Recommendations to use vasoconstrictors in dentistry and Oral surgery

**SOCIÉTÉ FRANCOPHONE DE MÉDECINE BUCCALE
ET DE CHIRURGIE BUCCALE**

www.societechirbuc.com

Working group

Carlos Madrid (Odontologiste, Toulouse), Rapporteur
Bruno Courtois (Odontologiste, Toulouse)
Marc Vironneau (Anesthésiste Réanimateur, Toulouse)

Reading group

Jacques Bayssière (Odontologiste, Montpellier)
Jean Pierre Bernard (Stomatologiste, Genève)
Jean Loup Coudert (Odontologiste, Lyon)
Damien Duran (Odontologiste, Toulouse)
Ahmed Feki (Odontologiste, Strasbourg)
Jean Christophe Fricain (Odontologiste, Bordeaux)
Patrick Girard (Odontologiste, Paris)
Jean Claude Harnet (Odontologiste, Strasbourg)
Jacques Jeandot (Stomatologiste, Bordeaux)
Benoît Lefèvre (Odontologiste, Reims)
Dan Longrois (Anesthésiste-Réanimateur, Nancy)
Louis Maman (Odontologiste, Paris)
Gilbert de Mello (Odontologiste, Rennes)
Guillaume Penel (Odontologiste, Lille)
François Prédine-Hug (Odontologiste, Brest)
Yvon Roche (Odontologiste, Paris)
Jacky Samson (Stomatologiste, Genève)
Jacques Henri Torres (Stomatologiste, Montpellier)
Daniel Viennet (Odontologiste, Nancy)

GENERAL METHODOLOGY

These recommendations on the use of vaso-constrictors in odonto-stomatology were worked out by a working group at the end of an analysis of the scientific literature and collection of the opinion of the members of the French-speaking Society of Oral Medicine and Oral Surgery at a scientific meeting in Metz on May 23, 2002. The text was then submitted to a reading group before being definitively adopted.

The members of the reading and working groups were designated by the French-speaking Society of Oral Medicine and Oral Surgery. The working group was chaired by a rapporteur who compiled the final document before proposing it and discussing it with the working group then submitting it to the reading panel. A systematic library search was carried out by interrogation of the Medline data bank. This bibliography obtained by automation was supplemented by a manual research. The members of the working group and the reading group transmitted articles. The lists of references quoted in the already identified articles were consulted.

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 2

The rapporteur with the working group used reading grids intended to assess the methodological quality and the level of scientific evidence of these documents. The documents were classified according to these grids in various categories. On the basis of this literature review, the working group proposed recommendations whenever possible. Those were based either on a scientific level of evidence, or, in the absence of evidence, on a professional agreement collected at the time of the scientific meeting of the French-speaking Society of Oral Medicine and Oral Surgery on May 23, 2002.

The bibliography obtained was almost completely used so that the working group did not consider it useful to separate selective bibliography and complementary bibliography. On the other hand the totality of the bibliography obtained was classified analytically according to the level of evidence (LoE) based on the following classification (US Agency for Health Care Policy and Research):

Level I a:	Meta-analysis evidence from randomised controlled trials (RCT)
Level I b :	Evidence from at least one RCT
Level II a :	Evidence from a non-randomised controlled study
Level II b :	Evidence from another well defined experimental study
Level III :	Evidence from a well defined descriptive experimental study (this includes comparative studies, cohort studies, and the study of case controls)
Level IV :	Opinion of experts or clinical experience

Grades A, B or C are assigned to the recommendations according to the level of evidence of the respective bibliography:

Grade A :	Based on level of evidence I
Grade B :	Based on level of evidence II or III
Grade C :	Based on level of evidence IV

Strategy of the documentary research

The automated research was based on the following key words:
- local anaesthesia
- general anaesthesia
- vasoconstrictors
- noradrenaline
- adrenaline
- levonordefrin
- corbadrine

The preceding key words were cross with:
- dentistry
- maxillofacial surgery
- side effects
- adverse effects
- special patients

Selected questions

• What is the place of vasoconstrictors in odonto-stomatology?

– Are vasoconstrictors necessary in odonto-stomatologic anaesthesia?

– Can vasoconstrictors be useful in odonto-stomatologic practice other than in association with a local anaesthetic substance?

– Can vasoconstrictors be associated with general anaesthetics during general anaesthesia in odonto-stomatology?

• How to choose the vasoconstrictive molecule in odonto-stomatology?

– Which are the advantages and disadvantages of adrenaline compared to noradrenaline?

– Which is the interest of other substances?

• What are the indications of vasoconstrictors in odonto-stomatology?

• Which dose of vasoconstrictors should be used in odonto-stomatologic anaesthesia?

• Which are the drug interactions of the vasoconstrictors used in odonto-stomatologic anaesthesia?

• Which are the pathologies which contraindicate the use of vasoconstrictors in odonto-stomatology?

• Do physiological states contraindicate the use of vasoconstrictors in odonto-stomatologic anaesthesia?

RECOMMENDATIONS

1. Injection technique

1. The injection of an anaesthetic solution with or without vasoconstrictor must always be carried out slowly (1 ml per minute) and in fractioned doses in order to supervise the possible signs of a noxious effect of the injection. When the injection takes place in a well vascularised territory, a negative aspiration test is a prerequisite to the injection of the anaesthetic solution with or without vasoconstrictor. The smallest effective dose is always recommended. **[Grade C]**

Indications

2. The association of a vasoconstrictor with an anaesthetic solution in local odonto-stomatologic anaesthesia by infiltration is indicated because the vasoconstrictor decreases the intravascular passage of the injected solution and thus ensures an increase in duration and depth of the anaesthesia while reducing the systemic effects of the solution. **[Grade A]**

3. It does not appear possible to conclude formally as for the harmlessness of retraction cords soaked with vasoconstrictor used in dental prosthetics. Evaluations based on the animal seem to show that haemodynamic changes are inconstant. The literature reports one serious accident in the human. **[GradeB]**

4. Local haemostasis techniques by using vasoconstrictors, pure or mixed with anaesthetic or astringent substances, have not been investigated in publications presenting a satisfactory level of evidence. Thus they are empirical. Although largely diffused, they have not led to the publication of an accident or an incident in connection with vasoconstrictors. **[Grade C]**

5. The use of an anaesthetic solution containing a vasoconstrictor as a means of decreasing the bleeding and of lowering the threshold of analgesia among patients operated in oral surgery under general anaesthesia contributes to decrease the sympathetic nerve response to the surgical aggression and to decrease the depth of the necessary general anaesthesia. **[Grade B]**

Choice of the molecule

6. Adrenaline is industrially and medically the leader of the vasoconstrictors used alone or in association with a local anaesthetic in odonto-stomatology. It has the broadest casuistry which confirms a great safety of this molecule. Non-catecholamine derivatives have not shown their superiority to date even among patients likely to badly tolerate catecholamines. **[Grade B]**

Indications according to the anaesthetic technique

7. The use of a vasoconstrictor in the techniques of intrapulpal, intraligamentary and intraseptal anaesthesia is not essential but considerably improves the success rate, the duration and the depth of the anaesthesia obtained. If the injection is carried out under adequate conditions, the local lesions directly ascribable to the vasoconstrictor are negligible and reversible. The systemic effects of these injections exist but are generally much lower than those observed in infiltration anaesthesias. **[Grade A]**

8. The use of a vasoconstrictor in local anaesthesia techniques (para-apical, anaesthesia of the lingual nerve, anaesthesia of the buccal nerve) is not essential, but appreciably improves the success rate, the duration and the depth of the anaesthesia obtained. **[Grade C]**

9. The addition of a vasoconstrictor to the anaesthetic solution is not essential for the anaesthesia of the lower alveolar nerve at the mandibular foramina. The addition of adrenaline increases the duration of the anaesthesia but does not seem to have a decisive effect on the incidence of failures. The results concerning the success rate of the anaesthesia are contradictory. Taking into account the relation which exists between the success rate and the volume

of injected solution, the addition of a vasoconstrictor could be considered in the prevention of the systemic effects of the local anaesthetic. **[GradeC]**

Dosage of the vasoconstrictor

10. The results are contradictory about the ideal dosage of adrenaline in 2% lidocaine solutions. The 1/200000 solution gives a sufficient duration of action for the majority of odonto-stomatologic acts. For 4% articaine and 2% mepivacaine, 1/200000 solutions should be preferred in the absence of a significant difference in the performances with the 1/100000 solution and because they are probably tolerated better. **[Grade A]**

Drug interactions

11. The attitude towards patients under tricyclic antidepressants must be to avoid noradrenaline in association with local anaesthetics and to inject reduced amounts of local anaesthetics associated with 1/200000 adrenaline. In practice the amount injected should be one the third of the total amount of that of the normal subject. **[GradeC]**

12. Patients under cardio-selective beta-blockers can receive local anaesthesias with vasoconstrictor (1/200000 adrenaline). Among patients receiving non-selective beta-blockers, it is recommended to use anaesthetic solutions with the lowest dose of vasoconstrictor. **[GradeC]**

13. Volatile halogenous general anaesthetics should not be used with adrenaline. The literature encourages prudence as for the use of a local anaesthetic with adrenaline in the event of association of thiopental + halothane during general anaesthesia. **[Grade C]**

14. Vasoconstrictors will be proscribed at least 24 hours after the consumption of cocaine to allow the elimination of the drug and its active metabolites. **[Grade C]**

15. No accident has been reported as for the administration of a local anaesthetic with adrenaline among patients under antipsychotic drugs or alpha-blockers. The risk of interaction between these substances is theoretical at the usual doses in odonto-stomatologic anaesthesia. **[Grade C]**

16. There is no contra-indication in the administration of a local anaesthetic with adrenaline in patients under selective MAOI. **[Grade C]**

Pathologies contraindicating vasoconstrictors associated with a local anaesthetic

17. Pheochromocytoma constitutes an absolute contraindication to the administration of vasoconstrictors. Patients suffering from this pathology must be dealt with in a hospital which disposes of a reanimation structure when a local anaesthesia with or without vasoconstrictor is necessary. **[GradeC]**

18. It appears desirable to avoid the association of vasoconstrictors with a local anaesthetic during conservative treatment and even more so during non-conservative treatment on bone irradiated beyond 40 Gy. **[Grade A]**

19. Intra-osseous injections of local anaesthetic with adrenaline must be avoided among patients presenting with arrhythmia. **[Grade A]**

Pathologies which do not contraindicate vasoconstrictors associated with a local anaesthetic

20. Stabilised hyper- and hypothyroid patients do not have major disorders when they are subjected to corrective treatment and put in the presence of catecholamines. Although the theoretical risk of thyroxine-adrenaline potentiation is serious, no clinical case has been reported. **[Grade C]**

21. Vasoconstrictors associated with an anaesthetic solution are not contraindicated in a

hypertensive subject stabilised by an antihypertension treatment. **[Grade A]**

22. In the event of unstable blood pressure associated with other elements burdening the prognosis, treatment implying a local anaesthesia with vasoconstrictor will have to be carried out under monitoring in a hospital disposing of a reanimation unit. **[Grade C]**

23. In auricular fibrillations stabilised by adequate treatment, the control of stress and the therapeutic heart rate is essential and the use of local anaesthetics with vasoconstrictor is indicated. **[Grade C]**

24. Patients under digoxin and those suffering from atrio-ventricular arrhythmias must be treated under monitoring in a hospital disposing of a reanimation unit when a local anaesthesia with or without vasoconstrictor is necessary. **[Grade C]**

25. Vasoconstrictors associated with an anaesthetic solution are not contraindicated in stabilised coronary cardiopathies. **[Grade C]**

26. Vasoconstrictors associated with an anaesthetic solution are not contraindicated in asthmatic subjects in order to control pain and avoid stress which is probably the principal source of asthma attack at the dental practice. In the event of cortico-dependent asthma, the resort to an anaesthetic without vasoconstrictor and thus without bisulphite is indicated. **[Grade C]**

27. Vasoconstrictors associated with an anaesthetic solution are not contraindicated among patients having presented previous and cured viral or toxic hepatic injury. In the event of evolutionary severe attack, the evaluation of the hepatic function is important. The total quantity injected may have to be reduced and intervals between the injections increased, without being detrimental to the use of an associated vasoconstrictor. **[Grade C]**

28. Vasoconstrictors associated with an anaesthetic solution are not contraindicated among stabilised type I or II diabetic patients. In the event of non-stabilised and unstable diabetes, with brutal passage from hypo- to hyperglycaemia, the quantities of local anaesthetic with vasoconstrictor will be reduced in order to take the hyperglycaemic character of adrenaline into account. **[Grade C]**

Physiological states and vasoconstrictors

29. Vasoconstrictors associated with an anaesthetic solution are not contraindicated during pregnancy and lactation. The usual amounts can be used. **[Grade C]**

30. Vasoconstrictors associated with an anaesthetic solution are not contraindicated in children beyond six months. The total amount of local anaesthetic with or without vasoconstrictor usually used in the healthy adult should be divided by 3 below 15 kg and 2 between 15 and 40 kg. **[Grade C]**

31. Vasoconstrictors associated with a local anaesthetic are not contraindicated in the elderly. The total amount of anaesthetic with or without vasoconstrictor should be adapted to the metabolic state of the considered subject. **[Grade C]**

ARGUMENTATION

1. 1. Vasoconstrictors in odonto-stomatology

Adrenergic vasoconstrictors are among the most administered therapeutic substances in odonto-stomatology. Their use in association with an anaesthetic substance started in 1904 when Heinrich Braun (1903) a reputed German specialist in local anaesthesia developed an adrenaline-procaine solution rapidly marketed by Hoechst under the Novocaine brand® which was to dominate the market for 50 years (Yagiela, 1995 [LoE IV]). Vasoconstrictors are also responsible for more drug interactions than the majority of other drug substances specific to the odonto-stomatologist (Yagiela, 1999 [LoE IV]). Adrenaline and the other sympathomimetic amine derivatives are injected routinely in association with local anaesthetics (LA) for pain control, or used alone on gingival retraction cords and in injectable or topic solutions intended for local bleeding control.

1.1. 1.1. Are vasoconstrictors necessary in stomatologic anaesthesia?

The advantages of vasoconstrictors in odonto-stomatologic anaesthesia are universally recognized by the scientific community and the principal handbooks of odonto-stomatologic local anaesthesia [LoE IV] refer to them as scientific evidence (Davies and Lefkowitz, 1981; Malamed, 1997; Berini and Gay, 1997; Gaudy and Arreto, 1999).

