



# Identification of the degree of knowledge of doctors about the use of vasoconstrictor in cardiac patients

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## Keywords

Cardiac, dental treatment, local anesthetic

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## Abstract

**Introduction:** There is a clear lack of knowledge among professionals about the use of local anesthesia during dental treatment in cardiac patients, coming to delay emergency care or to indicate the use of vasopressors erroneously since its use brings benefits to the patient and the professional.

**Objective:** To evaluate professionals' perception of the use of local anesthetics with vasoconstrictors to perform dental procedures in patients with heart disease.

**Methods:** This study was conducted by the application of a questionnaire that contained 12 questions which 100 professionals answered from January to September 2014.

**Results:** 61% of professionals recommend that the use of local anesthesia associated with a vasoconstrictor to dental treatment for a cardiac patient. Half of them did not know to answer, "What is the concentration of vasoconstrictor recommended for use in a cardiac patient?" 81 professionals choose the lidocaine as the best anesthesia.

**Conclusion:** The professionals demonstrate to know about the use of vasoconstrictors associated with local anesthetics in dental procedures; however, the total amount and concentration of the vasoconstrictors are unknown.

## Introduction

The local anesthesia is defined as a reversible blockade of the nervous stimuli conduction determined by the loss of sensations without a change in the consciousness level.<sup>[1]</sup>

It is known that the painful stimulus is transported by the nervous fibers from where they originate until the brain producing through transitory depolarization membrane of nerve cells through the influx of Na<sup>+</sup> by this. The action mechanism of local anesthetics acts by reducing or preventing the membrane permeability regarding these ions in the cell.<sup>[2]</sup>

All local anesthetics are amphipathic, i.e., have hydrophilic and lipophilic properties and characteristics which join together through an intermediary chain, classifying them in amino esters or oral anesthetics, these structures being directly linked to the modalities of biotransformation.<sup>[3]</sup>

The essential prerequisite in dentistry for the success of anesthesia is the local analgesia. Clinically local anesthetic agents, such as lidocaine and articaine, are used in conjunction

with vasoconstrictors, mainly adrenaline, to contribute with the increase of the anesthesia duration.<sup>[4]</sup>

Until recently, the American Dental Association in their Council on Dental Therapeutics advocated conservative maximum doses of local anesthetics. However, the Food and Drug Administration responsible for drugs and medicines control in the USA, encourages higher doses, which are the same as recommended for medical anesthesia.<sup>[2]</sup>

The vasoconstrictors are added to the anesthetic solutions so that they enable beneficial results to local anesthesia since they reduce the vasodilating action of anesthetics and promote the constriction of the blood vessel allowing greater hemostasis. They even lower the rate of absorption of the local anesthetic to the cardiovascular system, allowing the reduction of toxicity, further increasing the duration of most local anesthetics.<sup>[3]</sup>

During the treatment of patients with systemic problems (American Society of Anesthesiologists [ASA] II or ASA III), a constant deadlock for the professional is the use of anesthetic solutions containing epinephrine or other adrenergic

vasoconstrictors. Taking this as a basis, the surgeon dentist tends to forward the patient to the doctor and eventually adopt a conduct that violates the medical directions or that embrace, adopting, however, substances that do not allow a satisfactory anesthesia for the procedure. It is worth mentioning that guidelines and medical prescriptions are based on solutions used in medical emergencies that are different from the concentrations used in dentistry.<sup>[3]</sup>

Some physiological alterations caused by the solutions that contain local anesthetics associated with vasoconstrictors include alteration in blood pressure,<sup>[5]</sup> dysrhythmia, systemic alterations, and hypocalcemia. These changes are regulated by the control of the sympathetic and parasympathetic activities, and both the stress and pain can modify such responses.<sup>[6]</sup>

When these physiological events induced by vasoconstrictors exceed the normal average, the morbidity and mortality risk rates increase considerably. This fact is of particular relevance for cardiac patients despite the literature accept the adrenaline as safe; there is a controversy in relation to such patients.<sup>[7]</sup>

A study conducted by Neves *et al.*<sup>[8]</sup> asserts that there is a proportional increase in systolic and diastolic blood pressure in relation to the dose received of anesthetic solution. Such increase in systemic blood pressure occurred regardless of the presence or absence of vasoconstrictor in the anesthetic solution, and it should be indicated for the dental procedure act, in general, as responsible for the result.

