine	**Levobupivacaine**	**p**	**Articaine**	**Levobupivacaine**	**p**
Duration of operation, minutes	21.33± 4.72	21.50± 5.11	0.796	12.82± 2.53	12.60± 2.55	0.317
Durationof postoperative anesthesia, hours	3.01± 0.94	7.85± 2.49	**0.000**	3.10± 1.02	8.22± 2.25	**0.000**
Duration of postoperative analgesia, hours	3.07± 1.26	7.10± 2.88	**0.000**	2.58± 1.14	8.01± 2.04	**0.000**
Use of additional analgesic (pieces)	1.56± 1.16	0.76± 0.85	**0.000**	0.69± 1.01	0.30± 0.70	**0.014**
Bleeding	2.20± 0.40	1.86± 0.43	**0.004**	2.08± 0.28	1.52± 0.51	**0.000**

The mean additional painkiller requirement with articaine was 1.56 ± 1.16 in surgeries with osteotomy and 0.69 ± 1.01 in surgeries without osteotomy. The mean additional painkiller requirement with levobupivacaine was 0.76 ± 0.85 in surgeries with osteotomy and 0.30 ± 0.70 in surgeries without osteotomy. The need for additional painkiller was less in surgeries performed with levobupivacaine in both osteotomy (p =0.000) and non-osteotomy surgeries (p =0.014) (Table 2).

The mean amount of bleeding in patients who underwent osteotomy was 2.20 ± 0.40 with articaine, 1.86 ± 0.43 with levobupivacaine (p =0.004). In patients who did not undergo osteotomy, the mean amount of bleeding was 2.08 ± 0.28 for articaine and 1.52 ± 0.51 for levobupivacaine (p =0.000) (Table 2). The use of levobupivacaine was associated with less bleeding compared to articain. Evaluation of the hemodynamic parameters suggest that the anesthetics used did not affect systolic arterial pressure, diastolic arterial pressure or O2 saturation level during the surgeries (Table 3).

Table 3: Comparison of the effects of articaine and levobupivacaine on hemodynamic parameters in operations with and without osteotomy

	Surgeries With Osteotomy (n=30)			Surgeries Without Osteotomy		
	Articaine	**Levobupivacaine**	**p**	**Articaine**	**Levobupivacaine**	**p**
Pulse, (beats/min)						
Preoperative	87.83± 18.10	92.03± 16.98	0.202	82.95± 16.71	84.95± 12.92	0.411
After anesthesia	89.90± 16.15	90.83± 17.07	0.544	81.91± 13.42	84.86± 10.67	0.294
Postoperative	79.13± 13.15	81.40± 14.43	0.295	79.21± 11.57	79.86± 9.52	0.615
Saturation (%)						
Preoperative	97.43± 0.89	97.50± 0.82	0.790	97.52± 0.73	97.47± 0.79	0.782
After anesthesia	97.33± 0.66	97.46± 0.68	0.317	97.52± 0.66	97.43± 0.72	0.480
Postoperative	97.46± 0.57	97.46± 0.57	1.000	97.60± 0.58	97.69± 0.76	0.480
Systolic blood pressure (mmHg)						
Preoperative	123.86± 8.88	127.86± 9.44	0.017	122.86± 9.00	124.52± 11.35	0.266
After anesthesia	124.26± 9.60	123.56± 10.06	0.829	122.30± 10.81	123.13± 10.13	0.530
Postoperative	124.40± 12.61	124.03± 9.42	0.918	121.69± 9.84	122.95± 11.34	0.520
Diastolic blood pressure (mmHg)						
Preoperative	74.43± 5.70	75.50± 6.63	0.468	74.26± 5.85	75.60± 5.10	0.276
After anesthesia	74.53± 6.78	74.73± 6.28	0.795	77.60± 7.19	76.73± 5.84	0.749
Postoperative	75.93± 6.71	72.00± 5.25	0.014	75.34± 5.83	76.73± 6.93	0.552

There was no statistically significant difference in VAS values between the use of articaine and levobupivacaine at 0 and 15th minutes after surgery without osteotomy and at 0 minute after surgery with osteotomy. With the use of levobupivacaine, VAS values were lower between the 15th minute and the 4th hour after osteotomy surgeries, and between the 30th minute and the 4th hour after surgeries without osteotomy (Figure 1, Table 4).

