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Contraindications to vasoconstrictors in dentistry: Part I

Cardiovascular diseases

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This article reviews the main contraindications of vasoconstrictors in cardiac patients, notably unstable angina, recent myocardial infarction, recent coronary artery bypass surgery, refractory arrhythmias, untreated or uncontrolled hypertension, and untreated or uncontrolled congestive heart failure. Extensive survey of the literature has been completed, giving specific guidelines for a rational use of vasoconstrictors in this category of medically compromised patients.

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Epinephrine and levonordefrin (Neo-Cobefrin) are the main vasoconstrictors used today in dental medicine. Their role is to provide deeper anesthesia and good hemostasis, and to prevent toxic reaction to local anesthetic agents by retarding their absorption rate in the bloodstream and by decreasing their plasma concentration.^{1,2} Vasoconstrictors present many advantages and indeed can be used safely for most patients treated by dentists. However, the benefits they provide are sometime outweighed by potential risks of serious medical complications. General contraindications to vasoconstrictors are well documented,³⁻⁹ but one criticism regarding the current guidelines is their vagueness and ambiguity for medically compromised patients with cardiovascular disorders or other systemic conditions.

Depending on the potential risk and morbidity rate of medical complications, the contraindications to the use of vasoconstrictor in dentistry can be classified as

either absolute or relative (Table I). This article presents a critical review of the current guidelines and recommendations regarding the use of vasoconstrictors for patients with cardiovascular diseases.

ABSOLUTE CONTRAINDICATIONS General consideration for heart diseases

Epinephrine, a natural hormone released from the adrenal medulla, has an estimated basal secretion rate ranging from 0.17 to 0.54 $\mu\text{g}/\text{min}$ in a healthy 70 kg adult.^{10,11} The endogenous release of epinephrine and other catecholamines is reported to increase 20 to 40 times when persons are subjected to different kinds of stress.^{10,12} In 1955 the New York Heart Association made a recommendation and set the maximal dose for cardiac patients at 0.2 mg of epinephrine when used with a local anesthetic.¹³ This recommendation still holds today and has been used to derive the maximal dose of levonordefrin (1.0 mg) and other vasoconstrictors less commonly used in dentistry. The maximum doses are contained in 20 ml of local anesthetic with epinephrine 1:100,000 or levonordefrin 1:20,000; each milliliter of solution contains 0.01 mg and 0.05 mg of vasoconstrictor, respectively. Undoubtedly,

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Table 1. Contraindications to vasoconstrictors in dentistry

Absolute contraindications
Heart diseases
a. Unstable angina
b. Recent myocardial infarction
c. Recent coronary artery bypass surgery
d. Refractory arrhythmias
e. Untreated or uncontrolled severe hypertension
f. Untreated or uncontrolled congestive heart failure
Uncontrolled hyperthyroidism
Uncontrolled diabetes
Sulfite sensitivity; steroid-dependent asthma
Pheochromocytoma
Relative contraindications
Patients taking tricyclic antidepressants
Patients taking phenothiazine compounds
Patients taking monoamine oxidase inhibitors
Patients taking nonselective β -blockers
Cocaine abuser

cardiac patients are at higher risk from the massive release of endogenous catecholamines associated with the mismanagement of pain control and anxiety than they are from the small quantities of vasoconstrictors usually used in dentistry. This is one reason to advocate the use of local anesthetics with very small quantities of vasoconstrictor for the vast majority of cardiac patients.

In 1964 the American Heart Association officially endorsed this principle in a joint publication with the American Dental Association: "The concentration of vasoconstrictors normally used in dental local anesthetic solutions are not contraindicated for patients with cardiovascular disease when administered carefully with preliminary aspiration."¹⁴ Although the American Heart Association reiterated this principle by saying "a vasoconstrictor agent is generally indicated as a component of a local anesthetic solution," no mention was made of any possible contraindication. Neither did the American Dental Association nor the New York Heart Association ever take a stand on maximal doses of vasoconstrictors recommended for cardiac patients. Although the notion of maximal dose provides a useful guideline, it may also give an impression of false security in patients with cardiovascular disease. In fact, two authors^{9, 15} recommend a much smaller maximal dose of vasoconstrictor (0.04 mg) in any given session for patients with severe cardiovascular disease, but neither gives explicit criteria to categorize a patient as having severe heart disease.