A study conducted by Elad *et al.*<sup>[6]</sup> mentions that the risk of ischemia during dental treatment after the application of lidocaine or articaine is not clear. Nevertheless, the dentist must be aware that ischemic changes during the application of anesthetics are a risk for the patient's life especially in extensive surgeries; it is recommended in this way the use of techniques for the stress reduction.

The term "dental anxiety" has been reported in the literature as a shift on the emotions that go from apprehension, extreme anxiety, or dental phobia.<sup>[9]</sup> The anxiety, fear, and pain have an important role at complications in the dental treatment. Women usually have higher anxiety levels than men. All dental procedures can cause psychological changes. However, the anxiety related to anesthetic injection is probably one of the biggest.<sup>[10]</sup>

The administration of a vasoconstrictor associated to local anesthetics has been blamed for a rise of exogenous amines that, when added to the endogenous catecholamines released because of anxiety due to the dental procedures, can determine secondary effects or induce somatic changes that occurs by activation of adrenal - hypothalamus resulting in increased secretion of cortisol released in up to 10-40 times above what is released in basal levels.<sup>[2,3,11]</sup>

The role of catecholamines of the local anesthetics and of endogenous ones from adrenal medulla released during the anxiety and fear can be responsible for moderate to severe cardiovascular changes, with this, the general scenario of health can get compromised.<sup>[2,3]</sup>

The physiological response caused by stress of anesthetic injection is generally characterized by breath acceleration,

increase of the cardiac frequency, blood pressure elevation, followed by a deceleration of the cardiac frequency, and fall in blood pressure.<sup>[9]</sup>

Somatic changes induced by anxiety may occur due to activation of the hypothalamic-pituitary gland - adrenal gland axis that can result in an increase in cortisol secretion.<sup>[12]</sup>

The inadequate analgesia in dental procedures is associated to the increase of pain in the dental procedure, which in turn results in the production of endogenous epinephrine that brings cardiovascular alterations due to the increase of the pain and subsequently of stress.<sup>[13]</sup>

Based on scientific literature, this article aims to identify the knowledge of the doctors of Sao Luis do Maranhao on the use of local anesthetics with vasoconstrictors in patients with cardiopathy.

## Methods

100 professionals from diverse specialties, recorded at the Regional Council of Medicine of the State of Maranhao were selected for is research. The research was approved by the Permanent Ethics Committee of CEUMA University with number 851.110.

The criterion for inclusion in the research corresponded to professionals who have registration and authorization for the legal exercise of the profession and residing in the state of Maranhao. As exclusion criteria, those who do not possess the criteria to exercise this profession legally have become unfit to participate therein.

The individuals were evaluated always by the same examiner through a questionnaire, validated by professionals of the area, which presents closed questions in relation to the use of local anesthetic solutions with vasoconstrictors and methods for the control of anxiety [Table 1].

The data collected were organized in an Excel spreadsheet (Microsoft Office, 2007 version) and then a statistical analysis was performed of the same. The data were analyzed using the statistical program IBM SPSS statistics 20 (version 2011). Subsequently, to evaluate the association of the working area and the time of service of the doctor in the other variables the non-parametric test of Chi-square of independence was used. In all tests, the significance level ( $\alpha$ ) was of 5%, i.e. it was considered significant when  $P < 0.05$ .

## Results

Of the 100 professionals who participated in this research, 52% belonged to the medical clinic, 16% to the cardiology field, 7% of the intensive medicine care area, and 25% correspond to other expertises.

Regarding the time of professional exercise, 29% of the addressed professionals had between 1 and 5 years, 16% are in 6-10 years, 16% had from 11 to 15 years of professional exercise, and 39% of them had graduated more than 16 years ago.

