BioCore Exploring Scientific Community

International Journal of Dentistry and Oral Health

Research Article ISSN 2471-657X

Cardiovascular Effects Associated with Local Anesthetic Mepivacaine Containing Epinephrine

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Abstract

Introduction: Local anesthetics are most drug often used in dentistry, notably safe drug being considered when administered carefully and within limits therapeutic dosages. Demand to demonstrate possible cardiovascular changes of clinical significance relating to the use of local anesthetics associated to vasoconstrictors are extensive and aims to make sure about the safety of its clinical use. The aim of this study was to evaluate the cardiovascular effects resulting from infiltrative administration 3% mepivacaine hydrochloride (54mg) and 2% mepivacaine hydrochloride (36mg) associated with epinephrine hydrochloride 1: 100,000 (18mg).

Method: Twenty normotensive patients' volunteers were evaluated during low complexity restorative procedure in upper posterior teeth. During the experiment were monitored the blood pressure and heart rate through the oscillometric and fotopletismográfico method for non-invasive monitor. Mean values were recorded every minute and continuously during the Es of the experiment as follows: Phase 1 - control period (10 min.). On Phases 2 and 3 the Es were: (E1) baseline period (10 min.), (E2) preparation period (3 min.), (E3) anesthesia period (2 min.), (E4) anesthesia latency period (5 min) (E5) restorative period (10 min), (E6) final period (10 min).

Results: The changes observed in the cardiovascular parameters by the statistical analysis did not represent clinical manifestations or even patients' reports at any time during and after the experiment.

Conclusion: According to the results mepivacaine with or without vasoconstrictor did not induce significant changes in cardiovascular dynamics.

Key words: Epinephrine, Mepivacaine, Local anesthetic, Blood pressure, Heart rate

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Citation: Marcio Antonio Rodrigues Araujo et al. (2025), Cardiovascular Effects Associated with Local Anesthetic Mepivacaine Containing Epinephrine. Int J Dent & Oral Heal. 11:02, 58-63

Received: April 05, 2025 **Accepted:** April 17, 2025
Published: April 30, 2025

Introduction

Local anesthetics are most frequently drugs used in dentistry being considered remarkably safe when administered carefully and within limits of therapeutic dosages [1].

However, systemic side effects may occur in varying degrees of intensity and may be associated with the anesthetics or to vasoconstrictor present in most of the solutions administered. Thus, although the vasoconstrictors can reduce the maximum circulating levels of the local anesthetic they are not exempt from producing their own toxicity.

A common belief in medicine, dentistry and even among the patients is that the use of epinephrine is contraindicated in cardiovascular patients as epinephrine suddenly raises the blood pressure (BP) and heart rate (HR)[2]. On the other hand, some studies have shown that the amount of epinephrine in dental cartridges is so low that use of one to three cartridges of lidocaine with epinephrine is safe and has no considerable effect on the cardiac parameters like BP, HR, etc [3-4].

The search to demonstrate possible cardiovascular changes of clinical significance related to local anesthetics containing vasoconstrictors is extensive and aims to certify its safety [5-10].

Clinically relevant is the fact that epinephrine depending on the dose and the concentration administered produces different actions in the circulatory parameters, which may increase blood pressure and heart rate after its administration and promote its subsequent reduction [11-12]. Likewise these actions may also occur as a consequence of acci-

dental intravascular injection, local absorption or overdose [13].
In accidental intravascular injections the changes occur within the first minute of its administration, disappearing in ten minutes. Due to epinephrine is rapidly metabolized responses to intravascular injection rarely last longer than five minutes [14]. Otherwise, proper use of the local anesthetic does not result in any systemic alteration [5].
On the other hand, mepivacaine is commonly used in medically compromised patients - for whom elevation of blood pressure or heart rate is not advisable - in a vasoconstrictor or non-vasoconstrictor formulation [15].
The aim of this study is compare the cardiovascular effects in systolic, diastolic and mean arterial pressures and heart rate in normotensive patients during a low-complexity restorative procedure when intrabuccal infiltration of the local anesthetic 3% Mepivacaine Hydrochloride (54mg) and 2% Mepivacaine Hydrochloride (36mg) associated with Epinephrine Hydrochloride 1/100,000 (18µg).

