Journal of Craniomaxillofacial Research

Vol. 6, No. 1 Winter 2019

# Comparative study of articaine and lidocaine for third molar surgery

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**ARTICLE INFO**

*Article Type:*
**Original Article**

*Received:* 2 Sep. 2018
*Revised:* 8 Nov. 2018
*Accepted:* 15 Dec. 2018

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**ABSTRACT**

**Background**: This study aims to compare the anesthetic efficacy, postoperative pain, hemorrhage & dry sock incidence of articaine 4% versus lidocaine 2% in inferior alveolar nerve block during impacted lower third molar surgery.

**Materials and Methods**: A prospective randomized study was conducted on 20 subjects planned for elective surgical removal of bilateral impacted mandibular with similar difficulty indices. A single operator performed all surgeries on basis using 4% articaine or 2% lidocaine as an anesthetic agent and with the same concentration of vasoconstrictor (epinephrine 1:100,1000). Latency, duration of anesthetic effect, intra and post surgical pain experiences, hemorrhage & dry socket occurrences were evaluated with respect to the type of anesthetia. A visual analog scale was used to score pain. Data were analyzed by descriptive statistics, repeated measures ANOVA, Wilcoxon and McNemar's test ($\alpha$=0.05).

**Results**: Latency, Intra & Postoperative pain and hemorrhage showed clinical differences in favor of articaine, though statistical significance was not reached. In turn, the mean duration of anesthetic for articain was much extended and showed statistically significant difference. Dry socket incidence consisted of two occurrences (5%) and those two only occurred in Lidocain group.

**Conclusion**: Although 4% articaine offers better pharmacological performance than 2% lidocaine, both articaine and lidocaine have demonstrated adequate, negligible differences and acceptable clinical profiles. For this reason, their use in oral surgery should remain of the professional preference who will evaluate their use base on the necessary surgical time.

**Keywords**: Articaine; Bleeding; Dry socket; IAN bock; Impacted lower third molar; Lidocaine; Post operative pain.

## Introduction

The most frequent procedure at maxillofacial surgery clinics is the extraction of wisdom teeth [1]. Third molar eruption often occurs between 18-24 years of age. eruption failure and wide eruption time variation is expected. therefore, the impacted third molar surgery is counted as one of the most regular surgical procedures in the world [2,3,4]. Surgical interventions in dental office may induce pain and discomfort during surgery and in postoperative period of previously asymptomatic patient. Pain is considered as a critical factor which can deter patients from further dental treatments [5]. Hence, pain control is a crucial component in dental treatment [6]. In order to control the pain, local anesthetic agents are commonly used. Its preferred to opt anesthetic agent based on

three main clinical principals: anesthetic potency, latency (time to onset of anesthesia), and anesthetic effect duration [7]. The era of local anesthetics started with discovery of Cocaine in 1860 later, the developments of Novocain 1904 and then Lignocaine by Lofgren and Lumdquist in 1942 that revolutionized dental practice. Lignocaine (Lidocaine) soon became a gold standard drug against which all other new local anesthetics were compared and later several newer drugs such as Bupivacaine, Etidocaine, Articaine, Mepivacaine etc. were discovered [7]. Lidocaine is the safe local anesthetic which is extensively used for anesthesia. Its low toxicity and pharmacokinetic features are less in comparison with other ester-type anesthetics [7,8,9].The efficacy of Lignocaine although effective, unanimous and satisfactory, falls short of producing effective anesthesia in some instances which makes the clinician look for other options [2]. Recent evidence suggests that a newer anesthetic solution, articaine, offers better clinical performance [10]. It was first synthesized by Rusching et al. In 1969 with the name of carticaine, and was first marketed in Germany in 1976 [11]. As with lidocaine, articaine is also classified in the group of intermediate duration of action [2]. The aromatic ring with a Thiophenic ring is the pharmacological feature of this anesthetic which increases Lipo-solubility and multiplies its potency 1.5 times greater than lidocaine. These elements are accountable for its superiority considering other local anesthetics. In addition, articaine is the only amide-type local anesthetic which contains an ester group in its molecular structure–therefore, both plasma esterases and liver microsomal enzymes are in charge of its metabolization. articaine contains considerable advantages such as the anesthetic effect duration -only outshined by ultra-long acting anesthetics such as bupivacaine, ethidocaine and ropivacaine–and its high diffusion through bony tissue [2]. A number of studies have evaluated the advantage of articaine with respect to other local anesthetics [12,13,14,15,16,17]. However, many researchers haven't found a significant difference between its anesthetic efficacy compare to other agents e.g. 4% prilocaine 18 or 2% lidocaine [19]. Nevertheles, Malamed et al 10,20, declared articaine as a safe local anesthetic based on the results concluded after comparing articaine with 2% lidocaine and epinephrine 1:100,000, while its characteristic makes it able to compete with other local anesthetics [20,21]. Impacted lower third molars is inspected as the standard model in pain studies. Moderate to severe postoperative pain leads to more pain perception and causes discomfort in patients. Therefore, general patient compliance with oral surgery needs the efficient Intra and post-operative pain control [22]. Administration of intermediate action local anesthetics before sugary and use of analgesics after surgery, is the standard protocol for pain control in third molar surgery [23]. In addition to the analgesics commonly used to control pain after third molar surgery, the non-steroidal anti-inflammatory drug, ibuprofen 400 mg three times a day for 5 days was noted to be an effective analgesic regime [23,24].

