

## Influence of vasoconstrictors added to dental anesthetics on blood pressure and heart rate

### Influencia de los vasoconstrictores añadidos a la anestesia dental en la frecuencia cardiaca y la tensión arterial

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#### ABSTRACT

**Introduction:** vasoconstrictors are substances added to local anesthetics to lengthen their time of action, reduce their toxicity and enhance their local hemostatic effect. There is controversy about whether the use of vasoconstrictors in dental anesthetics has a negative effect on blood pressure and heart rate.

**Objective:** determine the influence of vasoconstrictors added to dental anesthetics on blood pressure and heart rate.

**Methods:** an experimental study was conducted with 120 patients divided in two groups of 60. These patients attended clinics in the Dental Academic Unit of the Autonomous University of Guerrero from July to December 2015. Group A was given just 3 % mepivacaine, whereas Group B was given mepivacaine with epinephrine at a concentration of 1:100 000. Measurements were taken of the patients' heart rate, systolic blood pressure and diastolic blood pressure at two moments: at baseline before infiltration and 5 minutes after infiltration. Statistical analysis was based on Student's t-test for independent samples.

**Results:** heart rate and systolic blood pressure did not yield any statistically significant value. Diastolic blood pressure was the only hemodynamic parameter showing a statistically significant difference ( $t= 2.3$ ;  $p= 0.02$ ).

**Conclusions:** the results obtained coincide with those reported by similar studies. At the doses recommended, epinephrine is safe for healthy patients as well as for those with controlled cardiovascular conditions.

**Keywords:** vasoconstrictors; blood pressure; heart rate.

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## RESUMEN

**Introducción:** los vasoconstrictores son sustancias que han sido añadidas a los anestésicos locales con la finalidad de aumentar su tiempo de acción, disminuir su toxicidad y aprovechar su efecto hemostático local. Existe controversia sobre si el uso de vasoconstrictores en los anestésicos dentales produce efectos negativos en la tensión arterial y la frecuencia cardiaca.

**Objetivo:** determinar la influencia de los vasoconstrictores añadidos a la anestesia dental en la frecuencia cardiaca y la tensión arterial.

**Métodos:** se realizó un estudio experimental en 120 pacientes divididos en dos grupos de 60, que acudieron a las clínicas de la Unidad Académica de Odontología de la Universidad Autónoma de Guerrero en el periodo julio-diciembre de 2015. Al grupo A se le administró mepivacaína simple al 3 %, y al grupo B se le administró mepivacaína con epinefrina a una concentración de 1:100 000. Se realizaron tomas de frecuencia cardiaca, tensión arterial sistólica y tensión arterial diastólica en dos momentos. Se realizó una toma basal de frecuencia cardiaca, tensión arterial sistólica y diastólica antes de la infiltración, y una segunda toma 5 min posteriores a la infiltración. Se realizó la prueba estadística t de Student para grupos independientes.

**Resultados:** la frecuencia cardiaca y la tensión arterial sistólica no obtuvieron significancia estadística. El único parámetro hemodinámico que tuvo una diferencia estadísticamente significativa fue la tensión arterial diastólica ( $t= 2,3$ ;  $p= 0,02$ ).

**Conclusiones:** los resultados obtenidos en esta investigación, coinciden con los reportados en otros estudios similares. La epinefrina puede ser utilizada de manera segura a las dosis recomendadas tanto en pacientes sin enfermedad cardiovascular, como en pacientes con compromiso cardiovascular en control.