Material And Methods

After being approved by the Ethics Committee of the Faculty of Dentistry of the University of São Paulo (nº11/00), the study was conducted by selecting 20 normotensive volunteers of both sexes (15 women and 5 men), age between 18 and 50 years, whose integration of the same was possible according to the fulfillment of the requirements, analyzed through anamnesis and including those who had a medical history which indicated cardiovascular and systemic normality. Patients with systolic blood pressure below 140 mm / Hg, diastolic blood pressure lower than 90 mm / Hg, and heart rate values ranging from 60 to 110 bpm measured at the first dental visit were included.
Each patient presented indication of restorative treatment of two bilateral posterior superior teeth with a similar occlusal extension cariogenic process and superficial depth to average observed in periapical radiographs, and being indicated for restoration by direct technique.
The non-invasive Scholar® II blood pressure monitor (CRITICARE System Inc .; USA) was used to monitor and record cardiovascular parameters for continuous reading of systolic (SBP), diastolic (DBP), mean blood pressure (MBP) and heart rate (HR) programmed to obtain the records every minute during the care sessions.The drugs used were the local anesthetic 3% Mepivacaine Hydrochloride (54mg) (Septodont) and 2% Mepivacaine Hydrochloride (36mg) associated with the vasoconstrictor Epinephrine Hydrochloride 1: 100,000 (18µg) (Septodont).
Patients attended three clinical sessions, conducted by the same operator, scheduled with the interval of one week between each, and in the first session which was called Phase 1 (control period) anamnesis, initial monitoring blood pressure and heart rate (to obtain baseline reference values), and clinical and radiographic examinations, as well as all the information about the study, the procedures to be performed, clarification of any doubts of the patient and signature of the patient consent form if it was in accordance with the research. In the following sessions (Phases 2 and 3) each patient received restorative treatment in only one tooth per clinical phase. The monitoring of the cardiovascular parameters was carried out in a continuous way, starting when the patient was sitting in the chair and extending until the end of the care.
The clinical sessions for the study were divided into six E: (E1) baseline period (10 minute monitoring with the patient in the dental chair to stabilize the cardiovascular parameters); (E2) period of preparation of the patient (for 3 minutes during the application of topical anesthetic based on 6% Lidocaine); (E3) anesthetic period (for 2 minutes during slowly anesthetic local infiltration with successive aspirations); (E4) anesthesia latency period (during the 5 minutes following administration of the local anesthetic); (E5) restorative period (for 10 minutes during caries removal and cavity preparation); (E6) final period (for 10 minutes after completion of the restorative procedure).
It was established that in Phase 2 the procedure would be performed with the local anesthetic containing the vasoconstrictor and in Phase 3 with the anesthetic without the vasoconstrictor. The dose used was one cartridge (1.8 ml) per session, given slowly and blood aspiration tests were performed to avoiding accidental intravascular injection through the local maxillary infiltration technique according to Malamed [16]. For the analysis of the results was used Hypothesis Test for the comparison of two averages with paired data, plus the confidence interval of the average of the differences of the population.

Results

The results represented by figures 1 to 4 it can be interpreted this way: the horizontal axis (x) corresponds to the average value of the parameters recorded in the control period (Phase 1) and the values represented above and below this (axis y) constitute the confidence intervals represent the mean differences that occurred during the experiment, that is, between the control period and the Es of the experiment whose positive values of the intervals mean reduction in the cardiovascular parameters and the negative values of the intervals represent increase in registrations.
Figure 1, 2 and 3 shows the behavior of blood pressures SBP, DBP and MBP respectively, in which the use of the local anesthetic 3% mepivacaine did not show a significant change in these parameters in Es 3, 4 and 5 of the experiment, after administration of the anesthetic. However, it can be noted that there were alterations in the final period (E 6) in which the mean differences intervals are entirely represented by negative values, meaning that there was an increase in blood pressure, as shown by the 3rd, 4th, 5th, 7, 8, and 10 minutes of SBP (Figure 1), and virtually all of E6 of the DBP (Figure 2) and the MBP (Figure 3), except in the 9th minute for the two parameters.
It can be verified that small increases occurred in the basal period (E1) of SBP, from 1 to 4 minutes; at the 1st, 2nd, 3rd, 5th and 6th minutes of the DBP and at the 3rd and 6th minutes of the MBP. Therefore, prior to administration of the anesthetic solution the increase in SBP in the 1st minute of the anesthetic period (E3) is due to needle puncture.
The analysis of the results regarding heart rate also revealed that there were no statistically significant changes in this parameter after administration of 3% mepivacaine as can be observed in figure 4. However, as in blood pressure it is possible observed that in the basal period (E1) there were heart rate elevations demonstrated on the 1st, 3rd, 7th and 10th minutes.
When administration of 2% mepvacaine epinephrine hydrochloride, it can also be observed in Figures 1, 2 and 3 that there was no significant change in blood pressures SBP, DBP and MBP in the Es immediately after administration of the anesthetic.
It may be noted that at some moments in the final period (E6) the intervals are entirely represented by negative values, meaning that blood pressure has increased as demonstrated by the 3rd, 6th, 7th and 10th minutes of the SBP (figure 1), 3rd, 4th, 5th, 6th, 8th and 10th minutes of DBP (figure 2) and 3rd, 7th and 10th minutes of MBP (figure 3).
Figure 2 shows small increases in diastolic blood pressure occurred in the basal period (E1) at the 1st and 4th minutes, only. Still, it can be noted that the heart rate remained unchanged during all stages during mepivacaine 2% with epinephrine was administered (figure 4).

