

Effect of Local Anesthetics with and without Vasoconstrictor Agent in Patients with Ventricular Arrhythmias

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Summary

Background: The use of local anesthetics associated to vasoconstrictors for the dental treatment of patients with cardiopathies is still controversial, due to the risk of adverse cardiovascular effects.

Objectives: To evaluate and compare the hemodynamic effects of the use of local anesthetics with a non-adrenergic vasoconstrictor in patients with ventricular arrhythmia, when compared to the use of anesthetics without vasoconstrictor.

Methods: A prospective randomized study evaluated 33 patients with positive serology for Chagas' disease and 32 patients with coronary artery disease that presented complex ventricular arrhythmia at Holter monitoring (>10 EV/h and NSVT), of which 21 were females, aged 54.73 ± 7.94 years, submitted to routine dental treatment with pterygomandibular anesthesia. These patients were divided in two groups: group I received prilocaine 3% associated with felypressin 0.03 IU/ml and group II received lidocaine 2% without vasoconstrictor. The number and complexity of extrasystoles were analyzed, as well as the heart rate and systemic arterial pressure of the patients on the day before, one hour before, during the procedure and one hour after the dental procedure.

Results: No hemodynamic alterations or increase in the number and complexity of the ventricular arrhythmia related to the anesthetic used in the dental procedure were observed in either group.

Conclusion: The results suggest that prilocaine 3% associated to a felypressin 0.03 IU/ml can be safely used in patients with Chagas' disease or coronariopathy with complex ventricular arrhythmia. (Arg Bras Cardiol 2008;91(3):128-133)

Key words: Arrhythmias, local anesthetics, vasoconstrictors, Chagas'ic myocardiopathy, coronariopathy.

Introduction

During routine dental treatment, when treating patients with cardiopathy and ventricular arrhythmia, the scarcity of objective information in the literature makes it difficult to choose the most adequate anesthetic agent and to reach a decision on the maximum dose to be used.

The fear of using local anesthetics containing vasoconstrictors is based on the potential adverse effect of these substances on the blood pressure and/or cardiac rhythm. The hemodynamic effects of local anesthetics can be caused by the direct action on the smooth or cardiac muscle or by the direct action on the autonomic innervation of the heart. All of them can cause, depending on the concentration, an increase in heart rate and

mean arterial blood pressure (MBP). When the anesthetic dose causes cardiovascular collapse, the predominant effect is tachycardia¹; however, the occurrence of most adverse reactions is due to inappropriate high-dose injections and accidental intravascular punctures².³. Moreover, with exception of allergic reactions, the other described anesthetic complications are caused by a higher adrenergic stimulation on the cardiovascular system, which justifies a certain restriction to the use of catecholaminergic vasoconstrictors in patients with cardiopathies.

Felypressin, a vasoconstrictor agent, does not cause significant alterations in heart rate⁴, as it does not act on adrenergic receptors, having a direct effect on the vascular smooth muscle. At the amounts required for local anesthesia, it acts on the venous circulation and does not have an arterial, cardiac or potential arrhythmogenic effect^{5,6}. Its vasoconstrictor action is lower than that of adrenaline, but the duration of the effect is similar⁷.

In Brazil, two types of vasoconstrictors are commercially available: felypressin and the sympathomimetic amines.

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Felypressin is only available when associated to the anesthetic prilocaine. As for lidocaine, it is available with and without the adrenergic vasoconstrictor, but not with felypressin.

Lidocaine and prilocaine are very similar in many aspects: both are classified as amides and have similar action and effect mechanisms². At the dose used and type of injected administration used for dental treatment, there are no significant differences regarding the time of latency and duration of the anesthetic effect.

Considering the non-adrenergic substances, evidence has suggested that, in the absence of overdose or puncture accident, the vasoconstrictors promote a protective effect as they increase the intensity and duration of the anesthetic effect, decrease their toxicity and reduce local hemorrhage⁸.

