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Effects of Epinephrine in Local Dental Anesthesia in Patients with Coronary Artery Disease

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Summary

Background: The use of vasoconstrictors for local anesthesia in patients with coronary heart disease is controversial in the literature, and there is concern regarding risk of cardiac decompensation.

Objective: To evaluate electrocardiographic and blood pressure parameters during restorative dental procedure under local anesthesia with and without a vasoconstrictor in patients with coronary artery disease.

Methods: Sixty-two patients were included in the study, ages ranging from 39 to 80 (mean 58.7 ± 8.8), 51 (83.2%) of whom were male. Thirty patients were randomly assigned to receive 2% lidocaine with epinephrine (epinephrine group), and the remaining patients, 2% lidocaine without epinephrine (non-epinephrine group) for local anesthesia. All patients underwent 24-hour ambulatory blood pressure monitoring and dynamic electrocardiography. Three periods were considered in the study: 1) baseline – recordings obtained during the 60 minutes prior to the procedure; 2) procedure – recordings obtained from the beginning of anesthesia to the end of the procedure and 3) 24 hours.

Results: There was an increase in blood pressure in both groups during the procedure, compared with baseline values; but when the two groups were compared no significant difference was detected between them. Heart rate remained unchanged in both groups. No ST-segment depression > 1 mm occurred either at baseline or during the procedure. Seven patients (12.5%) experienced more than ten arrhythmia episodes per hour during the procedure, four (13.8%) in the non-epinephrine group and three (11.1%) in the epinephrine group.

Conclusion: No difference was observed in blood pressure, heart rate, or evidence of ischemia and arrhythmias in either group. The use of vasoconstrictor has proved to be safe within the range of the present study.

Key words: Epinephrine/adverse effects; anesthesia, local; dental restoration, permanent; coronary arteriosclerosis.

Introduction

The literature is controversial regarding the use of vasoconstrictors in local dental anesthesia in patients with heart disease. Most studies were conducted either with healthy patients[1-10] or those with heart disease of various etiologies[11,12]. In addition, many authors[13-15] failed to include a control group comparing the effects of the anesthetic with and without a vasoconstrictor, making it difficult to extrapolate these results to CAD patients. We investigated the behavior of systemic blood pressure and 24-hour electrocardiogram (Holter monitoring) in patients with clinical symptoms of stable angina and on drug therapy, positive exercise testing, and angiographically proven coronary stenosis > 70% in at least one major artery and who underwent restorative dental treatment under anesthesia with and without a vasoconstrictor.

Methods

Sixty-two patients were followed up on at the outpatient clinic of the Coronary Care Unit of Incor (Hospital das Clínicas Heart Institute of the University of São Paulo Medical School), 51 (82.3%) of whom were male. Ages ranged from 39 to 80 (mean 58.7 ± 8.8), and body mass index (BMI), from 18.8 to 39.4 (mean 27.4).

Twenty-four patients (38.7%) were diagnosed with systemic hypertension and 24, with diabetes (38.7%) All patients continued their medication for coronary artery disease and possible comorbidities, especially beta-blockers (87.1%), lipid-lowering agents (87.1%), antiplatelets (83.9%), and nitrates (54.8%).

Patients were enrolled after Institutional Ethics Committee approval, and all of them read and signed an Informed Consent after receiving thorough verbal explanation of the study and its attendant risks.

Inclusion criteria were the following:

- Personal: patients of both genders from 30 to 80 years of age;

- Clinical: patients with coronary artery disease ($\geq 70\%$

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lumen stenosis) and exercise stress test positive for myocardial ischemia performed within less than three months in the absence of recent acute myocardial infarction;

- Dental: fully or partially dentate requiring lower molar, premolar, or canine restoration.

Exclusion criteria were the following:

- Clinical: neoplasias, septicemia, pregnancy, unstable angina, and malignant hypertension.

Coronary angiography revealed single-vessel disease in seven (11.3%) patients, two-vessel disease in 18 (29%) patients, and three-vessel disease in 37 (59.7%) patients.

Thirty patients were randomly assigned to receive 2% lidocaine and 1:100,000 epinephrine (epinephrine group), and 32 to receive 2% lidocaine without epinephrine (non-epinephrine group) for local anesthesia. In the epinephrine group, 15 patients were given one anesthetic cartridge (1.8 mL) of 2% lidocaine plus 1:100,000 epinephrine and 15 patients, two anesthetic cartridges (3.6mL). In the non-epinephrine group, 15 patients were given one cartridge of lidocaine 2% without vasoconstrictor and 17 patients, two cartridges.