Besides the concentration and volume of vasoconstrictor injected, the absorption and systemic response are influenced by the injection site; type of vasoconstrictor; and medication intake, age, and the current

health status of the patient.¹⁶⁻¹⁹ When a cardiac patient is treated, it is important to obtain a profound and prolonged local anesthesia with the lowest possible dose of vasoconstrictor. As a general rule epinephrine used at a concentration greater than 1:100,000 should be considered hazardous in patient with heart disease. Furthermore, the use of intraligamentary and intrabony injections, as well as epinephrine-impregnated retraction cords, should be strictly contraindicated.

According to Smith and Walton,²⁰ and Rawson and Orr,²¹ an important vascular penetration of local anesthetic takes place during intraligamentary injection. Smith and Pashley²² observed the same hemodynamic changes in blood pressure (hypertension) and heart rate (tachycardia) when they compared the effects of intraligamentary, intrabony, and intravenous injection of small quantity of local anesthetic with epinephrine 1:100,000. Although this technique presents several advantages, the depth and duration of anesthesia is highly dependent on the presence of a vasoconstrictor.²³⁻²⁶ Therefore intraligamentary injection should be considered dangerous and strictly contraindicated in any patient with heart disease, because the hemodynamic effects are likely to be similar to the one observed with an intravenous injection.

As pointed out by Buchanam and Thayer,²⁷ controversies still exist on the use of epinephrine-impregnated retraction cords in medically compromised patients. In a study of nine normotensive subjects, Hatch et al.²⁸ observed a 250% increase in the mean baseline plasma epinephrine level 60 minutes after placement of 1 inch of *r*-epinephrine impregnated retraction cord in an untraumatized gingival sulcus. Despite the rise in plasma epinephrine level, no hemodynamic change in heart rate, mean arterial pressure, or pulse pressure product was observed. Epinephrine absorption from an impregnated retraction cord is a function of time and is also influenced by the extent of the gingival vascular bed exposure. In a healthy gingival sulcus Shaw et al.²⁹ observed a sixfold increase in the mean plasma epinephrine level after 30 minutes of gingival retraction. These authors also reported a 25-fold rise 10 minutes after placement of 3 inches of epinephrine-impregnated gingival cord in a traumatized sulcus. Unfortunately, no data on hemodynamic factors were reported. Although the controversy remains, we should not underestimate the potential risks associated with sudden rises of plasma epinephrine level of even small magnitude in medically compromised patients. Notwithstanding these facts, retraction cords usually contain levels of epinephrine (approximately 0.2 to 0.1 mg/in) far greater than the maximal dose recommended by the New York Heart Association

and should therefore be contraindicated in patients with heart disease.

UNSTABLE ANGINA

Unstable angina is characterized by recent worsening of symptoms and poor response to medical treatment. Four clinical types are recognized: *de novo* angina, *crescendo* angina, angina at rest, and *postinfarction* angina.^{30, 31} Angina *de novo* refers to all recent angina of 4 weeks' duration or less whereas *crescendo* angina is mainly characterized by an increase in frequency, duration, severity of symptoms, and a decreased response to medication.