Third molar surgery may also be followed by other complications Including both iatrogenic (e.g., nerve injury, bone fractures, etc.) and inflammatory ones, such as dry socket, postoperative infection, hematoma, swelling, trismus, etc [2]. Reducing the incidence of these postoperative complications is imperative [25]. Hemorrhage might happen during (accident) or after (complication) the surgery, being classified as late or recur- rent hemorrhage. Bleeding can be minimized by using a good surgical technique and by avoiding the tearing of flaps or excessive trauma to bone and the overlying soft tissue. The most effective way to achieve hemostasis following surgery is to apply a moist gauze pack directly over the site of the surgery with adequate pressure for some minutes or use of bone wax, absorbable hemostats or electrocoagulation [23]. Both local anesthetics having the same concentration of adrenaline, but lidocaine being more vasodilator than articaine, one might assume that bleeding during surgery would be greater with lidocaine.

One of the most important and common complications following surgical removal of impacted teeth is dry socket (alveolar osteitis) [26,27]. It is one of the common problem that results in severe pain inside and around the extraction site [28]. Dry socket (DS) can be debilitating, and 45% of the patients with dry socket may require up to 4 additional postoperative visits to provide care for the condition. Most studies state that the incidence of dry socket is 1%-4% for all routine dental extraction, and 5%-30% for impacted mandibular third molars. The incidence of dry socket is higher in the mandible, occurring up to 10 times more often for mandibular molars compared with maxillary molars [26,27]. Typically, dry socket starts 1-3 days after tooth extraction and the duration usually ranges from 5 to 10 days. Clinical characteristics of dry socket are severe throbbing pain that starts 24-72 h after extraction, marked halitosis, and foul taste [28]. Based on the experience of surgeon, amount of trauma during extraction, site of extraction, local anesthesia, smoking status, inappropriate irrigation during surgery oral contraceptive, and preoperative infection the incidence of DS differs [28]. As an intervening factor some liter-

atures concerning the effects of local anesthetic on the incidence of dry socket [29]. However, some reports consider no role for local anesthesia in DS. Extraction under general anesthesia also result in DS when no local anesthesia is used [30].

## Objectives

The aim of this study was to compare the anesthetic efficacy, Intra and post operative pain of 4% articain against 2% lidocaine (both with epinephrine 1:100,000), in inferior alveolar nerve block (IANB) during standard clinical model of mandibular third molar surgery and comparing the incidence of hemorrhage and dry socket as two common surgical complications considering the type of anesthesia.

## Materials and Methods

A randomized prospective study was conducted of 20 patients aged 18-24 years old (12 males and 8 females; Mean age 20.4 years & SD:1.89), arranged for the bilateral lower third molars surgery considering the circumstances of Minor Surgery Clinic of the Oral and Maxillofacial Surgery Department of Isfahan University of Medical Sciences, Iran. The study was open to the investigators and blind to the patients. The study was approved by Ethics Committee of the School (#396473). Each participant was informed of the characteristics and objectives of the study and then an informed consent was obtained. 2 weeks was allowed between two operations as a minimum washout period using 4% articaine in one side and 2% lidocaine on the other side, randomly, both of them have epinephrine 1:100,000 as a vasoconstrictor, so that every patient had to be in both groups for examining with owns. Moreover, the present and previous medical and dental histories were compiled and obedience to the inclusion and exclusion criteria was established.