**Palabras clave:** vasoconstrictores; presión arterial; frecuencia cardiaca.

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## INTRODUCTION

Vasoconstrictors are substances that are added to local anesthetics to utilize their effect on the caliber (internal diameter) of blood vessels. Adrenaline or epinephrine is the most widely used vasoconstricting agent associated with local anesthetics in dentology.<sup>1-3</sup> These substances are naturally produced in the suprarenal medulla.<sup>4</sup>

Both the heart and the vessels have abundant alpha and beta adrenoceptors. In general, beta receptors tend to be more sensitive than alpha, therefore they respond to lower doses, so low concentrations actions predominantly beta, while in rapid intravascular injection also cause intense alpha actions. Adrenaline has

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chrono and inotropic effect by activation of beta 1 receptors. It causes vasodilation of arterioles muscle area, coronary and other area of the organism for action on b2 receptors; as a result, increases blood flow and reduces the diastolic pressure, by reflex mechanism, causing tachycardia. This effect is dominant at low doses of adrenaline. But high doses (above 0.1 mg/kg/min IV) activated receptors alpha 1 and alpha 2 arterioles of the skin, mucous membranes and the splanchnic area, including the renal circulation ; consequently a rise in blood pressure occurs,, preferably diastolic.<sup>5</sup>

This substances reduce blood vessel caliber in the mucosal membrane and the skin due to its effect on alpha adrenergic receptors, which counteracts the vasodilating effects of local anesthetics, while affecting beta 1 and beta 2 receptors by increasing arterial tension and vasodilation in muscles and internal organs, respectively.<sup>1,6</sup>

The advantages of administering an anesthetic combined with a vasoconstrictor are the following:

It prolongs the anesthetic effect by slowing down the blood flow in the infiltrated zone, increasing the block quality.

It slows down the absorption of the local anesthetic, reducing its systemic toxicity.

It reduces secondary blood flow by diminishing the vascular caliber, which promotes hemostasis, allowing for better visibility and reducing excessive bleeding during invasive surgical procedures.<sup>2-4,7,8</sup>

It is a widely held belief among doctors, dentists and even patients that epinephrine is not recommended for heart patients due to the possibility of increasing hart rate (HR) and arterial tension (AT). Nevertheless, it is well known that the amount of epinephrine contained in dental anesthesia cartridges (0.018 mg of epinephrine in 1.8ml cartridge at a concentration of 1:100 000) does not cause major changes to said factors. 1 to 3 cartridges of anesthesia with epinephrine at 1:100 000 (0.018 at 0.054 mg of epinephrine) can be safely administered to patients with cardiovascular disease.<sup>4</sup>

Other researchers agree with these findings and say that epinephrine dosages in cardiopathic patients should not exceed 0.036 mg of epinephrine contained in two dental anesthesia cartridges at a 1:100 000 concentration. If a greater dosage of anesthesia is required, one might consider an additional infiltration using pure anesthetic. The use of vasoconstrictors is justifiable in cardiopathic patients,<sup>9</sup> provided that extra precautions are taken not to deliver the anesthetic by way of intravascular injection.<sup>3</sup>

While there has been some debate regarding the procedure, previous literature denotes that, vasoconstrictors can be administered in patients with hypertension.<sup>10</sup>

Statistically significant changes in systolic arterial tension (SAT), diastolic arterial tension (DAT), and HR have been observed in patients with hypertension subjected to exodontic procedures using Lidocaine at 2 % with a 1:80 000 concentration of epinephrine, thereby emphasizing the importance of avoiding intravascular injection in such patients. <sup>11</sup>

In a meta analysis and after analyzing 6 studies on the subject, the use of different vasoconstrictors in dental anesthesia has been found to be justified even in cardiopathic patients and in patients with hypertension, provided that such use is controlled.<sup>6</sup> It has been demonstrated that other vasoconstrictors used in combination with local anesthetics, such as Felypressin, cause significant changes in DAT rates.<sup>12</sup>

Administering vasoconstrictors in combination with anesthetic solutions in odontological procedures allows for greater control over anxiety and pain without significantly impacting AT levels in any way,<sup>13</sup> and the quantities of adrenaline released endogenically are greater than those which are administered in dental anesthetics.<sup>14</sup>

Studies on healthy patients conclude that the effects of adrenaline associated with local anesthetic do not cause significant increase in factors such as AT and HR; rather, a potential increase in these factors is only due to the stress the patient is experiencing during the odontological procedure.<sup>6</sup>

