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Original Research Article

Comparison of the Effectiveness of 4% Articaine Hydrochloride and 2% Lignocaine Hydrochloride in Impacted Mandibular Third Molar Surgery- A Prospective, Parallel Arm, Randomized Controlled Trial

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Abstract

Objectives: This study aimed to compare the effectiveness of 4% articaine hydrochloride and 2% lignocaine hydrochloride in impacted mandibular third molar surgery. ***Materials and Methods:*** Sixty subjects randomly received either the 4% articaine injection (Group 1) or 2% lignocaine injection (Group 2) with 1: 200000 adrenaline via a pterygomandibular nerve block. The onset of the action of anesthesia, pulpal anaesthesia and its quality during the surgery, duration of anesthesia, duration of the surgery, the total volume of the anesthetic solution, hemodynamic statistics and pain levels were recorded. ***Results:*** The mean onset of anesthesia was significantly shorter in Group 1 (4.243 minutes) as compared to Group 2 (4.398 minutes). Onset of pulpal anesthesia was significantly shorter, with values as 4.287 ± 0.335 mins (Group 1) and 5.215 ± 0.3157 mins (Group 2). The duration of anesthetic effect in Group 1 was 3 hours (14.60 ± 9.76 mins), significantly higher than lignocaine -2 hours 43.33 mins (163.33 +-11.97 minutes). The duration of the procedure was marginally higher in Group 1- 41.67 ± 20.14mins; Group 2- 39.30 ±18.54mins. There was a statistically significant difference ($P < 0.05$) between qualities of anesthesia with pain scores lower in Group 1 as compared to Group 2. Articaine was found to have better cardiovascular stability than lignocaine. ***Conclusion:*** 4% articaine hydrochloride with 1:200000 adrenaline is more effective than 2% lignocaine hydrochloride with 1:200000 adrenalines in impacted mandibular third molar surgery in terms of onset, quality of anesthesia and hemodynamic parameters.

Keywords: Articaine; Epinephrine; Impacted tooth; Lignocaine; Mandibular third molar.

1. INTRODUCTION

Lignocaine hydrochloride, an amide group local anesthetic has revolutionized pain control in dentistry. Proven efficacy, low allergenicity, minimal toxicity through clinical use and research have confirmed the value and safety of this drug. The quest for a self-sufficient alternative saw a candidate in articaine hydrochloride, synthesized by Rusching and team in 1969. What started out as Carticaine in 1976 Germany ended up being the front-runner in all of Europe and Canada, with the United States however accepting it only in March 2000 (Rebolledo *et al*., 2007).

Articaine's unique identity stems from a thiophene ring-containing methyl ester link to its amide base. This increases its lipid solubility and potency (Rebolledo *et al*., 2007; Malamed *et al*., 2001), add to this the metabolization by both plasma esterases and liver microsomal enzymes (Claffey *et al*., 2004). It comes as no surprise that articaine was reported to be a safe local anesthestic for use in both children and adults (Malamed *et al*., 2000). It is considered to have superior diffusion through bony tissues in comparison to lignocaine, owing to its thiophene ring (Fan *et al*., 2009; Uckan *et al*., 2006; Oertel *et al*., 1997). Malamed *et al*. (2000, 2001) after comparing the drug efficacy of

4% articaine with 2% lignocaine (both with adrenaline 1:100,000) reported articaine to be safe local anesthestic that can be used both in children and in adults. Hersh *et al*. conducted a study comparing cardiovascular effects of 4% articaine with 1:100000 and 1:200000 adrenalines in which he concludes there is no significant difference between the two groups. There are few studies comparing the cardiovascular and central nervous system effects of lignocaine and articaine.

Thus the aim of this study was to further evaluate the effectiveness of 4% articaine hydrochloride against 2% lignocaine hydrochloride for surgical intervention of impacted mandibular third molars using the outcome parameters: onset, quality and duration of anesthesia, pain control, cardiovascular and central nervous system hemodynamic response.

2. MATERIALS AND METHODS

We conducted a triple blinded, parallel arm prospective randomized clinical study using 4 % articaine hydrochloride with 1:200000 adrenaline in study group [Group 1] and 2 % lignocaine hydrochloride with 1:200000 adrenaline in control group [Group 2] in surgical extraction of impacted mandibular third molars. Our study was in accordance with the tenets of the Declaration of Helsinki, CONSORT 2010 guidelines and was approved by the Institutional Review Board and Ethics Committee. The parameters analyzed in literature provide a base guideline of 5% α error, 10% β error and a minimum difference of 8 minutes between the study and control group. Incorporating this in the formula had narrowed down the sample size to 30 subjects per group. Simple randomization was selected as the sampling technique.

