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ALTERATIONS IN MONITORED VITAL CONSTANTS INDUCED BY VARIOUS LOCAL ANESTHETICS IN COMBINATION WITH DIFFERENT VASOCONSTRICTORS IN THE SURGICAL REMOVAL OF LOWER THIRD MOLARS

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KEY WORDS: Local anesthetics, vasoconstrictors, hemodynamic variables, blood pressure, heart rate, oxygen saturation.
MOTS CLES: Anesthesiques locaux, vasoconstricteurs, variables hemodynamiques, fréquence cardiaque, préssion arteriele, saturation d'oxygene.

ABSTRACT

The purpose of this study was to observe the hemodynamic changes during surgical extraction of lower third molars induced by three local anesthetics solutions associated with different vasoconstrictors.

A double-blind observational and longitudinal study was made of 45 healthy adult volunteers subjected to surgical removal of an impacted lower third molar under local anesthesia. Three groups were established (n = 15) according to the anesthetic solution and associated vasoconstrictor administered (4% articaine + epinephrine 1:200,000; 3% mepivacaine without vasoconstrictor; and 3% prilocaine + felypressin 1:1,850,000). Heart rate, systolic and diastolic pressure, and oxygen saturation were recorded at different times before, during and at the end of surgery, along with the type and amount of anesthetic solution administered.

The study variables were found to be more stable with articaine + epinephrine 1:200,000, although the three studied solutions caused no significant hemodynamic changes with respect to the basal values when administered in healthy patients subjected to surgical removal of a lower third molar.

RESUME

Altérations des constantes vitales monitorizéés, dues aux différents anesthesiques locaux associés à plusiers vasoconstricteurs pendant l'extraction chirurgicale des dents de sagesse inferieurs inclues.

Le but de cette étude consistait à observer les changements de variables hemodynamiques durant l'extraction chirurgicale des dents de sagesse inferieures inclues, en utilisant trois différents types de solutions anesthesiques locales associées a plusieurs vasoconstricteurs.

Nous allons réaliser une étude d'observation et longitudinale à double aveugle à 45 sujets adultes volontaires et sains, chez qui on va réalizer une extraction chirurgicale d'une dent de sagesse impacté avec anésthesie locale. Les patients sont repartis en 3 groupes, de 15 patients chacun, selon l'anésthesie utilisée (articaïne 4% avec epinephrine 1:200.000; mepivacaïne 3% sans vasoconstricteur, et prilocaïne avec felipressine 1:1.850.000). Nous registrons la fréquence cardiaque, la préssion arteriele systolique, la préssion arterial diastolique et la saturation d'oxygene en différents moments: avant, pendant et à la fin de l'intervention chirurgicale, pour chacun des groupes ainsi que la quantité de solution anésthesique utilisée.

Les variables plus stables ont apparu dans le groupe qui a été anesthésié avec articaïne 4% plus epinephrine 1:200.000, bien qu'aucune des trois solutions anesthésiques ne produisaient des changements significatifs au niveau des variables hemodynamiques étudiées chez les patients qui ont été sujets à des extractions chirurgicales des dents de sagesse inclues.

INTRODUCTION

Local anesthetics associated to vasoconstrictors are useful in dental practice, for they offer prolonged and deep pain control, less bleeding in the surgical zone, and delayed anesthetic absorption by the bloodstream-thereby reducing the risk of toxicity and overdose (Malamed S.F. et al. 1986; Holroyd S.V. et al. 1988; Cawson R.A. et al. 1992; Romero M.M. 1992; De Andrés-Trelles F. et al. 1993; Planas M.E. et al. 1992; Jage J. 1993; Norris L.H. et al. 1995; Bennett C.R. et al. 1984; Goodman C.S. et al. 1994; Dionne R.A. et al. 1984; Anderson L.D. et al. 1993; Salonen M. et al. 1988; Davenport R.E. et al. 1990; Meechan J.G. et al. 1988).