It is generally admitted that, whatever the path of injection, the bio-disponiblity of amino-amide LA is total. After injection, part of the dose reaches its target while another fraction passes into the systemic circulation. The passage through the endothelial vascular barrier is easy taking into account the good liposolubility of LA. An important capillary density, a local blood flow and a high blood/tissue division coefficient are as many factors increasing the systemic resorbtion which are found in the majority of target territories of local anaesthesia of the oral cavity. Various pharmacological interventions and in particular the addition of vasoconstrictors to the LA solution can modify the systemic resorbtion appreciably although it also varies with the effect of the LA itself upon local vascularisation (Viel and coll, 1997 [LoE IV]; Ackermann and coll, 1988 [LoE III]; Myers and Heckmann, 1989 [LoE IIb]).

The vasoconstrictor thus acts initially like a substance likely to slow down the speed of absorption of the anaesthetic solution at the point of injection (Fink and coll, 1978 [LoE IIb]; Jage, 1993 [LoE IV]). The reduction in systemic resorbtion is related to the local action of vasoconstrictors (adrenaline being selected as a reference) by stimulation of the alpha1 receptors of the smooth muscle of the peripheral vessels. The consequence of this action is a reduction in tissue perfusion which results in local ischaemia of the tissues (Allwood and coll, 1963 [Not classified]).

This ischaemia also relates to the vasa nervorum which supply the axons of sensitive nerve fibres concerned by the local anaesthesia; a significant reduction of the metabolism of the nerve cells then arises and thus of the transmission of the nerve impulse which leads to a deepening of the anaesthesia and an increase in its duration.

The effect of the vasoconstrictor also comprises a facilitating action on the penetration of the LA in nerve fibres by direct stimulation of anti-nociceptive adrenergic receptors. Such an action was demonstrated during peridural and intrathecal injections. (Bromage and coll, 1983 [LoE IIb]; Yaksh and Reddy, 1981 [LoE Ib]). From the clinical point of view, the reduction of the speed of absorption leads to two positive results known for a long time:

(1) An increase in the duration of the anaesthesia (Jage, 1993 [LoE IV]);

(2) (2) A reduction of the plasmatic peak of LA, which has, itself, two beneficial consequences: reduction in systemic toxicity and consequentially the possibility of increasing the amount injected. Covino and Vassallo (1976) [LoE V] thus reported that the addition of adrenaline made it possible to increase by 200% the duration of a lidocaine 0,5% anaesthesia while

decreasing the plasmatic peak by 50%. The behaviour of other LA tested is similar.

Let us note however that one of the unexpected side effects of vasoconstrictors, when they are associated with LA, is to slow down the induction time of the anaesthesia. Falaiye and Rood (1990) [LoE IIa] thus showed that the addition of adrenaline to a solution of lidocaine appreciably delayed the induction time of a deep anaesthesia appreciated with pulp-testing. This side effect would be dependent at the same time on a barrier effect of the vasoconstrictor towards the anaesthetic solution which it would block on the site of injection, at a distance of the targeted nerve fibre, and on an acidifying effect of the vasoconstrictor on the medium which is favourable to maintaining the anaesthetic in its inactive non-ionised form.

The association of a vasoconstrictor with an anaesthetic solution in odonto-stomatology is thus indicated because the vasoconstrictor decreases the plasmatic resorbtion of the injected mixture and thus ensures an increase in the duration and depth of the anaesthesia while reducing the systemic effects of the solution.

1.2. Can vasoconstrictors be useful in stomatologic practice other than in association with a local anaesthetic substance?

Two fields of odonto-stomatology call upon vasoconstrictors other than anaesthesia:

• on the one hand prosthetics: retraction cords intended to push back the gingiva below preparations of enamel and/or dentine at the time of taking impressions (Pallasch, 1998 [LoE IV]);

• on the other hand: oral surgery and in particular endodontic surgery where among other solutions the injection of vasoconstrictors or the installation of supports containing them is recommended to limit bleeding at the centre of the surgical zone (Syngcuk and Sivakami, 1997 [LoE IV]).

1.2.1. Vasoconstrictors on gingival retraction cords

Studies concerning the toxicity of gingival retraction cords impregnated with a vasoactive substance (in practice 8% racemic adrenaline)

are contradictory by divergence of the toxicological and pharmacokinetic results.

For 3 cm of cord Malamed (1997) [LoE IV] reports values varying from 225,5 to 661 µg of racemic adrenaline which actually represents 113 to 330 µg of the pharmacologically active L-form. Such a quantity is equivalent according to Pallasch (1998) [LoE IV] to 3,13 to 9,16 cartridges of 2 ml of anaesthetic solution with 1/100000 adrenaline.

Studies in the dog concerning tolerance showed spectacular rises in heart rate and blood pressure after placing cords. The plasmatic rate of adrenaline was measured in one patient passing from 15 pg.ml^{-1} to 316 pg.ml^{-1} after placing cords and this without a haemodynamic effect. Houston and coll (1970) [LoE IIb] took interest in the possible haemodynamic effects of these cords. They use a badly defined protocol on 9 subjects. Their results relate to blood pressure and heart rate at various times during impression-taking. They show negligible haemodynamic variations.

Other research highlights a significant difference in systemic resorbtion according to whether the gingival epithelium is intact or whether there is active gingivitis or that it is deteriorated by a prosthetic preparation: an intact crevicular epithelium seems to constitute an effective barrier against the plasmatic passage of adrenaline.

It should be noted finally that the various protocols are not easily comparable: duration of placing of the cords varying from 30 to 120 minutes, variable number of teeth concerned, size of the cords and variable doses, non discrimination of the quantities absorbed by plasma, the gingival fluid and saliva.

Pallasch thus proposes to retain some rules concerning the specifications of research on the tolerance of the cords impregnated with racemic adrenaline: (1) level of adrenaline indeed present on the cord; (2) duration of the presence of the cord in the sulcus; (3) state of the sulcus; (4) number of teeth concerned; (5) dilution by saliva and the gingival fluid; (6) metabolism of racemic adrenaline by catechol-O-methyltransferases ; (7) local vasoconstriction induced by adrenaline as a factor decreasing its own

absorption; (8) gingival traumatism during the placing of the cords; (9) individual sensitivity of the patient to even tiny variations of the circulating level of vasoconstrictor.

In the absence of concordant research, it does not appear possible to conclude as for harmlessness of the retraction cords used in dental prosthetics. Evaluations in the animal seem to show that the haemodynamic variations are inconstant, and that their symptomatic character is dependent either on the sensitivity of the subject, or on the experimental conditions. The literature reports only one serious incident in the human (Hilley, 1984) [Not classified: clinical case] related to halothane-adrenaline interaction.

1.2.2. Vasoconstrictors used for surgical haemostasis

Anaesthetic substances associated with high amounts of vasoconstrictors have been used with the only aim of controlling local bleeding by a broad infiltration of the operational site before incision (Gutman, 1993 [LoE IV]). The supporters of these techniques nevertheless observe that, on the one hand, it is often difficult to inject near the apexes without infiltrating skeletal muscle fibres which are rich in adrenergic beta$_2$ receptors which are responsible for vasodilation rather than vasoconstriction (Milam and Giovannitti, 1984 [LoE IV]); in addition, that this per operative vasoconstriction is generally followed by vasodilation by reactive hyperaemia: indeed, progressively with the resorbtion of the vasoconstrictor, the latter reaches a concentration on the surgical site which does not ensure stimulation of the alpha adrenergic receptors any more. The blood flow quickly finds its normal course then, by rebound phenomenon, gradually reaches a flow higher than normal by beta adrenergic reaction: this phenomenon is related to the local hypoxia of the tissues and to the acidosis caused by the prolonged vasoconstriction. When this local hyperaemia settles in, the complementary LA injections with vasoconstrictor are without effect (Gutman, 1993; Gutman and Harrison, 1994 [LoE IV]; Syngcuk and Sivakami, 1997 [LoE IV]).

Adrenaline, noradrenaline, phenyl-adrenaline were used <u>alone</u> in the control of local bleeding in endodontic surgery. Sommer (1962) [LoE IV] was the first to use various solutions: 1/1000 and 1/500 racemic adrenaline, 1/100 phenyl-adrenaline and 1/200 noradrenaline, the support always being gauze; Ingle (1965) [LoE IV] proposed to fill the osseous cavity with gauze saturated with a solution of 2% racemic adrenaline during 4 minutes. Grossman (1970) [LoE IV] recommends the use of salivary rolls of cotton soaked with 1/100000 adrenaline and also proposes the use of cotton pellets impregnated with a solution of 1,5 % racemic adrenaline.

Only the quantities of adrenaline present on the pellets could be evaluated, the other techniques not offering any standardisation. Besner (1972) [LoE IIb] could thus show that on n° 2 pellets one finds on average 1,15 mg of racemic adrenaline in the form of hydrochloride. The application of a n° 2 pellet during 4 minutes did not cause a variation of the heart rate in the series of Besner, which the author allots to the local vasoconstriction caused by adrenaline and which would lead to very weak and very slow absorption of the adrenaline itself.

Let us note that besides pellets impregnated with adrenaline alone, there also exists on the market pellets impregnated at the same time with adrenaline and astringent substances such as zinc phenol sulphonate and ferric sulphate. These specialities have not been tested in the literature and are not marketed in France to the knowledge of the working group. The local haemostasis techniques by use of vasoconstrictors, pure or mixed with anaesthetic or astringent substances have not been investigated in publications presenting a satisfactory level of evidence. They are thus empirical. Although broadly diffused, they have not led to the publication of an accident or incident in connection with vasoconstrictors.

1.3. Can vasoconstrictors be associated with general anaesthetics (GA) during general anaesthesia in odonto-stomatology?

The use of LA solutions associated with a vasoconstrictor for infiltration of the operative field

during general anaesthesia has often been recommended as a means of haemostasis in oral and maxillofacial surgery (Cantaloube and coll, 1991 [LoE IV]). It is a comfortable and bac-teriologically safe alternative compared to mani-pulations intended to manufacture an extempo-raneous serum containing adrenaline. The serum containing adrenaline is classically com-posed of 0,9% sodium chloride; the vasocons-trictive action being obtained by addition of 0,025% adrenaline in solution or 0,25 mg per cartridge of 1 ml of serum. Under these condi-tions, the usual amount of adrenaline not to be exceeded would be of 0,01 mg.kg^{-1} of weight of the patient.

The use of a LA as a vector of the vasoconstric-tor in addition to the advantages of handling mentioned above lowers the threshold of anal-gesia, increases the quality of per and post ope-rational control of pain as demonstrated by Engquist and coll (1977) [LoE IIa], Hosoda and coll (1991) [LoE Ib], Yuge and coll (1995) [LoE IV], for the peridural anaesthesia and espe-cially Mamiya and coll (1997) [LoE Ib] in oral sur-gery. Cantaloube recommends either 1% lido-caine hydrochloride with 1/100000 adrenaline or 2% with 1/80 000 adrenaline or articaine with 1/200 000 adrenaline or mepivacaine with 1/100000 noradrenaline for these infiltrations.

Tordoff and coll (1996) [LoE Ib] sought to know if the use of a loco-regional anaesthesia before incision under general anaesthesia for the extra-ction of lower third molars decreased post-ope-rative pain. In 36 patients they injected the same quantity of anaesthetic solution of 2% lidocaine with 1/200000 adrenaline on one side and a saline solution on the other. Injections were also made around the extracted teeth. Post-operative pain was evaluated by an analo-gical visual scale. No significant difference appeared between the physiological saline solution injected and the anaesthetic.

Mamiya and coll (1997) [LoE Ib] practised the following experiment on a group of 28 ASA 1 patients having to undergo a bilateral sagittal mandibular osteotomy: the 28 patients were divided into 4 groups. Groups 1 and 2 did not receive a loco-regional mandibular anaesthesia

and differed by an increasing level of the depth of the general anaesthesia by inhalation as quantified by minimal alveolar concentration (MAC: *minimum alveolar concentration*) passing from 1,3 MAC to 1,6 MAC. For groups 3 and 4 the patients underwent in addition to a bilateral loco-regional mandibular anaesthesia, a general anaesthesia by inhalation respectively 1,0 MAC and 1,3 MAC. It should be noted that the LA were identical in the two groups receiving the regional anaesthesia: 4 ml of 0,5% mepiva-caine. In both groups 3 and 4, a different vaso-constrictive solution was locally infiltrated (group 3: 8 ml of 1% lidocaine containing 10 µg.ml^{-1} of adrenaline; group 4: 8 ml of 3% pro-pitocaine containing 0,03 UI.ml^{-1} of felypres-sine). The general anaesthesia was carried out with the following general anaesthetics: induc-tion by thiopental (4 mg.kg^{-1}) then maintenance by isoflurane and a 40% mixture of nitrogen protoxide and oxygen. Controls of the haemo-dynamic effects of the surgery were as follows: blood pressure and heart rate. The sympathetic nerve response was evaluated by dosing the plasmatic noradrenaline. Measures started at the 4th minute after local infiltration and were repeated at various significant surgical times. The results show very significant differences between the groups with and without loco-regional anaesthesia. No significant difference was observed between groups 3 and 4. The same results are observed as for the plasmatic noradrenaline rates which are significantly lower in the groups with loco-regional anaesthesia.

The authors thus conclude that loco-regional anaesthetic infiltrations associated with the anaesthetic infiltration of a solution containing a vasoconstrictor in the operative site contribute, on the one hand, to decrease and prevent the auto-immune endocrine sympathetic nerve res-ponse to the surgical aggression which is at the origin of a great part of the post-operative pain, on the other hand, to decrease the depth of the general anaesthesia necessary to the intervention carried out.

A similar experiment was undertaken by Santoro and Marsicano (1998) [LoE IIb], with a different goal: to check the generated haemo-

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 10

dynamic modifications, this time, by injection of adrenaline while making the stress factors of coma vigil inoperative by general anaesthesia. The authors infiltrated 7 patients under general anaesthesia with 4 ml of a solution of 2% mepivacaine with 1/100000 adrenaline at the mandibular foramen. The patients were subjected to very different interventions in oral or maxillofacial surgery. The authors noted the variations of heart rate and blood pressure at various significant phases of the intervention. The authors conclude from a very debatable protocol that the variations of rhythm and heart rate observed at the time of a LA infiltration with vasoconstrictor under general anaesthesia are lower than those observed under local anaesthesia in the coma vigil. The use of an anaesthetic solution containing a vasoconstrictor as a means of decreasing bleeding and of lowering the threshold of analgesia among patients operated in oral surgery under general anaesthesia is a practice commonly reported in the literature. Recent experiments undertaken under peridural and block anaesthesia of the mandibular nerve show that this practice contributes to decrease the sympathetic nerve response to the surgical aggression and to decrease the depth of the general anaesthesia necessary.