The inclusion criteria were ASA-I patients between the age group of 18-47 years, with no history of allergy to the local anesthetics and those indicated for surgical removal of identically positioned impacted mandibular third molars. Exclusion criteria was patients with a recent history of consumption of antibiotics, anti-depressants, anti-platelet and anti-inflammatory drugs. Pregnant, lactating women, patients with systemic illness, acute infection or swelling, any previous complications associated with local anesthetics were also excluded from the study.

The defined variables to be assessed were blood pressure, pulse and SPO_2 levels, which were evaluated with a multi-parameter monitor preoperatively, 5, 10,15 minutes after the injection of local anesthetic and post-operatively in both the groups. The onset of the anesthetic action was calculated with the help of electronic pulp vitality tester after the point of needle withdrawal from the site of injection to the time; the pulp vitality test gave positive results. The quality of anesthesia was measured using a subjective, three-point rating scale, that categorizes pain into no, mild and significant discomfort requiring supplemental anesthesia. Intra-operative pain was measured using the VAS which ranged incrementally from "worst pain" to "no pain'. The duration of anesthesia was represented by lack of sensation experienced in the mucosa, tongue and lower lip, which was recorded as the time at which all soft tissue sensation was restored. Central nervous system effects of anesthesia were evaluated by the experiences given by the patient intra-operatively such as drowsiness, nausea, dizziness, slurred speech etc.

Total quantity of anesthetic solution was calculated in both the groups. Duration of the surgery was registered as the time between the first incision to the last suture placement. The standard operative protocol was followed for the surgical removal of anatomically symmetrical impacted mandibular third molars on an orthopantomogram. The patients were prescribed routine antibiotics and analgesics for a period of 5 days.

3. STATISTICAL PROCEDURES

Data obtained was compiled on a MS Office Excel Sheet (v 2010, Microsoft Redmond Campus, Redmond, Washington, United States) & was subjected to statistical analysis using Statistical package for social sciences (SPSS v 21.0, IBM). Comparison of mean of outcome variables like onset (minutes), pulpal anesthesia (minutes), Duration of anesthesia (minutes) & VAS score between the groups articaine & lignocaine & blood pressure -systolic, diastolic, pulse & SPO_2 between the groups at various time intervals has been done using t test. For all the statistical tests, P <0.05 was considered to be statistically significant, keeping α error at 5% and β error at 20%, thus giving a power to the study as 80%.

4. RESULTS

The inter-group comparison of the quality of anesthesia is enlisted in Table I. In our study, in an age group of 18-47 year old enrolled subjects, the mean age was 31.6 years. There were 36 (56.7%) males and 24 (43.3%) females. There was statistically, a highly significant difference seen when mean of the onset of anesthesia was compared between the 2 groups (p= 0.00); with mean higher in group 2[4.39] as compared to 1[3.84]. Thus, the onset of anesthesia was significantly longer in Group 2 than Group 1. The mean onset of pulpal anesthesia was longer in Group 2[4.81] as compared to Group 1[4.28] with a statistical significance (p= 0.00). Also, the duration of anesthesia was significantly prolonged in Group 1[194.60 minutes] as compared to group 2[163.33 minutes] with a statistically significant p value. The mean VAS scores statistically showed a significant difference [p=0.001] with higher score recorded in Group 2[2.72] as compared to Group 1[1.50]. Hence overall the quality of anesthesia was considerably better in Group 1 than Group 2.

Table-I: Inter-group comparison of the quality of anesthesia

Subjects		N	Mean	Standard. Deviation [SD]	Standard Error Mean [SEM]	P value of t test
Onset of local anesthesia in min	Group 1	30	3.84366	0.3642989	0.0665116	0.000
	Group 2	30	4.39833	0.2670023	0.0487477	
Onset of pulpal anesthesia in min	Group 1	30	4.28700	0.3350466	0.0611709	0.000
	Group 2	30	4.81500	0.3157230	0.0576429	
Duration of anesthesia in min	Group 1	30	194.60	9.768	1.783	0.000
	Group 2	30	163.33	11.987	2.188	
VAS score	Group 1	30	1.50533	1.3909281	0.2539476	0.001
	Group 2	30	2.72333	1.2322347	0.2249742	

The details of inter-group comparison of cardiovascular variables is depicted in Table II. Statistically, a highly significant difference seen when mean of SPO_2 was compared between the 2 groups ($p<0.05$); with mean higher in group 2 as compared to group 1 pre-operatively, 5, 10, 15 minutes and post-operatively. There was a statistically significant difference seen when mean of BP diastolic, Pulse & SPO_2 was compared between the 2 groups ($p<0.05$) with mean higher in group 2 as compared to 1, at 5 minutes post injection. There was a statistically highly significant difference seen when mean of, Pulse & SPO_2 was compared between the 2 groups ($p<0.05$) with mean higher in group 2 as compared to group 1 at 10 minutes. Thus, articaine has more cardiovascular stability than lignocaine. However, statistically insignificant difference was seen with SBP, DBP & pulse between the groups ($p>0.05$). Significant difference was also found ($p<0.05$) when comparing pulse: pre-operative vs 5 min , pre-operative vs 10 min and 10 min vs post operatively in the lignocaine group, which suggests that articaine has a considerably lesser effect on cardiovascular system.