Nevertheless, the combined administration of anesthetics and vasoconstrictors may cause some complications and alter certain hemodynamic parameters. In this context, local anesthetics at the doses habitually employed are known to increase heart rate and cardiac output as a result of increased sympathetic activity, which may also induce a slight rise in blood pressure (Malamed S.F. et al. 1986). In the event of overdosing, marked hypotension results as a consequence of diminished myocardial contractility, lessened cardiac output and a decrease in peripheral resistance caused by a drop in vascular smooth muscle tone (Malamed S.F. et al. 1986).

Ester-type local anesthetics cause greater vasodilatation than amide compounds, and are now practically discarded for parenteral use. In turn, prilocaine and mepivacaine are the amide-type anesthetics with the least vasodilatory effects (Martindale W. 1993).

Epinephrine, which causes α receptor-mediated vasoconstriction, is the most widely employed vasoconstrictor in combination with local anesthetic solutions, for such receptors predominate within the periodontium and oral mucosa and submucosa. In contrast, the main inconvenience of epinephrine is increased myocardial excitability resulting from β receptor action (Cawson R.A. et al. 1992). As a result of these effects, the combined use of local anesthetics and vasoconstrictors has been debated-criticism centering on its potential for inducing adverse systemic cardiovascular effects secondary to an increase in heart rate and output (Malamed S.F.et al. 1986; Romero M.M. 1992; Jage J. 1993; Norris L.H. et al. 1995; Bennett C.R. et al. 1984; Goodman C.S. et al. 1994; Hirota Y. et al. 1986). In contrast, other studies have found local anesthesia with epinephrine to increment plasma epinephrine concentrations without causing significant hemodynamic repercussions (Davenport R.E. et al. 1990; Chernow B. et al. 1983; Cioffi G.A. et al. 1985; Barber W.B. et al. 1985).

Felypressin is a vasoconstrictor with scant local action against bleeding; as a result, it does not alter cardiovascular response. In addition, it appears to have no arrhythmogenic potential or effects upon the central nervous system (Malamed S.F.et al. 1986; De Andrés-Trelles F. et al. 1993)

Monitoring of vital constants is required to rapidly correct possible hypoxia in patients subjected to oral surgery. In this sense, hypoxemia is defined as infranormal arterial blood oxygenation (Poiset M. et al. 1990), and can be assessed in terms of oxygen saturation (SaO_2) - a parameter that measures arterial oxyhemoglobin saturation -. Although little information on this subject is available in the oral surgical literature, hypoxemia is only related to healthy patients when they are under sedation (Poiset M. et al. 1990; Gandy S.R. et al. 1995).

The pulse oxymeter (Fig. 1) affords noninvasive, immediate and continuous Monitoring of heart rate and blood oxygen saturation (i.e., the proportion between oxygenated and non-oxygenated hemoglobin) (Gandy S.R. et al. 1995). Heart rate is defined by the arteriolar pulse, and SaO_2 is determined from the transmission of red and infrared waves through vascularized tissues. The wave emitting source and recording photodiode both form part of the pulse oxymeter sensor (Berini-Aytés L. et al. 1997).

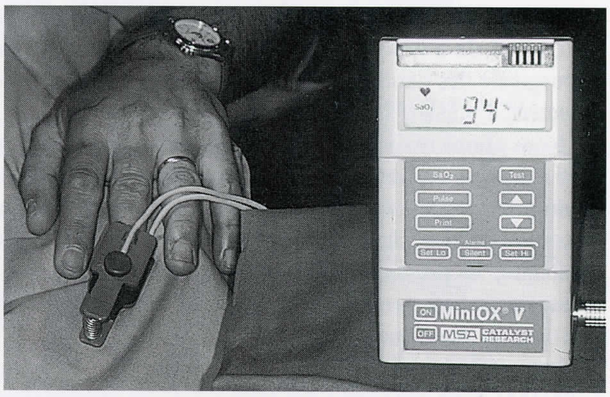

Fig. 1. *MiniOX Printer (MSA Instrument Division) pulsioxymeter.*

The purpose of the present study was to observe the hemodynamic changes during surgical extraction of lower third molars induced by three local anesthetics solutions associated with different vasoconstrictors. The parameters studied were heart rate (HR) and $Sa0_2$. Recordings were also obtained of systolic (SAP) and diastolic arterial pressure (DAP), to allow calculation of the mean arterial pressure (MAP), defined as [DAP + (SAP-DAP) / 3], and the following myocardial oxygen consumption indicators: cardiac rate-pressure product (RPP = SAP x HR) and pressure-rate quotient (PRQ = MAP / HR) (Campbell R. L. et al. 1995).