**Table 1:** The questionnaire applied in this research

- 
1. What is your field area?
    - a. Medical clinic
    - b. Cardiology
    - c. Intensive medicine
    - d. Other which? \_\_\_\_\_
  2. What is your professional exercise time?
    - a. 1-5 years
    - b. 6-10 years
    - c. 11-15 years
    - d. 16 or more years
  3. How often are you required to answer an opinion from dental surgeons regarding the use of anesthetics and vasoconstrictors in dental procedures?
    - a. Frequently (more than 20 times in the year)
    - b. Sometimes (between 10 and 20 times in the year)
    - c. Rarely (<10 times in the year)
    - d. Never
  4. In your opinion, which is the anesthetic of choice for hypertensive patients?
    - a. Lidocaine
    - b. Prilocaine
    - c. Ropivacaine
    - d. Bupivacaine
  5. When prompted, do you guide the dental surgeon to use anesthetics associated to vasoconstrictors?
    - a. Yes
    - b. No
  6. Which is the quantity of vasoconstrictor you would indicate to hypertensive compensated degree I patients per kg/weight that would be submitted to dental procedures?
    - a. 0.04 mg/day
    - b. 0.4 mg/day
    - c. 0.004 mg/day
    - d. 4 mg/day
  7. What is the concentration of the anesthetic with vasoconstrictor you recommend for hypertensive compensated degree I patients that would be submitted to dental procedures?
    - a. 1:1000
    - b. 1:10,000
    - c. 1:100,000
    - d. 1:1,000,000
  8. What is the type of the anesthetic with vasoconstrictor you recommend for hypertensive compensated degree I patients that would be submitted to dental procedures?
    - a. Epinephrine
    - b. Noradrenaline
    - c. Levonordefrin
    - d. Phenylephrine
  9. In your opinion, can stress and anxiety caused by dental procedures interfere in the levels of endogenous adrenaline of the patient?
    - a. Yes
    - b. No
- 

*Contd...*

**Table 1: Contd...**

- 
10. In the event of a positive response to the previous question, would you indicate the use of anxiolytics for hypertensive patients who will undergo dental procedures?
    - a. Yes
    - b. No
  11. In the event of a positive response to the previous question, what would be your anxiolytic of choice?
    - a. Diazepam
    - b. Lorazepam
    - c. Alprazolam
    - d. Midazolam
    - e. Triazolam
  12. With a good control of anxiety, in your opinion, do you believe that local anesthetics with vasoconstrictors would interfere with blood pressure in hypertensive individuals?
    - a. Yes
    - b. No
- 

In relation to the frequency with which a physician was asked to answer an opinion ensued by dental surgeons regarding the use of local anesthetics with vasoconstrictors in dental procedures in patients with heart disease, 12% of the physicians reported that such fact often occurred, 8% said that sometimes, 30% rarely, and 50% that had never been addressed about the theme.

About the best anesthetic for the use in hypertensive patients during dental procedures, 81% of the physicians reported being lidocaine anesthetic the solution of choice, 7% prilocaine, 1% the ropivacaine, and 11% the bupivacaine.

When the professionals were asked about the guidelines of the use of anesthetic solutions containing vasoconstrictors, 61% stated that they indicate the use of vasopressors in patients with heart disease, while 39% said they did not do such indication when asked for an opinion from dental surgeons.

On the quantity of vasoconstrictor that should be used in patients with heart diseases, 38% indicated 0.04 mg/day.

On the concentration of the vasoconstrictor in anesthetic solutions for cardiac patients, 50% of the physicians reported being 1:100,000 the most indicated, 19% 1:10,000, 14% 1:1000, and 13% 1:1,000,000.

Regarding the vasoconstrictor indicated for patients with cardiopathy, 59% of the evaluated physicians indicated the epinephrine as the substance of choice for patients with cardiopathies. It was still questioned in this research if the stress and anxiety caused by dental procedures could interfere in the levels of endogenous adrenaline of cardiac patients where 97% reported that yes and 3% reported that not according to the data presented in Graph 1. Still in the present study, 77% of the physicians said that they indicate the use of anxiolytics for the control of anxiety during dental treatment and 23% do no such thing for this case.

Regarding the anxiolytic of choice for dental procedures, 26% of the covered professionals said to indicate diazepam,

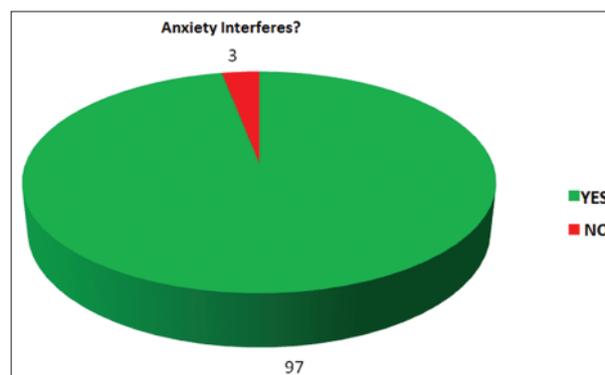
**Table 2:** Frequency distribution of the variables studied