Table-II: Inter-group comparison of cardiovascular variables

Subjects		N	Mean	SD	SEM	P value of t test
SBP pre-op	Group 1	30	123.60	8.024	1.465	0.327
	Group 2	30	121.33	9.675	1.766	
SBP 5min	Group 1	30	125.73	6.943	1.268	0.325
	Group 2	30	127.93	9.944	1.816	
SBP 10min	Group 1	30	146.07	111.274	20.316	0.381
	Group 2	30	128.07	9.606	1.754	
SBP 15min	Group 1	30	125.13	7.496	1.369	0.674
	Group 2	30	126.07	9.476	1.730	
SBP post-op	Group 1	30	124.53	7.500	1.369	0.353
	Group 2	30	122.53	8.989	1.641	
DBP pre-op	Group 1	30	76.93	5.601	1.023	0.878
	Group 2	30	77.20	7.658	1.398	
DBP 5min	Group 1	30	78.40	5.593	1.021	0.024
	Group 2	30	82.20	7.053	1.288	
DBP 10min	Group 1	30	78.33	5.460	.997	0.164
	Group 2	30	80.53	6.580	1.201	
DBP 15min	Group 1	30	99.57	118.228	21.585	0.333
	Group 2	30	78.47	6.902	1.260	
DBP post-op	Group 1	30	76.73	4.968	0.907	0.632
	Group 2	30	77.47	6.704	1.224	
Pulse pre-op	Group 1	30	78.60	6.881	1.256	0.576
	Group 2	30	79.97	11.412	2.084	
Pulse 5min	Group 1	30	80.40	8.601	1.570	0.000
	Group 2	30	91.20	12.896	2.354	
Pulse 10min	Group 1	30	81.27	6.351	1.160	0.003
	Group 2	30	89.17	12.545	2.290	
Pulse 15min	Group 1	30	81.20	6.515	1.189	0.064
	Group 2	30	85.43	10.411	1.901	
Pulse post-op	Group 1	30	79.57	7.356	1.343	0.416
	Group 2	30	81.37	9.521	1.738	
SpO2 pre-op	Group 1	30	98.50	0.509	0.093	0.000
	Group 2	30	99.00	0.000	0.000	
SpO2 5min	Group 1	30	98.20	0.714	0.130	0.000

	Group 2	30	98.83	0.461	0.084	
SpO2 10min	Group 1	30	98.20	0.610	0.111	0.000
	Group 2	30	98.90	0.305	0.056	
SpO2 15min	Group 1	30	98.20	0.664	.121	0.000
	Group 2	30	98.97	0.183	.033	
SpO2 post-op	Group 1	30	98.37	0.556	0.102	0.000
	Group 2	30	99.00	0.000	0.000	

5. DISCUSSION

The introduction of amide local anesthetics like lignocaine in 1942 provided a relief to clinicians from the shortcomings of previously used esters, which were higher incidence of allergic reactions, shorter duration of action and less profound pulpal anesthesia (Malamed *et al*., 2001). Many studies especially in the western countries have been conducted over the years to compare the anesthetic potency between articaine and lignocaine, in terms of the clinical setting, concentration of anesthetic solution and vasoconstrictor, and the type of anesthetic administration (nerve block, infiltration or both). Evans G *et al*. (2008), Kanaa *et al*. (2006) and Abdulwahab *et al*. (2009) have found articaine to be more efficient than lignocaine. In contrast, Oliveira *et al*. (2004) and Vahatalo *et al*. (1993) have shown no significant differences between the two anesthetic agents. In India, lignocaine is still considered the standard of care in minor oral surgical procedures, inspite of newer alternatives being available today. With this in view, our study aimed to compare the anesthetic efficacy and cardiovascular effects 4% articaine (with 1:2, 00,000 epinephrine) with 2% Lignocaine (with 1:2, 00,000 epinephrine) in surgical extraction of impacted mandibular third molars. We took up the latter as it is the most predictable and commonly done procedure by maxillofacial surgeons and articaine is known for its optimal hard and soft tissue penetration.