A restriction must be made with halogenous volatile GA (halothane) which should not be used with adrenaline. Indeed halogenous GA cause a potentiation of the depressor effects of catecholamines on the speed of conduction of Purkinje fibres in the cardiac autonomous system (Camara and coll, 2001 [LoE IIb]).

2. Choosing the vasoconstrictive molecule in odonto-stomatology

2.1. Adrenaline versus noradrenaline

Adrenaline and the closely related adrenergic amines cause vasoconstriction by stimulating specific membrane receptors of the cells of the smooth muscles of the vessels.

Two principal types of adrenergic $alpha_1$ and $alpha_2$ receptors can initiate vasoconstriction. Anatomically, alpha1 receptors are located close to the sympathetic nerves which innervate the vessels whereas $alpha_2$ receptors are disseminated in order to respond more easily to circulating catecholamines. The cascade of events which go from the stimulation of the receptor to vasoconstriction is now well established (Ruffolo and coll, 1991 [LoE IV]).

The adrenergic receptors are connected to effector enzymes and ionic channels by G proteins, i.e. polypeptides which bind guanosine triphosphate when these receptors are stimulated by adrenaline. The activation of the G proteins bound to $alpha_1$ adrenergic receptors causes the opening of the calcic channels of the plasma membrane and the stimulation of a phospholipase C. The calcium ions then penetrate into the cell and activate a kinase from the light chain of the calmodulin-dependent myosin. It is this which, in turn, initiates the muscular contraction. During this time, the hydrolysis of certain components of the cellular membrane by the phospholipase C leads to the formation of diacylglycerol and inositol triphosphate. These second messengers induce contraction by facilitating the release of intracellular calcium reserves and by maintaining the activation of the protein kinase C which contributes to the metabolic support of the contraction.

Stimulation of the $alpha_2$ receptors by vasoconstrictors also opens calcium channels by activation of the G proteins. Moreover adenylcyclase is inhibited by a specific inhibiting G protein. The adrenergic $beta_2$ receptors activate, on the contrary, adenylcyclase and consequently cause vasodilation. $Beta_2$ receptors are widespread in the vessels of the skeletal muscles and in certain internal organs, they are rare in mucous membranes and the skin.

Noradrenaline shares with adrenaline the capacity to stimulate $alpha_1$ and $alpha_2$ receptors but it does not interact with $beta_2$ receptors so that the only direct effect of noradrenaline on vessels is to favour their constriction.

This purely alpha-adrenergic character was initially taken advantage of by the industry as proof of specificity of this catecholamine. In fact, the affinity of noradrenaline for alpha receptors is less than that of adrenaline which

implies the use of more important noradrenaline doses to obtain the same vasoconstriction (Knoll Kohler, 1988 [LoE IV]).

Noradrenaline is thus approximately 4 times less vasoconstrictive locally than adrenaline. The first consequence is a shorter action by faster plasmatic absorption. An intravascular injection of noradrenaline has more severe consequences than that of adrenaline: rise in the systolic blood pressure (> 200 mm Hg), increase of 75 to 80% of the average blood pressure and increase in myocardial oxygen consumption (Boakes, 1972 and 1973 [LoE IV]) which makes it a difficult molecule to handle in patients suffering from myocardial ischaemia. The absence of action of noradrenaline on beta$_2$ receptors produces an increase in peripheral vascular resistances which largely explains its toxicity. Moreover noradrenaline has a severe and paradoxical bradycardic action as it is active on the cardiac beta$_1$ receptors, it should cause in all logic an acceleration of the heart rate. In fact, noradrenaline could also cause a reflex stimulation of the aortic and carotid baroreceptors in response to a rise in the diastolic and systolic pressures and lead to brutal bradycardia (Berini and Gay, 1997 [LoE IV]). The duration of the rise in blood pressure consecutive to a noradrenaline injection is 4 minutes and that of the bradycardic effect is 15 minutes (Knoll Kohler, 1988 [LoE IV]).

Anaesthetic solutions containing an association of adrenaline and noradrenaline have been marketed. Although no specific study has been published on this subject, the opinion of the literature is unfavourable asserting that the beneficial effects of these associations are not higher than those of adrenaline alone whereas they add the disadvantages of noradrenaline (Jage, 1993 [LoE IV], Berini and Gay, 1997 [LoE IV]).

2.2. Other vasoconstrictors

Facing the risks identified with catecholamines, the researchers and the industrialists thought of using non-catechol vasoconstrictive substances derived from a natural hormone secreted by the post-pituitary gland: vasopressin.

Felypressine (phenyl alanine 2-lysin-vasopressin 8) is the leader of the synthetic analogues of

vasopressin, it has its local vasoconstrictive characteristics without having its powerful diuretic effects nor the vasoconstrictive effects on the coronary arteries (approximately one third of the coronary action of vasopressin) (Goldman and coll, 1971 [LoE IIb]).

It does not seem to act on blood pressure nor on the central nervous system (Von Tsakiris and Bultmann, 1961).

Recent well documented research (Sunada and coll, 1996 [LoE IIa]) relativises the systemic advantages of felypressine which was regarded at a time as the vasoconstrictor of choice in patients with a history of myocardial ischaemia (Johnson and Widrich, 1977 [LoE Ib]). In this article, the myocardial effects of various solutions of 2% propitocaine associated with doses varying from 0 (reference group) to + 0,25 IU.ml^{-1} of felypressine are compared in 26 patients suffering from essential hypertension. The results show that the systolic pressure is increased in the groups with high doses of felypressine compared to the reference but that all the groups have a rise in diastolic pressure compared to the reference.

Even if myocardial ischaemia is not highlighted formally because of experimental skews, the authors observe a reduction of the myocardial contractility in the 3 groups with the highest doses of felypressine.

They conclude by recommending a dose of 0,18 IU of felypressine in patients with essential hypertension which corresponds to 6 ml of 3% propitocaine with 0,03 IU of felypressine.

Volpato (1999) [LoE Ib] shows that with a high dose in the animal, the toxicity of adrenaline and felypressine are comparable but that adrenaline would have a "protective" effect as for the onset of convulsions when it is associated with lidocaine.

Shanks (1963) [LoE III] showed that the effects of the interaction of felypressine with halogenous general anaesthetics are close to those of adrenaline. Roberts and Sowray (1987) [LoE IV] recommend not to use felypressine in pregnant women because of a possible inhibitory action on placental circulation by interfering with uterine tonicity.

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 12

Ornipressin (POR-8) is another synthetic analogue of vasopressin which has local vasoconstrictive properties. It was at one time described as the vasoconstrictor of choice in infiltration of the operative field but severe complications (Kleemann and coll, 1986 [LoE IV]; Cantaloube, 1991 [LoE IV]) showed its powerful constrictor effect on the coronary arteries and led it to be abandoned.

Mixed with a LA ornipressin has much lower performances than adrenaline: it takes approximately 10 minutes to obtain its maximum vasoconstrictor effect (Jage, 1993 [NdP IV]) which complicates its use.

Corbadrine is still found in association with aptocaine, a LA having known a renaissance recently because of a good tolerance in some hepatic porphyries. Corbadrine is an alpha-methyl noradrenaline much less toxic than noradrenaline itself. Nevertheless its vasoconstrictive activity is much weaker. Doses 10 times higher than that of noradrenaline have to be given to obtain a comparable effect. Moreover, this synthetic substance is slowly eliminated which prolongs its action which can constitute an obstacle. This prolongation of the duration of action is related to the presence of a methyl group which prevents the degradation of corbadrine by mono-oxydase (Jacquot and coll 1978 [LoE IV]).

Adrenaline is industrially and medically the leader of vasoconstrictors used alone or in association with LA in odonto-stomatology. It has the broadest casuistry which confirms the great safety of this molecule. The non catechol derivatives have not shown their superiority to date even among patients likely to badly tolerate catecholamines.

3. Indications of vasoconstrictors in odonto-stomatology

The characteristics of vasoconstrictors associated with LA solutions have been reminded in this work and justify the very broad use of these associations in infiltration anaesthesias in odonto-stomatology. The working group questioned two anatomically opposed anaesthetic techniques for which the use of vasoconstrictors poses different problems. They are: on the one hand local anaesthesias known as intrapulpal, intraseptal, intradiploic and intraligamentary anaesthesia; on the other hand loco-regional anaesthesias at the mandibular foramen which are carried out in a richly vascularised territory as well on the arterial level as on the venous level which raises the risk of endovascular injection of an anaesthetic substance containing adrenaline.

3.1. Do vasoconstrictors have to be used at the time of intrapulpal, intraseptal, intradiploic and intraligamentary anaesthesias?

These anaesthesias have in common the fact that the anaesthetic solution is infiltrated in an anatomically closed space where diffusion will be minimal so that the quantity injected will be low and that the addition of a vasoconstrictor could appear useless even harmful because of the aggressiveness of the local vasoconstriction it causes on the tissues (Madrid and coll, LoE [NdP IV]).

Intra-osseous or intradiploic anaesthesia has been the subject of many studies aiming at studying in particular the contribution of these techniques as a complement of the loco-regional techniques of anaesthesia of the mandibular nerve at the mandibular foramen. Reitz and coll (1998) [LoE Ib] tested 0,9 ml of a solution of 2% lidocaine with 1/100000 adrenaline in intra-osseous injections in the region of the 2nd molar, 1st molar and 2nd premolar in 38 subjects. Guglielmo and coll (1999) [LoE Ib] followed a strictly identical protocol with a solution of 2% mepivacaine containing 1/20000 levonordefrine in 40 subjects. In both cases no local complication was reported by the authors with the use of a vasoconstrictor in intra-osseous injections. Dunbar and coll (1996) [LoE Ib] and Coggins (1996) [LoE IIa] have, as for them, noted inflammation and suppuration at the point of injection but in both cases the authors accuse the injection technique and not the possible effect of the vasoconstrictor.

Replogue and coll (1998) [LoE Ib] has, as for him, established the superiority of an intra-osseous injection of 2% lidocaine with 1/100 000 adrenaline compared to a solution of 3% mepivacaine without vasoconstrictor during the anaesthesia of the 1st mandibular molar which does seem to indicate an interest in the use of vasoconstrictors since mepivacaine is practically neutral as for vasodilation even slightly vasoconstrictive. These results are concordant with those of Petrikas (1990) [LoE III] who studied on 22 subjects the efficiency of a solution of lidocaine with and without adrenaline during a series of intraseptal injections: he concluded that the addition of adrenaline improves the depth of the anaesthesia, its success rate and its duration, contributes to the pulpal dissemination of the anaesthesia and does not increase the local noxious effects.

For intraligamentary anaesthesia, the research of Tagger and coll (1994) [LoE Ib] clearly showed that the anaesthesia results more from intra-osseous diffusion than from direct diffusion to the apex so that the remarks made for the intra-osseous techniques should apply to the intraligamentary techniques. In fact, the work of Gray and coll (1990) [LoE IIa] showed at the same time the absence of noxious effects of vasoconstrictors associated with an anaesthetic solution injected into the ligament (lidocaine + adrenaline or prilocaine + felypressine) and the marked superiority of the success rates with vasoconstrictors compared to LA alone.

The work of Walton (1982) [LoE IIb] and of Galili and coll (1984) [LoE IIb] show a complete recovery of the periodontal ligament after 8 to 15 days of healing in the monkey having undergone intraligamentary injections of solutions comprising a vasoconstrictor. Tsirlis and coll (1992) [LoE IIa] showed in a study group of 305 mandibular tooth extractions that the frequency of dry socket after intraligamentary anaesthesia was not increased compared to a reference group with a conventional anaesthesia. Mc Lean and coll (1992) [LoE Ib] showed the superiority of a solution of bupivacaine with 1/200 000 adrenaline over a solution of lidocaine with 1/100 000 adrenaline.

Finally in a methodologically rigorous study, Handler and Albers (1987) [LoE IIb] compared the use of 4 different solutions during intraligamentary anaesthesias: 2% lidocaine, 2% lidocaine with 1/50000 adrenaline, 2% lidocaine with 1/100000 adrenaline and finally 1/100000 adrenaline alone. Their surprising results show that contrary to what is usually reported, there is no relation of proportionality between the amount of adrenaline present in the solution and the duration of the anaesthesia measured with the pulp tester. There is no difference between the 4 solutions as for the frequency of success of the anaesthesia. The anaesthesia is also obtained with the solution of adrenaline alone which the authors explain by the fact that the anaesthesia in this case would be related to the pressure and not to the pharmacological action of the vasoconstrictor. The use of a vasoconstrictor in intrapulpal, intraseptal, intradiploic and intraligamentary anaesthesia techniques is not essential but considerably improves the frequency, the duration and the depth of the anaesthesia obtained. If the injection is carried out under adequate conditions: controlled pressure, slow injection, small volumes – 0,2 ml on average per dental root, (Handler and Albers, 1987) [LoE IIb] – the local lesions directly ascribable to the vasoconstrictor are negligible and reversible.

Systemic effects of these injections exist but are generally much lower than those observed in anaesthesias by infiltration.

3.2. Do vasoconstrictors have to be used during loco-regional anaesthesias of the mandibular nerve?

For a long time the risk of an intravascular injection of an anaesthetic solution with adrenaline was suggested as an argument in favour of the proscription of the use of a vasoconstrictor in the anaesthesia technique at the mandibular foramen (Gaudy and Aretto, 1999) [LoE IV]). This argument is opposed to the consensual feeling in the profession that the success rate of the loco-regional mandibular anaesthesia is related to the presence and the dose of the vasoconstrictor. The literature does not confirm this

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 14

impression. Keesling and Hinds (1963) [LoE Ib] compared 5 solutions of 2% lidocaine containing respectively 1/50 000, 1/250 000, 1/750 000, 1/1000000 adrenaline and without adrenaline for anaesthesia at the mandibular foramen. The authors report a success rate with the pulp tester of 87,5% for an average duration of anaesthesia of 44 ± 5,7 minutes for lidocaine without adrenaline. To be compared for example with a success rate of 96% and an average duration of 66,9 ± 8,7 minutes for the 1/750 000 solution. There does not seem to be a significant difference between the solutions with 1/50 000 and 1/250 000, neither for the success rates, nor for the duration of the anaesthesia.