Variables	n (%)
Field	
Medical clinic	52 (52.0)
Cardiology	16 (16.0)
Intensive medicine	7 (7.0)
Other	25 (25.0)
Prof. exercise time	
1-5	29 (29.0)
6-10	16 (16.0)
11-15	16 (16.0)
16 or more	39 (39.0)
Frequency that answers to dental surgeon opinion	
Frequently (more than 20× in the year)	12 (12.0)
Sometimes (10 and 20× in the year)	8 (8.0)
Rarely (<10× in the year)	30 (30.0)
Never	50 (50.0)
Anesthetic for hypertensive patients	
Lidocaine	81 (81.0)
Prilocaine	7 (7.0)
Ropivacaine	1 (1.0)
Bupivacaine	11 (11.0)
Ask the dentist to use vasoconstrictor	
Yes	61 (61.0)
No	39 (39.0)
Quantity kg/weight	
None	4 (4.0)
0.04 mg/day	38 (38.0)
0.4 mg/day	21 (21.0)
0.004 mg/day	26 (26.0)
4 mg/day	11 (11.0)
Total	100 (100)
Concentration of the anesthetic	
None	4 (4.0)
1:1000	14 (14.0)
1:10,000	19 (19.0)
1:100,000	50 (50.0)
1:1,000,000	13 (13.0)
Type of vasoconstrictor	
None	4 (4.0)
Epinephrine	59 (59.0)
Noradrenaline	23 (23.0)
Levonordefrin	7 (7.0)
Phenylephrine	7 (7.0)

Contd...

**Table 2: Contd...**

Does anxiety interfere?	
Yes	97 (97.0)
No	3 (3.0)
Has use of anxiolytic?	
Yes	77 (77.0)
No	23 (23.0)
Anxiolytic	
None	23 (23.0)
Diazepam	26 (26.0)
Lorazepam	22 (22.0)
Alprazolam	12 (12.0)
Midazolam	17 (17.0)
With controlled anxiety, vasoconstrictors interfere in the AR	
Yes	29 (29.0)
No	71 (71.0)
Total	100 (100)

**Graph 1: ???**

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while 22% lorazepam, 17% midazolam, and 12% the alprazolam [Table 2].

As can be observed in Table 3, the working area presented a significant association ( $P < 0.05$ ) with the types of anesthetics for hypertensive, which verifies that the lidocaine was the most indicated anesthetic mainly by the intensivist physician (100%), while the doctors with other specializations indicated other anesthetics such as prilocaine (20%), ropivacaine (4%), and bupivacaine (12%).

There is a significant association ( $P < 0.05$ ) of medical specialties with the orientation or not to the dentist to use vasoconstrictors. It can be verified that the general practitioners (75%) and the cardiologists (81.2%) are the ones who most guide dentists to use the vasoconstrictors while intensivists (28.6%) and of other specialties (28%) guideless.

As can be observed in Table 4, the variables frequency of responding to the opinions, anesthetics for hypertensive

**Table 3:** Association of other variables with the physician's field of activity

Variable	Field								P
	Medical clinic	%	Cardiology	%	Intensive medicine	%	Other	%	
Frequency that answers to dental surgeon opinion									
Frequently (more than 20× in the year)	3	5.8	5	31.3	1	14.3	3	12.0	0.130
Sometimes (10 and 20× in the year)	4	7.7	2	12.5	1	14.3	1	4.0	
Rarely (<10× in the year)	20	38.5	4	25.0	2	28.6	4	16.0	
Never	25	48.1	5	31.3	3	42.9	17	68.0	
Anesthetic for hypertensive patients									
Lidocaine	46	88.5	12	75.0	7	100.0	16	64.0	0.046
Prilocaine	2	3.8	0	0.0	0	0.0	5	20.0	
Ropivacaine	0	0.0	0	0.0	0	0.0	1	4.0	
Bupivacaine	4	7.7	4	25.0	0	0.0	3	12.0	
Ask the dentist to use vasoconstrictor									
Yes	39	75.0	13	81.2	2	28.6	7	28.0	0.000
No	13	25.0	3	18.8	5	71.4	18	72.0	
Quantity kg/weight									
None	3	5.8	0	0.0	0	0.0	1	4.0	0.127
0.04 mg/day	17	32.7	10	62.5	3	42.9	8	32.0	
0.4 mg/day	10	19.2	5	31.3	1	14.3	5	20.0	
0.004 mg/day	12	23.1	1	6.3	3	42.9	10	40.0	
4 mg/day	10	19.2	0	0.0	0	0.0	1	4.0	
Type of vasoconstrictor									
None	3	5.8	0	0.0	0	0.0	1	4.0	0.165
Epinephrine	23	44.2	12	75.0	4	57.1	20	80.0	
Noradrenaline	14	26.9	3	18.8	3	42.9	3	12.0	
Levonordefrin	5	9.6	1	6.3	0	0.0	1	4.0	
Phenylephrine	7	13.5	0	0.0	0	0.0	0	0.0	
Total	52	100	16	100	7	100	25	100	