Due to the necessity of obtaining more objective information on patients considered to be high-risk ones, this study was carried out to evaluate the safety of the use of local anesthetics with non-adrenergic vasoconstrictor in patients with ventricular arrhythmias associated to Chagas'ic and coronary cardiopathies.

The objective of the present study was to evaluate the effects of lidocaine without vasoconstrictor and prilocaine with felypressin on the number and the complexity of extrasystoles, the heart rate and rhythm and the systemic arterial pressure in patients with Chagas' disease or coronary artery disease with complex ventricular arrhythmia, during routine dental treatment.

Methods

This was a prospective, randomized and non-double blind study. The inclusion criteria were:

- Age between 18 and 70 years;
- Positive serology for Chagas' disease or stable coronary artery disease (CAD);
- Presence of complex ventricular arrhythmia at the 24-hour ambulatory electrocardiogram (Holter) monomorphic, polymorphic, repetitive, non-sustained and also sustained ventricular tachycardia;
 - With or without specific medication;
- Indication for dental treatment in the lower maxillary region.

The exclusion criteria were:

- Other cardiopathies (recent infarction, unstable angina);
- Signs and symptoms of functional class IV heart failure, even if clinically controlled.

A total of 65 consecutive patients were selected: 33 with positive serology for Chagas' disease and 32 patients with CAD and previous myocardial infarction, with or without prior myocardial revascularization. All patients presented frequent and complex ventricular extrasystoles (VES), >10/hour with or without repetitive beats or NSVT, documented by the 24-hour Holter.

Nine patients from the coronary group and 18 from the Chagas'ic group were medicated with amiodarone, one Chagas'ic patient used quinidine and one patient from the coronary group used propaphenone; four patients had definitive artificial pacemakers, of whom one was from the coronary group and three from the Chagas'ic group; and seven patients had implantable cardioverter defibrillators (ICD): one from the coronary group and six from the Chagas'ic group. Thirty-three patients used a platelet anti-aggregant drug (ASA) and 12 used an oral anticoagulant (Warfarin).

All patients presented a previous diagnosis of arterial hypertension controlled with specific medication prescribed at the ambulatory where the patient was originally treated, such as enalapril, captopril, lisinopril, losartan, diltiazem, hydralazine, furosemide, spironolactone and hydrochlorothiazide.

After the preliminary evaluation and after the need for dental treatment was verified, the patients were referred to the Dentistry Unit and informed in written form on the protocol. After signing the free and informed consent form, they were scheduled for the dental procedures. At the first dental assessment, they were submitted to anamnesis, clinical examination and periapical X-ray. A panoramic X-ray was requested and the clinical file was filled out. The Holter monitoring was started on the day before the procedure. The ECG recording was carried out in a portable recorder (Dýnamis 3000 ECO) and the recording was made in a magnetic tape. The patients were instructed to come back on the following day to undergo the dental treatment. The treatment was carried out in the morning period and all patients took medications on the day of the procedure.

The arterial blood pressure and heart rate monitoring was carried out with a Critikon Dinamap TM Plus device, attached to the patient by a standard cuff (24 x 32 cm); the recordings were made from oscillometric measurements according to the following protocol: at the waiting room, ten minutes before the start of the treatment; at the moment of the patient's arrival at the dental office; five minutes after the anesthetic injection; every 15 minutes during the 50-minute treatment session and 10 minutes after the end of the treatment session. The dental procedures were carried out in the mandibular, molar and premolar regions (first and second, right or left).

The anesthesia was carried out by regional pterygomandibular block with a carpule syringe and 3G needle.

For each procedure, 2 to 4 vials, with 1.8 ml of anesthetic each, were used. The patients were divided in groups according to the anesthetic agent they received, sequentially:

- 1. Chagas'ic patients with prilocaine associated to felypressin,
- 2. Chagas'ic patients with lidocaine without vasoconstrictor, 3. Coronary patients with prilocaine associated to felypressin and
- 4. Coronary patients with lidocaine without vasoconstrictor.