In our study duration of surgery was found to be 41.67±20.14 mins and 39.30±18.54 mins for Group1 and Group 2 respectively. There was no statistical significance (p=0.541) between the two groups as the operating surgeon was same for both the groups. The average onset of anesthesia was significantly shorter in Group 1(4.243 minutes) than Group 2 (4.398 minutes); [p= 0.000]. Our results were in accordance with the theory that, the onset of anesthesia depends on a number of factors, such as the intrinsic property of the drug used and the anesthetic technique employed. It is most often influenced by its corresponding pKa value i.e. smaller pKa is associated with shorter onset of anesthesia, that is pka of articaine is 7.8 while that of lignocaine is 7.9 (Malamed. 2004). In comparison with lignocaine, articaine comprises better diffusion properties through bone and soft tissues (Claffey *et al*., 2004; Kanaa *et al*., 2006). In the present study quantity of local anesthetic used was 2millilitres for both the groups and in none of the cases additional local anesthetic was required.

In a study by Berlin *et al*. (2005), the mean onset times of pulpal anesthesia for the first molar were 1.3 minutes with articaine solution and 2.2 minutes with lignocaine and the outcome was statistically significant (p= 0.008). Likewise, the onset of pulpal anesthesia in Group 1 and Group 2 in our study too showed a high statistical significance (P =0.000) as 4.287±0.335mins and 5.215±0.3157 mins in Group 1 and Group 2 respectively. Articaine presents one of the greatest protein binding percentages of all amide local anesthetics, comparable to ultra-long acting substances such as bupivacaine, ropivacaine and etidocaine, implying longer anesthetic effect (VanEaden *et al*., 2002).

In this study, articaine's anesthetic effect lasted significantly longer than the post-operative anesthesia obtained in Group 2 (P < 0.000), being 3 hours 14.60± 9.76 mins (194.60 mins) 43.33 mins(163.33+-11.97 minutes) in Group 2. This is in accordance with a study by Kambalimath *et al*. (2013) which recorded an average total anesthetic duration of 195 minutes and 175 minutes for articaine and lignocaine respectively. Claffey *et al*. (2004), Kanaa *et al*. (2006), Jakobs *et al*. (1995), Moore *et al*. (2006) in their studies showed an even higher duration of action of articaine with an average ranging between 220.8 – 245.10 minutes. The mean VAS scores were significantly lower (P = 0.001) in Group 1 (1.50 ± 1.39) as compared to Group 2 (2.72 ± 1.23), in our study. However in a study by Jakobs *et al*. (1995), results obtained showed no statistical difference in VAS scores between the two anesthetic solutions. In both our groups, VAS score has a positive correlation with pulpal anesthesia, suggesting that higher latency in pulpal anesthesia gives higher score. A statistically significant difference (P <0.05; 0.091) was found in or study when comparing the quality of anesthesia with VAS scores in Group 1, emphasizing that articaine is more comfortable to the patient with low scores. According to Tofoli *et al*. (2003) and Moore *et al*. (2006), better quality of anesthesia was achieved with articaine. Articaine's better diffusibility and low latency in pulpal anesthesia help in making it more comfortable than lignocaine. All the hemodynamic parameters studied showed a statistically significant difference (P <0.05) in our study. A comparison of mean of DBP, pulse & SPO_2 were compared between the 2 groups (P < 0.05) which depicted a higher mean in Group 2 as compared to Group 1. This implies that articaine is more cardio-protective than lignocaine, suggesting it to be a more stable alternative. This development leads the

research where comparisons between the two groups in studies by Elad *et al*. (2008), Colombini *et al*. (2006), Martinez *et al*. (2008), Santos *et al*. (2007) describe statistically significant difference (P< 0.05) in terms of the blood pressure and oxygen saturation at different time intervals in articaine and lignocaine was found. Significant difference was also found (p<0.05) when comparing mean pulse values in the present study: pre-operative vs 5 min, pre-operative versus 10 min and 10 min versus post operatively higher in the lignocaine group, which suggests that articaine has a considerably lesser effect on cardiovascular system.

Meral *et al*. (2005) reported an increase in pulse rate immediately after injection was likely an expression of endogenous catecholamine because of the injection pain. Kambalimath *et al*. (2013) found that articaine had better cardiovascular stability as compared to lignocaine; thereby it can be a better alternative to lignocaine. In our study none of the patients complained of any CNS symptoms in both the groups so we can conclude that, there is no CNS toxicity associated with both the anesthetic solutions.

6. CONCLUSION

In tandem with the results, we conclude that 4% articaine hydrochloride is more effective than 2% lignocaine hydrochloride in impacted mandibular third molar surgery. It has proved its mettle as a safer alternative from a cardiovascular standpoint, making it better suited over lignocaine. The higher anesthetic efficacy makes articaine patient-centric, which helps maximise patient compliance.

Within the limitations of this study design, future research with special consideration to medically compromised patients can be carried out to document the evaluation of anesthetic safety and cardiovascular stability between articaine and lignocaine.

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9. Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms.

Abbreviations: ASA: American Society of Anesthesiologists, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure, VAS: Visual Analog Scale, Cardiovascular: CVS, Central nervous system: CNS, oxygen saturation; SPO_2, CONSORT – Consolidated standards of reporting trials.

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