patients, guidance for dentists, the amount of anesthetics and the type of vasoconstrictor had a statistically significant association ( $P < 0.05$ ) with the service time of the physician.

## Discussion

There are no reports in the literature about a consensus, among physicians, on the use of vasoconstrictors in local anesthetics for the dental treatment.

In the face of the increase in the prevalence of cardiovascular diseases in the population, it is essential that the surgeon dentist and physician in a joint, cohesive, and integral fashion possess the correct knowledge to develop their activities with the use of the best and most accurate techniques aiming the well-being of the patient.<sup>[14]</sup>

This study showed that 61% of the physicians guide dentists to use vasoconstrictors. This percentage meets the present literature studies when it comes to promoting beneficial effects as regards to the control of pain.<sup>[15]</sup>

Entering in confrontation with 39% of the doctors that contraindicated the use of vasoconstrictors, Rettore<sup>[16]</sup> considers contraindicated, in dentistry, only in very specific cases, on malignant, untreated hypertension or not controlled patient.

In the present work, 81% of the physicians pointed to lidocaine as the best anesthetic to use in patients with heart disease, and 59% indicated epinephrine as ideal vasopressor, while for Meehan *et al.*<sup>[17]</sup> in line with Serra and Muniz<sup>[15]</sup> and Neder *et al.*,<sup>[18]</sup> the prilocaine 3% with felypressin at 0.03 UI/ml is the best solution for this type of patients, possessing lower vasoconstrictor action mechanism than epinephrine and norepinephrine, but the duration of effect is similar. Without act on adrenergic receptors, it does not act on the myocardium, not causing arrhythmic reactions,<sup>[19]</sup> and not presenting another significant cardiovascular response.<sup>[20]</sup>

The New York Heart Association, in 1955, defined 0.2 mg as the maximum dose of adrenaline per session treatment for

**Table 4:** Association of other variables with the physician's service time

Variable	Professional exercise time								P
	1-5	%	6-10	%	11-15	%	16 or more	%	
Frequency that answers to dental surgeon opinion									
Frequently (more than 20× in the year)	2	6.9	1	6.3	2	12.5	7	17.9	0.027
Sometimes (10 and 20× in the year)	1	3.4	2	12.5	3	18.8	2	5.1	
Rarely (<10× in the year)	3	10.3	7	43.8	6	37.5	14	35.9	
Never	23	79.3	6	37.5	5	31.3	16	41.0	
Anesthetic for hypertensive patients									
Lidocaine	19	65.5	12	75.0	16	100.0	34	87.2	0.009
Prilocaine	2	6.9	0	0.0	0	0.0	5	12.8	
Ropivacaine	1	3.4	0	0.0	0	0.0	0	0.0	
Bupivacaine	7	24.1	4	25.0	0	0.0	0	0.0	
Ask the dentist to use vasoconstrictor									
Yes	19	65.5	11	68.8	15	93.8	16	41.0	0.002
No	10	34.5	5	31.3	1	6.3	23	59.0	
Quantity kg/weight									
None	0	0.0	0	0.0	0	0.0	4	10.3	0.001
0.04 mg/day	8	27.6	5	31.3	11	68.8	14	35.9	
0.4 mg/day	9	31.0	3	18.8	0	0.0	9	23.1	
0.004 mg/day	4	13.8	8	50.0	5	31.3	9	23.1	
4 mg/day	8	27.6	0	0.0	0	0.0	3	7.7	
Type of vasoconstrictor									
None	0	0.0	0	0.0	0	0.0	4	10.3	0.000
Epinephrine	14	48.3	6	37.5	8	50.0	31	79.5	
Noradrenaline	11	37.9	8	50.0	1	6.3	3	7.7	
Levonordefrin	1	3.4	1	6.3	5	31.3	0	0.0	
Phenylephrine	3	10.3	1	6.3	2	12.5	1	2.6	
Total	29	100.0	16	100.0	16	100.0	39	100.0	

cardiac.<sup>[21]</sup> Such definition, approved by the Association of Cardiology altogether with the Council of North American Dental Treatment 1964, stated that vasoconstrictors were not contraindicated in these types of patients, they are recommended since it is executed a proper anesthetic technique and with the lowest possible anesthetic dose. However, the use of these substances should be avoided in patients classified as high risk.<sup>[22]</sup>