The heart rhythm, number and the complexity of ventricular extrasystoles (VES) were analyzed by the Holter system, according to the following protocol: at the same time of dental procedure on the day before and one hour before and during the procedure, totaling 25 hours of monitoring. The BP and HR measurements and number and complexity of VES were compared in the four groups of patients (according to the type of anesthetic used) at three phases: before the dental procedure, during the procedure and after its end.

Initially, all variables were analyzed descriptively. For the quantitative variables, this analysis was made through

the observation of the minimum and maximum values and the calculation of means and standard deviations, as well as medians. For the qualitative variables, the absolute and relative frequencies were calculated. The level of significance was set at 5%.

Results

The dental treatment was well tolerated by all patients and all of them remained asymptomatic. There were no complications due to the procedure, such as bleeding or puncture accidents.

The comparison of the four groups of patients regarding the number of anesthetic vials used and concerning their clinical characteristics is described in Tables 1 and 2.

The clinical and demographic characteristics were similar and there was no difference regarding the dose of anesthetic used, as well as in the degree of ventricular dysfunction between Chagas'ic and coronary patients that received anesthetics with or without vasoconstrictor.

Cardiac rhythm

When analyzing the number of VES, no difference was observed at the different assessed moments (on the day before, before the dental procedure and during the procedure) or regarding the use of anesthetics with or without vasoconstrictor, in the Chagas'ic as well as in the coronary patients (Charts 1 and 2). The complexity of the extrasystoles also remained stable at the different moments, with a similar behavior in both groups.

Blood pressure

Regarding the behavior of the mean blood pressure (MBP) before, during and after the procedure, we did not observe any difference related to the types of anesthetic solution used, in Chagas'ic as well as coronary patients (Charts 3 and 4).

Heart rate

The behavior of heart rate (HR) in the studied patients is shown in Charts 5 and 6. No difference was observed among the groups related to the types of anesthetics used.

Discussion

The present study did not demonstrate adverse cardiovascular effects in Chagas'ic and coronary patients with complex ventricular arrhythmia, submitted to dental treatment under local anesthesia. Regardless of the type of anesthetic used, there were no variations in the number and complexity of the ventricular extrasystoles, in the systemic arterial pressure and in the behavior of heart rate.

We chose the dental procedures carried out in the mandibular region under the regional block technique, as this technique allows the drug to reach the bloodstream and thus, the potential effects on the cardiovascular system could be analyzed. At the upper jaw region, the regional block technique is replaced by infiltration anesthesia. With the infiltration technique, the concentration of the anesthetic drug in the bloodstream is negligible, and therefore, we would not reach our objectives.

The studies by Oliveira et al⁹ reported that the alterations in blood pressure and heart rate due to the use of local anesthetics with vasoconstrictor occur immediately after the injection of these drugs, showing a tendency to rapidly normalize. It is interesting to mention that, according to the authors, significant alterations occurred only when the drug administration (lidocaine with noradrenaline or prilocaine with felypressin) was carried out by intravenous route (simulating a technique accident) and not by the intrabuccal or infiltrative routes. Tsakiris and Buhlmann¹⁰ reported a systemic vasopressor effect when 0.5 IU or more of felypressin was administered by intravenous route. They also observed that 1 IU of IV felypressin was capable of increasing the systolic pressure by 25 mmHg and the diastolic pressure by 13 mmHg.

Table 1 - Amount of anesthetic vials used in the four groups

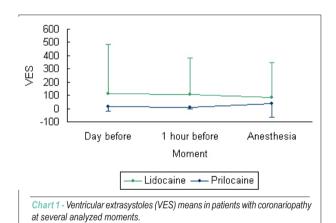
Group	Anesthesia								
	number of	Lidocaine		Prilocaine + felypressin		*			
		n	%	n	%	- p*			
Chagas'ic	2 (78 mg)	10	71.4	18	94.7	- 0.152			
	3 (108 mg)	2	14.3	1	5.3				
	4 (144 mg)	2	14.3	0	0.0				
Coronariopathy	2 (108 mg)	10	66.7	13	76.5	0.191			
	2.5 (135 mg)	0	0.0	2	11.8				
	3 (162mg)	5	33.3	2	11.8				

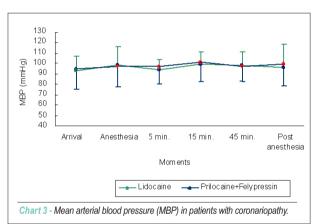
^{*}Descriptive level of Fisher exact probability test.