Unstable angina is usually associated with major pathologic changes of the coronary arteries.³⁰ Many factors play a role in the pathogenesis of this condition. Coronary thrombosis and ulcerated atheromatous plaques have been documented in *crescendo* angina,³²⁻³⁴ whereas coronary artery vasospasm is one of the leading causes of angina at rest.^{30, 35} All forms of unstable angina eventually lead to a temporary decrease of coronary blood flow. Unless adequately treated, the prognosis is poor considering the proportion of patients who may eventually have myocardial infarction or sudden death. In a recent study of 100 patients admitted and treated for unstable angina, Mulcahy et al.³⁶ observed eight deaths, 14 nonlethal infarctions, and three cases of readmission within a year after the initial hospital stay. Such results are not surprising because angiographic studies are highly suggestive of a pathophysiologic continuum between unstable angina and myocardial infarction. This is supported by Ambrose et al.,³⁷ who observed similar changes of coronary thrombosis and ulcerated plaques in both conditions. Because of serious cardiovascular impairment, unstable angina is considered a medical emergency requiring immediate hospitalization.

During the past few years several investigators studied the hemodynamic effects of local anesthetic injection with epinephrine in normal healthy subjects before the subjects underwent dental procedures. Whereas the injection of 1.8 ml of local anesthetic with epinephrine 1:100,000 (0.018 mg [18 μ g]) in normotensive healthy subjects was not associated with significant changes in heart rate and mean arterial blood pressure,³⁸⁻⁴¹ injection of a larger quantity of local anesthetic with epinephrine may not be as safe and may not be without significant hemodynamic changes when administered to patients with severe cardiovascular disease. In fact, Dionne et al.⁴² observed a 19% and 30% increase in cardiac rhythm and cardiac output, respectively, after injecting 5.4 ml of lidocaine 2% with epinephrine 1:100,000 (0.054 mg [54 μ g]), thus confirming previous results reported by

Goldstein et al.⁴³ Overall, these results suggest that in normotensive healthy subjects injection of a moderate quantity of local anesthetic with vasoconstrictor can lead to significant increase in cardiac stroke volume and oxygen consumption. Regardless of the risk associated with an accidental intravenous injection, there is no certainty that such hemodynamic changes could not compromise the cardiovascular status of a patient with unstable angina.

Cardiovascular effects of intravenous epinephrine infusion in normal subjects have also been extensively studied in the last few years. Although these studies were not meant to replicate the effects of an accidental intravascular injection of a small quantity of epinephrine, we must recognize that it could potentially lead to serious hemodynamic changes in patients with unstable angina. In a controlled study, Fellows et al.⁴⁴ observed a 30% increase in heart rate (19 beats/min \pm 3) during an intravenous infusion of epinephrine 50 ng/kg/min (3.5 μ g/min). Despite a gradual fall in plasma epinephrine concentration to baseline level 15 minutes after the infusion, the cardiac rhythm was still elevated 30 minutes after cessation of the infusion. Stratton et al.,⁴⁵ using isotopic ventriculography (radionuclide left ventricular angiography), reported 58% and 74% increases in cardiac output with an intravenous infusion of 50 and 100 ng/kg/min (3.5 and 7.5 μ g/min) of epinephrine, respectively. A dose-dependent increase in cardiac rhythm in the order of 20% to 30% (12 beats/min \pm 2 to 17 beats/min \pm 1) was also observed. A similar effect on cardiac output was reported by Freyschuss et al.⁴⁶ through cardiac catheterization.

More recently, Sung et al.⁴⁷ infused epinephrine in graded doses of 60, 120, 180, and 240 ng/kg/min (4.2, 8.4, 12.6, and 16.8 μ g/min) to assess the effects of elevated plasma epinephrine level on cardiovascular performance in patients with coronary artery disease. Although the dose response curves to epinephrine were similar in control and patient subjects with coronary artery disease, significant increase in heart rate, rate-pressure product, systolic blood pressure, cardiac output, and stroke volume index were frequently observed even at the lowest infusion rate (60 ng/kg/min [4.2 μ g/min]). At the lowest infusion rate the rise in plasma epinephrine concentration was comparable to the transient increase reported by several investigators^{38, 41, 42} after the injection of 1.8 to 5.4 ml of local anesthetic with epinephrine 1:100,000. We can hardly compare the results of these studies because of major differences in study design. However, we must not underestimate the clinical significance of the hemodynamic changes reported, because the amount of epinephrine infused in most of these

studies was only one fifth of the epinephrine currently contained in 1.8 cc of local anesthetic 1:100,000 (18 μg).