MATERIAL AND METHODS

A double-blind, longitudinal observational study was conducted between September 1995 and July 1996. The study sample was non-randomized, involving 45 healthy volunteers (29 females and 16 males) aged 18-50 years (mean age 24.3) and consecutively enrolled for the surgical extraction of an impacted lower third molar under local anesthesia. Only ASA I (Berini-Aytés L. et al. 1997) individuals without a history of significant pathology were included.

Personal data were recorded for each patient, along with the classification of molar extraction difficulty according to Pell, Gregory and Winter (Gay-Escoda C. et al. 1999), the type and amount of local anesthetic used, and the previously established surgical times at which the different study variables were determined. Immediately before surgery, SAP and DAP were determined using a Littman 3M phonendoscope and Waitch sphygmomanometer.

A MiniOX Printer (MSA Instrument Division) pulse oxymeter was fitted contralateral to the pressure cuff for digital Monitoring of HR and $Sa0_2$ throughout the operation.

Three groups were established (n = 15) on a randomized basis, according to the anesthetic solution and associated vasoconstrictor administered (4% articaine + epinephrine 1:200,000 (Ultracain 0.5®); 3% mepivacaine without vasoconstrictor (Scandinibsa®); and 3% prilocaine + felypressin 1:1,850,000 (Citanest®)). The anesthetic carpules were concealed with stickers bearing a color code indicating the type of anesthetic involved. Both the patient and operator were blinded to the color code, and only the upper portion of the cartridge was left exposed, to reflect the number of aspirations made. The anesthetic technique comprised truncal block of the inferior dental nerve, with infiltrating anesthesia of the vestibular zone of the lower third molar. A maximum total of three carpules (1.8 ml per carpule) was established per patient.

All variables determined before anesthesia were again recorded upon completing wound suture and on removing the stitches one week after surgery (these being regarded as basal values). During surgery, the variables were determined immediately after administering the anesthetic; one minute after beginning to use the micromotor for the ostectomy; upon commencing the application of dental extraction pressure; and, where necessary, at the time of repeat anesthesia. At these times only HR and $Sa0_2$ were recorded, to avoid undue patient and surgeon inconvenience caused by manual determinations of arterial pressure during the operation.

All surgery and postoperative controls were performed by the same surgical team.

Statistical analysis

The results obtained were subjected to a multifactorial analysis of variance (MANOVA) using the SPSS version 6.1 statistical package under Windows (license no.: 1250352). Seven MANOVA tables were constructed to identify any statistically significant changes in the study variables over time, and to determine whether such changes are attributable to the type of anesthetic used.

RESULTS

Third molar extraction proved very difficult in three patients (score 7-10 according to the Pell, Gregory and Winter classification), simple in 7 (score 3-4) and moderately difficult in the rest (score 5-7). The mean duration of surgery (i.e., from immediately after anesthesia injection and thus including anesthetic latency, to suture completion) was 40.3 minutes. Less than two carpules were needed in 28 patients, while the remaining 17 required more than two.

Within each anesthetic group, statistically significant variations in HR were observed at different times in the course of surgery ($F(2.99, 160) = 12.94$, $p<0.001$). No significant changes in Sa02 were recorded, however ($F(2.90, 160) = 1.11$, $p = 0.348$)(Tab. 1).