In consensus to this study, where 38% of physicians recommend a daily quantity of 0.04 mg of vasopressor, Malamed<sup>[3]</sup> recommends that maximum dose of adrenaline, per session, in a healthy patient is of 0.2 mg, and for patients with cardiopathies, the maximum dose is 0.04 mg, corresponding to four vials of adrenaline 1:200,000 per session, opposing to the definition of the American Heart Association.<sup>[21]</sup>

Ferreira<sup>[1]</sup> stipulated that the recommended dosage in cardiac patients per session of treatment must be of 3-6 vials dependent on concentrations present in the solutions employed 1:100,000 or 1:200,000. Now, Mello<sup>[23]</sup> and Neves *et al.*<sup>[8]</sup> also

do not contraindicate the use of vasoconstrictors, and can be used both the felypressin or adrenaline (1:100,000 or in smaller concentration) in lower doses, which is in agreement with this study, with employment of proper technique performing always foresaw intakes and slow injections, being ideal not to exceed two vials per session.

Regarding to the concentration of 1:100,000, considered by 50% of the evaluated dentists in this study as their default use, this is due to the fact that physicians do not have an intimate knowledge of dental practice and by thinking of the adrenaline in terms of extremely high doses that are used in emergency medicine and not in much more diluted doses used for the local anesthetic technique in dentistry.<sup>[14]</sup>

Furthermore, valuing the decrease in the level of stress to achieve a physical and psychological comfort of the patient<sup>[6,9]</sup> did 97% of the evaluated state that anxiety interfere in blood pressure and 77% recommended the use of anxiolytics. Rates proven by Willemann<sup>[14]</sup> where it is said that elevations in blood

pressure should be credited yet to the environment and dental procedure.

Still on the use of anxiolytics, 26% of the respondents indicated diazepam as the drug of choice and only 17% have recommended midazolam. As for benzodiazepines, it is known that diazepam presents greater duration of effect while the others (lorazepam, alprazolam) are of intermediary action.<sup>[2,24]</sup> Midazolam stands out, another anxiolytic also of this group, of shorter duration, but that also causing amnesia and presenting hypnotic action (induction of physiological sleep); it still has the faster beginning of the action and lower half-life when compared to the other drugs of the same family.<sup>[2]</sup>

Thus, when evaluated their properties, midazolam, becomes the ideal drug for dentistry employment to promote the anxiety control. It is recommended to use a single dose of the selected benzodiazepine, from 30 to 45 min before the procedure.<sup>[24]</sup>

## Conclusion

In agreement with the data obtained in this research and the researched literature, physician addressed in the study demonstrate to know that vasoconstrictors associated to local anesthetics should be used in dental procedures. However, they are unaware of their quantity and concentration. This result reflects the lack of scientific knowledge about the subject, emphasizing the scarce scientific literature involving the areas of obstetrics and dentistry about this content in academic training of its professionals.

## References

1. Ferreira MB. Local anesthetics. In: Wannmacher L MB Ferreira. Clinical Pharmacology For Dentists. Rio de Janeiro: Guanabara-Koogan; 1999. p. 104-16.
2. Andrade ED. Drug Therapy in Dentistry. 3<sup>rd</sup> ed. São Paulo: Artes Médicas; 2014.
3. Malamed SF. Local Anesthesia Manual. 5a ed. São Paulo: Elsevier; 2005.
4. Moore PA, Boynes SG, Hersh EV, DeRossi SS, Sollecito TP, Goodson JM, et al. The anesthetic efficacy of 4 percent articaine 1:200,000 epinephrine: Two controlled clinical trials. J Am Dent Assoc 2006;137:1572-81.
5. Cheraskin E, Prasertsuntarasai T. Use of epinephrine with local anesthesia in hypertensive patients. IV. Effect of tooth extraction on blood pressure and pulse rate. J Am Dent Assoc 1959;58:61-8.
6. Elad S, Admon D, Kedmi M, Naveh E, Benzki E, Ayalon S, et al. The cardiovascular effect of local anesthesia with articaine plus 1:200,000 adrenalin versus lidocaine plus 1:100,000 adrenalin in medically compromised cardiac patients: A prospective, randomized, double blinded study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:725-30.
7. Middlehurst RJ, Gibbs A, Walton G. Cardiovascular risk: The safety of local anesthesia, vasoconstrictors, and sedation in heart

disease. Anesth Prog 1999;46:118-23.