Table 4: Comparison of visual analogue scale (VAS) values in the use of articaine and levobupivacaine in operations with and without osteotomy

	Surgeries With Osteotomy (n=30)			Surgeries Without Osteotomy		
	Articaine	**Levobupivacaine**	**p**	**Articaine**	**Levobupivacaine**	**p**
VAS 0	2.10± 2.12	1.53± 1.69	0.062	2.21± 2.67	1.43± 1.90	0.150
15th minute VAS	2.73± 2.21	1.76± 1.67	**0.012**	2.17± 2.26	1.60± 1.92	0.149
30th minute VAS	3.33± 2.24	1.96± 1.69	**0.001**	2.47± 2.27	1.69± 1.86	**0.038**
45th minute VAS	3.73± 2.37	2.10± 1.64	**0.001**	2.69± 2.51	1.65± 1.66	**0.011**
60th minute VAS	4.03± 2.39	2.40± 1.81	**0.000**	2.73± 2.30	1.47± 1.44	**0.002**
2nd hour VAS	4.53± 1.97	3.10± 2.23	**0.001**	3.17± 2.49	1.52± 1.78	**0.003**
4th hour VAS	5.36± 2.09	4.00± 2.11	**0.002**	3.60± 2.23	2.30± 2.24	**0.008**
8th hour VAS	3.80± 2.12	4.23± 2.09	0.481	2.52± 1.90	2.91± 2.27	0.294
24th hour VAS	2.53± 2.16	2.00± 1.72	0.091	1.60± 1.80	1.13± 1.25	0.141
48th hour VAS	1.13± 1.50	1.00± 1.53	0.604	1.13± 1.71	0.60± 0.83	0.138

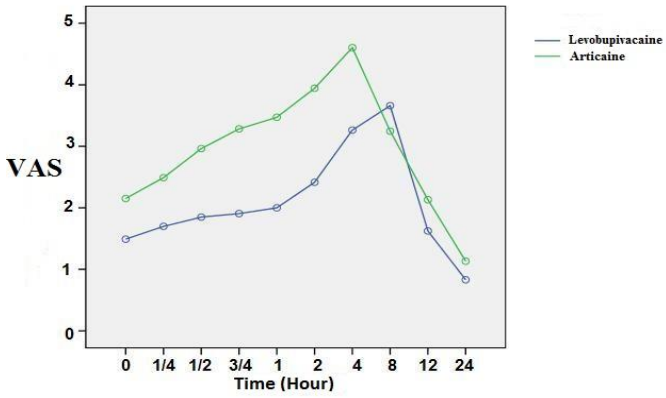

Figure 1: Postoperative mean visual analogue scale (VAS) values

4. Discussion and Conclusion

In this study, we investigated the anesthetic and analgesic effects of articaine and levobupivacaine in bilateral lower third molar surgery. We found that the time to onset of anesthesia as well as the duration of postoperative anesthesia and analgesia were longer, and the bleeding and VAS scores were lower in patients treated with levobupivacaine compared to the patients treated with articaine.

Elderly patients, female patients, less experienced surgeons, longer duration of surgical procedures and anesthesia support during the surgical procedure are some of the variables that affect the level of

discomfort in patients during third molar extraction and in the postoperative period [10]. The pain that occurs after the third molar tooth extraction is considerable and pain relief after the surgery is being addressed in many studies. The level of pain that occurs after impacted tooth operations depends on the position of the buried tooth, bone or mucosal retention, extraction pattern of the buried tooth, irrigation, trismus, swelling, duration of operation, ability of the physician and closure of the operation area as primary or secondary [11,12].

Depending on the oral health of patients, there is a decrease in the quality of life in the postoperative period. Postoperative pain, edema and trismus can cause functional and social loss in patients after third molar dental surgery. Several studies have evaluated the use of analgesics, antibiotics and mouthwashes to reduce these complications and improve postoperative quality of life [13-15]. In the current study, we compared the effects of articaine and levobupivacaine on the postoperative quality of life in impacted third molar dental surgery.

