Influence of local anesthethics with adrenalina 1:100.000 in basic vital constants during third molar surgery

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Abstract

Objective: The present study consists of a double-blind randomized clinical trial of paired samples. The purpose of the present study was thus to examine the effect of four different local anesthetics of the amida group (2% lidocaine with 1:100.000 adrenaline; 3% prilocaine with 0.30 IU felipressine; 2% mepivacaine with 1:100.000 adrenaline; and 4% articaine with 1:100.100 adrenaline) in patients undergoing extraction of lower third molars and verify the changes in systolic, diastolic and mean blood pressures, heart rate (HR) and oxygen saturation (SpO_2).

Study design: The sample comprised 168 extractions of lower third molars performed on 84 patients, divided into three groups, in whom lidocaine was the control anesthetic. The anesthetic solution applied differed from one side of the mouth to the other (control and experimental) in the same patient at different time periods.

Results: The following significant variations were observed: increase in systolic blood pressure with mepivacaine and articaine; decrease in diastolic blood pressure with lidocaine; increase in heart rate with all the anesthetics, but with no statistical significance in the case of prilocaine. The variations in mean blood pressure and oxygen saturation were not statistically significant. All the hemodynamic changes returned to normal with no need for any further treatment. No complications were observed in any of the 168 procedures performed.

Conclusion: All the anesthetics studied behaved, in relation to lidocaine, within the parameters of hemodynamic safety, although the best performance was that of prilocaine, followed by lidocaine. The measurement of systolic blood pressure, diastolic blood pressure and heart rate are appropriate monitoring methods for patients under the effects of local anesthetic, even healthy ones.

Key words: *Anesthetics, local, molar, third, tooth, unerupted, surgery, oral, blood pressure, heart rate, oximetry.*

Introduction

The discovery of local anesthetics at the end of the nineteenth century permitted the use of regional anesthesia as an option in patients undergoing surgical procedures. In 1948 lidocaine became the first local amida anesthetic to be marketed, and is the most widely used local anesthetic in many countries. It is currently the "gold standard" (1) against which all the new local anesthetics are measured (2-4).

Prilocaine presents a pharmacological profile similar to that of lidocaine, causing less vasodilation, however, which enables the anesthetic effect to last longer in the absence of a vasoconstrictor. Mepivacaine has an important role in dental practice on account of its minimal vasodilation and ability to promote deep local anesthesia without the need for a vasoconstrictor (5). Its pharmacological properties are similar to those of lidocaine, but it appears to offer a slightly greater safety margin than lidocaine. The time it takes to produce its effect is similar to that of lidocaine, although its duration is around 20% greater, even in the absence of a vasoconstrictor. Articaine is the first and only anesthetic of the amida group to have a tiophenic ring as a lipophilic portion (6). Articaine succeeds in spreading through the hard and soft tissues with a greater reliability than the other local anesthetics (4).

It is imperative that professionals be alerted to the proper use of local anesthetics and to the care needed when choosing and administering these anesthetic agents, bearing in mind that the local anesthetics currently available are marketed in different kinds of solutions, with various concentrations of both anesthetic salt and vasoconstrictor. The use of an inappropriate volume or concentration of anesthetic solution can produce systemic complications, which are frequently serious (7,8).

The purpose of the present study was thus to examine the effect of four different local anesthetics of the amida group in patients undergoing extraction of lower third molars and verify the changes in systolic, diastolic and mean blood pressures, heart rate (HR) and oxygen saturation (SpO_2).

Material and Methods

This is an analytic study in the form of a randomized, double-blind clinical trial, with paired samples, in which the anesthetic solution used in the extraction of lower third molars on one side of the mouth was different from that used on the other side of the mouth in the same patient at different periods of time. The patients were randomly allocated into groups by draw, the examiner thus having no influence on the form of treatment each group was submitted to.