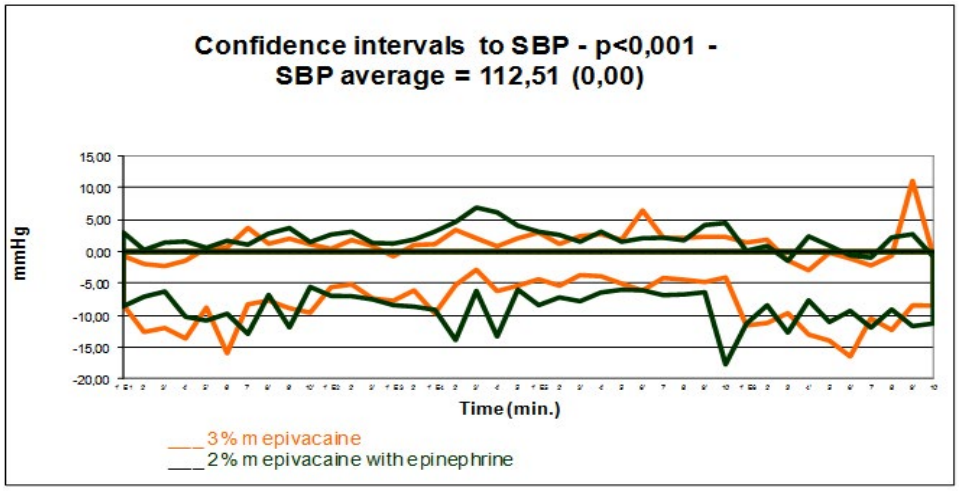

Figure 1: Confidence interval of values obtained for systolic blood pressure (SBP)

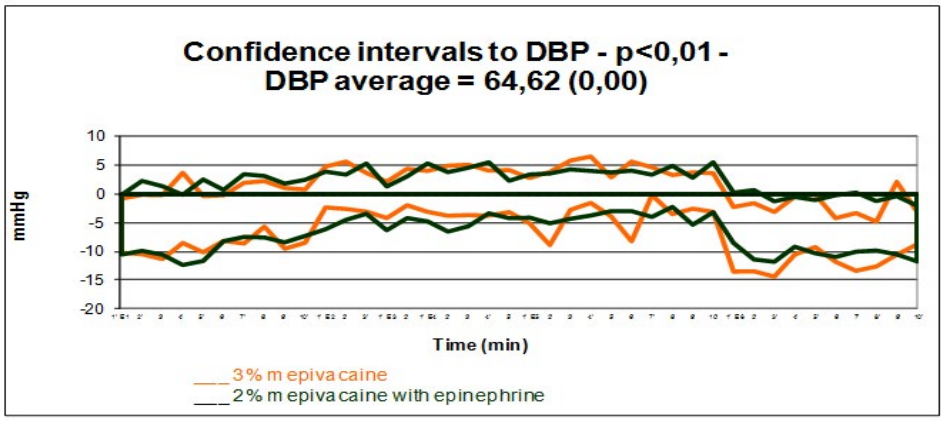

Figure 2: Confidence interval of values obtained for dyastolic blood pressure (DBP)

