ORIGINAL ARTICLE

Clinical evaluation of different epinephrine concentrations for local dental anesthesia*

Avaliação clínica da epinefrina em diferentes concentrações para anestesia local odontológica

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ABSTRACT

BACKGROUND AND OBJECTIVES: Clinical trials comparing lidocaine associated to different epinephrine concentrations are scarce. This study aimed at comparing cardiovascular parameters, anesthetic efficacy and level of discomfort during the injection of two 2% lidocaine solutions associated to 1:100,000 or 1:200,000 epinephrine.
METHODS: Participated in this cross-sectional double blind study 30 patients (24.3±4.7 years) who were submitted to anamnesis, vital signs evaluation and baseline threshold measurement of right upper canine tooth. In each clinical session, with 15 days interval, 1.8mL of one of the anesthetic solutions were administered. Anesthetic efficacy was measured with electric stimulation and vital parameters were evaluated in three periods: 5 minutes before, during and soon after anesthesia. At the end of each session, the visual analog scale was applied to evaluate injection pain sensitivity, which was repeated 24h later.
RESULTS: All volunteers had satisfactory pressure levels to carry out the trial. There has been no statistically significant differences in systolic blood pressure (p=0.33), diastolic blood pressure (p=0.1505), heart rate (p=0.9464) and oxygen saturation (p=0.9297) considering each local anesthetic solution in each moment (during and after anesthesia). Formulations of 2% lidocaine with 1:100,000 and 1:200,000 epinephrine have shown no statistical differences for all anesthetic parameters (p>0.05).
CONCLUSION: Considering the volume used in this study, decreased epinephrine concentration on lidocaine solution has not affected its clinical efficacy and has not influenced cardiovascular parameters.
Keywords: Epinephrine, Local anesthesia, Vasoconstrictors.

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RESUMO

JUSTIFICATIVA E OBJETIVOS: Estudos clínicos comparando o uso da lidocaína associada a diferentes concentrações de epinefrina na odontologia são escassos. O objetivo deste estudo foi comparar parâmetros cardiovasculares, eficácia anestésica e grau de desconforto durante a injeção de 2 soluções de lidocaína a 2% associadas a epinefrina 1:100.000 ou 1:200.000.
MÉTODOS: Trinta pacientes (24,3±4,7 anos) foram incluídos (estudo cruzado e duplamente encoberto) e submetidos a anamnese, avaliação de sinais vitais e mensuração do limiar basal do dente canino superior direito. Em cada sessão clínica, com intervalo de 15 dias, foram administrados 1,8mL de uma das soluções anestésicas. A eficácia anestésica foi mensurada com estímulo elétrico, e os parâmetros vitais foram avaliados em 3 períodos: 5 minutos antes, durante e logo após a anestesia. Ao final de cada sessão foi aplicada a escala analógica visual para avaliação da sensibilidade dolorosa da injeção, e repetida após 24h.
RESULTADOS: Todos os voluntários apresentaram níveis pressóricos satisfatórios para realização do estudo. Não houve diferenças estatisticamente significativas entre os valores de pressão arterial sistólica (p=0,33), pressão arterial diastólica (p=0,1505), frequência cardíaca (p=0,9464) e saturação de oxigênio (p=0,9297) considerando cada anestésico local em cada momento (durante e após a anestesia). As formulações de lidocaína a 2% com epinefrina a 1:100.000 e 1:200.000 não apresentaram diferença estatística para todos os parâmetros anestésicos (p>0,05).
CONCLUSÃO: Considerando o volume utilizado no presente estudo, a redução da concentração da epinefrina na solução de lidocaína não afetou sua eficácia clínica e não influenciou os parâmetros cardiovasculares.
Descritores: Anestesia local, Epinefrina, Vasoconstritores.

INTRODUCTION

Local anesthetics are the most widely used drugs in Dentistry to control perioperative pain, being critical for the success of clinical procedures. However, factors such as inadequate choice of anesthetic solution, anesthetic salt overdose, accidental vasoconstrictor intravascular injection and fast administration of the solution may lead to increased blood concentration of the drug and to a higher potential for toxic effects[1,2]. Systemic complications of intravascular injection of local an-

esthetics are basically induced by the interaction of adrenergic vasoconstrictors and sympathetic autonomous nervous system receptors, because its vasoconstrictor therapeutic action occurs by means of binding to α1 receptors. In addition, vasoconstrictors may act on other receptors, changing cardiovascular parameters such as blood pressure and heart rate[3].