All patients underwent 24-hour electrocardiography (Holter) and ambulatory blood pressure monitoring (ABPM). They were instructed to report any chest pain or discomfort, noting the time of the event in the diary provided by the Holter Laboratory. Three recording periods were considered: 1) baseline – one hour before anesthesia; 2) procedure – from the beginning of anesthesia until the patient left the dental chair; post-procedure – until the 24 hours were completed.

To assess systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR), the mean values recorded during these three periods were considered.

An ischemic episode was defined as either ST-segment elevation ≥ 1-mm or horizontal or downsloping ST-segment depression ≥1mm from baseline, lasting for at least one minute and reverting to baseline levels for at least one minute during the study periods (baseline, procedure and post-procedure).

The presence of cardiac arrhythmia was considered when more than ten ventricular extrasystoles (VES) and supraventricular extrasystoles (SVES)[16] occurred per hour during the study periods.

Dental procedure - Each patient (30 in the epinephrine group and 32 in the non-epinephrine group) underwent a single restorative procedure under inferior alveolar nerve block anesthesia.

Statistical analysis - For quantitative variables, minimum and maximum values were observed and means, medians, and standard deviations were calculated. For qualitative variables, the absolute and relative frequencies were calculated.

The following tests were used: Student's *t* test to compare means between two groups; one-way analysis of variance (ANOVA)[19], using Bonferroni's multiple comparison test[18], to compare four groups; Fisher's exact test for proportions; repeated-measures ANOVA[19] to assess groups behavior taking into account the medical conditions studied; in addition to Friedman's nonparametric test and the Mann-Whitney nonparametric[18] test when the assumption of data normality was rejected. The significance level was set at 5% (p = 0.05).

Results

Duration of procedures: length range was wider in the epinephrine group (12 to 94 minutes, mean 35 ± 15) than in the non-epinephrine group (22 to 69 minutes, mean 40 ± 2). However, means between both groups did not differ (p = 0,200). No clinical events were observed.

Blood pressure behavior - There was a rise in systolic and diastolic blood pressure from baseline to the procedure in both groups (14 mm Hg and 5 to 7 mmHg, respectively), when they were evaluated separately. However, when the epinephrine and non-epinephrine groups were compared, no significant difference was found (Tables 1 and 2). Moreover, no differece was found when mean systolic (p = 0.2076) and diastolic (p = 0.5936) blood pressure were compared between the baseline, procedure, sleep and wake periods (Figure 1).

The number of anesthetic cartridges used, one (1 c) or two (2 c) with or without epinephrine, did not differ between the epinephrine and non-epinephrine groups regarding mean systolic (p = 0.2083) and diastolic (p = 0.1183) blood pressure (Figure 2), and there was no influence by the use or not of beta-blockers.

24-hour ambulatory electrocardiography - Fifty-six patients underwent 24-hour electrocardiography. For technical reasons (motion artifacts and noise > 2%), six patients were excluded from the study: three from the non-epinephrine group and

Table 1 - Distribution of means, standard deviation, minimum, and maximum SBP at baseline and during the procedure according to the presence or not of epinephrine in the anesthetic solution

| | SBP | | | | | | | | | |
| | Epinephrine group | | | | | Non-epinephrine group | | | | |
Period	Mean	Standard deviation.	Minimum value	Maximum value	n	Mean	Standard deviation.	Minimum value	Maximum value	n
Baseline	124.17	17.08	94.00	166.00	30	129.84	21.54	95.00	169.00	32
Procedure	137.97	21.35	93.00	196.00	30	144.28	24.69	109.00	205.00	32

SBP - systolic blood pressure; Epinephrine group - lidocaine plus epinephrine; Non-epinephrine group - lidocaine without epinephrine. Comparing groups - p = 0.8025. Comparing periods - p = 0.2614. Individual groups – p < 0.001.

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Table 2 - Distribution of means, standard deviation, minimum, and maximum DBP at baseline and during the procedure according to the presence or not of epinephrine in the anesthetic solution

	DBP									
	Epinephrine group					Non-epinephrine group				
Period	Mean	Standard deviation.	Minimum value	Maximum value	n	Mean	Standard deviation.	Minimum value	Maximum value	n
Baseline	75.70	10.34	51.00	96.00	30	79.28	13.76	56.00	106.00	32
Procedure	81.33	10.83	59.00	109.00	30	83.75	14.22	66.00	117.00	32

DBP - diastolic blood pressure; Epinephrine group - lidocaine plus epinephrine; Non-epinephrine group - lidocaine without epinephrine. Interaction between groups and periods - p = 0,.567. Comparison between periods p = 0.2614. Individual groups – p < 0.001.
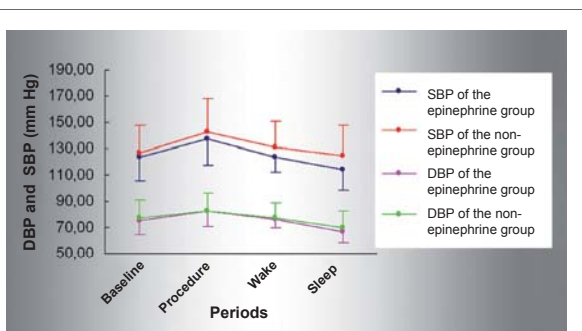

Fig. 1 - *Distribution of SBP and DBP means during the baseline, procedure, sleep, and wake periods according to the presence (epinephrine group) or not (non-epinephrine group) of epinephrine in the anesthetic solution. SBP - systolic blood pressure; DBP - diastolic blood pressure.*

three from the epinephrine group.