The criteria for inclusion in the study were as follows: normal healthy patients with no apparent systemic changes, patients who had an indication for the bilateral extraction of lower third molars and teeth in the mesioangular and vertical position in Winter's classification. The following exclusion criteria were adopted: failure to meet the inclusion criteria at the radiological evaluation, patients presenting systemic problems contraindicating surgery and patients who did not follow the instructions they were given for the purposes of the study. A total of 84 patients were operated on. The patients were operated on by a single professional Master in Oral and Maxillofacial Surgery. The length of procedure didn't exceed 40 minutes.

Three groups were constituted, 1, 2 and 3. In Group 1 the anesthetics used were 2% lidocaine (alphacaine; DFL, Brazil) with 1:100,000 adrenaline (control) and 2% mepivacaine (mepiadre; DFL, Brazil) with 1:100.000 adrenaline (experimental). In Group 2 those used were 2% lidocaine (alphacaine; DFL, Brazil) with 1:100.000 adrenaline (control) and 3% prilocaine (prilonest; DFL, Brazil) with 0.03 IU felipressine (experimental). In Group 3 the ones used were 2% lidocaine (alphacaine; DFL, Brazil) with 1:100.000 adrenaline (control) and 4% articaine (articaine; DFL, Brazil) with 1:100.000 adrenaline (experimental). All the local anesthetics were conditioned in glass tubes containing 1.8 ml. The tubes of anesthetic were covered with a colored tape in one of six colors: green, blue, white, black, red and yellow, thereby constituting the blind element of the study, the color code being known only by the research supervisor. It was used two cartridges on average for each procedure not exceeding 50% of the maximum safety dose of each anestethic solution.

Following the initial screening by means of a clinical examination, the model adopted by the School of Dentistry of Pernambuco, and an objective and thorough history taking, all the patients were evaluated by checking their vital signs, thereby determining the baseline values used for control purposes at the trans- and postoperative evaluations, as well as the body mass index (BMI).

The BMI is calculated by dividing the weight in kilograms by the square of the height in meters (9-11). Another parameter assessed was the mean blood pressure (MBP). It is calculated by the following formula: MBP=DBP+1/3(SBP-DBP), SBP being systolic blood pressure and DBP diastolic blood pressure (12).

All patients were given dexametasone 8 mg, two 4-mg tablets by mouth one hour before surgery. For the procedures the patients were submitted to local anesthesia by regional blockage of the inferior alveolar, lingual and buccal nerves and infiltration anesthesia. The patients were monitored by pulseoxymetry and by checking the blood pressure before, during and after surgery. Once the patient was anesthetized, the operation was performed in accordance with the routine procedures for the extraction of lower third molars and suture. None of the patients were submitted to reanesthesia. The suture was removed one week after surgery (12).

The independent variables in this study were age, gender, weight, heigh and BMI. The dependent variables studied

were SBP, DBP, MBP, HR and SpO_2. All these variables directly or indirectly affect the systemic effects of the drugs analyzed.

The measurements of the patients' BP were made at clinical examination (baseline moment), in the operating room prior to surgery (preanesthesia, moment 1), immediately after the administration of anesthesia (postanesthesia, moment 2) and following suture (end of the surgical procedure, moment 3). To measure the blood pressure a sphygmomanometer was placed on the right arm at the level of the heart, with the patient partly inclined in the dorsal position.

The patients had their staging established in relation to arterial hypertension in accordance with the values determined by Chobanian et al (13). The autors classified the SBP in normal (<120), Prehypertensive (120-139), Grade 1 hypertension (140-159) AND Grade 2 hypertension (>160). Mean blood pressure was calculated from the results of the measurements of SBP and DBP. The patients were monitored throughout the surgical procedure by pulseoxymetry (oxymeter Emai –OXP-Model). The equipment has a measure strip of 0 to 100% for oxymetry and of 30 to 254 for pulse. The degrees of hypoxaemia considered were following: normal (97-100%), Normal oxygenation of the tissues (>95%), Mean hypoxemia (>90-95%), Moderate hypoxemia (75-90%) and Severe hypoxemia (<75%) (14).