Local anesthetics cause transient sensory, motor and autonomic function loss when delivered at appropriate concentrations, resulting in electrophysiological activity changes in all nerve fibers, neurons, and other excitable tissues in the body. Local anesthetics are used both as anesthetics and analgesics in dental surgery. Rapid incubation time, excellent quality of the anesthetic, low toxicity and short-term hydrolytic breakdown are the reasons for the widespread use of articaine in dentistry [16]. Although bupivacaine has been preferred for many years in clinical use, the presence of cardiotoxicity has led to the need for discovery of new drugs. For this reason, the more reliable S (-) enantiomer of bupivacaine, known as levobupivacaine, has come into use. Human and animal studies have shown that levobupivacaine is as effective as bupivacaine and provides a longer duration of sensory block [17-19].

Various studies have been conducted to determine the mean time to the onset of anesthesia. Branco et al. [20] reported 1.5 minutes (range 0-4 minutes) for levobupivacaine and 1 minute (range 0-21 minutes) for bupivacaine. Gregorio et al. [21] reported 1.66 ± 0.13 minutes for articaine and 2.51 ± 0.21 minutes for bupivacaine while Thakare et al. [2] reported 42.53 ± 16.65 seconds for articaine and 61 ± 26.63 seconds for bupivacaine. We found in the current study that the time to the onset of anesthesia was 136.69 ± 33.52 seconds for levobupivacain and 80.28 ± 19.27 seconds for articaine. This difference in duration between articaine and levobupivacaine could be related to the difference in pKa values. The pKa value of articaine (7.8) is lower than the pKa value of levobupivacaine (8.1). The pKa of a drug is the pH at which the ionic and non-ionic forms of the drug are found in equal amounts. If the pKA value is close to the physiological pH, the concentration of the non-ionic base form of the drug is higher; therefore, a greater amount of the drug is likely to cross the neuronal membrane and the onset of action is faster.

Colombini et al. [22] reported that the duration of postoperative anesthesia in a third mandibular molar surgery was 273.80 ± 15.94 minutes for articaine. Branco et al. [20] reported a duration of postoperative anesthesia of 612 minutes (range 403-740 minutes) for levobupivacain and 643 minutes (range 240-864 minutes) for bupivacaine. Gregorio et al. [21] reported that the duration of postoperative anesthesia was 260.31 ± 20.49 minutes for articaine and 319.68 ± 34.26 minutes for bupivacaine in a patient who underwent osteotomy. The duration was 245.10 ± 16.60 minutes for articaine and 310.92 ± 49.86 minutes for bupivacaine in patients who did not undergo osteotomy. In the current study, the duration of postoperative anesthesia was 3.01 ± 0.94 hours for articaine, 7.85 ± 2.49 hours for levobupivacaine in patients who underwent osteotomy, and 3.10 ± 1.02 hours for articaine and 8.22 ± 2.25 hours for levobupivacaine in patients who did not undergo osteotomy. The longer duration of postoperative anesthesia observed with levobupivacaine compared to articaine in the current study is therefore consistent with previously published data.

Pain is highly subjective; previous encounters with pain may vary with factors such as education level and pain threshold, which makes the objective measurement of pain very difficult. Despite these limitations, VAS is universally regarded as the most appropriate instrument for pain measurement, and is commonly used to measure postoperative pain after surgical excision of the third major molar [23,24]. VAS was used to assess pain in the current study as well. Rood et al. [8] reported that patients who underwent anesthesia with levobupivacaine in impacted third molar surgery had lower VAS scores than those using lidocaine. Similarly, Crincoli et al. [25] found that postoperative VAS scores of patients using levobupivacaine were lower than those using mepivacaine at the 1st and 2nd