In turn, no significant differences were recorded among the three groups at the different times in the course of surgery in terms of either HR (F (2.32) = 1.00, p = 0.378) or SaO_2 (F (2.32) = 0.91, p = 0.414)(Tab. 2). Lastly, each anesthetic combination induced similar HR variations, with maximum values during surgery (from immediately after anesthetic injection to extraction of the impacted third molar). In all cases, HR tended to decrease towards basal values after the operation (F (5.98, 160) = 1.77, p = 0.114)(Fig. 2). SaO_2 remained very stable at all times (F (5.79, 160) = 1.46, p = 0.204)(Fig. 3)(Tab. 3).

Tab. 1. - *Differences in heart rate and blood oxygen saturation within each anesthetic group over time.*

	F	p
Heart Rate (HR)	**(2.99, 160) = 12.94**	**< 0.001***
Oxygen Saturation (SaO_2)	**(2.90, 160) = 1.11**	**= 0.348**

* *statistically significant difference*

Tab. 2. *Differences in heart rate and blood oxygen saturation among the different anesthetic groups at given times.*

	F	p
Heart Rate (HR)	**(2.32) = 1.00**	**= 0.378**
Oxygen Saturation (SaO_2)	**(2.32) = 0.91**	**= 0.414**

Tab. 3. *Differences in heart rate and blood oxygen saturation among the different anesthetic groups over time.*

	F	p
Heart Rate (HR)	**(5.98, 160) = 1.77**	**= 0.114**
Oxygen Saturation (SaO_2)	**(5.79, 160) = 1.46**	**= 0.204**

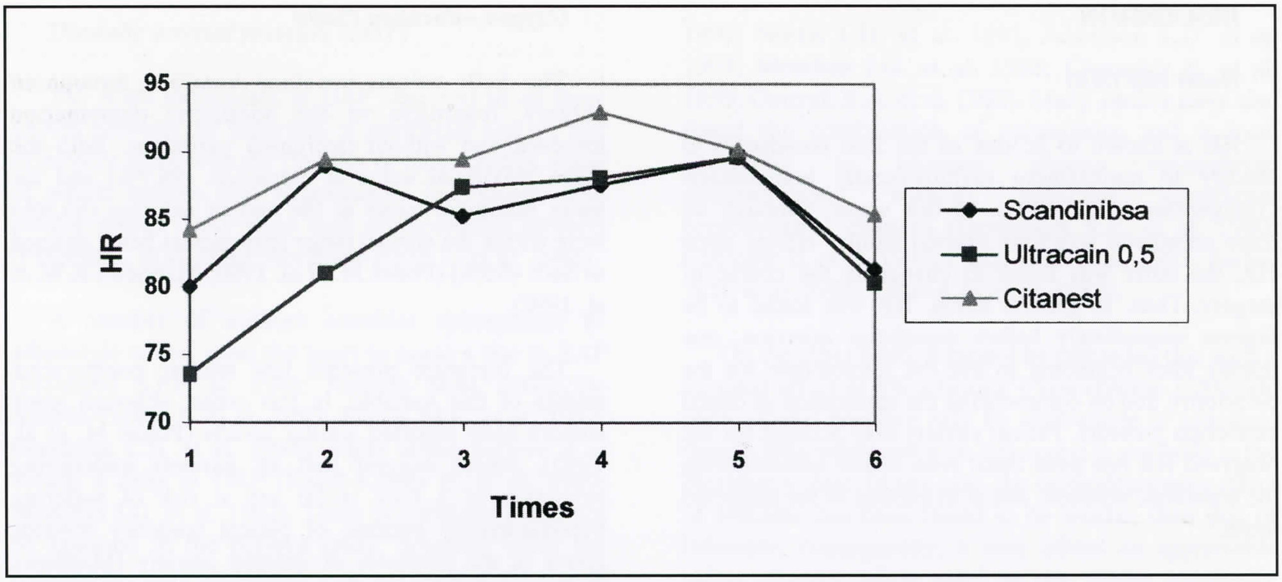

Fig. 2. *Heart rate (HR) recordings over time, for the different anesthetic solutions studied. 1. Basal. 2. Before local anesthetic injection. 3. After local anesthetic injection. 4. One minute after starting to use the micromotor for ostectomy. 5. Pressure application at extraction. 6. End of wound suturing.*