Overall, these studies show that epinephrine infusion does produce an increase in cardiac output and myocardial oxygen consumption at low infusion rate when plasma concentration levels are similar to those achieved after the injection of 1.8 to 5.4 ml of local anesthetic with epinephrine 1:100,000 (18 to 54 μg). No study has attempted to measure the magnitude of the hemodynamic changes resulting from an accidental intravascular injection of local anesthetic with epinephrine 1:100,000. In normotensive healthy patients the effect of a transient sudden increase in plasma epinephrine level is likely minimal, but we must not overlook the serious consequences it could lead to in patients with unstable angina. In fact, cases of severe myocardial ischemia and myocardial infarction have been reported after the intravenous and subcutaneous injection of epinephrine for the treatment of allergic reactions.^{48, 49}

Therefore vasoconstrictors as well as any dental treatment are strictly contraindicated in patients with unstable angina. Through their chronotropic and inotropic properties, epinephrine and other vasoconstrictors possess a powerful cardiovascular effect on oxygen consumption, increasing the risk of myocardial ischemia.

RECENT MYOCARDIAL INFARCTION

The current recommendation for patient with a history of recent myocardial infarction is to postpone dental treatment for at least 3 to 6 months.³⁻⁹ This widely accepted principle is supported by the fact that after a myocardial infarction, higher risk of reinfarction is reported during surgery with the patient under general anesthesia.^{50, 51} It is further substantiated by the results of a recent longitudinal study showing a peak in the mortality rate within the first year after a myocardial infarction.⁵² This delay period is therefore critical because of the electrical instability of the myocardium, which accounts for most of the sudden deaths reported during the recovery period.^{53, 54}

The infarcted myocardium is the site of many electrophysiologic abnormalities. In postinfarction patients Kienzle et al.⁵⁵ noted an elevation in the excitability threshold, an increase in conduction time, and a lengthening of the refractory period. These sequelae may lead to the sudden onset of all kinds of cardiac arrhythmias. Federman et al.⁵⁶ estimated at approximately 50% the incidence of ventricular arrhythmias in the first year after a myocardial infarction (R-on-T phenomenon, multifocal ventricular extrasystoles, bigeminy, trigeminy, salvos, ventricular tachycardia).

More recently, Cocco et al.⁵⁷ studied a group of asymptomatic patients between the tenth and the sixteenth weeks after the infarction. They observed multifocal extrasystoles, salvos extrasystoles, and ventricular tachycardia in 46%, 38%, and 16% of the patients, respectively. A very high incidence (70%) of ischemic abnormalities was also reported by Starling et al.⁵⁸ in patients undergoing a treadmill exercise stress test 6 weeks after infarction.

All these results substantiate the presence of an important electrical instability of the myocardium for months after an infarction. Electrophysiologic experiments assessing the facility of induction of certain types of arrhythmias through programmed cardiac stimulation also support these findings. According to Richard et al.⁵⁹ and Roy et al.,⁶⁰ sustained episodes of ventricular fibrillation or ventricular tachycardia can easily be provoked artificially in more than 25% of recent infarct patients. On the other hand, evidence indicates that epinephrine and other catecholamines possess important arrhythmogenic properties. By speeding up the repolarization of the calcium channels, catecholamines induce changes in the refractory period that predispose ischemic areas to reentrance arrhythmias and fibrillation.^{61, 62}

Because of their chronotropic, inotropic, and arrhythmogenic properties, epinephrine and other vasoconstrictors are strictly contraindicated for patients recovering from myocardial infarction. In the postrecovery period local anesthetic with vasoconstrictor should be employed only in patients whose heart condition has been followed closely and judged stable by the treating cardiologist. Furthermore, dentists should rule out the presence of unstable angina, refractory ventricular arrhythmias, and uncontrolled congestive heart failure, which are frequent in the patient after infarction.