For each procedure a single anesthetic solution was used, randomly chosen by draw. A table of dose proportionality was prepared, in which a standard quantity was used, according to the weight of each patient, corresponding to 50% of the maximum safety dosage of each solution (15). In this way possible systemic changes due to the toxicity of the anesthetic were avoided.

Data analysis consisted of the following: absolute distributions, percentage distributions and the statistical measurements minimum value, maximum value, mean, median, standard deviation and coefficient of variation (techniques of descriptive statistics), Fisher's Exact test, F test for repeated measurements, Student's paired t-test and F test (ANOVA) for independent groups. It is emphasized that, in the event of significant differences in the use of test F for repeated measurements, the Bonferoni tests of paired comparisons were used and, in the case of test F, for independent groups, those of Tukey. The level of significance used in the statistical test was 5% ($P = 0.05$). The data were entered using the Excel spreadsheet and the software program used was the SPSS Version 11.

Results

In Table 1, it is possible to see that, in Groups 1 and 3, the mean SBP values were lower at the baseline evaluation than at the other three evaluations. In Group 2, the highest mean values were recorded at moment 1, the values at baseline evaluation and moment 3 being quite similar. At none of the moments were significant differences found between the lidocaine (control) and any of the experimental anesthetics ($P > 0.05$). To obtain these results the repeated measurements model was used. SBP significant differences were found when lidocaine was used: in Group 1, between the baseline evaluation and that of moment 2; in Group 2, between evaluation 1 and moment 3; in Group 3, between the baseline evaluation and moment 2. When mepivacaine was used, significant difference were found between the evaluation at moment 2 and with each of the other evaluations. When prilocaine was used, no significant differences were detected. When articaine was used, a significant difference was observed between moments 1 and 2.

In relation to DBP, Table 1 shows that the only significant difference between the control and experimental groups was recorded at moment 1 in Group 3. Among the moments of each group it was observed that, when lidocaine was used, there was a significant difference from baseline to moment 2 in Group 1 and from moment 1 to moment 2 in Group 2. When the three other anesthetic solutions were used, no significant differences were found between the corresponding groups.

With regard to the mean values of MBP the table 1 showed that the greatest variations were recorded in Group 2 and in Group 3. The only two significant differences between the control and experimental groups at the level of 5% were recorded between lidocaine and articaine at moments 1 and 2. When the different moments of evaluation were compared, the following facts stood out: when lidocaine was used, no significant differences were found between moments in Group 1; in Group 2, between moments 1 and 2 and between moments 1 and 3, while in Group 3 significant differences were found. When the experimental anesthetics were used, no significant differences were found between the moments of evaluation.

In all the groups and with all the anesthetics there was a significant increase in mean HR from baseline to moment 2 (postanesthesia) and a decrease from moment 2 to moment 3 (end of the surgery). Significant differences at the level of 5% were revealed at moment 2 between lidocaine and prilocaine (Group 2) and between lidocaine and articaine (Group 3). Among the moments significant differences were found for the following: lidocaine, in any group between all the moments, except between moments 1 and moment 3; between all the moments when mepivacaine was used; between moments 2 and 3 when prilocaine was given, with a decrease in HR; when articaine was given at all the moments, with higher means than lidocaine (Table 2).

Minor differences are found in the mean values for SpO_2, with an increase from moment 1 to moment 2 with all anesthetics. With the exception of mepivacaine (Group 1), there was a decrease from moment 2 to moment 3 with all the anesthetics. At the level of 5% no significant differences

Table 1. Systolic blood pressure (SBP), Diastolic blood Pressure (DBP) and Mean Blood Pressure (MBP) by time of evaluation and group and results of comparative tests between groups.