hours. Kakagia et al. [26] also reported that the use of levobupivacaine in abdominoplasty surgery was accompanied by significantly lower postoperative VAS scores between the 4th and 24th hours after surgery compared to ropivacaine. Olmedo-Gaya et al. [27] reported that the intensity of pain measured by VAS was significantly higher in the patients provided with articaine compared to the patients provided with bupivacaine at all time points except for the 8th hour postoperatively. Sancho-Puchades et al. [28] reported lower pain levels between 5th and 9th hours after surgery in patients treated with bupivacaine. While Pellicer-Chover et al. [29] found no significant difference in pain levels post-surgery in patients treated with these anesthetics, Trullenque-Eriksson et al. [30] observed lower levels of pain at the 6th and 12th hours after surgery with articaine compared to bupivacaine. In the current study, no statistically significant difference was found in the VAS scores with the use of either articaine or levobupivacaine at 0 and 15 minutes after the surgeries without osteotomy. However, a difference in outcome with the two anesthetics was observed starting at the 30th minute after the operation, and the VAS scores with levobupivacaine from 45th minute to the 4th hour after surgery were found to be statistically significantly lower compared to the surgeries performed with articaine. The VAS scores with levobupivacaine from the 15th minute to the 4th hour after osteotomy surgeries were also found to be statistically significantly lower than those performed with articaine. Our data therefore corroborate data from previous studies that have reported lower VAS scores with the use of levobupivacaine.

The lower VAS scores observed with levobupivacaine can be attributed to a longer duration of anesthesia along with an analgesic effect. This is supported in the current study by a significantly reduced use of additional painkiller with levobupivacaine (0.76 ± 0.85 with osteotomy, 0.30 ± 0.70 without osteotomy) compared to articaine (1.56 ± 1.16 with osteotomy, 0.69 ± 1.01 without osteotomy). Demiraran et al. [31] found that postoperative analgesic requirements of patients using levobupivacaine was lower compared to patients using lidocaine after rhinoplasty. Olmedo-Gaya et al. [27] reported that rescue analgesia was required by 13 (52%) patients using articaine and 8 (32%) patients using bupivacaine; however, this difference did not reach statistical significance. Gregorio et al. [21] found that the duration of postoperative analgesia was 195.68 ± 27.74 minutes with articaine and 281.72 ± 68.62 minutes with bupivacaine in surgeries without osteotomy; the same was 193.14 ± 24.56 minutes with articaine and 226.21 ± 60.25 minutes with bupivacaine in surgeries with osteotomy. Colombini et al. [22] reported a duration of postoperative analgesia of 198 ± 25.86 minutes with articaine in impacted third molar dental surgery. In the current study, the duration of postoperative analgesia was 3.07 ± 1.26 hours with articaine and 7.10 ± 2.88 hours with levobupivacaine in osteotomy patients; 2.58 ± 1.14 hours with articaine and 8.01 ± 2.04 hours with levobupivacaine in surgeries without osteotomy. This difference is most likely due to the analgesic effect of levobupivacaine.

Intraoperative bleeding was found to be higher in surgeries that were performed using articaine compared to levobupivacaine. Neither anesthetic agent contains any vasoconstrictor. Therefore, the lower bleeding observed with levobupivacaine could be due to lower induction of vasodilation as well as some induction of vasoconstriction with this agent compared to other local anesthetics [17].

Surgical extraction of impacted lower third molars is a highly complex procedure and complications such as lingual nerve damage [32], alveolar nerve damage [33] and mandibular fracture [34] have been reported in previous studies. However, in the current study, such complications were not observed in any of the patients.

In conclusion, the use of 0.5% levobupivacaine provided prolonged postoperative analgesia, less hemostasis, a longer duration of soft tissue anesthesia with better postoperative pain control and lower postoperative VAS scores compared to the use of 2 % articaine in impacted third molar dental surgery. Thus, levobupivacaine can be considered as a viable alternative to the established local anesthetics for the surgical removal of lower third molars.

Declaration of Ethical Code

In this study, we undertake that all the rules required to be followed within the scope of the "Higher Education Institutions Scientific Research and Publication Ethics Directive" are complied with, and that none of the actions stated under the heading "Actions Against Scientific Research and Publication Ethics" are not carried out.

(Gulhane Medical Academy Command Pharmaceutical Research Local Ethics Committee, 17.04.2009; 1491-64209/15399).

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