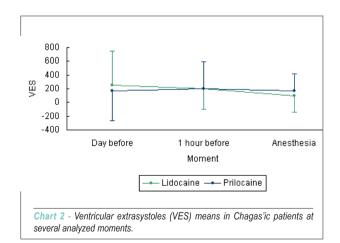
Table 2 - Type of anesthetic used and ventricular function in patients with coronariopathy and Chagas'ic ones

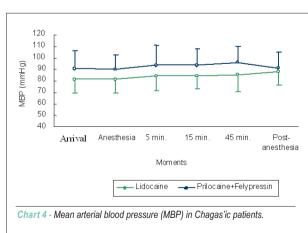
		Lido	ocaine	Prilocaine +	Prilocaine + felypressin	
	FE %	n	%	n	%	p*
Coronariopathy	< 30	6	46.1	3	20.0	
	30-50	2	15.4	5	33.3	0.351
	> 50	5	38.5	7	46.7	
	Total	13	100.0	15	100.0	
Chagas'ic	< 30	1	7.1	1	5.3	0.637
	30-50	9	64.3	9	47.4	
	> 50	4	28.6	9	47.3	0.037
	Total	14	100.0	19	100.0	

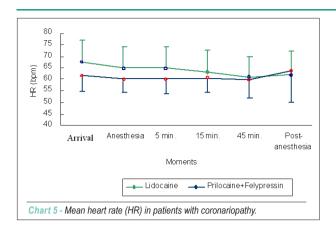
^{*}Descriptive level of Fisher exact probability test; EF-ejection fraction.

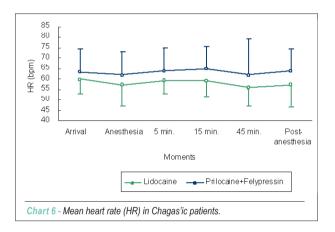












Aochi et al¹¹ reported an increase of 40 mmHg in the systolic pressure and of 25 mmHg in the diastolic pressure when 1 IU of felypressin was administered by IV route. Johnson and Widrich¹² observed that the cardiovascular disorders rarely occurred with felypressin at doses < 0.2 IU/ml.

We did not observe any hemodynamic alterations after the infusion of the assessed anesthetics in the present study, certainly due to the administered dose appropriateness (0.03 IU/ml of felypressin) and due to the lack of puncture accidents. The observed cardiovascular effects were not different from those observed with the use of the anesthetic without vasoconstrictor. These data confirm that, in patients with clinical characteristics similar to those of the studied population and at ideal doses, the non-adrenergic vasoconstrictors can be safely used to optimize the anesthetic effect.

The literature recommends that the use of adrenergic vasoconstrictors should be avoided in patients with unstable angina, recent myocardial infarction or revascularization surgery, in refractory arrhythmias, non-controlled arterial hypertension and decompensated congestive heart failure³. Newcomb and Waite⁶ suggest the use of anesthetics with non-catecholaminergic vasoconstrictor in the dental surgeon's routine procedures and contraindicate the use of catecholaminergic ones in patients with cardiovascular problems, hyperthyroidism, those receiving antidepressants or anti-hypertensive drugs and when used in association with sedation or general anesthesia.

The patients in the present study represent a population that reflects the reality of dental practice associated to cardiology. The patients with ventricular arrhythmia, although clinically stable under optimized clinical treatment, were hypertensive and presented variable degrees of ventricular dysfunction. Some had pacemakers or defibrillator implants, with a history of previous myocardial infarction, presented multiple coronary artery involvement and used platelet antiaggregants and anticoagulants, factors that characterize a higher-risk population.