RECENT CORONARY ARTERY BYPASS SURGERY

There is a lack of information in the dental literature regarding treatment guidelines for patients who underwent coronary artery bypass surgery. In a recent study of 92 patients treated by coronary artery bypass, Rubin et al.⁶³ showed that 56% still had complex ventricular arrhythmias (couplets, ventricular tachycardia, R-on-T phenomenon) at the time of their release from the hospital. Other investigators^{64, 65} have even questioned the treatment outcome of this procedure for the prevention of cardiac arrhythmias. Thus it would be prudent to adopt the same attitude as previously mentioned for patients who had a recent myocardial infarction. Both the injection of local anesthetic with vasoconstrictor and regular dental treat-

ments could indeed be risky within 3 months after coronary artery bypass surgery. This corresponds to the delicate healing period during which significant ischemic alterations can take place.

Percutaneous transluminal coronary angioplasty is now considered an excellent alternative to coronary artery bypass surgery in certain circumstances. This procedure should not be seen as a contraindication to the use of vasoconstrictors, because it is associated with a lower morbidity rate than coronary bypass surgery, is technically easier, and has a shorter recovery period. However, the cardiac status of the patients and the possibility of residual angina before undergoing any dental treatment must be carefully assessed.

REFRACTORY ARRHYTHMIAS

Refractory arrhythmias put patients at high medical risk and thus represent one of the major contraindications to the use of vasoconstrictors in dentistry. Refractory arrhythmias refer to any disturbance of heart rhythm, heart rate, and conduction that are unresponsive to medical treatment. Ventricular tachycardia and ventricular fibrillation are among other dangerous types of arrhythmias associated with an increased risk of sudden death.^{53, 54, 59, 66, 67} Because complex cardiovascular imbalance characterizes refractory arrhythmias, treatment usually requires close electrophysiologic monitoring and perfect drug balance.⁶⁸⁻⁷¹ Any history of infarction, absorption of many different antiarrhythmic agents, or current intake of some last-generation drugs listed in Table II should alert the dental practitioner to suspect the presence of refractory arrhythmias.⁷²⁻⁷⁷ The use of local anesthetics with vasoconstrictors in patients with refractory arrhythmias is therefore too risky and must be contraindicated.

UNTREATED OR UNCONTROLLED SEVERE HYPERTENSION

Controversies still exist about the use of vasoconstrictor in hypertensive patients. One major concern has always been a sudden and dramatic increase in blood pressure that could lead to a life-threatening complication. By enhancing the duration of local anesthesia and providing better pain control, vasoconstrictors may reduce the massive release of endogenous catecholamines often associated with anxiety and stress related to dental treatment. This is an important consideration in the hypertensive person, but instances exist where the use of vasoconstrictor should be avoided.

As mentioned previously, several investigators^{38, 39, 41, 42} did not observe any significant changes in the mean arterial pressure in normal subjects after

Table II. New antiarrhythmic drugs

Amiodarone
Encainide
Flecainide
Lorcainide
Mexiletine
Pirmenol
Propafenone
Tocainide