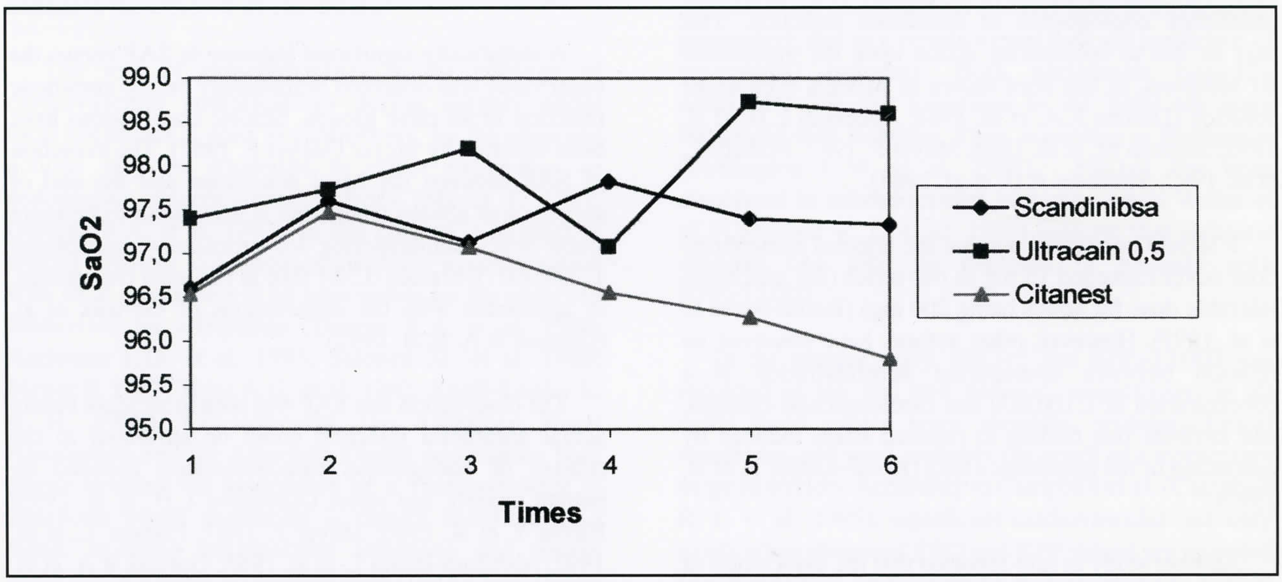

Fig. 3. *Blood oxygen saturation (SaO_2) recordings over time, for the different anesthetic solutions studied. 1. Basal. 2. Before local anesthetic injection. 3. After local anesthetic injection. 4. One minute after starting to use the micromotor for ostectomy. 5. Pressure application at extraction. 6. End of wound suturing.*

DISCUSSION

Heart rate (HR)

HR is known to be one of the first parameters to modify in maintaining cardiovascular homeostasis (Tresguerres J.A.F. 1993). In this sense, although all three anesthetic solutions exerted similar effects upon HR, the latter was found to change in the course of surgery. Thus, in general terms, HR was found to be highest immediately before anesthesia injection, one minute after beginning to use the micromotor for the ostectomy, and on commencing the application of dental extraction pressure. Patient anxiety may account for the observed HR rise from basal even before administering the anesthetic solution, and at extraction of the impacted tooth.

As could be expected, at the end of the operation, the absence of pain and tension tended to restore the HR to the initial basal values. These observations coincide with those of other authors (Dionne R.A. et al. 1984; Anderson L.D. et al. 1993; Hirota Y. et al. 1986; Meyer F. 1987; Frabetti L. et al. 1992; Abraham-Inpijn L. et al. 1988; Beck F.M. et al. 1981; Cheraskin E. et al. 1959; Pateromichelakis S. 1992).