When 2 % Lidocaine with a 1:100 000 concentration of epinephrine was administered to patients free of major systemic illness, significant increases in HR were identified between the first pre-infiltration measurement and the second, post-infiltration measurement, but no significant changes related to SAT, DAT or breathing rate were observed.<sup>7</sup>

When the effects of administering pure Lidocaine and Mepivacaine were compared with those same substances combined with epinephrine in healthy patients, no significant changes to experimental factors observed such as HR, SAT, DAT, and other electrocardiographic levels were detected.<sup>15</sup>

Following the infiltration of local anesthetic with varying concentrations of adrenaline in healthy patients, hemodynamic changes in HR and AT were observed but without exhibiting any significant differences between the three levels of concentration administered (1:200 000, 1:100 000, 1:80 000), but less effects were observed on AT at a concentration of 1:200 000 than observed in the 1:100 00 and 1: 80 000 levels, indicating that the lowest concentration used in the study (1:200 000) is the safest level for use on healthy patients.<sup>3</sup>

Due to the release of secondary endogenic catecholamines caused by stress on the patient during the odontological procedure, adverse cardiovascular effects tend to be greater than the dose of adrenaline in the anesthetic solution actually used. The administration of pure anesthetic fails to deliver sufficient anesthesia and/or produce the desired hemostasis, which can cause hemorrhage and transoperative pain, resulting in the subsequent release of a greater quantity of endogenic catecholamines than those present in the therapeutically administered local anesthetic solution, which can be reflected in the hemodynamic factors under study.<sup>10,15</sup>

The increase seen in hemodynamic factors such as HR, SAT, DAT is caused more by the anxiety patients experience during dental procedures subsequently leading to a release of endogenic catecholamines than the by the effect of vasoconstrictors administered in combination with local anesthetic.<sup>10,16</sup> Adequately controlling anxiety and pain, scheduling short appointments in the morning, using topical anesthesia before infiltration with the local anesthetic, and not showing the needle to the patient beforehand are some ways to reduce the release of such endogenic adrenaline and its resulting impact on hemodynamic factors such as DAT, SAT, and HR.

The objective of this study is to determine whether administering epinephrine has significant effects on the AT and HR during dental procedures.

## METHODS

An experimental study was carried out before and after under complete control of each patient using a convenience sample of 120 patients. The universe were patients who attended the clinics of the Academic Unit of Dentistry of the Autonomous University of Guerrero in the period July-December 2015 who were undergoing periodontal treatments, dental extraction, mouth surgeries, and dental operative techniques. The sample was divided into two groups of 60 patients.

The variables studied were age, gender, SAT, DAT and HR. Patients were assigned to the groups based on the type of procedure they were about to undergo. Group A comprised of patients undergoing non-surgical treatments (operative techniques and prosthesis), while group B was composed of patients undergoing invasive surgical procedures (periodontal and mouth surgery, as well as dental extraction procedures) to prevent excessive bleeding in the absence of the vasoconstrictor.

Pure Mepivacaine at 3 % was administered to Group A, while Group B was given Mepivacaine combined with epinephrine at a 1:100 000 concentration. Group A was infiltrated with a dental cartridge containing 36 mg of Mepivacaine, while Group B was giving 36 mg of Mepivacaine combined with 0.018 mg of epinephrine.

The fact that Group B knew that they were going to be exposed to invasive procedures may have skewed the results of the study, as the resulting stress may have caused an elevation of the experimental factors.

A supraperiostic infiltration technique was used in procedures carried out on the upper maxillary, and a troncular technique was used during procedures on the lower jaw. Intravascular injection was not done in this study.

Two measurements of the HR, SAT, and DAT were taken with a digital Microlife BP A100 ONBO ELECTRONIC (SHENZHEN) CO., LTD. baumanometer. The first measurement was taken 30 min after the patient arrived to the clinic, to eliminate the influence of fatigue on the experimental factors resulting from the patient having just climbed stairs or traversed other distances within the institutional facility on their way to the clinic. The second measurement was taken 5 min after the first one, before initiating the procedure and following infiltration.