Mean heart rate did not differ between the epinephrine and non-epinephrine groups at baseline, during the procedure (p = 0.1967), and over the 24 hours (p = 0.8417) (Tables 3 and 4), as well as in the assessment based on the number of anesthetic cartridges used, that is, one or two with or without epinephrine.

ST-segment depression - Ten patients (17.9%) had ST-segment depression greater than 1 mm from baseline, six (20.7%) in the non-epinephrine group (14.8%) and four

(14.8%) in the epinephrine group, but no significant difference was found between both groups (p = 0.731). No events were recorded at baseline or during the procedure, and all episodes occurred at least two hours after the dental procedure had been completed.

Cardiac arrhythmias - Sinus rhythm prevailed throughout the 24-hour monitoring period. Over the 24 hours, 17 patients (30.4%), ten (34.5%) belonging to the non-epinephrine group and seven (25.9%) belonging to the epinephrine group, experienced supraventricular extrasystoles (SVES) and/or ventricular extrasystoles (VES). During the procedure, however, only seven (12.5%) patients had arrhythmias, four (13.8%) in the non-epinephrine group and three (11.1%) in the epinephrine group, but no significant difference was found between the two groups (p = 1.00).

Discussion

This study included CAD patients with ≥ 70% of lumen stenosis; most of them (59.7%) had triple-vessel disease. In keeping with the literature[20,21], the study sample was predominantly male (82.3%) .

The presence of classical risk factors for coronary artery disease was common, particularly metabolic disorders, such as diabetes mellitus (38.7% *vs* 7.5% of the population mean), and circulatory conditions, such as systemic hypertension (38.7% *vs* 20% of the population mean)[22].
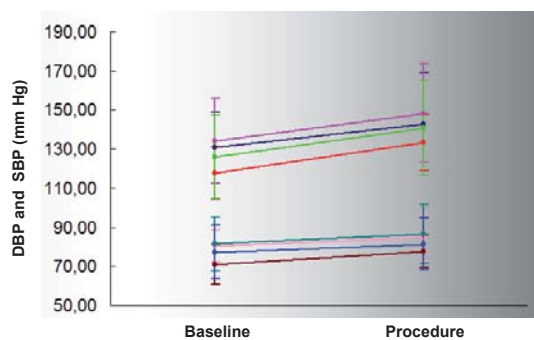

Fig. 2 - *Distribution of SBP and DBP means at baseline and during the procedure according to the presence (epinephrine group) or not (non-epinephrine group) of epinephrine in the anesthetic solution and the number of cartridges used (one cartridge - 1 c; two cartridges - 2 c). SBP - systolic blood pressure; DBP - diastolic blood pressure.*

Table 3 - Distribution of means, standard deviation, minimum, and maximum HR at baseline and during the procedure according to the presence or not of epinephrine in the anesthetic solution

	HR (bpm)									
	Epinephrine group					Non-epinephrine group				
Period	Mean	Standard deviation.	Minimum value	Maximum value	n	Mean	Standard deviation.	Minimum value	Maximum value	n
Baseline	63	8.2	48	90	27	66	11.8	48	108	29
Procedure	63	8.4	48	95	27	66	10.8	48	103	29

HR - heart rate; Epinephrine group - lidocaine plus epinephrine; Non-epinephrine group - lidocaine without epinephrine. Comparing groups = p = 0.8025. Comparing the same periods in both groups – p = 0.1967. Comparing periods in a single group – p = 0.4038.

Table 4 - Distribution of means, standard deviation, minimum, and maximum HR over 24 hours according to the presence or not of epinephrine in the anesthetic solution

	HR (bpm)									
	Epinephrine group					Non-epinephrine group				
Period	Mean	Standard deviation.	Minimum value	Maximum value	n	Mean	Standard deviation.	Minimum value	Maximum value	n
24 hours	68	7.8	45	86	27	69	8.8	53	86	29

HR - heart rate; Epinephrine group - lidocaine plus epinephrine; Non-epinephrine group - lidocaine without epinephrine. p = 0.8417.