In the present study, only the 4% articaine + epinephrine 1:200,000 (Ultracain 0.5®) anesthetic combination induced an actual increase in HR as an immediate consequence of anesthesia injection. This may be due to epinephrine action upon the myocardial ß1 receptors, as has been shown in patients even under sedation (Dionne R.A. et al. 1984; Anderson L.D. et al. 1993; Salonen M. et al. 1988; Meyer F. 1987; Frabetti L. et al. 1992; Struthers A.D. et al. 1983).

It should be pointed out that the injected epinephrine dose never exceeded 15 mg in our series (the maximum tolerable dose for adults being 200 mg) (Berini-Aytés L. et al. 1997). However, other authors have observed no relation between epinephrine administration at a concentration of 1:100,000 and cardiovascular changes, and attribute this finding to reduced stress induced by deepening of the anesthetic effect (Knoll-Köhler E. et al. 1991).

Another study in turn reported that the association of epinephrine to the anesthetic solution in young healthy individuals ensures cardiovascular stability, with only a slight and non-significant increase in HR following injection (Tolas A.G. et al. 1982).

Oxygen saturation (SaO_2)

The SaO_2 values remained constant throughout surgery, regardless of the anesthetic combination involved and without intergroup variations. Both the mean maximum value at extraction (98.7%) and the mean minimum value at the end of suturing (95.8%) were within the normal range (hypoxemia being defined as SaO_2 <95%) (Poiset M. et al. 1990; Matthews R.W. et al. 1992).

The literature presents few similar comparative studies of this variable. In this sense, although some authors have reported similar results (Poiset M. et al. 1990), others suggest that all patients undergoing extraction of a third molar are at risk of suffering hypoxia-mainly because of patient tendency towards apnea in the moments of greatest anxiety (Matthews R.W. et al. 1992; Lowe T. et al. 1992).

On the other hand, a number of studies relate hypoxia during and at the end of surgery to patient sedation (Gandy S.R. et al. 1995; Matthews R.W. et al. 1992), hypoxia in the end phase of surgery has even been attributed to increased tissue oxygen demands due to the increased presence of catecholamines in the bloodstream secondary to accumulated stress (Matthews R.W. et al. 1992).

Systolic arterial pressure (SAP)

A statistically significant increase in SAP versus the basal value was observed immediately before anesthetic injection in all three groups. Similar observations have been reported by Meyer (Meyer F. 1987). The evolution of SAP between the basal conditions and the end of surgery was always stable, but it was found to be more stable when administering 4% articaine + epinephrine 1:200,000 (Ultracain 0.5®) than in the other two groups, in agreement with the observations of Gortzak et al. (Gortzak R.A. et al. 1992).

The observation that SAP was seen to increase before actual anesthesia injection could be attributed to the release of endogenous catecholamines induced by patient anxiety and stress (Anderson L.D. et al. 1993; Hirota Y. et al. 1986; Meyer F. 1987; Frabetti L. et al. 1992; Abraham-Inpijn L. et al. 1988; Gortzak R.A. et al. 1992). Nevertheless, a number of authors are of the opinion that such stress does not affect blood pressure in either adults or hypertensive subjects (Beck F.M. et al. 1981; Meiller T.F. et al. 1983).

Diastolic arterial pressure (DAP)

The scant increments in DAP observed in all three groups between the induction of anesthesia and the end of surgery agree with the findings of other studies, some of which include also hypertensive individuals, who exhibit greater DAP rises than normotensive subjects (Frabetti L. et al. 1992; Abraham-Inpijn L. et al. 1988).

A number of authors consider epinephrine ß-adrenergic action upon the heart to cause a rise in SAP (Malamed S.F.et al. 1986; Romero M.M. 1992; De Andrés-Trelles F. et al. 1993; Planas M.E. et al. 1992; Goodman C.S. et al. 1994), while others believe it to induce a drop in DAP (Knoll-Köhler E. et al. 1989; Meechan J.G. et al. 1992). These possibilities could not be assessed in the present study, however, since the required pressure recordings were not made in the course of surgery. Other authors support both actions: epinephrine activity upon the central α-adrenergic receptors would yield vasoconstriction and hence an increased SAP, while ß-adrenergic action upon the skeletal muscle would lead to vasodilatation and thus a diminished DAP.