Mac Lean and coll (1993) [LoE Ib] thus showed by testing on 30 subjects 3 anaesthetic solutions (2% lidocaine with 1/100 000 adrenaline, 4% prilocaine alone and 3% mepivacaine alone) that there was no significant difference in the success rates of the anaesthesia at the mandibular foramen controlled with the pulp tester.

Dagher and coll (1997) [LoE IIa] tested 3 solutions of 2% lidocaine with respectively 1/50000,1/80 000 and 1/100 000 adrenaline. According to the methodology of Mac Lean (1993) out of 30 subjects in good health, the 3 solutions appear equivalent as for the success rate, the rate of failure and the frequency of the anaesthesia. Malamed (1997) [LoE IV] recommends the block anaesthesia of the alveolar nerve with vasoconstrictor only if a prolonged duration of the anaesthesia is required.

Knoll-Kohler and Fortsch (1992) [LoE Ib] tested, on 10 students, two solutions of 2% lidocaine without adrenaline, one with a pH of 3,5, the other with a pH of 6,8, and three solutions of 2% lidocaine with 1/50 000, 1/100 000 and 1/200 000 adrenaline. According to these authors lidocaine without adrenaline whatever the pH shows a high rate of failures and a lower duration. The addition of 1/100 000 or 1/200 000 adrenaline improves the success rate and the duration of the anaesthesia but does not make the latency time vary. These results are in agreement with those of Kabambe and coll (1982) [LoE Ib] who observe, by comparing a solution of lidocaine with and without adrenaline, a failure in more than half of their subjects during anaesthesia of the lower alveolar nerve.

The addition of a vasoconstrictor to the anaesthetic solution is not essential for anaesthesia of the lower alveolar nerve at the mandibular foramen. The addition of adrenaline increases the duration of the anaesthesia but does not seem to have a decisive effect on the success rate. The results concerning the success rate of the anaesthesia are contradictory. Taking into account the relation which exists between the success rate and the volume of solution injected (Vreeland, 1989) [LoE IIb], the addition of a vasoconstrictor could prove to be judicious in the prevention of the systemic effects of LA.

Another argument called upon to dispute the use of a vasoconstrictor in loco-regional anaesthesia of the mandibular nerve is the fact that the vasoconstrictor could lengthen the duration of the labio-mental anaesthesia and consequently favour wounds by lip biting which constitute one of the most frequent adverse effects of these injections (Wahl, 2000). In fact, research has shown that only the pulpal anaesthesia is lengthened during loco-regional anaesthesias of the mandibular nerve with vasoconstrictor and not the labio-mental anaesthesia (Hersh and Hermann, 1995 [Not classified: clinical case]; Yaguiela, 1985 [LoE Ib]).

4. Dose of vasoconstrictors in odonto-stomatologic anaesthesia

There does not exist a definitively conclusive work concerning the ideal dose of adrenaline in LA. Fink (1978) [LoE IIb] showed that the duration of the local anaesthesia (all techniques taken into account) was directly dependent on the amount of adrenaline present in the solution: the duration obtained for a solution of 1% lidocaine with 1/50000 adrenaline is 210 minutes, 160 minutes with 1/100 000 and 130 minutes with 1/200 000. Taking into account the average duration of dental acts, Himuro and coll (1989) propose to replace lidocaine with 1/80 000 by lidocaine with 1/200 000 after a comparative test on only 6 volunteers. Since 1967, Gangarosa

and Halik [LoE Ib] showed that the solution of lidocaine with 1/100000 or with 1/300000 were equivalent for the speed of onset and the efficacy evaluated according to the experience of a group of 17 dental surgeons in a prospective double blinded series of 542 patients. With regard to the duration of the anaesthesia, which is believed since Braun (1924) [LoE III] to be dose-dependent; the results of the same study show a negligible gain in terms of duration while passing from the anaesthetic solution with 1/300 000 adrenaline to the solution with 1/100 000 adrenaline. Knoll-Kohler (1992) [LoE Ib] after studying 10volunteers affirms that only lidocaine with 1/100000 gives constant results. Obviously, the dosing of adrenaline must be adapted to the characteristics of the LA molecule. In addition to lidocaine, carticaine and articaine are also available and marketed with 1/100000 and 1/200000 adrenaline.

Vahatalo and coll (1993) [LoE Ib] tested 2% lidocaine with 1/80000 adrenaline and 4% articaine with 1/200000 adrenaline for latency time and duration of the anaesthesia controlled with the pulp tester. There was no statistically significant difference between the two groups which would make it possible to choose the molecule containing the lowest dose of adrenaline.

Knoll-Kohler and coll (1992) [LoE Ib] compared 4% articaine with 1/100000 and the solution with 1/200000 during the extraction of a 3rd mandibular molar by measuring the variations of heart rate, the concentration of cyclic AMP and the level of noradrenaline. These parameters were correlated to the plasmatic levels of adrenaline as a reference of endogenous secretion. The resorbtion of adrenaline from the site of injection appeared to be dose-dependent which should have made the authors lean in favour of the solution with 1/200000 adrenaline.

In fact, in earlier research, Knoll-Kohler (1991) [LoE Ib] estimated that the risk of cardiovascular accident was all the more high as the operational gesture was prolonged and that the dose of adrenaline was low.

This result is disputed by the work of Daublander and coll (1997) [LoE III] who note that the sympathomimetic side effects of the LA injections with vasoconstrictor are significantly more important in their retrospective series of more than 2700 subjects for the solution of articaine with 1/100000 in comparison with the solution of articaine with 1/200000. Jage (1993) [LoE IV] estimates that the best concentration in the healthy patient is (all molecules taken into account) 1/100000 to 1/200000 knowing that the individual maximum dose is 0,25 mg. On the other hand in the patient presenting a vascular pathology the obligatory concentration would be 1/200000. Let us recall that for 1 ml of anaesthetic solution a solution with 1/1000accounts for 1 000µg of adrenaline while a solution with 1/200 000 contains 5µg of adrenaline.

For mepivacaine Berling's research (1958) [LoE IIb] shows an absence of statistically significant difference between the 2% solutions with respectively 1/100000 and 1/200000 adrenaline for the success rate and the duration of the pulpal anaesthesia.

Work is still contradictory concerning the ideal dose of adrenaline in 2% solutions of lidocaine. The solution with 1/200000 gives more than two hours of anaesthesia which represents a sufficient duration for the immense majority of all odonto-stomatologic acts. For 4% articaine and 2% mepivacaine, 1/200 000 solutions should be preferred in the absence of significant difference in performance with the 1/100000 solution.

Finally the work of Jorkjend and Skoglung (2000) [LoE Ib] clearly shows:
• On the one hand that the increase in the volume of adrenaline and local anaesthetic solution injected can have an adverse effect which is the increase in post-operative pain without counterparts in terms of duration or quality of the anaesthesia;
• On the other hand that the increase in the dose of adrenaline in the anaesthetic solution also significantly increases post-operative pain by rising the level of cyclic AMP in gingival tissues which enhances the accumulation of noxious substances or pro-algesic mediators.

5. Drug interactions

Vasoconstrictors used in association with LA but also as topic or injectable haemostatic agents and finally on gingival retraction cords have the potential to interact with a broad variety of drugs (Hansten, 1981) [LoE IV].

Local reactions go as far as local ischaemia and necrosis (Yagiela, 1999; Damm and Fantasia, 1992). They are related to the relative overdose by saturation of the tissues with the vasoconstrictor and with too rapid injections (Meechan, 1998) Most of the systemic reactions

are of short duration mainly because of the rapid inactivation of the vasoconstrictors once that they are absorbed in the blood flow (Yaguiela, 1999) [LoE IV]. Nevertheless serious lesions or even the death of the patient can result from fibrillation of medicamentous origin, a myocardial infarction or a cerebro-vascular accident (Hilley, 1984; Okada, 1989; Massalha, 1996) [Not classified: clinical cases].

5.1. Tricyclic antidepressants

They are gradually replaced by selective inhibitors of the recapture of serotonin, nevertheless they remain used among patients who are intolerant or resistant to these new drugs. Tricyclic antidepressants block the active recapture of biogenic amine neurotransmitters (catecholamines and serotonins) by the nervous terminations where they were released. The result is a potentiation of the concerned neurotransmitters: the adrenergic vasoconstrictors but especially noradrenaline are prone to the same phenomenon of recapture. Tricyclic antidepressants block the muscarinic and alpha1 adrenergic receptors and depress the myocardium what can in turn modify the cardiovascular response to vasoconstrictors.

According to Boakes and coll (1972) [LoE IV] out of 15 case of patients having presented severe disorders with noradrenaline, 5 took tricyclic antidepressants.

Such accidents can occur for injections of 2,5 cartridges of 1/100000 adrenaline (Persson and Siwers, 1975) [LoE IV]. Cawson and coll (1983) [LoE IV] drew aside the possibility of cli-

nically significant interactions between tricyclic antidepressants and LA containing adrenaline. Actually if the theoretical risk is high the clinical signs are rare. Several factors contribute to it:
– the competition between the vasoconstrictor (α adrenergic) and vasodilator (β_2 adrenergic) effect leads to a compensation of the haemodynamic variations at the usual doses in odonto-stomatology;
– the prescription of these drugs is often done on a long term basis which causes a desensitisation to adrenergic vasoconstrictors and consequently a reduction in the risk of interaction (Moyer and coll,1979) [LoE Ib].

The attitude toward patients under tricyclic antidepressants must be to avoid noradrenaline in association with LA and to inject measured doses of LA associated with 1/100 000 or 1/200000 adrenaline. In practice the amount injected should be one third of the maximum amount in the normal subject (Yaguiela, 1999 [LoE IV]).

5.2. Monoamine oxydase inhibitors

The only selective inhibitors still used do not present an interaction with adrenaline. Studies repeated in human subjects and the animal did not show any significant interaction with the doses used in odonto-stomatology (Boakes and coll, 1973 [LoE IV]; Wong and coll, 1980 [LoE Ib]).

5.3. Beta-blockers

Although broncho- and vasoconstrictor effects can theoretically appear when taking cardio- or beta1 selective beta-blockers (which are thus likely to cause asthma attacks), there does not exist any incident described among patients in whom beta-blockers, cardio-selective drugs and adrenaline anaesthetic solutions were associated (Pallash, 1998 [LoE IV]).

Thus it is mainly non cardio-selective beta-blockers that competitively block the stimulation of the $beta_1$ and $beta_2$ receptors by endogenous catecholamines which are the cause. They also block the activation of the beta receptors by exogenous catecholamines. It is mainly upon the $beta_2$ receptors that the beta-blockers act

by transforming adrenaline into an exclusively alpha-adrenergic drug. The consequences are an increase in peripheral resistances and, directly in connection with the dose, an increase in blood pressure and a deceleration of the heart rate which can lead to major and well documented accidents (Hansbrough and Near, 1980; Foster and Aston, 1983 [Not classified: clinical cases]).

This risk must be moderated for non cardio-selective beta-blockers with an intrinsic sympathomimetic activity (ISA) for which the partial beta-agonist activity leads to a limitation of the bradycardia and vasoconstrictor effect. Let us note that beneficial local effects have been described for beta-blockers like lengthening of the duration of the pulpal anaesthesia and soft tissues (Zhang, 1999 [LoE Ib]).

The precautions will include a split and slow injection of LA containing no more than 1/100000 adrenaline after negative aspiration.

5.4. General anaesthetics

We have discussed the possible interactions with halogenous derivatives. The mechanism by which GA potentiate the arythmogenous effects of catecholamines are unknown. It is probably a simultaneous stimulation of the alpha1 and beta receptors. Adrenaline is in turn able to activate the two types of receptors and to generate rhythm disorders during general anaesthesia (Hayashi, 1993 [LoE Ib]).

Thiopental is also able to exaggerate the arythmogenous potential of adrenergic substances. As thiopental is often used during induction with halogenous derivatives, its interaction was initially under estimated.

When thiopental is used alone, a dose of adrenaline of 2 µg.kg^{-1} will be allowed in per-operative injection under general anaesthesia. This dose will be 1 µg.kg^{-1} if the thiopental is associated with halothane (Christensen and coll, 1993 [LoE IV]). One death has been reported under halothane, due to an interaction with a retractor cord containing racemic adrenaline (Hilley and coll, 1984 [Not classified: clinical case]).

5.5. Cocaine

Animal experiments and human cases have given proof of the interaction of cocaine with adrenergic vasoconstrictors. (Lathers and coll, 1988) [Not classified: clinical case]. Several deaths whose study is well documented, appear in the literature (Chiu, 1986) [Not classified: clinical case]. The mechanism is a facilitator effect of cocaine on the release of adrenergic neurotransmitters and the intensification of postsynaptic responses to adrenaline-like substances. The blocking of muscarinic cardiac receptors and the central deterioration of the vegetative nervous system can moreover contribute to worsen the reactions to the injection of vasoconstrictors.

No dental treatment should be carried out in patients under the effects of narcotics. Vasoconstrictors will be proscribed for at least 24 hours after the consumption of cocaine to allow the elimination of the drug and its active metabolites.

5.6. Antipsychotic drugs and alpha-blockers

These drugs (chlorpromazine, thioridazine, risperidone) have as a side effect blocking of the alpha-adrenergic receptors and thus causing orthostatic hypotension reactions. In the event of overdose, the plasmatic passage of adrenaline would be worsening since only beta$_2$ receptors would be activated leading to vasodilation. It is in fact a strictly theoretical risk: no seriously documented accident has been reported with the doses used in odonto-stomatology.

5.7. Guanethidine

Being a substance inhibiting the release of noradrenaline at the terminal sympathetic nerve fibres, it is used in the treatment of severe arterial hypertension: used over a long period it could cause a multiplication of adrenergic receptors or a decrease in their sensitivity threshold.
This risk is theoretical for a rare drug.

5.8. Adrenergic anorectics

These are sympathomimetic drugs that affect the metabolism of catecholamines and are chemically similar to amphetamines. These drugs

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 18

increase the adrenergic neurotransmission and stimulate the central nervous system, their anorectic activity follows from this stimulation of the SNC.

Their effects can be potentiated by the concomitant use of vasoconstrictive substances. It is the case of *mazindol* for which the FDA and the manufacturer recommend caution before use with vasoconstrictors (Wynn, 1997 [LoE IV]).