In terms of the ethical aspects not new medications or new techniques were used in this study. The protocol was approved by the Bioethics Committee at the Academic Unit of Dentistry at the Autonomous University of Guerrero. Informed consent was obtained from each participant in the trial, as a prerequisite for participating in the trial, in accordance with the ethical principles set forth in the Helsinki Declaration (2008 version).

Sociodemographic variables such as age and gender were analyzed using CIETMap software. Student t statistical analysis for independent groups was used to analyze the differences between the two groups before after infiltration. The latter analysis was run using statistical software GraphPad QuickCalcs (GraphPad Software, Inc 20014 S.D. CAL USA). A value p less than 0.05 was consider statistically significant. t and p values were reported.

## RESULTS

Of the 120 patients included in the study, 60 were men and 60 were women, with an average age of 40.5 years within a range of 14 to 77 years of age (SD 16). Group A (pure Mepivacaine) were represented with an average age of 38.6 years within a range of 20 to 74 (SD 14.4), while Group B (Mepivacaine with epinephrine) was represented by an average age of 42.4 years within a range of 14 to 77 (SD 17.4).

Increased levels were recorded in all measured variables after infiltration, with the exception of DAT, which exhibited no change in both groups ([table 1](#)).

**Table 1.** List of the experimental factors examined for Groups A and B before and after infiltration

Group	HR bi <sup>(1)</sup>	HR ai <sup>(2)</sup>	Dif <sup>(3)</sup>	SAT bi <sup>(4)</sup>	SAT ai <sup>(5)</sup>	Dif <sup>(3)</sup>	DAT bi <sup>(6)</sup>	DAT ai <sup>(7)</sup>	Dif <sup>(3)</sup>
A	73.7	75.5	1.82	119.7	120.7	1	75.4	75.4	0
B	76.8	77	0.27	117.1	122.7	5.6	72	77.6	5.6

<sup>(1)</sup> Heart rate before infiltration; <sup>(2)</sup> heart rate after infiltration; <sup>(3)</sup> difference; <sup>(4)</sup> systolic arterial tension before infiltration; <sup>(5)</sup> systolic arterial tension after infiltration; <sup>(6)</sup> diastolic arterial tension before infiltration; <sup>(7)</sup> diastolic arterial tension after infiltration.

Increase in HR for Group A was greater than for Group B. Nevertheless, these differences did not carry any statistical significance (t= 0.73; p= 0.46) ([table 2](#)).

**Table 2.** Changes in average HR between the study groups, taking into consideration that the changes were not statistically significant

HR <sup>(1)</sup>	Average	SD <sup>(2)</sup>	T <sup>(3)</sup>	p <sup>(4)</sup>
Group A	1.82	9.63	0.73	0.46
Group B	0.27	13.13		

<sup>(1)</sup> Heart rate; <sup>(2)</sup> standard deviation; <sup>(3)</sup> value T.

In respect to SAT, an increased level was more notable in Group B than in Group A. However, as in the the case with HR, the slight change in values did not carry any statistical significance (t= 1.38; p= 0.16) ([table 3](#)).

**Table 3.** Differences between average SAT between both study groups, taking into consideration that the changes reported were not statistically significant

SAT <sup>(1)</sup>	Average	SD <sup>(2)</sup>	T <sup>(3)</sup>	p <sup>(4)</sup>
Group A	0.95	14.09	1.38	0.16
Group B	5.58	21.67		

<sup>(1)</sup> Systolic arterial tension; <sup>(2)</sup> standard deviation; <sup>(3)</sup> value T.; <sup>(4)</sup> value p.

In respect to DAT, Group B again registered greater changes than Group A, but in this case, the changes reported were in fact statistically significant (t= 2.3; p= 0.02) ([table 4](#)).