	Time of evaluation			
Vital Sign/ Group/ anesthetic	Baseline Mean	Moment 1 mean	Moment 2 mean	Moment 3 mean
Systolic Blood Pressure				
• **Group 1**				
Lidocaine	110.12	114.92	118.84	116.60
Mepivacaine	110.12	113.92	121.12	115.68
Value of P (1)	**	P=0.7247	P=0.4728	P=0.6804
• **Group 2**				
Lidocaine	110.61	117.39	114.65	111.81
Prilocaine	110.61	115.23	112.06	109.55
Value of P (1)	**	P=0.2532	P=0.2539	P=0.2941
• **Group 3**				
Lidocaine	113.00	117.82	122.36	118.75
Articaine	113.00	113.89	118.86	116.57
Value of P (1)	**	P=0.0411	P=0.1051	P=0.3040
Diastolic Blood Pressure				
• **Group 1**				
Lidocaine	71.00	68.48	65.84	68.84
Mepivacaine	71.00	69.12	68.08	68.56
Value of P (1)	**	P=0.7405	P=0.2651	P=0.8826
• **Group 2**				
Lidocaine	70.52	72.16	67.65	67.65
Prilocaine	70.52	68.87	67.55	68.00
Value of P (1)	**	P=0.1057	P=0.9566	P=0.8024
• **Group 3**				
Lidocaine	70.14	73.00	69.64	70.32
Articaine	70.14	69.07	66.57	66.71
Value of P (1)	**	P=0.0237*	P=0.0575	P=0.0951
Mean Blood Pressure				
• **Group 1**				
Lidocaine	84.04	83.96	83.51	84.76
Mepivacaine	84.04	84.05	85.76	84.27
Value of P (1)	**	P=0.9626	P=0.2808	P=0.7892
• **Group 2**				
Lidocaine	83.88	87.24	83.31	82.37
Prilocaine	83.88	84.32	82.39	81.85
Value of P (1)	**	P=0.0892	P=0.5792	P=0.7084
• **Group 3**				
Lidocaine	84.43	87.94	87.21	86.46
Articaine	84.43	83.85	84.00	83.33
Value of P (1)	**	P=0.0057*	P=0.0209*	P=0.0558

(*) – Significant difference at 5.0%
(**) – Only one measurement taken at baseline evaluation
(1) – Using the t-Student paired test

Table 2. Heart rate (HR) and SPO_2 by time of evaluation and group and results of comparative tests between groups.

	Time of evaluation			
Group/ anesthetic	Baseline Mean	Moment 1 mean	Moment 2 mean	Moment 3 mean
Heart rate				
• Group 1				
Lidocaine	74.24	85.84	96.32	90.60
Mepivacaine	74.24	84.16	98.64	90.72
Value of P (1)	**	P=0.4337	P=0.3902	P=0.9703
• Group 2				
Lidocaine	73.13	86.23	97.81	86.19
Prilocaine	73.13	85.45	88.90	82.39
Value of P (1)	**	P=0.7245	P=0.0037*	P=0.2043
• Group 3				
Lidocaine	72.32	82.54	96.04	85.96
Articaine	72.32	82.64	101.07	86.04
Value of P (1)	**	P=0.9698	P=0.0354*	P=0.9766
SPO2				
• Group 1				
Lidocaine	Not measured	97.44	97.72	95.80
Mepivacaine	Not measured	97.12	97.72	97.84
Value of P (1)		P=0.3563	P=1.000	P=0.1483
• Group 2				
Lidocaine	Not measured	97.65	98.00	97.03
Prilocaine	Not measured	97.26	97.68	96.97
Value of P (1)		P=0.2592	P=0.1607	P=0.9255
• Group 3				
Lidocaine	Not measured	97.61	98.21	97.93
Articaine	Not measured	97.21	97.79	97.46
Value of P (1)		P=0.1837	P=0.1901	P=0.3203

(*) – Significant difference at 5.0%
(**) – Only one measurement taken at baseline evaluation
(1) – Using the t-Student paired test

are seen between the control (lidocaine) and each of the anesthetics at the moments evaluated. The only significant differences recorded between the moments were between moments 1 and 2 in Group 3, when lidocaine was used, and between moments 2 and 3, when prilocaine was used.