The subjects aged between 18 and 25, without systemic diseases, and presenting impacted symmetrical lower third molars requiring tooth sectioning with ostectomy for surgery were the inclusion criteria. the presence of acute infection and/or swelling during extraction, were the exclusion criteria, known or suspected allergies to the local anesthesia, pregnancy/lactation, subjects who are on antidepressant drugs, subjects who had taken aspirin, acetaminophen, NSAIDS 24 hours prior to administration of local anesthetic. All 20 patients had symmetrical bilateral impacted lower third molar (Horizontal, Moderate, Class A Gregory & Pell). A questionnaire form was designed for evaluating pain, bleeding and dry socket. Before the surgery patients were asked to evaluate pain based on VAS scoring from 0 to 10 and ones who scored 0 only were involved in this trial. In this study we provided a Spanish brand of articaine 4% with 1:100,000 epinephrine (Artinibsa®, Inibsa, Barcelona, Spain) and an Iranian brand of lidocaine 2% with 1:100,000 epinephrine (Xylopen®, Exir Darou, Tehran, Iran). Using the conventional nerve trunk technique, 1.5 ml of anesthesia was enforced to inferior alveolar nerve and the lingual nerve blocking, and the remaining 0.3 ml of that carpule applied for the anesthesia of the long buccal nerve. Time interval between anesthesia and surgery was fixed to 10 minutes and if cases required administration of higher quantities of anesthesia, it would be excluded from the study. The operation lasting more than 60 minutes was also determined as the other excluding factor. Full mucoperiostal envelope flap was used then bony tissue over the tooth removed which was followed by tooth sectioning. Once the third molar was removed, the mucoperistal flap was repositioned and sutured with 3/0 silk and the patients were instructed on the normal postoperative recommendations.

The duration of surgery, latency for onset of anesthesia and Intraoperative pain and hemorrhage was recorded in a questionnaire. A questionnaire with accurate instructions was given to the patients in order to collect the post-operative parameters after operation. The patients were asked to put small gauze on the socket with a mild pressure on the area until one hour and to avoid any intake of food up to two hours. The patients could have cold and soft food thereafter.

The patients were also asked not to use any other drug for his/her pain until the first 2 hours after surgery. The intensity of pain was recorded using visual analog scale or VAS. The scale consisted of a horizontal 10cm line with two points on both sides considered between pain absence 0 and intolerable pain 10. The proforma was filled by the patients based on their pain experiences during surgery, 24 , 48 and 72 hours after surgery. After the surgery the operator recognized the bleeding during the surgery (mild, moderate, sever) and Ibuprofen 400 (Brufen®, Arya Darou, Tehran, Iran) consumption as painkiller were reminded to patients. It was prescribed as PRN (when necessary). We assessed post-operative hemorrhage by numbers of sterile gauze 2×2 inch replacing by the patients. The sum of analgesics used in 12, 24 and 48 hours after surgery was required to record by them. Standard post-operative follow-ups were arranged for the fourth and seventh days after the operation. In the first visit post operative complications like hemorrhage and dry sock-

et development were evaluated.

## Statistical Analysis

Data was analyzed by descriptive statistics, repeated measures ANOVA for comparison of pain during intervals, Wilcoxon test to compare bleeding and Ibuprofen intake and McNemar's test to compare dry socket incidence among two study groups using Statistical Package for the Social Sciences 22 (SPSS, IBM, NY, USA) at the significance level of 95%.