The results of the present study suggest that the less evident changes induced by articaine plus epinephrine versus the other anesthetic combinations could be explained by epinephrine acting as a vasoconstrictor that enhances the efficacy of anesthesia.

The role of catecholamines in the etiology of cardiovascular complications during surgery under local anesthesia is open to controversy, for the observed actions may be attributed to either exogenous or endogenous catecholamine activity (Meyer F. 1987; Gortzak R.A. et al. 1992). In this context, a number of studies consider exogenous epinephrine in combination with local anesthetics to be responsible for the observed cardiovascular alterations (Dionne R.A. et al. 1984; Anderson L.D. et al. 1993; Salonen M. et al. 1988; Meyer F. 1987; Tolas A.G. et al. 1982; Knoll-Köhler E. et al. 1989). Consequently, the American Heart Association and the American Dental Association both advise limiting the association of a vasoconstrictor to situations where anesthesia is clearly benefited as a result, avoiding intravascular injections and always using the minimum acceptable dose (De Andrés-Trelles F. et al. 1993; Anderson L.D. et al. 1993). On the other hand, the endogenous epinephrine released as a result of inadequate analgesia may be worse than exogenous epinephrine (Holroyd S.V. et al. 1988; Planas M.E. et al. 1992; Norris L.H. et al. 1995; Anderson L.D. et al. 1993; Meechan J.G. et al. 1988; Cheraskin E. et al. 1959; Gortzak R.A. et al. 1992). Many studies have also found the combination of epinephrine and a local anesthetic to increase plasma epinephrine concentrations without inducing significant hemodynamic changes (Davenport R.E. et al. 1990; Chernow B. et al. 1983; Cioffi G.A. et al. 1985; Barber W.B. et al. 1985; Tolas A.G. et al. 1982).

On the other hand, it cannot be discarded that such a minimal effect of 4% articaine + epinephrine 1:200,000 upon arterial pressure may be attributable to articaine, though little information on this aspect is available in the literature to date. In any case, the cardiodepressive effect of articaine has been found to be weaker than that of lidocaine; consequently, it may afford an appreciable safety margin when used at the doses habitually administered in oral surgery (Lefevre P.B. et al. 1991). On the other hand, other studies have reported no differences in favor of the anesthetic superiority of this particular solution (Haas D.A. et al. 1991; Brinklov M.M. et al. 1977).

Cardiac rate-pressure product (RPP) and pressure-rate quotient (PRQ)

Few studies in the literature have addressed these parameters in detail. Both RPP and PRQ constitute mathematical combinations derived from hemodynamic parameters, and to a certain extent they are predictive of myocardial ischemia. Both parameters basically underscore HR, for variations in the latter are more associated with ischemia. Thus, according to Buffington (Buffington C.W. et al. 1985), PRQ<1 has been associated to subendocardial ischemia, while Waller et al. (Campbell R. L. et al. 1995) indicate that ischemic changes can also be detected in patients with RPP>12,000.

In the present study, PRQ<1 and RPP>12,000 was recorded in ten and two patients, respectively; in all cases these values were sporadic, without clinical symptoms, and were probably the result of a momentary surge in anxiety. According to Campbell et al. (Campbell R. L. et al. 1995), significant cardiovascular risk only exists when abnormal PRQ and RPP values are recorded simultaneously. This condition was observed in four of our patients before administration of the anesthetic solution, a fact that suggests the need for prophylactic measures in the form of anxiolytic medication in certain oral surgery patients who show marked anxiety.

CONCLUSIONS

1. - At the concentrations used in the present study, articaine + epinephrine, mepivacaine without vasoconstrictor, and prilocaine + felypressin caused no significant changes in either heart rate or blood oxygen saturation.

2. - The results obtained suggest that the anesthetic solutions studied can be administered indistinctly in healthy non-sedated patients, though the 4% articaine + epinephrine 1:200,000 combination was found to afford the most stable heart rate and arterial pressure values.

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