The addition of vasoconstrictors to anesthetic solutions has several clinical advantages, because they increase anesthesia duration and quality, decrease anesthetic salt plasma levels and, as a consequence, the probability of adverse effects and toxicity. In addition, they decrease the necessary concentration for adequate anesthesia and control hemorrhage during surgical procedures[3-5].

However, accidental sympathomimetic vasoconstrictor intravascular injection or its use in excessive doses may induce systemic manifestations such as cardiovascular disorders, hypertension, tachycardia, arrhythmias, shivering and headache. According to Laragnoit et al.[6], healthy patients tolerate plasma epinephrine increase, but the same may be not true for patients with cardiovascular problems. The literature is controversial about the use of local anesthetics associated to epinephrine in patients with cardiovascular problems, although the administration of this solution is used to prevent patients' pain and discomfort during dental assistance[7].

Previous studies have shown the clinical safety of 1:100,000 epinephrine in controlled cardiac patients[8,9], but studies comparing lidocaine associated to epinephrine in different concentrations are still scarce. So, this study aimed at comparing cardiovascular parameters, anesthetic efficacy and the level of discomfort during injection of two 2% lidocaine anesthetic solutions associated to different epinephrine concentrations.

METHODS

Participated in the study 30 volunteers, being 18 females and 12 males. Age between genders has not shown statistically significant difference (t test, p=0.3243), being mean age of females 22.6±3.7 years and of males 24.3±4.7 years. All volunteers have gone through medical evaluation and were in good health. In addition, they were not using any drug that could change pain perception, as observed by written history and oral questioning.

Inclusion criteria were having right upper canine teeth without decay or extensive restorations, traumas, endodontic treatment and responsive to electric stimulation (Pulp Tester); not having used any drug that could change pain perception (anti-inflammatory, analgesic, anxiolytic, antidepressant). Exclusion criteria were pregnancy, history of hypersensitivity to studied drugs (lidocaine) and to preservatives of tested solutions (sodium bisulfite), evidence of organic dysfunction or significant deviation from normal, history of psychiatric disease that could impair the ability of giving written consent, history of drug addiction or abusive alcohol consumption.

The study was carried out in three sessions, being the first session for history and evaluation of baseline vital signs: blood pressure by means of aneroid sphygmomanometer with stethoscope (AccumedGlicomed®, Registered before ANVISA Sphygmomanometer n° 10385180030, Registered before ANVISA Stethoscope nº 80275310014), partial oxygen concentration (SpO2), heart rate (OX-P-10, Transmai Equipamentos Médicos Hospitalares Ltda., Registered before ANVISA n° 80052640002), and evaluation of right upper canine baseline response threshold with the electric impulses-emitting device Pulp Tester (Vitality Scanner model 2006, Analytic Technology, Redmond, USA, Registered before the Ministry of Health nº 103.1111.0033). For this latter parameter, the mean of three different measurements was considered.

Volunteers were submitted to two more clinical sessions, with a previously defined randomized order for the application of both tested solutions and with a minimum interval of two weeks between anesthesias. In each session, 1.8mL (1 tubete) of solution A (2% lidocaine with 1:100,000 epinephrine - DFL®, Rio de Janeiro), or solution B (2% lidocaine with 1:200,000 epinephrine - DFL®, Rio de Janeiro) were administered on the apical vestibular region of right upper canine (subperiosteal infiltrative technique) and each patient was his/her own control. Upper canine infiltration was administered with anesthetic tubete with 2% lidocaine with 1:100,000 epinephrine or tubete with 2% lidocaine with 1:200,000 epinephrine along the apex of right upper canine root. In each session all vital parameters were evaluated in three periods: 5 minutes before anesthetic administration; during anesthetic injection; immediately after injection.

Solutions were always administered by a single operator using the good anesthetic technique practice with slow injection (mean of 2 minutes per tubete, that is, 1mL/min) for better patients' comfort[10]. The investigator-operator was not involved in the evaluation of anesthetic parameters, characterizing a double-blind study. At the end of each session, the visual analog scale (VAS) was applied to evaluate injection painful sensitivity. The same scale was applied 24 hours after each session to evaluate pain after anesthetic procedure at puncture site.

VAS is a 10-cm line without numbers or marks, except for the edges where there are marks between zero and 10. Zero corresponds to no pain, and 10 to the most severe pain (Figure 1). Pain was classified by placing a vertical mark on the line; the distance between the mark and the zero edge was measured with a digital caliper rule (Pantec, São Bernardo do Campo, Brazil), to evaluate patients' pain sensation. Patients were oriented to mark the level of pain they were feeling at that moment[11,12].