6. Does there exist pathologies contraindicating vasoconstrictors?

One must keep in mind that 45% of the patients presenting at a dental practice have one or more intercurrent pathologies with the oral pathology and that 20% of them present a cardiovascular pathology. Daublander and coll (1997) [LoE III] estimate in their series at 0,07% the risk of a serious accident in connection with a local anaesthesia at the dental surgery which is comparable with the incidence of serious complications of general anaesthesia (0,05%). But these figures must be balanced by the status of the patient. Thus the side effects observed under dental local anaesthesia concern 5,7% of the patients presenting risks against 3,5% of the healthy patients. These figures are to be put in relation with those of general anaesthesia for which the side effects affect 12,3% of ASA 1 patients and 34,9% of ASA III and IV patients. Daublander shows clearly that the found side effects are independent of the anaesthetic molecule used (articaine, lidocaine or mepivacaine) and of the presence or not of an associated vasoconstrictor but rather depend on the dose employed.

Local anaesthesia with vasoconstrictor is thus, in odonto-stomatology, a very safe technique whose contraindications appear to be largely exaggerated.

6.1. Hyperthyroidism
Hyperthyroidism can result from a disease or follow from a chronic overdose in thyroxine. Hyperthyroidism will result in cardiovascular disorders which reproduce the effects of an overdose in adrenaline: tachycardia and other arrhythmias, widening of the amplitude of the pulse, myocardial ischaemia... It was believed for a long time that adrenaline and noradrenaline took part in the disorders of hyperthyroidism in a synergistic manner to that of thyroxine; It is not the case: in hyperthyroidism, the haemodynamic responses to the action of adrenaline and noradrenaline are not fundamentally changed. (Yaguiela, 1999 [LoE IV]).

Recent studies (Johnson, 1995 [LoE Ib]) have shown that hyper- and hypothyroid patients do not present major disorders when they are subjected to corrective treatment and put in the presence of catecholamines before the beginning of this treatment. Although the theoretical risk of thyroxine-adrenaline potentiation is serious, no clinical cases have been reported.

6.2. Hypertension
Hypertension and its relationship with vasoconstrictors are the subject of an abundant literature. It is now largely accepted that the plasmatic passage of the vasoconstrictor is practically negligible in terms of cardiovascular effect (increase in the heart rate and the blood pressure) in comparison with endogenous catecholamine secretion in case of pain and stress. The totality of the debate on the cardiovascular changes induced by the possible addition of a vasoconstrictor to LA thus focuses on the evaluation of the exogenous contribution (about $20 \mu g.l^{-1}$) caused by the injection of a cartridge as compared with the level of the plasmatic concentration which is around $300 \mu g.l^{-1}$. If one considers the physiological capacity to absorb such an exogenous contribution, certain well documented facts can be taken into account: at the time of the childbirth without peridural the labour pains can multiply the level of plasmatic adrenaline by a factor 4 to 6 (Bonica, 1999 [LoE IV]); at the time of a dental extraction the stress alone without pain multiplies the plasmatic adrenaline by a factor 10 or 20. The passage into the blood at the time of the resorbtion of 2,2 ml of lidocaine with 1/100000 adrenaline causes only a doubling of the rate of plasmatic adrenaline (Tolas, 1982 [LoE IIa]).

Chernow and coll (1983) [LoE Ib] compared the LA injection associated with adrenaline and without vasoconstrictor in 14 healthy subjects for variations in blood pressure, heart rate and dose of endogenous catecholamines. They point out significant results after injection of the solution with adrenaline for the rise in catecholamine concentration during 60 minutes after injection: the concentration passing from 27+/4 pg.l⁻¹ to 94+/-13 pg.l⁻¹ in a 1:3 ratio. The same team (Cioffi, 1985 [LoE IIb]) reported an increase in a 1:3,5 ratio in the concentration of circulating catecholamines after anaesthesia with adrenaline for conservative treatment. These concentrations being divided by two from the very start of the treatment procedure (dental dam placement).

In 1993, Lipp and coll [LoE Ib] tried to identify in the increase of catecholamines which follows an anaesthetic injection the part which results from the exogenous contribution by the anaesthetic solution with vasoconstrictor from the part which results from the rise in endogenous catecholamines related to stress due to the infiltration and the global fear of the operational act. In order to do so the authors used an injection of 4 % articaine with 20 µg of marked adrenaline. They observed a rise in the total adrenaline concentration (exogenous and endogenous) 5 to 10 times higher than in the reference group treated without anaesthesia. They also observed two serum peaks of adrenaline: one 5 minutes after the beginning of the injection, the other after the beginning of the dental treatment. The authors affirm that the increase in total catecholamines is mainly the result of the exogenous contribution and explain the peak which marks the beginning of the treatment by the increase in the rate of the plasmatic resorbtion of the anaesthetic due to the inevitable massage of the site of injection by the fingers of the operator.

Niwa and coll (2000) [LoE Ib] in a particularly detailed and sophisticated work established that the infiltration of 3,6 ml of 2 % lidocaine with 1/80000 adrenaline was equivalent, in terms of haemodynamic effects and plasmatic catecholamine rates, to the perfusion of 10ng.kg.mn⁻¹ of adrenaline alone. The plasmatic catecholamine rate passing from 52+/ 24pg.l⁻¹ to 363 +/- 105 pg.l⁻¹ for the anaesthetic infiltration with adrenaline and from 32+/ 18pg.l⁻¹ to 214 +/- 69 pg.l⁻¹ for the perfusion of 10 ng.kg.min⁻¹, i.e. being multiplied by a factor 7.

But if one could show a significant increase in total catecholamines after LA injection with vasoconstrictor and even show the dominating share of exogenous catecholamines in this increase, it is impossible to know with precision the cardiovascular repercussion of this increase because other additional factors make the interpretation of the results random. Thus, Di Angelis and Luepker (1983) [LoE IIa] showed that the only fact of going to the dental surgeon's for a simple check-up caused a rise in the blood pressure of 4,5 mm Hg higher than that of a check-up at the doctor's. Work of Gortzack and coll (1992) [LoE Ib] confirm these results and show that there is no difference between normo- and hypertensive subjects on this point. Many authors finally think that it is impossible to establish proportionality between increase in total catecholamines and cardiovascular effects, since if the majority observe this increase after LA injection with vasoconstrictor, they agree that they have not observed manifest clinical repercussions in healthy or hypertensive subjects (Sack and Kleeman, 1992 [LoE IIa]).

Cheraskin and coll (1958) [LoE Ib] have shown that the main factor in the rise in blood pressure took place in the waiting room and not during the operational phase. This rise in blood pressure was not significantly different between hypertensive and normotensive patients but it was significantly reduced in the hypertensive subjects who received a sedative premedication 45 minutes before the time of the appointment. This work thus clearly highlighted the role of stress in comparison with the discrete role of the exogenous catecholamine injection at the time of the LA.

The same authors showed in later work (Cheraskin and Prasertsuntarasai, 1959 [LoEIb]) that the phase of 5 to 10 minutes which follow the anaesthetic injection with or without adrena-

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 20

line is marked by no significant change in blood pressure or pulse, whether the patient is initially normo or hypertensive. They foresee the later results of Campbell (1996) [LoE IIb] by specifying that it is at the beginning and the end of the operational act itself that the most significant changes are observed.

Their conclusion is that the use of a preoperative sedative and of a vasoconstrictor associated with a LA in hypertensive subjects gives significantly better results in terms of control of the blood pressure and pulse compared to hypertensive subjects who receive neither a sedative nor a vasoconstrictor. This result is to be put in relation with the work of Goldstein (1982) [LoE Ib] which shows that the haemodynamic variations observed are principally due to the endogenous noradrenaline secretion under the effect of the operational stress, secretion well compensated by the administration of a sedative premedication by diazepam.

Meyer (1987) [LoE Ib] compared the variations of blood pressure in 60 healthy subjects receiving for 30 of them a LA injection with adrenaline and for the 30 others a LA injection without vasoconstrictor. The results show that the blood pressure of the patients of the group without vasoconstrictor are significantly worse, in terms of control of the blood pressure, than those of the group with vasoconstrictor. The author logically explains these results by the bad quality of the anaesthesia obtained when the LA was injected alone and thus by the endogenous catecholamine hypersecretion. It should be noted that in the two groups half of the subjects underwent only the anaesthesia while the others were subjected to an anaesthesia followed by a tooth extraction. In the group without vasoconstrictor, those who underwent the extraction presented significant variations in blood pressure.

Thus there is no contraindication to use of a LA associated with adrenaline in particular for acts requiring a prolonged and deep local anaesthesia in hypertensive subjects stabilized by an antihypertensive treatment.

The maximum recommended dose is 0,04 mg in total which corresponds to 2 cartridges or 4,4 ml of LA with 1/100000 adrenaline. (Budentz, 2000 [LoE IV]).

For the great majority of stabilised hypertensive subjects, it is possible to exceed this limit while taking into account the rules of overdose (Meechan, 1998 [LoE Ib]). In patients with non-stabilised blood pressure, one will be able to continue the anaesthesia beyond two cartridges with adrenaline with an anaesthetic without vasoconstrictor.

Massalha and coll (1996) [Not classified: clinical case] report 2 cases of intracerebral haemorrhages having resulted in the death of the patient during dental care. We quote them to recall attention. They carry out a review of the literature and put, like the majority of the authors, these major hypertensive pushes leading to death on the account of a hyperstimulation of the trigeminal nerve.

Indeed, in addition to the sensitivity of the face and the masticatory motricity, the trigeminal ganglion, ensures the vasomotor innervation of all the cerebral blood vessels (Moskowitz, 1984 [LoE IV]). They conclude that there is a simultaneous effect of this hyperstimulation and haemodynamic changes induced by the rise in the serum peak of catecholamines after anaesthetic injection. Their point of view is purely conjectural. In the event of unstable blood pressure associated with other elements burdening the prognosis, the treatment will have to be carried out in a hospital disposing of a reanimation structure and under vital function monitoring.

6.3. Rhythm disorders

The literature concerning the study of the variations of the heart rate induced by the injection of LA with vasoconstrictor is rich and often of a very good level of evidence (Meyer, 1987 [LoEIb]; Montebugnoli, 1990 [LoE Ib]; Blinder, 1996 [LoE IIb]; Campbell, 1996 [LoE IIb]; Replogue, 1999 [LoE Ib]).

A very well documented work by Campbell and coll (1996) [LoE IIb] allowed to study the variations of the heart rate in a population of 40 old-aged subjects (20 reference subjects and 20 subjects with arrhythmia (treated or not)) at various times of the intervention: preoperative,

anaesthetic injection, per-operational, post-operative. The results made possible the downfall of some common beliefs: (1) there was no significant difference between the reference group and the arrhythmia group as for the onset of an episode of benign arrhythmia (17 subjects); (2) the results show in a paradoxical way that the rise in the heart rate is definitely lower during the anaesthetic injection compared to the pre and per operational rise of the heart rate; (3) the authors show moreover that the injection of an anaesthetic solution with vasoconstrictor is probably not implied in the episodes of benign arrhythmia observed: the serum peak of the vasoconstrictor was reached on average 5 minutes after the injection whereas the episodes of arrhythmia were after half of the surgical time, i.e. well after the serum peak of the vasoconstrictor.

This work can be compared to the results of Blinder and coll (1996) [LoE IIb] on the electrocardiographic changes observed by Holter monitoring among 40 cardiac patients followed-up 1 hour before an extraction under LA without vasoconstrictor and 23 hours afterwards. These results show that 14 patients presented significant changes on the ECG and 12 of them presented an arrhythmia although no vasoconstrictor was present in the solution.

Another result is that 12 of the 14 patients having presented a significant change on the ECG were under digoxin, either for ischaemic accidents or for auricular fibrillation. These results seem to show the capacity of the anaesthetic injection to cause alone, via the physiological and psychological stress which are associated to it and via the interaction of the pro-arrhythmogenic effects of LA, acute modifications of the heart rate in a significant percentage of patients whether they have healthy cardiovascular functions or not (Malamed, 1996).

The authors in agreement with Stanley Malamed [LoE IV] recommend the monitoring of patients under digoxin at the time of a local anaesthesia. The intra-osseous injections which cause a more important rise in the heart rate and blood pressure must be avoided (Chamberlain, 2000 [LoE IIb]). Replogue and

coll (1999) [LoE Ib] propose the use of a 3% solution of mepivacaine as an alternative to the injection of a LA solution with adrenaline in these patients.

The rhythm disorders met in daily practice are essentially auricular fibrillations stabilised by an adapted treatment (Anguera Camos and Brugada Terradellas, 2000 [LoE IV]).

Under these conditions the control of stress and the therapeutic heart rate is essential and the use of anaesthetics with vasoconstrictors is indicated. The dosing rules are the same as those discussed previously.

6.4. Coronary cardiopathies

These pathologies are frequently related to the two preceding ones and it appears obvious that close answers can be given, nevertheless taking into account the extreme frequency of this pathology and the confusion which exists in our minds on their subject, as well in the general practitioners or specialists as in the dental surgeons, the working group made a point of devoting a specific paragraph to it.

Episodic myocardial ischaemias during stable or unstable known coronary artery disease fr.:coronaropathies??) pass clinically unperceived in more than 2/3 of cases (Quyyumi and coll, 1985 [LoE IIa]). Extra cardiac surgery, even minor, is one of the identified sources of episodes of myocardial ischaemia in known coronary patients (Deanfield, 1984 [LoE IIa]).

Much work has shown that anomalies of the ST segment of the ECG translate episodes of myocardial ischaemia. In 1989, Vanderheyden and coll [LoE Ib] studied these anomalies of the ST segment during periodontal treatment under LA with a vasoconstrictor among known and treated coronary patients, placed under monitoring in order to evaluate the anomalies of the ST segment in the immediate LA post injection phase. They show that the use of a LA with vasoconstrictor does not cause any significant modification of the ST segment taken as an indicator of myocardial ischaemia.

The recommendations of the American Dental Association and American Heart Association (1964) specify that vasoconstrictors are not

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 22

contraindicated in these diseases when a safe anaesthetic technique is used, when an aspiration test is practised and when the smallest effective dose is used.

6.5. Asthma

Vasoconstrictors associated with an anaesthetic solution can be used in asthmatic subjects in the aim of controlling pain and of avoiding stress which is probably the principal source of passage to an asthma attack at the dental surgery.