8. Neves RS, Neves IL, Giorgi DM, Grupi CJ, César LA, Hueb W, et al. Effects of epinephrine in local dental anesthesia in patients with coronary artery disease. Arq Bras Cardiol 2007;88:545-51.
9. Ng SK, Stouthard ME, Keung Leung W. Validation of a Chinese version of the dental anxiety inventory. Community Dent Oral Epidemiol 2005;33:107-14.
10. Malamed SF, editor. Pain and anxiety in dentistry. In: Sedation: A Guide to Patient Management. 4<sup>th</sup> ed. St. Louis: Mosby; 2003. p. 2-6.
11. Paiva LC, Cavalcanti AL. Anestésicos Local anesthetics in dentistry: A literature review. UEPG Ci Biol Saúde 2005;11:35-42.
12. Dimsdale JE. Psychological stress and cardiovascular disease. J Am Coll Cardiol 2008;51:1237-46.
13. Liao FL, Kok SH, Lee JJ, Kuo RC, Hwang CR, Yang PJ, et al. Cardiovascular influence of dental anxiety during local anesthesia for tooth extraction. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008;105:16-26.
14. Willemann A. Vasoconstritores. Rev Bras Cirur Implant 2002;9:125-9.
15. Serra MA, Muniz RB. The use of antiinflammatories nonsteroidal in the dental clinic. Goiania; 2008. Available in: <http://www.portaleducacao.com.br/odontologia/artigos/2584/o-uso-dos-anti-inflamatorios-nao-esteroides-na-clinica-odontologica>. [Last accessed on 2014 Set 15].
16. Rettore RJ. Anestesia odontológica. Jornal do CROMG, 2000. p. 15. Disponível em: [http://www.gruponitro.com.br/atendimento-a-profissionais/%23/pdfs/artigos/anestescos\\_locais/anestesia\\_odontologica.pdf](http://www.gruponitro.com.br/atendimento-a-profissionais/%23/pdfs/artigos/anestescos_locais/anestesia_odontologica.pdf). [Last accessed em 2014 Set 28].
17. Meechan JG, Parry G, Rattray DT, Thomason JM. Effects of dental local anaesthetics in cardiac transplant recipients. Br Dent J 2002;192:161-3.
18. Neder AC, Nouer DF, Renci J, Arbex ST, Garlipp Olympio F, Saliba R, et al. Citocaina 3% (high pH) with felypressin. Comparative study with other similar preparations on the market: Clinical observations in 653 patients. Rev Paul Odontol 1989;11:34-7.
19. Louro RS, Moreira LM, Miranda MS, Medeiros PJ. Comparative study of the use of prilocaine hydrochloride 3 percent felypressin 0 to 03 UI and lidocaine hydrochloride 2 percent with epinephrine 1:100,000 in hypertensive patients. Rev Bras Odontol 2001;58:228-31.
20. Yagiela JA. Local anesthetics. In: Neidle EA, Kroeger DC, Yagiela JA, editors. Pharmacology and Therapeutics For Dentists. Rio de Janeiro: Guanabara Koogan; 1991. p. 85-200.
21. Use of epinephrine in connection with procaine in dental procedures: Report of the Special Committee of the New York Heart Association. J Am Dent Assoc 1955;157:854.
22. Akutsu A, Chiba T, Takahashi H, Shimoda M, Suematsu T. American Dental Association and American Heart Association. Management of dental problems in patients with cardiovascular disease. J Am Dent Assoc 1964;68:333-42.
23. Mello HS. Considerations geriatric dentistry; Vascular and cardio-respiratory problems. In: Geriatric dentistry. São Paulo: Santos; 2005. p. 10-41; 81-93.
24. Andrade ED. Care with the use of drugs in diabetes, hypertension and heart disease. In: 15o Conclave Odontológico Internacional de Campinas. Campinas: São Paulo; 2003. p. 1678-899.

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