## Results

All of 20 patients who had been participated in this study were included in the trial (12 males, 8 females) because they primarily met all inclusion criteria. A total of 40 interventions were included in the study, 20 performed with 2% lidocaine, and 20 with 4% articain (with epinephrine 1:100,000 in both cases. The mean duration of surgery was 18.1 minutes (SD: 3.15) in lidocaine group and 17.7 in articaine group (SD:2.89), there were no significant deferences between two groups. The average of anesthetic latency for lidocaine was 92.05 seconds (SD:10.56) in contrast with 59.76 (SD:8.47) for articaine that this difference was not statistically significant. The latency was measured from the moment of needle withdrawal from the patients' soft tissue. In turn, the mean duration of anesthetic effect was 211 minutes (SD: 9.23) and 148.20 minutes (SD: 10.05). The difference in this case was statistically significant (Table 1). For assessing pain in four periods of time we asked patients to scale intensity of pain from 0 to 10 (0=painless, 10=severely painful) in VAS questionnaire. Subjective intraoperative pain scoring by the patients showed no differences between the two groups, with mean VAS scores of 5.07 mm (SD: 3.07) and 3.78 (SD: 3.06), respectively (Table 2). Intra surgical & post surgical pain was measured and compared in 0, 24, 48 and 72 hours after surgery between two anesthetic solution groups. VAS means of post 24, 48 and 72 hours were reported more in lidocaine group but the surgery pain mean was greater in articaine group (Table 2). In both groups, patients reported the maximum VAS mean in the first 24 hours following the surgery. How ever the differences between two anesthetic solutions in the severity of pain was not statistically significant (P value=0.266, 0.2, 0.23, 0.138 respectively) but the differences among measured VAS means in each group performed significant difference which presented in a linear diagram (Fig 1). Numbers of Ibuprofen consumption in 12, 24 and 48 hours after the surgery were compared between two groups, there was no significant differences in measured times between means (P value=0.317, 0.592, 0.837 respectively). Mean of Ibuprofen consumption in the first 12 hours was more in articaine group but its increasing trend in the followed couple of times was seen in both groups although smoothly in articaine group (Figure 2). Bleeding is the third parameter which was analyzed, surgeon opinion about the surgery bleeding was put into an ordinal quantitative classification (1. mild 2. moderate 3. sever) and in this case there was not significant differences between means. 85.7% of surgeries were done with help of articaine had mild bleeding and the rest of surgeries had moderate bleeding but in lidocaine group 71.4% of surgeries were reported mild bleeding and 28.6% with sever bleeding and bleeding during first two time (12 and 24 hours after surgery) decreased in either groups but during 48 hours after surgery in Lidocaine increased in contrast with articaine group which had a decreasing trend (Figure 3). However the differences in means between two groups in 12, 24 and 48 hours after the surgery were not statistically significant (P value=0.236, 0.317, 0.10 respectively). Dry socket incidence consisted of two occurrences (5%) and those two only occurred in Lidocaine group (10% surgeries in Lidocaine group).

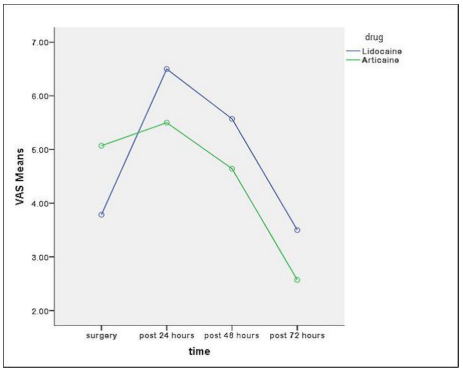


*Figure 1.* Linear diagram of VAS during surgery, 24, 48 and 72 hours after surgery among study groups.

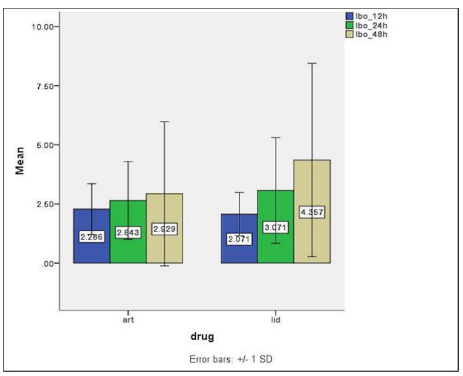


*Figure 2.* Distribution of Ibuoprofen intake by patients 12, 24 and 48 hours after surgery among study groups.