Besides adrenaline alone is used for its broncho-dilating properties in the treatment of asthma and a recent systematic review reports level 3 and 4 clinical studies which confirm the absence of adverse effects at the time of its use (Safdar and coll 2001 [LoE IV]). In the particular case of cortico-dependant asthma (Bush and Taylor, 1986 [LoE IIb]; Perusse and coll 1992, 2 [LoE IV]) the problem of the hypersensitivity to sulphites, conservative of the vasoconstrictor, can be posed. It seems however that 96% of asthmatic subjects are not sensitive to the metabisulphite in question (Send, 1986). Besides Wahl (2000) pointed out that a meal at the restaurant contains on average from 25 to 200 mg of sulphite i.e. 27 times the amount contained in a cartridge of lidocaine with 1/100000 adrenaline (0,9 Mg). The recourse to an anaesthetic without vasoconstrictor and bisulphite however is indicated in the event of cortico-dependent asthma.

6.6 Hepatic insufficiency

Patients having presented a previous and cured viral or toxic hepatic attack may be treated like healthy patients.

In the event of evolutionary severe attack, the evaluation of the hepatic function is important. The total quantity injected can have to be reduced and the intervals between the injections increased without detriment to the use of an associated vasoconstrictor.

6.7. Diabetes

Chez les patients diabétiques équilibrés de typeI ou II, l'utilisation de vasoconstricteurs est indiquée. En cas de diabète déséquilibré et instable, avec passage brutal de l'hypo à l'hyperglycémie, les quantités d'AL avec vasoconstricteur seront modérées de façon à tenir compte du caractère hyperglycémiant de l'adrénaline (Meechan, 1996 [NdP Ib]).

6.8. Pheochromocytoma

It is a tumour of the adrenal medulla or paravertebral sympathetic ganglion which causes severe hypertension because of the endogenous hypersecretion of adrenaline. Because of the risk of potentiation of cardiovascular disorders, **pheochromocytoma and all the tumours of the adrenal medulla constitute an absolute contraindication to the use of vasoconstrictors** (Kaufman and coll, 2002 [LoE IV]; Gaudy and Arreto, 1999 [LoE IV]; Perusse and coll, 1992 [LoE IV]). The anaesthetic injection of a solution without vasoconstrictor when it is necessary in the patient suffering from pheochromocytoma must take place in a hospital and under vital function monitoring taking into account the difficulties of per-operational stabilisation of the blood pressure in these patients (Niruthisard and coll, 2002 [LoE III]; Tanaka and coll, 1991 [LoE III]; Pratilas and Pratila, 1979 [LoE IV]).

6.9. Irradiated bone

Any irradiation of the maxillofacial structures in a therapeutic aim, may it be in the form of brachy- or of teleradiotherapy, reduces the vascularisation of the bone so that the bone tissue is not able to defend itself against aggressions any more. Oedema followed by endothelial necrosis induces successively hyalinisation, fibrosis and thrombosis within the wall of the irradiated vessels. The vessels are obliterated and the tissue hypoxia leads to the lysis of collagen then to degeneration of the bone medulla (Marx, 1983 [LoE III]). Osteoradionecrosis (ORN) or radio osteitis constitutes one of the major complications of maxillofacial therapeutic irradiations.

It is easily understood that such a process which generally occurs for irradiations higher than 60 Gy can be favoured by the local ischaemia caused at the point of injection of a LA

containing a vasoconstrictor. In the animal, Heiss and Grasser (1968) [LoE Ib] showed under extreme experimental conditions the significant increase in the risk of ORN after injection of vasoconstrictor substances in irradiated rat mandibles.

Obviously there does not exist a comparable protocol in the human. On the other hand, Maximiw and coll 1991 [LoE IIb] showed that the use of low doses of vasoconstrictors or LA solutions without vasoconstrictor led to, for a group of 449 extractions undertaken in a bone having received on average 50 Gy (values ranging from 25 to 84 Gy), a total absence of post extraction osteoradionecrosis and this after a post-extraction follow-up for 4,8 years on average.

Although the mandible is a clearly identified risk factor of post-extraction ORN, the total amount delivered and the mode of irradiation (Curi and Dib, 1997 [LoE III]) and that there is no evaluation in the human of the direct risk related to the use of vasoconstrictors; **it appears desirable to avoid the association of vasoconstrictors with LA during conservative and especially non-conservative treatment on bone irradiated beyond 40 Gy.**

7 Physiological states and vasoconstrictors

7.1. Pregnancy and breast-feeding

Although vasoconstrictors (especially noradrenaline) have a potential for reducing the placental perfusion, studies undertaken on this subject did not show any adverse effect of adrenaline on the foetus (Haas and coll, 2000 [LoE III]). Actually, the amounts of adrenaline used in the marketed local anaesthetic solutions are so weak that it is very improbable that they can affect the uterine blood flow. As for breast-feeding the only data available is the opinion of authors. They confirm the possibility of using vasoconstrictors in association with LA in women during breast-feeding (Gibbs and Hawkins, 1994 [NdP IV]; Malamed, 1997 [LoEIV).

7.2. Children

In children, taking care of pain is done classically by avoiding a systematic recourse to vasoconstrictors. This practice has no relationship with the toxic risk. It rises from the increase in the severe risk of biting the labial area anaesthetised for a long time after the end of the treatment because of the lengthening of the duration of the anaesthesia in the presence of a vasoconstrictor (Walh, 1997 [LoE IV]; Gaudy and Aretto, 1999 [LoE IV]). This concerns mainly the loco-regional anaesthesia of the mandibular nerve and the danger of biting the lower lip.

Hersh and Hermann (1995) [LoE Ib] nevertheless showed that there was no significant difference in the duration of the labio-mental anaesthesia after injection of mepivacaine without vasoconstrictor when one compares it with an injection of lidocaine + adrenaline. According to these authors, the recourse to an anaesthetic without vasoconstrictor in the child is thus without interest and they recommend on the contrary the use of lidocaine 2% with adrenaline up to a total amount of 4,4cartridges of 1,8 ml in a child of 25 kg against 2,8cartridges of mepivacaine 3% without adrenaline.

Let us note that Hersh and coll (1991) [Not classified: clinical case] reported a mortal overdose in a 5 year old child weighing 16,4 kg and in whom 5 cartridges of 1,8 ml of mepivacaine 3% without vasoconstrictor had been injected.

There are various complex methods for calculating the dose in the child depending on the amount of anaesthetic in the adult, and according to the body surface in relation to the weight. The different formulas of Clark and Young lead to nearby results. The ADA and the FDA propose the conversion charts appearing in tables 1 and 2.

Although in practice the problem seldom arises, the use of local anaesthetics and a vasoconstrictor in a child of less than 6 months is contraindicated taking into account the low metabolic capacities which can lead to an overdose or an accumulation of the free fraction.

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 24

Table 1 : Child dose according to weight calculated according to the usual amount in the adult. According to Berini and Gay, 1997.

Weight of the child in kg	Fraction of the adult dose
10	0,27
15	0,36
20	0,48
25	0,55
30	0,62
35	0,69
40	0,75

Table 2 : Comparison of the total amounts recommended by the Food and Drug Administration in 2% lidocaine with adrenaline and mepivacaine in the adult and the child. According to Wahl, 1997.

	Mepivacaine 3%	Lidocaine 2% + adrenaline
Quantity of anaesthetic per 1,8 ml cartridge	54 mg	36 mg
Maximal number of cartridges per 24 hours for a 70 kg adult	7,4	13,9
Maximal number of cartridges per 24 hours for a 25 kg child	2,8	4,4

7.3. The elderly

The elderly are often the target of the various pathologies which have already been reviewed in this report. It is moreover traditional to consider subjects beyond 70 years of age as suffering from chronic renal insufficiency (after 40years the glomerular filtration drops by 1 ml per minute and per annum) which forces us to decrease the total amounts by a third from 70 to 80 years of age and by half beyond (Commissionnat and Rimet, 1992 [LoE IV]).

BIBLIOGRAPHY

1 - ACKERMAN B, HELBERG IB, TROSSVIK C. Primary evaluation of the local anesthetic properties of the aminoamide agent ropivacaine. Acta Anaesthesiol Scand 1988; 32: 571-8.

2 - ALLWOOD MJ, COBBOLD AF, GINSBURG J. Peripheral vascular effects of nor adrenaline, isopropyl nor adrenaline and dopamine. Br Led Bull 1963; 19: 132-8.

3 - American Dental Association and American Heart Association. Management of dental problems in patients with cardiovascular disease: report of a working conference jointly sponsored by the American Dental Association and American Heart Association. J Am Dent Assoc 1964; 68: 333-42.

4 - ANGUERA CAMOS I, BRUGADA TERRADELLAS P. Nuevas Perpspectivas en el tratamiento no farmacologico de la fibrilacion auricular. Med Clin 2000; 114: 25-30.

5 - BERINI L, GAY C. Anestesia Odontologica. Avances Editeur, Madrid 1997.

6 - BERLING C. Carbocain in local anesthesia in the oral cavity. Odont Rev y 1958, 9: 254-8.

7 - BESNER E. Systemic effects of racemic epinephrine when applied to the bone cavity during periapical surgery. Va Dent J 1972; 49: 9-12.

8 - BLINDER D, SHEMESH J, TAICHER S. Electrocardiographic changes in cardiac patients undergoing dental extractions under local anaesthesia. J Oral Maxillofac Surg 1996; 54: 162-5.

9 - BOAKES AJ. Adverse reactions to local anesthetic vasoconstrictors preparations. Br Dent J. 1972; 1: 133-7.

10 - BOAKES AJ. Interactions between sympathomimetic amines and antidepressant agents in man. Br Dent J 1973; 1: 311-4.

11 - Bonica JJ. Labour pain in Textbook of pain (pp624-6). Churchill Livingstone Editeurs, 3e edition, 1999.

12 - Borea G, Montebugnoli L, Capuzzi P, Vaccaro MA. Ciruclatory dynamics during dental operations in patients with heart transplants. Quintessence Int1993; 24: 749-51.

13 - Brand HS, Van der Wal JHA, Palmer Bouva CCR, de Vries DR. Cardiovascular changes during subgingival debridement. Int Dent J 1997; 47 : 110-4.

14 - Brand HS, Abraham-Inpijn L. Cardiovascular responses induced by dental treatment. Eur J Oral Science 1996; 104: 245-52.

15 - Braun H. Über dein Einfluss der Vitalitat der Gewebe auf die Örtlichen und allgemeinen giftwirkjung lokaler anästhesierender mitteln und über bedeutjung des Adrenalins für die lokalanesthasie. Arch Klin Ckr 1903; 69: 541-91.

16 - Braun H. Local Anesthesia Lea et Febinger Publishers, New York 1924.

17 - Britz-Mckibbin P, Kranack AR, Paprica A, Chen DDY. Quantitative assay of epinephrine in dental anesthetic solutions by capillary electrophoresis. Analyst 1998; 123: 1461-3.

18 - Britz-Mckibbin P, Wong J, Chen DDY. Analysis of epinephrine from fifteen different dental anesthetic formulations by capillary electrophoresis. J Chromat 1999; 853: 535-40.

19 - Bromage PR, Camporesi EM, Durant PA. Influence of epinephrine as an adjuvant to epidural morphine. Anesthesiol 1983; 58: 257-61.

20 - Bush RK, Taylor SL. Prevalence of sensitivity to sulfiting agents in asthmatic patients. Am J Med 1986; 74: 687-91.

21 - Budentz A. Local anaesthetics and medically complex patients. J Calif Dent Ass 2000; 28: 611-19.

22 - Camara AK, Turner LA, Bosnjak ZJ. Interactions of halothane with isoproterenol and epinephrine on canine epicardial conduction velocity at normal and elevated potassium levels. Acta Anaesth Scand 2001; 45: 885-92.

23 - Campbell JH, Huizinga PJ, Das SK, Rodriguez JP, Gobetti JP. Incidence and significance of cardiac arrhythmia in geriatric oral surgery patients. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996; 82: 42-6.

24 - Cannell H. Evidence of safety margins of lignocaine local anesthetics for peri-oral use Br Dent J 1996; 181: 243-9.

25 - Cantaloube D, Rives JM, Daize E, Salleras JP. Traitement préventif et curatif des hémorragies opératoires. Encycl Med Chir Editions techniques Editeur, Paris 22090G10, 1991.

26 - Cawson RA, Curson I, Whittington DE. The hazards of dental local anaesthetics. Br Dent J 1983; 154: 253-8.

27 - Chamberlain TM, Davis RD, Murchinson DF, Hansen SR, Richardson BW. Systemic effects of an intra osseous injection of 2 % lidocaïne with 1/100 000 epinephrine. Gen Dent 2000; 48: 299-302.

28 - Chen J, Dohi S, Tan Z, Banno Y, Nozawa Y. The inhibitory effect of local anesthetic s on bradykinin-induced phospholipase D activation in rat pheochromocytoma PC12 cells. Anesth Analg 2002; 95: 88-97.

29 - Cheraskin MD, Prasertsuntarasai MS. Use of epinephrine with local anaesthesia in hypertensive patients. Effects of sedation on blood pressure and pulse rate in the waiting room. J Am Dent Assoc 1958; 56: 210-8.

30 - Cheraskin MD, Prasertsuntarasai MS. Use of epinephrine with local anaesthesia in hypertensive patients. Effects of tooth extraction on blood pressure and pulse rate. J Am Dent Assoc 1959; 58: 61-8.

31 - Chernow B, Balestrieri F, Ferguson CD, Terezhalmy GT, Fletcher JR, Lake CR. Local dental anaesthesia with epinephrine. Minimal effects on the sympathetic nervous system or on hemodynamic variables. Arch Intern Med 1983; 143: 2141-3.

32 - Chiu YC, Brecht K, Das Gupta DS, Mhoon E. Myocardial infarction with topical cocaine anaesthesia for nasal surgery. Arch Otolaryngol Head Neck Surg 1986; 112: 988-90.

33 - Christensen LQ, Bonde J, Kampmann JP. Drug interactions with inhalational anaesthetics. Acta Anaesth Scand 1993; 37: 231-44.

34 - Cioffi GA, Chernow B, Glahn RP, Terezhalmy GT, Lake CR. The hemodynamic and plasma cathecolamine responses to routine restorative dental care. J Am Dent Assoc 1985; 111: 67-70.

35 - Coggins R, Reader A, Nits Beck M, Meyers W. Anaesthetic efficacy of intraosseous injection in maxillary and mandibular teeth. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1996; 81: 634-41.

36 - Commissionat Y, Rimet JL. Anesthésie Locale. Complications. Actual Odontostomatol 1992; 179: 497-506.