Anesthetic depth was monitored with electric stimulation (Pulp Tester). Immediately after local anesthetic injection, right upper canine was stimulated with the Pulp Tester every

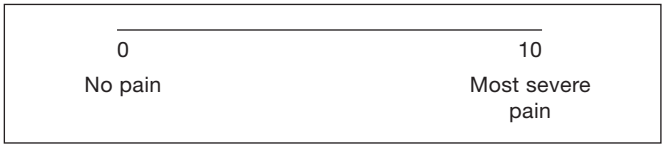

Figure 1. Visual analog scale

two minutes until lack of response to maximum stimulation (80), being then stimulated every 10 minutes until return to response baseline threshold. Lack of response until maximum stimulation in the Pulp Tester (80) was considered pulp anesthesia. Anesthesia was considered successful when presenting two consecutive lack of responses within the 10 initial minutes. Onset time was considered as the period between the end of anesthetic injection until lack of stimulation perception[13].
After the anesthetic technique, volunteers were submitted to the pinprick test being the vestibular mucosa pricked with the bevel of a 30G gingival needle every 10 minutes, until total recovery of anesthesia in soft tissue[14].

Statistical analysis
Data were analyzed by BioEstat, version 5.0 (Mamirauá Institute, Belém, PS, Brazil). Age, pain, onset time and anesthesia duration were compared by Student *t* test. Other variables were compared by Friedman test. Significance level was 5%.
This study was approved by the Research Ethics Committee, São Leopoldo Mandic College (CEP/SL Mandic- Protocol 07/125) and before anesthesia sessions all volunteers have signed the Free and Informed Consent Term agreeing to participate in the research.

RESULTS

All volunteers had satisfactory pressure levels to participate in the study. With regard to oxygen saturation, there has been no variation of initial observed levels, which have remained around 96% of saturation. There have been no significant variations in heart rate that could interfere with study results. Figure 2 shows values of vital signs obtained during and after anesthesia using both 1:100,000 (1:100) or 1:200,000 (1:200) epinephrine solutions. There have been no statistically significant differences in systolic blood pressure (Friedman, p=0.33), diastolic blood pressure (Friedman, p= 0.1505), heart rate (Friedman, p=0.9464) and oxygen saturation (Friedman, p=0.9297) considering each local anesthetic in each moment (during and after anesthesia). Table 1 shows general sample characteristics.