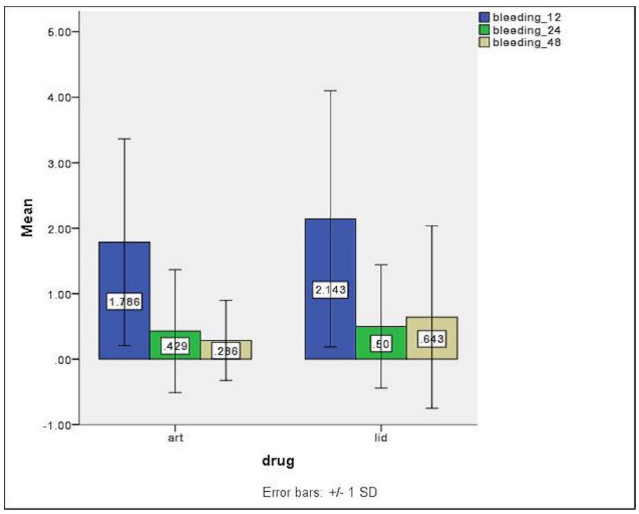


*Figure 3.* Distribution assessment of bleeding according to postsurgical gauze number used by patients in 12, 24 and 48 hours after surgery.

| | | N | Mean | SD |
|---|---|---|---|---|
| *Duration of surgery(min.)* | *L* | *20* | *18.1* | *3.15* |
| *(p=0.35)* | *A* | *20* | *17.7* | *2.89* |
| *Latency(sec.)* | *L* | *20* | *92.05* | *10.56* |
| *(p=0.2)* | *A* | *20* | *59.76* | *8.47* |
| *Duration of Anesthesia(min.)* | *L* | *20* | *211* | *9.23* |
| *(p=0.012)* | *A* | *20* | *148.20* | *10.05* |

*Table 1.* Duration of impacted third molar surgical extraction, anesthetic latency and duration with 4% articain (A) and 2% lidocaine (L) (both with epinephrine 1:100,000 as vasoconstrictor).

| *Drug* | | *Surgery pain* | *24 hours pain* | *48 hours pain* | *72 hours pain* |
|---|---|---|---|---|---|
| *Articaine group* | *Mean* | *5.0714* | *5.5000* | *4.6429* | *2.5714* |
| | *Std. Deviation* | *3.07507* | *2.84875* | *2.43712* | *2.20887* |
| | *Minimum* | *.00* | *1.00* | *2.00* | *.00* |
| | *Maximum* | *10.00* | *10.00* | *10.00* | *8.00* |
| | *N* | *20* | *20* | *20* | *20* |
| *Lidocaine group* | *Mean* | *3.7857* | *6.5000* | *5.5714* | *3.5000* |
| | *Std. Deviation* | *3.06791* | *2.56455* | *2.76557* | *2.92864* |
| | *Minimum* | *0.00* | *2.00* | *1.00* | *0.00* |
| | *Maximum* | *10.00* | *10.00* | *10.00* | *10.00* |
| | *N* | *20* | *20* | *20* | *20* |
| *Total* | *Mean* | *4.4286* | *6.0000* | *5.1071* | *3.0357* |
| | *Std. Deviation* | *3.08435* | *2.70801* | *2.60113* | *2.58890* |
| | *Minimum* | *.00* | *1.00* | *1.00* | *0.00* |
| | *Maximum* | *10.00* | *10.00* | *10.00* | *10.00* |
| | *N* | *40* | *40* | *40* | *40* |

*Table 2.* Pain distribution according to Visual Analogue Scale among study groups.

## Discussion

One of postsurgical morbidity expected after third molar surgery is pain. The post surgical pain begins when the effect of the local anesthesia subsides and reaches peak level in 6 to 12 hours postoperatively [31]. It is well-documented that surgical trauma and subsequent inflammation induce the sensitivity of peripheral nociceptors (primary hyperalgesia). It has been clinically observed as increased postoperative pain emanating from the site of surgery. Inadequate and short-lasting nerve blocks may cause prolonged and enhanced postoperative pain, leading to central neural sensitization which results in pain hypersensitivity beyond the area of surgery (secondary hyperalgesia) [32]. This study supports the argument that articaine as compared with lidocaine provides a higher rate of postsurgical pain control with comparable safety to lidocaine when used as IANB injection. Our results showed that the analgesic efficacy of articain local anaesthetic was seen up to 72 hours postoperatively, long after local anaesthetic action had finished. It may be attributed to that Inadequate and short-lasting nerve blocks in lidocaine group may cause prolonged and enhanced postoperative pain, leading to central neural sensitization which results in pain hypersensitivity beyond the area of surgery. In addition, the total amount of rescue analgesics is higher in lidocaine group over a two-day period in spite of the difference was not statistically significant that could be related to the central sensitization.