The prevailing use of beta-blockers, acetylsalicylic acid, lipid-lowering agents, and nitrates is also consistent with that found in a series of CAD patients[20,23,24]. The percentages of patients on beta-blockers and nitrates (87.1% and 54.8%, respectively) were similar to those reported by Leviner et al[25] (60% and 85%, respectively), in 1992; nevertheless, these rates were higher than those reported by Cintron et al[13] (27.5% and 32.5%) in a sample of 40 patients with recent acute myocardial infarction.

In order to make all study phases homogeneous, patients were enrolled based on their need of dental care. This approach enabled the length of the procedure and anesthetic dosages to be standardized, something that usually is not seen in endodontic and surgical procedures, thereby contributing to reduce the influence of stress, which has always been borne in mind.

Moreover, for practical purposes, caries treatment is the predominant procedure in dental office daily routine. In spite of this, few researchers, among them Leviner et al[25], Cioffi et al[26], Corah[27,] and Oliver et al[28], have studied the effects of vasoconstrictors in patients undergoing dental anesthesia for restorative treatment.

In this study, there was a significant increase in SBP and DBP in both groups of patients from baseline to the procedure, when they were analyzed separately. However, when both groups were compared, no significant difference was found (baseline, procedure, sleep, and wake periods).

The same was true regarding the anesthetic solution dosage delivered: 1.8 ml (one cartridge) and 3.6 ml (two cartridges). Therefore, in our opinion, blood pressure increase was independent of the presence or absence of vasoconstrictor in

the anesthetic solution, and should be attributed to the dental procedure in general.

Our rates contrast with those reported by Cintron et al[13], who did not detect changes in blood pressure before, during or after the procedure, using the same kind of anesthetic solution. These authors, however, used a lower amount of anesthetic agent and, thus, less vasoconstrictor (10 μg vs 18 or 36 μg in our study).

Vaderheyden et al[15] and Findler et al[29] reported lower rates than ours, but in smaller samples (20 and 26 patients, respectively); in addition, they failed to include a control group to compare the effects of anesthetics with and without vasoconstrictors.

Other authors[11,12] have evaluated heterogeneous groups, that is, patients with heart diseases of various etiologies, thus making it difficult to compare their results with our findings.

It has been suggested that adverse drug interactions between nonspecific beta-blockers[30, 31] may cause an excessive rise in blood pressure; however, this was not the case with our patients, most of whom (54.8%) were taking nonselective beta-blockers.

No change in HR was found from baseline to the procedure in both of the study groups, with either one or two cartridges of anesthetic solution; however, beta-blocker influence should be considered. Our rates are similar to those reported by other authors who studied CAD patients, such as Cintron et al[13] and Findler[29], but unlike those reported by Leviner et al[25].

ST-segment assessment showed no evidence of myocardial ischemia either at the baseline period or during the procedure. Ten patients experienced ischemic episodes, and all of them

occurred at least two hours after the procedure had been completed. In our opinion, there were no grounds to associate these results to vasoconstrictor use, since as many as six patients who had ischemia belonged to the non-epinephrine group and, thus, were free of the vasoconstrictive effect of this drug.

Analyzing the data in the patients' diaries, we could not correlate the time of ischemia with their reports. Our data strongly suggest that the recorded ischemic episodes were secondary to the heart disease itself. However, this might be explained by the fact that all patients were medicated, since other investigators[32] have found that the use of medication may reduce both the incidence and duration of ischemia episodes during normal daily life activities.

Our data superimpose those reported by Vanderheyden et al (1989)[15]. In the study of Hasse et al[12], however, the incidence of ST-segment depression was significantly higher in CAD patients than in non-CAD patients. These authors, though, established a criterion of 0.5 mm, rather than 1 mm, considered indicative of ST-segment depression or elevation by cardiologists[33,34], thus producing false positives.

Several authors[12,35] have detected arrhythmias in normal patients undergoing dental treatment, but these are particularly exacerbated in patients with cardiovascular disease. In our study, 12.5% patients experienced more than ten cardiac arrhythmias per hour during the dental procedure[16], a figure that rose proportionally over the 24 hours. However, no difference was found between the epinephrine and non-epinephrine groups.

The use of 0.018 mg or 0.036 mg of epinephrine in the local anesthetic solution was safe and well tolerated by all patients. Further studies with specific groups of cardiac patients are needed for the benefit of the dentist-physician-patient relationship.

Conclusion

We came to the conclusion that blood pressure did not behave differently with epinephrine-containing and epinephrine-free anesthetic solution. Heart rate did not change during the procedure, nor was there evidence of myocardial ischemia and cardiac arrhythmia, using anesthetic solution with and without vasoconstrictor, in patients taking drugs, the majority of whom were on beta-blockers.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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