37 - Covino BG, Vassallo HG. Local anesthetics: mechanism of action and clinical use. Grune and Stratton Editeur, New York 1976.

38 - Curi MM, Dib LL. Osteoradionecrosis of the jaws: a retrospective study of the background factors and treatment in 104 cases. J Oral Maxillofac Surg 1997; 55: 545-6.

39 - Dagher FD, Ghassan MY, Machtou P. An evaluation of 2% lidocaïne with different concentrations of epinephrine for inferior alveolar nerve block. J Endod 1997; 23: 178-80.

40 - Damm DD, Fantasia JE. Recurring palatal ulceration Gen Dent 1992; 40: 102 et 148

41 - Daublander M, Roth W, Lipp M. Effects of different lidocaïne sprays for topical anesthesia on cardiovascular parameters and oxygen saturation. Anesth Pain Cont Dent 1992; 1: 161-6.

42 - Daublander M, Muller R, Lipp MDW. The incidence of complication associated with local anaesthesia in dentistry. Anesth Prog 1997; 44: 132-41.

43 - DAVIES AP, LEFKOWITZ RJ. Regulation of adrenergic receptors in Lefkowitz Receptors regulation. Chapmann and Hall Editor, New York 1981.

44 - DEANFIELD JE, RIBIEROV P, OAKLEY K, KRIKLER S, SELWYN AP. Analysis of ST segment changes in normal subjects: implication for ambulatory monitoring in angina pectoris. Am J Cardiol 1984; 54: 1321-5.

45 - DI ANGELIS N, LUEPKER RC. The effect of the dental setting on blood pressure measurement. Am J Public Health 1983; 73: 1210-2.

46 - DIONNE RA, GOLDSTEIN DS, WIRDZEK PR. Effects of diazepam premedication and epinephrine-containing local anaesthetic on cardiovascular and plasma catecholamine responses to oral surgery. Anesth Analg 1984; 63: 640-6.

47 - DUNBAR D, READER A, NIST R, BECK M, MEYERS W. Anaesthetic efficacy of intraosseous injection after an inferior alveolar nerve block. J Endod 1996; 22: 481-6.

48 - ENGQUIST A, BRANDT MR, FERNANDES A, KEHLET H. The blocking effects of epidural analgesia on the adrenocortical and hyperglycaemic responses to surgery. Acta Anaesth Scand 1977; 21: 330-5.

49 - EZZAT ABOULEISH MB, KLIONSKY BL, TAYLOR FL. Lidocaine effects on leucocytes and erythrocytes. Anesthesiology 1978; 48: 295.

50 - FALAIYE VO, ROOD JP. Influence of adrenaline on the onset time of lignocaine anaesthesia. J Dent 1990; 18: 221-3.

51 - FINK BR, AASHEIM GM, LEVY BA. Neural pharmacokinetics of epinephrine. Anesthesiology 1978; 48: 263-8.

52 - FOITZIK C, DAUBLANDER M, VIETOR K, PROTSCH VON ZIETEN A. Management and care of patients at risk in a surgical dental practice. Anesth Prog 1996; 43: 73-7.

53 - FOSTER CA, ASTON SJ. Propanolol-epinephrine interaction: a potential disaster. Plast Reconstr Surg 1983; 72: 74-8.

54 - GALILI D, KAUFMAN E, GARFUNKEL AA, MICHAELI Y. Intraligamentari anaesthesia: a histological study. Int J Oral Surg 1984; 13: 511-6.

55 - GANGAROSA LP, HALIK FJ. A clinical evaluation of local anaesthetic solutions containing graded epinephrin concentrations. Arch Oral Biol 1967; 12: 611-21.

56 - GAUDY JF, ARRETO CD. Manuel d'analgésie en odontostomatologie. Masson Editeur, Paris 1999.

57 - GERMISHUYS PJ. Hyperresponders and adrenaline in local anaesthetic solutions. South Afr Dent J 2001; 56: 175-7.

58 - GIBBS CP, HAWKINS JL. Anesthesia for the pregnant patient requiring no obstetrical surgery. ASA Refresher course in anaesthesiology 1994; 22: 127-40.

59 - GOLDMAN V, ASTROM A, EVERS H. The effect of tricyclic antidepressants on the cardiovascular effects of local anaesthetic solutions containing different vasoconstrictors. Anaesthesia 1971; 26: 91-6.

60 - GOLDSTEIN DS, DIONNE R, SWEET J, GRACELY R, BREWER B, GREGG R, KEISER HR. Ciruclatory plasma catecholamine lipid and psychological responses to real-life stress (third molar extraction): effects of diazepam sedation and of inclusion of epinephrine with the local amesthetic. Psychosomatic Med 1982 44: 259-72.

61 - GORTZAK RAT, ABRAHAM INPIJN L, PETERS G. Non invasive 27 hour blood pressure registration including dental checkups in some dental practice. Clin Prevent Dent 1992; 14: 5-10.

62 - GORTZAK RAT, ABRAHAM INPIJN L, OOSTING J. Blood pressure response to dental checkup: a continuous, non-invasive registration. Gen Dent 1991; 39: 339-42.

63 - GORTZAK RAT, ABRAHAM INPIJN L, PETERS G. Non invasive 27 hour blood pressure registration including dental checkups in some dental practice. Clin Prevent Dent 1992; 14: 5-10.

64 - GRAY RJ, LOMAX AM, ROOD JP. Periodontal ligament injection: alternative solutions. Anesth Prog 1990; 37: 293-5.

65 - GROSSMAN LI. Endodontic practice Lea et Febiger editor, 7e ed, Philadelphia 1970.

66 - GUGLIELMO A, READER A, NIST R, BECK M, WEAVER J. Anesthetic efficacy and heart rate effect of the supplemental intraosseous injection of 2% mepicacaine with 1/20000 levonordefrin. Oral surgery Oral Med Oral Pathol 1999; 87: 284-93.

67- GUTMAN JL. Parameters in achieving quality anaesthesia and hemostasis in surgical endodontics. Anesth Pain Control Dent 1993, 223-6.

68 - GUTMAN JL, HARRISON JW. Surgical endodontics, Ishiyaku Euro America Editor, St Louis 1994.

69 - HAAS DA, LENNON D. A 21 year retrospective study of reports of paresthesia following local anaesthetic administration J Can Dent Assoc 1995; 4: 319-30.

70 - HAAS DA, PYNN BR, SANDS TD. Drug use for the pregnant or lactating patient. Gen Dent 2000; 48: 54-60.

71 - HANDLER LE, ALBERS DD. The effect of the vasoconstrictor epinephrine on the duration of pulpal anesthesia using the intraligamentary injection J Am Dent Assoc 1987; 114: 807-9.

72 - HANSBROUGH JF, NEAR A. Propanolol -epinephrine antagonism with hypertension and stroke. Ann Int Med 1980; 92: 717-21.

73 - HANSTEN PD. Drug interactions affecting the cardiovascular response to sympathomimetics. Drug Interac Newsletter 1981; 1: 21-6.

74 - HAYACHI Y, KAMIBAYASHI T, SUMIKAWA K, YAMATODANI A, KURO M, YOSHIYA I. Adrenoreceptor mechanism involved in thiopental-epinephrine induced arrhythmias in dogs. Am J Physiol 1993; 265: 1380-5.

75 - HEISS J. GRASSER H. Behaviour of the rat mandible following maximum irradiation with simultaneous administration of vaso-active and vasoconstricting substances. Dtsch Zahnarztlz 1968; 23: 1410-7.

76 - HERSH EV, HELPIN ML, EVANS OB. Local anesthetic mortality: report of a case. J Dent Child 1991; 58: 489-91.

77 - HERSH EV, HERMANN DG. Assessing the duration of mandibular soft tissue anaesthesia J Am Dent Assoc 1995; 126: 1531-6.

78 - HILLEY MD, MILIAM SB, GIESKE AH, GIOVANNITTI JA. Fatality associated with the combined use of halothane and gingival retraction cord. Anesthesiology 1984; 60: 587-8.

79 - HIMURO H, MURATA T, TAMESUE A, NAKAJIMA T, HIRATSUKA M, TSUBAKI T, AONO K. Determination of the desirable epinephrine concentration containing in dental local anaesthetic solution. Comparison between two lidocaïne solutions containing1/80000 and 1/200000 epinephrine. Fukuoka Shika Daigaku Gakkai Zasshi 1989; 16: 323-7.

80 - HONDRUM SO. Hypertensive episode in the dental office. Gen Dent 1985; 33: 134-9.

81 - HOSODA R, HATTORI M, SHIMADA M, SHIMOMURA Y, MATSUURA M. Favourable effects of epidural analgesia on hemodynamics, oxygenation, and metabolic variables in the immediate post anaesthesic period. J Jap Soc Clin Anesth 1991; 11: 570-9.

82 - HOUSTON JB, APPLEBY R, DE COUNTER L, CALLAGHAN N, FUNK DC. Effect of repinephrine-impregnated retraction cord on the cardiovascular system. J Prosth Dent 1970; 24: 373-6.

83 - ICHINOHE T, FUKUDA K, KANEKO Y. Epinephrine at doses used in dentistry deteriorates platelet retention rate. Anesth Prog 1997; 44: 59-63.

84 - INGLE JL. Endodontics, Lea et Febiger éditeur, Philadelphie 1965.

85 - JACQUOT C, RAPIN JR, VIEILLEFOSSE R. Pharmacologie dentaire pratique, Julien Prélat Editeur, Paris 1978.

86 - JAGE J. Circulatory effects of vasoconstrictors combined with local anaesthetics. Anesth Pain Cont Dent 1993; 2: 81-6.

87 - JOHNSON WC, WIDRICH WC. Control of bleeding varices by vasopressine: a prospective randomised study. Ann Surg 1977; 186: 369-75.

88 - JORKJEND L, SKOGLUND LA. A doses response study of adrenaline with lignocaine 2%: effect on acute postoperative pain after oral soft tissue surgery. Br J Clin Pharmacol 2000; 51: 335-41.

89 - JORKJEND L, SKOGLUND LA. Increase in volume of lignocaine/adrenaline containing local anaesthetic solution causes increase in acute postoperative pain after gingivectomy. Br J Oral Maxillofac Surg 2000; 38: 230-4.

90 - KABAMBE WM, ROOD JP, SOWRAY JH. A comparison of plain 2 per cent lignocaine and 2 per cent lignocaine with adrenaline in local analgesia for minor oral surgery. J Dent 1982; 10: 136-9.

91 - KAUFMAN E, GARFUNKEL A, FINDLER M, ELAD S, ZUSMAN SP, MALAMED SF, GALILI D. Emergencies evolving from local anesthesia. Refuat Hapeh Vehashinayim 2002; 19: 13-8.

92 - KEESKLING GR, HINDS EC. Optimal concentration of epinephrine in lidocaïne solutions. J Am Dent Assoc 1963; 66: 337-40.

93 - KENNEDY M, READER A, BECK M, WEAVER J. Anesthetic efficacy of ropivacaine in maxillary anterior infiltration. Oral Surg Oral Med Oral Pathol 2001; 91: 406-12.

94 - KHOURY F, HINTERTHAN A, SCHURMAN J, ARNS H. Clinical comparative study of local anesthetics. Random double blind study with four commercial preparations. Dtsch Zahnarztl 1991; 46: 822-4.

95 - KLEEMANN PP, LANZ E, SCHMITT B, VON DOMARUS H. Ist das Risiko einer Lokalinjektion von ornipressin wohnend der Vollnarkose vertretbar? Dtsch Z Mund Kiefer Gesichtschir 1986; 10: 14-8.

96 - KNOLL-KOHLER E. Sicherheit bei der lokalanasthesiell. Pharmakologie vasokonstriktorischer. Zusatze. Phillip J 1988; 1: 79-87.

97 - KNOLL-KOHLER E, BRANDT K, BECKER J. Cardiohemodynamic and serum catecholamine response to surgical removal of impacted mandibular third molars under local anaesthesia: a randomised double blind parallel group and crossover study. J Oral and Maxillofacial surg 1991; 49: 957-62.

98 - KNOLL-KOHLER E, FORTSCH G. Pulpal anaesthesia dependent on epinephrine dose in 2% lidocaine. Oral Surg Oral Med Oral Pathol 1992; 73: 537-40.

99 - KNOLL KOHLER E, BRANDT K, KNOLLER M. The beta mimetic effects following the endoral injection of epinephrine with articaine. Schweiz Monatsschr Zahnmed 1992; 102: 172-7.

100 - LATHERS CM, TYAU LS, SPINO MM, AGARWAL I. Cocaine induced seizures, arrhythmias and sudden death. J Clin Pharmacol 1988; 28: 584-93.

101 - LIPP M, DICK W, DAUBLANDER M, FUDER H, STANTON-HICKS M. Exogenous and Endogenous plasma levels of epinephrine during dental treatment under local anaesthesia. Reg Anesthesia 1993; 18: 6-12.

102 - MAC LEAN ME, WAYMAN BE, MAYHEW RB. Duration of anesthesia using the periodontal ligament injection: a comparison of bupivacaine to lidocaïne. Anesth Pain Cont Dent 1992; 4: 207-13.

103 - MAC LEAN C, READER A, BECK M, MERYERS WJ. An evaluation of 4ù prilocaine and 3% mepivacaine compared with 2% lidocaïne (1/100 000 epinephrine) for inferior alveolar nerve block. J Endod 1993; 19: 146-50.

104 - MADRID C, CABALLERO R, DURAN D, BRU DE SALA C. L'anesthésie Mandibulaire. Réal Clin 1991; 2: 51-68.

105 - MALAMED S. Electrocardiographic changes in cardiac patients undergoing dental extractions under local anesthesia Discussion. J Oral Maxillofacial Surg 1996; 54: 165-6.

106 - MALAMED SF. Handbook of local anesthesia. Mosby Editor, 4e Edition, St Louis 1997.

107 - MAMIYA H, ICHINOHE T, KANEKO Y. Effects of block analgesia on attenuating intraoperative stress response during oral surgery. Anesth Prog 1997; 44: 101-5.

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 28

108 - Marx RE. Osteoradionecrosis a new concept of its pathophysiology. J Oral Maxillofac Surg 1983; 41: 283-8.

109 - MASSALHA R, VALDMAN FARKASH P, MERKIN L. Fatal intracerebral haemorrhage during dental treatment Int J Med Sci 1996; 32: 774-6.

110 - MAXIMYW WG, WOOD RE, LIU FF. Post radiation dental extractions without hyperbaric oxygen. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1992; 74: 155-7.