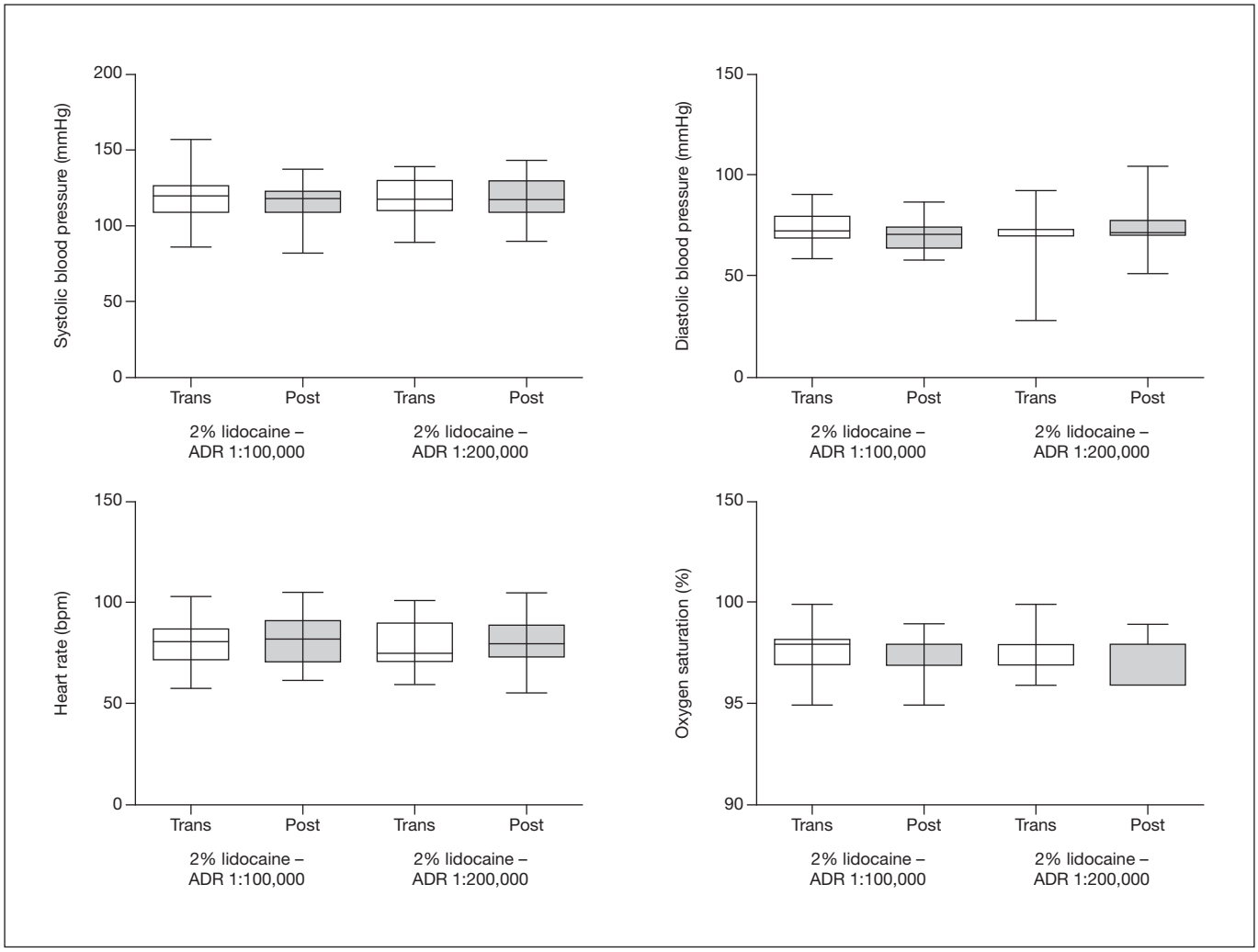

Figure 2. Values of vital signs during and after anesthesia using both solutions

Table 1. General characteristics of evaluated volunteers

Variables	Categories	Distribution	p value
Gender (n and %)	Female	18 (60)	-
	Male	12 (40)	-
Age (years)*	Female	22.6±3.7	0.3243
	Male	24.3±4.7	

* Values in mean ± SD.

Table 2 shows pulp anesthesia success percentage and onset time, and pulp anesthesia duration in soft tissues. Formulations of 2% lidocaine with 1:100,000 and 1:200,000 epinephrine have not shown statistically significant differences for all evaluated anesthetic parameters (p>0.05).

Table 2. Success of anesthesia, pulp anesthesia onset (minutes), pulp anesthesia duration (minutes) and soft tissue anesthesia duration (minutes) with both solutions

	2% Lidocaine with 1:100,000 epinephrine	2% Lidocaine with 1:200,000 epinephrine	p value
Success of anesthesia (%)	100	100	-
Pulp anesthesia onset (min)	1.29±1.90	1.10±1.47	0.67
Pulp anesthesia duration (min)	41.61±14.16	41.03±17.79	0.88
Soft tissue anesthesia duration (min)	148,06±58,10	137,93±70,67	0,54

Table 3 shows pain reported by volunteers on VAS (in millimeters) during anesthetic solutions administration and pain on anesthetized region 24h after sessions. Formulations were not different with regard to pain during anesthetic injection (p>0.05). With regard to pain after anesthetic procedure, volunteers have not reported sensitivity the day after injection with 2% lidocaine with 1:200,000 epinephrine, differently from 2% lidocaine and 1:100,000 epinephrine (p=0.001). In addition, no volunteer had any type of associated symptom, such as headache, tachycardia and dizziness.

Table 3. Pain during injection and 24 hours after administration of both solutions

	2% Lidocaine with 1:100,000 epinephrine	2% Lidocaine with 1:200,000 epinephrine	p value
Pain during injection (mm)	29.03±22.01	19.24±17.83	0.06
Pain after injection (mm)	2.58±7.28	0±0.0	*0.001

DISCUSSION

This study has evaluated the efficacy of two commercial 2% lidocaine solutions associated to different epinephrine concentrations (1:100,000 and 1:200,000) using the volume of one anesthetic tubete (1.8 mL), to minimize vasoconstrictor concentration (18 and 9µg, respectively) and the possible interference on cardiovascular parameters. 1:200,000 epinephrine was already present in other anesthetic salts, such as articaine and bupivacaine. However, the association with lidocaine was only recently made available in the Brazilian market, and there are still few studies comparing lidocaine anesthetic solutions associated to different epinephrine concentrations.

The methodology used for pulp anesthesia evaluation was the electric test (pulp tester), recognized as the standard for this type of study since 1946, being considered a safe, accurate and reproducible method, because it mimics functional nervous responses[15-17] without injuring the dental pulp[18]. Electric stimulation response is characterized as a subjective sensation; however, volunteers were their own controls, thus adding reliability to the study. The pulp tester may be used as an effective tool to estimate the level of anesthesia before a dental procedure, calling the attention of the clinician for possible anesthetic problems[17].