the injection of 1.8 to 5.4 ml of lidocaine 2% with epinephrine 1:100,000. Vernale,⁷⁸ in a study on normotensive and hypertensive subjects, injected 2 cc of lidocaine 2% with epinephrine 1:100,000 and observed a higher rise in systolic blood pressure among the hypertensive group. No significant variation, however, was observed in the magnitude of the pressor changes between both groups of subjects. Other evidence suggests that significant changes in the systolic blood pressure take place when the steady state of epinephrine concentration achieved by intravenous infusion falls within a certain concentration range. Fellows et al.⁴⁴ infused 50 ng/kg/min (3.5 $\mu\text{g}/\text{min}$) of epinephrine in normal healthy subjects and noted a mean increase in systolic blood pressure of 17 mm Hg. During graded epinephrine infusion of 100 ng/kg/min (7 $\mu\text{g}/\text{min}$) Stratton et al.⁴⁵ observed a mean increase of 30 mm Hg in the systolic blood pressure of normotensive subjects. Similar changes were also reported by Clutter et al.⁷⁹ and Duff and Swan⁸⁰ with intravenous infusion of 2.5 $\mu\text{g}/\text{min}$ and 10 $\mu\text{g}/\text{min}$, respectively. In addition, and concomitant with an increase in systolic pressure, these studies showed either no change or a slight decrease in the mean arterial pressure brought about by a simultaneous decrease in diastolic pressure induced by the activation of β -adrenoreceptors located in the vascular smooth muscles.

The results of these studies suggest a dose-dependent hemodynamic change in the systolic blood pressure during epinephrine infusion. On the basis of the current literature we cannot predict whether changes of significant magnitude could occur after an accidental intravascular injection in normotensive or hypertensive subjects. We can, however, question the safety of using vasoconstrictors in severely hypertensive patients. In fact, potential risk of severe cardiovascular or cerebrovascular complications appears too great in patients with severe or uncontrolled hypertension if changes in systolic blood pressure such as those observed with low-dose epinephrine infusion take place. Although severe or unresponsive hypertension has never been defined beyond the upper limit guideline for high blood pressure, we believe that lo-

cal anesthetic with vasoconstrictors should be avoided for any patient with blood pressure equal to or greater than 180/100 mm Hg. Moreover, these patients should never undergo any dental treatment unless their condition has been assessed and adequately treated. We reiterate, however, that it is safe and beneficial to use local anesthetic with vasoconstrictor for hypertensive patients whose blood pressure is only slightly or moderately elevated, when all precautions to prevent accidental intravascular injection and stress control are undertaken by the care provider.

UNCONTROLLED OR UNTREATED CONGESTIVE HEART FAILURE

Uncontrolled congestive heart failure reflects a state of decompensation to an underlying cardiac disorder such as ischemic heart disease, hypertension, or rheumatic or congenital cardiopathy⁸¹⁻⁸⁴ and thus represents a major contraindication to any dental treatment. Several studies have clearly shown that uncontrolled congestive heart failure carries a poor prognosis and a high risk of sudden death resulting mainly from ventricular arrhythmias.⁸⁵⁻⁸⁷ These arrhythmias involve many complex mechanisms. The most important seems to be the electrolytic depletion often associated with severe ventricular dysfunctions (ejection fraction <40%).⁸¹ Certain arrhythmias, however, can result from ischemia, and thus represent as such an independent risk factor unrelated to the ventricular performance itself.^{82, 83}

Whatever the underlying mechanism responsible for severe congestive heart failure, there is a concomitant electrical instability of the myocardium and a significant decrease in cardiac reserve. Patients with uncontrolled congestive heart failure are therefore at high risk for morbid complications, and as such administration of local anesthetic with vasoconstrictor becomes contraindicated.

CONCLUSION

Undoubtedly incorporation of vasoconstrictor to local anesthetic provides better pain control, which in turn reduces apprehension and stress often associated with dental treatment. Their proper administration can benefit most patients with heart disease, but in certain instances the benefits vasoconstrictors provide are sometime outweighed by potential cardiovascular complications. As health care providers, dentists have a responsibility to prevent exposing patients with severe or uncontrolled cardiovascular diseases to additional risk factors.

The contraindications reviewed in this article should not raise any doubt when a medically compromised patient has one of the cardiovascular conditions listed

in Table I. The administration of epinephrine or any congener substance may induce significant hemodynamic changes and eventually lead to life-threatening complications. However, these restrictions should be reassessed with consideration to the availability in the future of new vasoconstrictor agents.

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