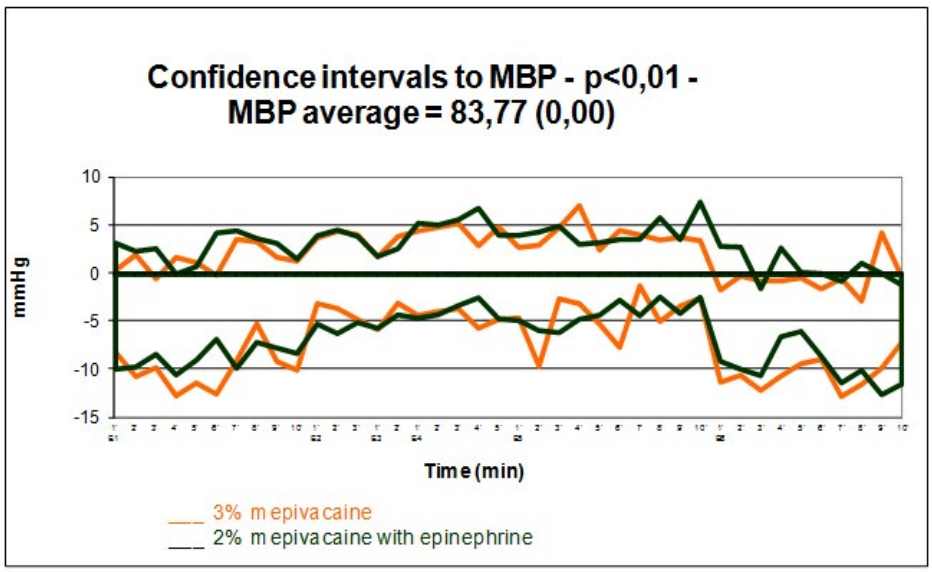

Figure 3: Confidence interval of values obtained for mean blood pressure (MBP)

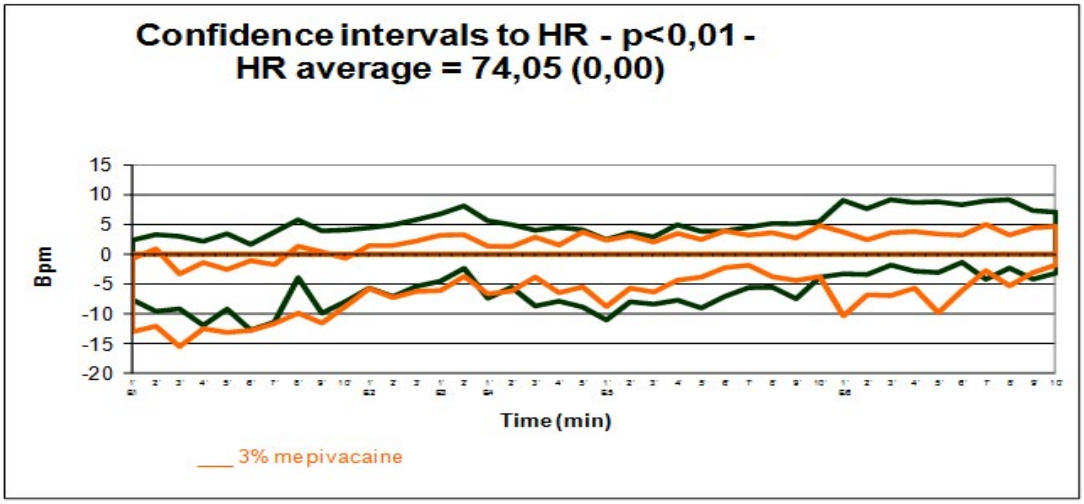

Figure 4: Confidence interval of values obtained for Heart Rate (HR)

Discussion

In our study there was no change in any cardiovascular parameters (SBP, DBP, MBP and HR) after the administration of local anesthetic containing epinephrine. This may be related to the dose administered (18 µg) being very small even though infrequently the epinephrine influences on hemodynamics are observed within a few minutes after its administration and disappear completely in 10 to 15 minutes, with the peak of influence in 5 -10 minutes after its administration, declining rapidly after this period [6]. In this sense significant changes would have been observed in Es 4 and 5 of this study.

The results presented here are similar to other studies that used lidocaine and articaine associated with epinephrine at the same concentration that was used in our study. No significant changes were observed in the cardiovascular parameters measured after administration of the local anesthetic to a simple restorative procedure [5, 17].