**Table 4.** Observed differences between the averages of both groups for DAT were reported statistically significant

DAT (1)	Average	SD (2)	T (3)	p (4)
Group A	0	12.21	2.3	0.02
Group B	5.67	14.53		

(1) Diastolic arterial tension; (2) standard deviation; (3) value T; (4) value p.

## DISCUSSION

Epinephrine is the vasoconstrictor most widely used as a supplement to local anesthetics in general medicine as well as in odontology. It is typically added to Lidocaine or Mepivacaine at 2 % for its vasoconstricting benefits, which slow down bleeding, prolong the anesthetic's effects and increase its overall effectiveness by slowing down the absorption of the anesthesia, thereby reducing its toxicity and transoperative bleeding.

In respect to variations in HR, our findings coincide with those documented by Rodríguez Alfaro et al. whose reports, based on comparative studies using pure Lidocaine and pure Mepivacaine versus dosages administered using a combination of same local anesthetics with a vasoconstrictor, confirm that vasoconstrictors did not significantly influence HR. Contrary results were observed by Núñez et al. who reported a significant increase in HR after infiltration with Lidocaine at 2 % combined with epinephrine at a concentration of 1:100 000.<sup>7</sup>

Findings related to variations of SAT levels coincide with previous study results that reported variations in this factor, none of which reached statistical significance.<sup>7,15,17</sup>

Our results showed that vasoconstrictors exert a positive influence on DAT, as changes in this factor reached statistical significance. This result differs from those found by other similar studies that in contrast reported that DAT levels had no statistical significance.<sup>17</sup>

In respect to Abu Mustafa's findings, our results coincide in terms of variations in HR and SAT levels, but differ in terms of DAT levels. In contrast to Mustafa's results, we did in fact find statistically significant increased levels in this hemodynamic factor.<sup>3</sup> Nevertheless, we consider the use of anesthetics with vasoconstrictors to be safe, as it provides advantages over using pure anesthetics, provided that safe dosages are administered on healthy patients, and controlled dosages on cardiopathic patients.

Some elevated levels of the experimental factors observed in patients about to undergo surgical procedures compared to patients who were about to receive other treatments were considered of little value, as any patient who is aware that any kind of odontological treatment is imminent, surgical or not, experiences a certain degree of stress.

Administering epinephrine in dental anesthesia cartridges does not produce significant changes to HR and SAT levels, even though our study did show significant changes to DAT levels. Nevertheless, we do not consider it necessary to use pure anesthetics on healthy patients. Pure anesthetics can be used on cardiopathic patients, but as long as the patient is controlled, they can also be administered safe doses of local anesthetics with vasoconstrictors. The advantages of using vasoconstrictors in these cases still outweigh the disadvantages.

Epinephrine can be used safely at recommended doses on both healthy patients and on those with cardiovascular compromise. According to American Heart Association the maximum dose of epinephrine in local anaesthesia for a healthy subject is 0.2 mg, though this can be lowered to 0.04 mg if patient has severe cardiovascular disease. Therefore, if a dental anesthetic cartridge with epinephrine at a concentration of 1: 100 000 contains 0.018 mg of adrenaline, the maximum dose in healthy patients that is 0.2 mg, it is contained in just over 11 cartridges 1.8 mL, while the dose in patients with cardiovascular disease is 0.04 decreases to 2.2 cartridges.<sup>18</sup>

We recommend conducting similar studies on a larger scale and on patients with cardiovascular disease to examine the effects of the pharmaceuticals on such patients, similar to studies done previous by other researchers.

## CONCLUSION

The results obtained in this research coincide with results reported in other similar studies. Epinephrine can be used safely at recommended doses on both healthy patients and on those with cardiovascular compromise under control, since administering epinephrine in dental anesthesia cartridges does not produce significant changes to HR and SAT levels.

## Conflict of interest

No conflict of interest exists among the participants in the study, nor with any national or international institute.

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