While our findings were also with agree that articaine injection can cause slightly more post injection pain than lidocaine, the differences was not statistically significant, and none of the studies reported this occurrence as a problem from the patients' perspective [33]. Hass and Lennon have demonstrated that articaine increased the risk the risk of non-surgical postoperative paresthesia [34]. This finding, however, could not be confirmed in a recent study by Pogrel [35]. The first author of this article also has not found, in her more than 500 experiences of IANB by articaine nor in this study, temporary or permanent effect or injury to the IAN. Our findings are also consistent with the manufacturer's information on articaine that suggests an improved anesthetic effect. This may be explained to its chemical structure that increases its lipo-solubility that permits it to diffuse to the bone in addition to the main action of blocking nerve action potential. Malamed in 2000 stated "clinical observations indicates that articain has faster onset of anesthesia" [10]. The latency of an anesthetic depends on number of factors. One factor is pKa values, smaller pKa values being associated to shorter latency. Thus 4% articaine (pKa=7.8) would at least in theory present a shorter latency than 2% lidocaine (pKa=7.9). Khoury stated that the better results of 4% articaine compared to 2% lidocaine were statistically not significant [36]. Beside this study, we similar to the Sierra et al [16] and Martinez et al [37] studies, reported no significant difference in respect to the anesthetic latency. The duration of the effect of an anesthetic is proportional to its degree of protein binding. As the injection site and vasoconstrictor concentration were similar in both study groups the higher mean duration of anesthesia in articaine is because of its intrinsic characteristic as presents one of the greatest protein binding percentages of all amide local anesthetics, comparable only to ultra-long action anesthetics such as bupivacaine, ropivacaine and ethidocaine [7]. These values in our study coincided with other studies [16,20,21,37] and were significantly longer than in the case of lidocaine. Regarding the patient's satisfaction with the overall treatment, significantly higher number of patients marked articaine than lidocaine with epinephrine. It could be postulated that the overall patient's satisfaction is in strong correlation with satisfaction with the achieved analgesia, while prolonged analgesia after surgery seemed to favor the patients' choice of a articaine. Moreover, the quality of life after oral surgical interventions can have a major impact on a patient's future perception of pain and preoperative anxiety.

In comparing hemorrhage with gender, age, position of the tooth, classification of the tooth, retention, angle, systemic conditions, bad habits, use of oral contraceptives and menstruation, there were not any statistically significant differences [23]. Anesthetics listed in decreasing order of vasodilatory potential includes procaine, bupivacaine, lidocaine, articaine, prilocaine, mepivacaine, ropivacaine, and cocaine [38]. Although one might assume that bleeding during surgery would be greater with lidocaine, in our study the differences in bleeding were not statistically significant. As an intervening factor some literatures concerning the effects of local anesthetic on the incidence of dry socket [29]. Dry socket incidence in our study consisted of two occurrences and those two only occurred in lidocaine group. How ever the difference between two groups was not statistically significant that could be due to limited number of patients. In summary, in spite of the fact that 4% articaine offers higher pharmacological performance than 2% lidocaine, especially in terms of latency, anesthetic effect period and less post-surgical pain experiences, and thereafter less analgesic intake

by the patients, less hemorrhage and dry socket occurrences in our study, both articaine and lidocaine have showed sufficient, negligible differences and acceptable clinical profiles. For this reason, their use in oral surgery should remain of the professional preference who will evaluate their use base on the necessary surgical time.

## Conflicts of interest

There is no conflict of interest to declare.

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*Please cite this paper as:*
Shahnaseri Sh, Mohammadi N, Tamizifar A, Mousavi A; Comparative study of articaine and lidocaine for third molar surgery. J Craniomaxillofac Res 2019; 6(1): 26-33