111 - MEECHAN JG. Epinephrine Magnesium and dental local anaesthetic solutions. Anesth Prog 1996; 43: 99-102.

112 - MEECHAN JG. Plasma potassium changes in hypertensive patients undergoing oral surgery with local anaesthetic containing epinephrine. Anesth Prog 1997; 44: 106-9.

113 - MEECHAN JG, SKELLY AM. Problems complicating dental treatment with local anaesthesia or sedation: prevention and management. Dental Update 1997; 24: 278-83.

114 - MEECHAN JG, ROOD JP. Adverse effects of dental local anaesthesia. Anaesthesia, 1997; 24: 315-8.

115 - MEECHAN J. How to avoid local anaesthetic toxicity. Br Dent J 1998; 184: 334-5.

116 - MEECHAN JG, DAY PF, MC MILLAN AS. Local anesthesia in the palate: a comparison of techniques and solutions. Anesth Prog 2000; 47: 139-42.

117 - MEECHAN JG, COLE B, WELBURY RR. The influence of two different dental local anaesthetic solution on the haemodynamic responses of children undergoing restorative dentistry: a randomised, single-blind, split-mout study. Br Dent J 2001; 190: 502-4.

118 - MEYER FU. Haemodynamic changes under emotional stress following a minor surgical procedure under local anaesthesia. Int J Oral Maxillofac Surg 1987; 16: 688-94.

119 - MITO RS, YAGIELA JA. Hypertensive response to levonordefrin in a patient receiving propanolol : report of a case. J Am Dent Assoc 1988; 116: 55-7.

120 - MONTEBUGNOLI L, PELLICCIONI GA, BORGHI C. Effetti del vasocostricttore durante l'aestesia locale. Dental Cadmos 1990; 58: 62-71.

121 - MOORE PA, GAGE TW, HERSH EV, YAGIELA JA, HAAS DA. Adverse drug interaction in dental practice. J Am Dent Assoc 1997; 130: 47-54.

122 - MOSKOWITZ MA. The neurobiology of vascular head pain. Ann Neurol 1984; 16: 157-68.

123 - MOYER JA, GREENBERG LH, FRAZER A, BRUNSWICK DJ, MENDELS J, WEISS B. Opposite effects of acute and repeated administration of desmethylimipramine on adrenergic responsiveness in rat pineal gland. Life Sci 1979; 24: 2237-44.

124 - MUZYKA B. Atrial fibrillation its relationship to dental care. J Am Dent Assoc1999; 130: 1080-5.

125 - MYERS RR, HECKMANN HM. Effects of local anaesthetics on nerve blood flow using lidocaine with and without epinephrine. Anesthesiology 1989; 71: 757-62.

126 - NAKAI Y, MILGROM P, MANCL L, COLDWELL S, DOMOTO PK, RAMSAY DS. Effectivemess of local anesthesia in pediatric dental practice. J Am Dent Assoc 2000; 131: 1699-705.

127 - NIRUTHISARD S, CHATRKAW P, LAORNUAL S, SUNTHORNYOTHIN S, PRASERTSRI S. Anesthesia for one-stage bilateral pheochromocytoma resection in a patient with MEN type IIa : attenuation of hypertensive crisis by magnesium sulfate. J Med Assoc Thai 2002; 85: 125-30.

128 - NIWA H, SHIBUTANI T, HORI T, KIM Y, AKITA M, MATSUURA H. The interaction between pindolol and epinephrine contained in local anesthetic solution to the left ventricular diastolic filling velocity in normal subjects. Anesth Prog 1996; 43: 78-84.

129 - NIWA H, SATOH Y, MATSUURA H. Cardiovascular response to epinephrine containing local anaesthetics for dental use: a comparison of haemodynamic responses to infiltration anesthesia and ergometer stress testing. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2000; 90: 171-81.

130 - ODOR TM, PITT FORD TR, MC DONALD F. Andrenaline in local anaesthesia: the effect of concentration on pulpal circulation and anaesthesia. Endod Dent Traumatol 1994; 10 : 167-73.

131 - OERTEL R, RAHN R, KIRCH W. Clinical pharmacokinetics of articaine. Clin Pharmacokin 1997; 33: 417-25.

132 - OKADA Y, SUZUKI H, ISHIYAMA I. Fatal subarachnoid haemorrhage associated with dental local anesthesia. Australian Dental J 1989; 34: 323-5.

133 - PALLASCH TJ. Vasoconstrictors and the heart. J Calif Dent Assoc 1998; 26: 668-73.

134 - PALMER BOUVA C, OOSTING J, DE VRIES R, ABRAHAM-INPIJN L. Stress in elective dental treatment : epinephrine,norepinephrine, the VAS, ansd CDAS in four different procedure. Gen Dent 1998; 46: 356-60.

135 - PERSSON G, SIWERS B. The risk of potentialting effect of local anesthesia with adrenaline in patients treated with tricyclic antidepressants. Sven Tandlak Tidskr 1975; 68: 9-18.

136 - PERUSSE R, GOULET JP, TUTCOTTE JY. Contraindications to vasoconstrictors in dentistry Part I: cardiovascular diseases. Oral Surg Oral Med Oral Pathol 1992; 74: 679-86.

137 - PERUSSE R, GOULET JP, TUTCOTTE JY. Contraindications to vasoconstrictors in dentistry Part II: hyperthyroidism, diabetes, sulphite sensitivity, cortico-dependent asthma and pheochromocytoma. Oral Surg Oral Med Oral Pathol 1992; 74: 687-91.

138 - PETRIKAS AZ. A clinico-pharmacologic study of intraseptal spongiosa dental anesthesia with lidocaine and with/without adrenaline. Stomatologia 1990; 69: 27-9.

139 - PRATILAS V, PRATILAS MG. Anaesthetic management of phaeochromocytoma. Can Anaesth Soc J 1979; 26: 253-9.

140 - Quyyumi AA, Mockus L, Wright C, Fox KM. Morphology of ST segment changes in patients with varying severity of coronary artery disease: investigation of the frequency of nocturnal ischaemia and coronary spasm. Br Heart J 1985; 53: 186-93.

141 - Reitz J, Reader A, Nist R, Beck Meyers WJ. Anesthetic efficacy of the intraosseous injection of 0.9ml of 2% lidocaine (1:100 000 epinephrine) to augment an inferior alveolar nerve block. Oral Surg Pral Pathol Oral Med 1998; 86: 516-23.

142 - Replogue K, Reader A, Nist R, Beck M, Meyers W. Cardiovascular effects of the intraosseous injection of 2 % lidocaine with 1:100 000 epinephrine and 3 % mepivacaine. J Am Dent Assoc 1999; 130: 649-57.

143 - Roberts DH, Sowray JH. Local analgesia in dentistry. Wright éditeur, 3ᵉ édition, Bristol 1987.

144 - Rood JP. Local Anesthesia dosage. Br Dent J 1998; 185: 59.

145 - Rood JP. Safety of adrenaline. Br Dent J 1999; 186: 104.

146 - Ruffolo RR, Vichols AJ, Stadel JM, Hieble JP. Structure and function of α adrenoreceptors. Pharmacol Rev 1991; 43: 475-505.

147 - Sack U, Kleeman PP. Intraoral conduction anesthesia with epinephrine containing local anaesthetics and arterial epinephrine plasma concentration. Anesth Pain Cont Dent1992; 1: 77-80.

148 - Safdar B, Cone DC, Pham KT. Subcutaneous epinephrine in the prehospital setting. Prehosp Emergency Care 2001; 5: 200-7.

149 - Sakyray M. Effect of epinephrine in local dental anesthetics on plasma catecholamine concentration and circulation. Dentistry in Japan 1990; 27: 135-9.

150 - Santoro V. Marsicano C. Variazione dei parametri emodinamici in pazienti in anestesia generale sottoposti ad infiltrazione sottomucosa con miscela di anestesico locale/adrenalina. Minerva Stomatologica, 1998; 47: 649-53.

151 - Seng GF, Gay BJ. Dangers of sulphites in dental local anaesthetic solutions: warning and recommendation. J Am Dent Assoc 1986; 113: 769-70.

152 - Shanks CA. Intravenous octapressin during halothane anaesthesia: a pilot study. Br J Anaesth 1963; 35: 640-7.

153 - Silvrestre FJ, Verdu MJ, Sanchis JM, Grau D. Penarrocha M. Efectos de los vasoconstrictors usados en odontologia sobre la presion arterial sistolica y diastoloca. Med Oral 2001; 6: 57-63.

154 - Sommer R, Ostrander F Crowley M. Clinical Endodontics, Saunders Editor, Philadelphia, 1962

155 - Sunada K, Nakamura K, Yashimoro M, Sumitomo M, Furuya H. Clinically safe dosage of felypressin for patients with essential hypertension. Anesth Prog 1996; 43: 108-15.

156 - Syngcuk K, Sivakami R. Haemostasis in endodontic surgery. Dent Clin North Amer 1997; 41: 499-511.

157 - Tagger E, Tagger M, Sarnat H, Mass E. Periodontal ligament injection in the dog primary dentition: spread of local anaesthetic solution. Int J Paediatr Dent 1994; 4: 159-66.

158 - Tanaka S, Miyabe M, Ohyama I, Seki S, Tsukamoto T, Namiki A. Sevoflurane with continuous epidural anesthesia for removal of pheochromocytoma. Masui 1991; 40: 1261-4.

159 - Tolas AG, Pflug AE, Halter JB. Arterial plasma epinephrine concentrations and haemodynamic responses after dental injection of local anaesthetic with epinephrine. J Am Dent Ass 1982; 104: 41-3.

160 - Tordoff SG, Brossy M, Rowbotham DJ, James JN, James R, Raphael JH. The effect of preincisional infiltration with lignocaine on postoperative pain after molar teeth extraction under general anesthesia. Anesthesia 1996; 51; 585-7.

161 - Tsirlis A,T Iakovidis DP,Parissis NA. Dry socket: frequency of occurrence after intraligamentary anesthesia. Quintessence Int 1992; 23: 575-7.

162 - Tsuchihashi T, Takata Y, Kurokawa H, Miura K, Maruoka Y, Kajiyama M, Fujishima M. Blood pressure response during dental surgery. Hypertension research, clinical and experimental 1996; 19: 189-94.

163 - Vahatalo K, Antila H, Lehtinen R. Articaine and lidocaine for maxillary infiltration anesthesia. Anesth Prog 1993; 40: 114-6.

164 - Vanderheyden PJ, Williams RA, Sims TN. Assessment of ST segment depression in patients with cardiac disease after local anesthesia. J Am Dent Assoc 1989; 119: 407-12.

165 - Viel E, Bruelle P, La Coussaye JE, Eledjam JJ. Pharmacologie des Anesthésiques locaux. In Brasseur L. Douleurs, Maloine Editeur, Paris 1997

166 - Volpato MC, Ranali J, Amaral IMG, Demetrio CGB, Chalita LVAS. Acute toxicity of lidocaine and prilocaine in combination with adrenaline and felypressin. Indian J Dent Tes 1999; 10: 138-44.

167 - Von Tsakiris A, Buhlmann A. Experimentelle Untersuchjungen beim Menschen über die wirkjung von vasopressin auf die Leberdurchblutung und den Portalen Druck. Hel Med Acta 1961; 4: 615-21.

168 - Vreeland L, Reader A, Beck M, Meyers Weaver J. An evaluation of volumes and concentration of lidocaïne in human inferior alveolar nerve block. J Endod 1989; 15: 6-12.

169 - Wahl MJ. Local anesthetics and vasoconstrictors: myths and facts. Pract Period Aest Dent 1997; 9: 649-52.

170 - Wahl MJ. Demystifying medical complexities. Calif Dent Assoc J 2000; 28: 510-8.

171- Walton RE, Garnick JJ. The periodontal ligament injection: histological effects on the periodontium in monkeys. J Endod 1982; 8: 22-6.

172 - Wang HH. The effects of 2-PHE, 8-Lys vasopressin, angiotensin, and nor-epinephrine on coronary blood flow and arterial blood pressure. Fed Proc 1964; 24: 565.

173 - WATERS BD. Providing Dental treatment for patients with cardio-vascular disease. Ontario Dent 1995; 72: 24-32.

174 - WONG KC, PUERTO AX, PUERTO BA, BLATNICK RA. Influence of imipramine and pargyline during halothane, enflurane or methoxyflurane anesthesia in dogs. Life Sci 1980; 27:2675-8.

175 - WYNN RL. Dental drug interactions with the greatest potential for serious adverse effects. Gen Dent 1994; 42: 116-7.

176 - WYNN RL. Dental considerations of patients taking appetite suppressants. Gen Dent 1997; 45: 324-8.

177 - WYNN RL. Hypertension medications and dental considerations. Gen Dent 2000; 48: 126-31.

178 - YAGUIELA JA. Local anaesthetics: a century of progress. Anesth Prog 1985; 32: 47-56.

179 - Yaguiela JA, Duffin SR, Hunt LM. DRUG INTERACTIONS and vasoconstrictors used in local anaesthetic solutions. Oral Surg Oral Med Oral Pathol 1985; 59: 565-71.

180 - YAGUIELA JA. Vasoconstrictors Agents for local anesthesia. Anesth Prog 1995; 42: 116-20.

181 - YAGUIELA JA. Adverse Drug Interactions in dental practice. Interactions associated with vasoconstrictors. J Am Dent Assoc 1999; 130: 701-9.

182 - YAKSH TL, REDDY SV. Studies in the primate on the analgesic effects associated with intrathecal actions of opiates, alpha-adrenergic agonists and baclofen. Anesthesiology 1981; 54: 451-6.

183 - YOSHIMURA Y, OKA M, KISHIMOTO H, MATSUURA R, MISHIMA K. Hemodynamic changes during dental extraction and post-extraction bleeding in patients with prosthetic heart valves. Int J Oral Maxillofac Surg 1987; 16: 425-31.

184- YUGE M, KAWAMOTO M, MORIWAKI K. Balanced anesthesia today: the meanings of balanced anesthesia. The epidural anesthesia with general anesthesia. J Jap Soc Clin Anesth 1995; 153-5.

185 - ZHANG C, BANTING D, GELB A, HAMILTON JT. Effects of β adrenoreceptors blockade with nadolol on the duration of local anesthesia. J Am Dent Assoc 1999; 130: 1773-80.

nédecine
buccale
chirurgie
buccale

L. 9, N° 2
2003

page 30