Otherwise a comparative meta-analysis study revealed that 3% Mepivacaine had superior inhibition of heart rate increase, as Mepivacaine 2% with vasoconstrictors is better than 2% Lidocaine with vasoconstrictors under dental treatment, given the efficacy and safety of the two solutions, and in relation to the greater success rate of anesthesia, a similar time of onset of pulpal anesthesia and superior control of pain during the injection phase. However, 3% mepivacaine is better for patients with heart disease [18].

Similarly, no changes in cardiovascular parameters were observed when 1:100,000 epinephrine was administered in patients undergoing more stressful procedures such as dental avulsion and periodontal surgery or even when using a higher dose epinephrine (1:80,000) for unit implants placement, or endodontic, restorative and periodontal procedures [2, 19-24].

Although there was no change in heart rate (HR) as demonstrated in other studies using local anesthetic containing epinephrine for minor surgical procedures [11, 25], the results presented here share the opinion that its use can be considered a safe practice, when well-conducted even in patients with cardiovascular disorders and controlled hypertension [10,15,26-28]. In any case, we must be very careful with the choice and execution of the anes¬thetic technique, being it possible to use a dose between 1.8 and 3.6 ml, on a general basis [29].

Even the endogenous release of epinephrine in the event of stress is much larger and therefore responsible for the cardiovascular changes observed in patients who undergo dental treatment [16].

In addition, the increase in heart rate observed prior to anesthesia (E1) in this study may have been due to the release of endogenous catecholamines associated with stress [5,30-31], as well as the statistically significant increase observed in SBP at the 1st minute of E 3, when needle puncture was performed at 3% mepivacaine (figure 1) may also be associated with the stress resulting from the procedure performed, that is, possible pain or fear during the needle bite.

Comparably, in figure 2 an increase in diastolic blood pressure can be observed only at the 1st and 4th minutes during the initial phase (E1) and therefore before administration of the local anesthetic containing epinephrine which may be associated with anxiety prior to dental treatment, as well as it was registered statistically significant elevations in E1 of the 3rd Phase of all measured cardiovascular parameters (Figures 1, 2, 3, and 4), thus also predating the administration of no vasoconstrictor local anesthetic, but no clinical importance according to other studies [30,32]. These changes can be due to the compensatory cardiovascular responses associated with dental treatment anxiety, or physiological process of postural adjustment of blood pressure [33,34] at the beginning of the session and at the end of the procedure when the patient returned to the sitting position.

It is important to remember that factors such as inadvertent intravascular injection, overdosage, vascularization at the site of injection, anesthetic and vasoconstricting agents characteristics, or patient susceptibility have been identified as responsible for toxicity, and their and systemic effects attributed to local anesthesia in dentistry even when using low concentrations of the drug [13,35].

According to Becker and Reed [14] (2012), even small doses of epinephrine can produce cardiovascular responses. The question is whether this represents a significant risk for patients with varying degrees of cardiovascular impairment and this should be assessed individually and in accordance with the operative context.

To Hashemi, Ladez, Moghadam [36] (2016), no significant changes in blood pressure were observed in all dental procedures on the group of controlled hypertension patients that had to be performed under careful monitoring and aspiration. Moreover, the maximum epinephrine dose (0.04mg) should never be exceeded in these patients.

Nevertheless it must be considered that multiple variable factors exist,

such as technique variability, anatomic variations, complexity of procedure and reporting error. Pain itself is multifactorial; and perception and pain reaction vary greatly among individuals [25].

The changes observed in the cardiovascular parameters by the statistical analysis did not represent clinical manifestations or even patients' reports at any time during and after the experiment.

However, it can be considered that the results demonstrated in this study are in agreement with the safe practice of local anesthesia in Dentistry, in which the administration of small doses of local anesthetics injected slowly and with successive aspirations so that there is no risk of accidental intravascular administration and systemic adverse effects, in addition to adequate indications.

Conclusions

There were no statistically significant changes at a significance level of 1%, in blood pressures or heart rate due to mepivacaine administration with or without vasoconstrictor during the low complexity restorative procedures. However, alterations were observed in moments that preceded the administration of the drugs, which could be related to the stress and anxiety caused by dental treatment.

Conflict Of Interest

The current research is free of conflict of interest.

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