Discussion

Clinical examination and measurement of the patients' vital signs were conducted in order to enhance the safety of the operation and allow the patients to totally satisfy the criteria for inclusion in the study. As an additional safety precaution to prevent complications, 50% of the maximum safety dose of each anesthetic solution was used, as this was an amount sufficient for performing the dental procedures (two cartridges approximately).

The evaluation of the variables age, height and BMI by group showed little variability, which characterized the sample as homogenous, a highly important consideration for this kind of study. The coefficient of variation for these measurements was 25.56% at the most. The monitoring, with methods of observation and recording of data, of a surgical patient should not be confined to measurements of BP but a set of parameters forming part of the "vital signs" that may undergo changes due to the type of anesthetic solution and degree of anxiety. For this reason, in addition to the SBP, DBP and MBP, HR and SpO_2 were also monitored as tools of evaluation (2, 7).

When the mean SBP values were observed at moments 2 and 3 in relation to the baseline evaluation by group, a significant increase was found with mepivacaine in comparison with lidocaine in Group 1 at moment 2, producing a mean increase of 11 mmHg, a variation that was greater than that found by Frabetti et al (17) and similar to that found by Silvestre et al (18). In Group 2 (lidocaine and

prilocaine), there were no significant differences for SBP, the results being similar to those of Meechan et al. (8) and Araújo et al (19). In Group 3 (lidocaine and articaine), there were likewise no statistically significant differences and the values are in agreement with those of Oertel et al (20) and Malamed et al (15) at moments 2 and 3.

With regard to DBP, no significant difference was seen between controls and trial subjects in either of these groups under the effect of the anesthetic, both remaining within the normal range for the classification of arterial hypertension according to Chobanian et al (13).

In an evaluation of Groups 1, 2 and 3 at the various moments in relation to MBP, no statistically significant differences were found for any of the anesthetic solutions.

As regards HR, when Groups 1, 2 and 3 were evaluated at moments 2 and 3 in relation to baseline, a significant difference was found between these moments for all the anesthetics, with mean increases in HR ranging from the 15.77 bpm for prilocaine from baseline to moment 2 to 28.75 bpm for articaine, in agreement with Salonen et al (21); Frabetti et al. (17) and Niwa et al. (22), unlike what occurred in the study of Mestre Aspa et al. (12), who stated that there was no change in HR resulting from the use of anesthetic solutions.

When moment 3 is evaluated in relation to moment 1, i.e. under the effect of the anesthetic, it is seen that all the anesthetics produced an increase in HR means with the exception of prilocaine, which presented a negative variation. Mepivacaine was the anesthetic that produced the greatest increase in mean HR.

It is important to emphasize that, at no moment of evaluation in all the groups, even under the effect of the anesthetics, was any mean of the measurement of SPO_2 outside the normal range, in agreement with Poiset et al (14). Nonetheless, we agree with Lowe & Brook (23), who suggested that all patients submitted to surgery for removal of third molars are at risk for hypoxia. Short episodes of hypoxia may have only minor consequences in healthy patients, but those not in good health may develop serious complications. Our findings are in agreement with the studies of Matthews et al. (24) and Aeschliman et al. (16).

In the 168 surgical procedures carried out on 84 patients no systemic changes having clinical repercussions were observed. The variations in BP, HR and SpO_2 returned to normal without the need for any additional treatment. Our findings are in agreement with those of Wong & Jacobsen (25), Simon et al (26), Matsumura et al (27), Silvestre et al (18), Mestre Aspa et al. (12), Niwa et al. (22) and Colombini et al. (28). Local anesthetics, when used in dentistry, produce limited and safe hemodynamic effects. The rates of BP and SPO_2 are due to endogenous catecholamines or are associated with the adrenaline secondary to the local anesthetic. Fewer alterations were seen in the cases in which felypressin rather than adrenaline was used.

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