Neves et al.[8] have compared 2% lidocaine without vasoconstrictor associated to 1:100,000 epinephrine in inferior alveolar nerve block in patients with coronary problems. Authors have evaluated blood pressure and ECG and have observed no difference in blood pressure or changes in heart rate, concluding that the use of vasoconstrictor is safe for this type of patient. The technique used has a higher incidence of accidental intravascular injection and yet the study has shown that there has been no interference with cardiovascular parameters. In addition, the study of Neves et al.[8] has used 1:100,000 epinephrine, while our study has also evaluated lidocaine associated to 1:200,000 epinephrine, thus further decreasing vasoconstrictor concentration. Conrado et al.[9] have shown that the use of vasoconstrictor (1:100,000 epinephrine) in anesthetic solution for tooth extraction has not caused additional risks to patients with cardiovascular problems, as compared to the use of anesthetic without vasoconstrictor. In our study, both 1:100,000 and 1:200,000 concentrations have shown to be safe in the volume used, thus in line with mentioned authors. In addition, Cáceres et al.[19] have concluded that local anesthetic effect, with or without vasoconstrictor, has not induced significant cardiovascular parameters change, and Morais et al.[2] and Bispo et al.[20] have also concluded that different epinephrine concentrations associated to lidocaine and articaine have not changed cardiovascular parameters of volunteers.

Similar to literature results, our study has shown that vasconstrictors in concentrations of 1:100,000 or 1:200,000 have not changed cardiovascular parameters and oxygen saturation. So, the lowest concentration (1:200,000) tested in our study may be an even safer alternative for patients with systemic disorders, such as the elderly, giving a higher safety margin for such patients. However, further clinical trials should be carried out to confirm this.

Notwithstanding epinephrine exerting less interference on blood pressure for acting on adrenergic β-2 receptors[3], as compared to other adrenergic vasoconstrictors, maximum recommended dose for controlled cardiac patients is just

0.04/session, that is, 2 anesthetic tubetes with 1:100,000 epinephrine[21]. Additionally, the literature shows that the results of our study suggest that it is possible to use 2 tubetes of lidocaine with 1:100,000 epinephrine with good anesthetic efficacy or even to use twice the tubetes with the same clinical safety with lidocaine associated to 1:200,000 epinephrine. When higher local anesthetic volumes are needed, it is also recommended to use the lowest epinephrine concentration (1:200,000)[7,22].

Hershet et al.[23] have compared cardiovascular parameters of volunteers submitted to infiltrative anesthesia in right upper canine region with high doses of 4% articaine associated to 1:100,000 or 1:200,000 epinephrine. Similarly to our study, articaine formulations with 1:200,000 and 1:100,000 epinephrine had similar anesthetic efficacy. However, researchers have observed increased systolic blood pressure and heart rate during anesthesia with 1:100,000 epinephrine and have concluded that lower vasoconstrictor concentrations are safer for patients with systemic disorders.

Similarly to our results, Eladet et al.[24] have shown that articaine associated to 1:200,000 epinephrine and lidocaine associated to 1:100,000 epinephrine had the same clinical efficacy and have not interfered with cardiovascular parameters, such as systolic blood pressure, diastolic blood pressure, heart rate and oxygen saturation. Cassidy et al.[25] have recommended 2% lidocaine associated to 1:200,000 epinephrine due to the lower possibility of cardiovascular changes as compared to the potential risk with 1:100,000 concentration in some patients with systemic disorders.

Although our study has not evaluated surgical procedures to evaluate the anesthetic efficacy in volunteers, it is important to stress the influence of this vasoconstrictor concentration difference on clinical parameters such as homeostasis, because a study by Moore et al.[26] has shown that in patients submitted to periodontal surgery, both epinephrine concentrations have provided adequate pain control; however authors emphasize that the highest epinephrine concentration (1:100,000) favors better visualization of the surgical field, as well as there is less bleeding and this association should be indicated for patients who tolerate the highest vasoconstrictor concentration. So, we hope that our study may contribute for the scientific proof of the efficacy of the association of 2% lidocaine and 1:200,000 epinephrine. However, considering the importance of the subject and the size of the evaluated sample, it is imperative that new clinical trials are carried out to further evidence the use of epinephrine in lower concentrations in Dentistry.

CONCLUSION

Considering the anesthetic volume used, the results of our study have shown that decreasing epinephrine concentration in lidocaine solution has not affected its clinical efficacy and has shown clinical safety for evaluated cardiovascular parameters.

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