Our results are original ones and their relevance is based on the lack, in the specialized literature, of publications that validate the safety of using of local anesthetics with non-adrenergic vasoconstrictors during dental procedures in a population with these characteristics.

Conclusions

We conclude that during the routine dental treatment:

- 1) The effects of the local anesthetics, with or without non-adrenergic vasoconstrictors, on the cardiovascular system are not significant;
- 2) In spite of the known variability in the behavior of ventricular arrhythmias at 24-hour Holter monitoring, no significant alterations in their number or complexity pattern were observed, after both anesthetic interventions and throughout the procedure;
- **3**) The use of anesthetics with non-adrenergic vasoconstrictors at adequate doses can be safely used in Chagas'ic and coronary patients with complex ventricular arrhythmia.

Limitations

The present study was carried out with two different anesthetic salts, due to the commercial unavailability, in the national market, of lidocaine associated to felypressin and isolated prilocaine. We did not think there would be any obstruction to attain the objectives, as both lidocaine and prilocaine, at the dose and type of administration used (injected) have similar mechanisms and effects. Moreover, our objective was not to compare the two drugs, but to evaluate the possible deleterious effect of the vasoconstrictor on the cardiovascular system in high-risk patients. Therefore, we considered that it would be clinically more relevant to use different anesthetic salts, but with similar effects and that are available in the Brazilian daily clinical routine.

Potential Conflict of Interest

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

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Study Association

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References

- Groban L, Deal DD, Vernon JC, James RL, Butterworth J. Ventricular arrhythmias with or without programmed electrical stimulation after incremental overdosage with lidocaine, bupivacaine, levobupivacaine, and ropivacaine. Anesth Analg. 2000; 91 (5): 1103-11.
- 2. Yagiela JA, Duffin SR, Hunt IM. Drug interactions and vasoconstritors used local solutions. Oral Surg Oral Med Oral Pathol. 1985; 59: 565-71.
- Perusse R, Goulet JP, Turcotte JY. Contraindications to vasoconstrictor in dentistry: Part I. Cardiovascular diseases. Oral Surg Oral Med Oral Pathol. 1992; 74 (5): 679-86.
- Tortamano N, Soares MS, Migliorati CA. Anestésicos locais. In: Tortamano N. Terapêutica medicamentosa em odontologia. São Paulo: Moreira Jr. Ed Médica; 1980. p. 56-62.
- Jastak JT, Yagiela JA. Vasoconstrictors and local anesthesia: a review and rationale for use. J Am Dent Assoc. 1983; 107: 623-30.
- 6. Newcomb GM, Waite IM. The effectiveness of two local analgesic preparations in reducing hemorrhage during periodontal surgery. J Dent. 1972; 1: 37-42.
- 7. Akerman B. On felypressin (octapressin) as an adjunct to lidocaine and prilocaine

- an experimental study in animals. Acta Pharmacol Toxicol (Copenh). 1966; 24: 377-88.
- Meyer FU. Hemodynamics changes under emotional stress following a minor surgical procedure under local anaesthesia. Int J Oral Maxillofac Surg. 1987; 16: 688-94
- Oliveira MA, Tortamano N, Armonia PI, Rocha RG. Comparative study of the effects of lidocaine with noradrenaline and prilocaine with felypressin on the cardiovascular system of dogs, according to variations in dosage, time and route of administration. Rev Fac Odontol Univ São Paulo. 1986; 24 (2): 75-92.
- Tsakiris A, Buhlmann A. Experimentelle untersuchungen beim Menschen uber die Wirkung von Vasopresssin auf die leberdurchblutung und den portalen druck. Helv Med Acta. 1961; 4: 615-21.
- 11. Aochi O, Takesita T, Kawaguchi T, Goto Y, Yasunaka H. Fundamental and clinical study on PLV2 (octapressin). Massui. 1966; 15 (5): 436-43.
- 12. Johnson WC, Widrich WC, Ansell JE, Robbins AH, Nabseth DC. Control of bleending varices by vasopressin: a prospective randomized study. Ann Surg. 1977; 186: 369-76.