
Contraindications to vasoconstrictors in dentistry: Part II

Hyperthyroidism, diabetes, sulfite sensitivity, cortico-dependent asthma, and pheochromocytoma

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Dentists are aware of contraindications to the use of vasoconstrictors in patients with cardiovascular diseases. However, there are some other noncardiac conditions we should know. This article discusses the absolute contraindications to the use of vasoconstrictors in patients with a history of hyperthyroidism, diabetes, allergy to sulfites, asthma, and pheochromocytoma. (ORAL SURG ORAL MED ORAL PATHOL 1992;74:687-91)

Absolute and relative contraindications to the use of vasoconstrictors in dentistry depend on the potential risk of cardiovascular and metabolic complications after their use in medically compromised patients. In that regard the dental literature has focused primarily on cardiovascular diseases, and as dentists we have been prompted to be cautious with their use mainly when dealing with cardiac patients. In Part I we reviewed the guidelines published by the American Heart Association and discussed the contraindications to the administration of local anesthetic with vasoconstrictor for patients with cardiovascular disease. Too often, however, we forget that other noncardiac conditions should also be carefully assessed because they may preclude the use of local anesthetic with vasoconstrictor. This second part presents and discusses the absolute contraindications dentists should be aware of when treating patients with a history of hyperthyroidism, diabetes, sulfite allergy, asthma, or pheochromocytoma (Table I).

ABSOLUTE CONTRAINDICATIONS Uncontrolled hyperthyroidism

Hyperthyroidism is characterized by a constellation of symptoms reflecting an increased metabolic activity of the body tissues. The most common clinical

Table I. Contraindications to vasoconstrictors in dentistry

Absolute contra-indications
Heart diseases
Unstable angina
Recent myocardial infarction
Recent coronary artery bypass surgery
Refractory arrhythmias
Untreated or uncontrolled severe hypertension
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 abusers

manifestations are weight loss, diffuse goiter, exophthalmos, and characteristic stare with widened palpebral fissures.^{1,2} Because of the direct effect of the thyroid hormone on the myocardium, patients with hyperthyroidism frequently have hypertension, atrial tachydysrhythmias, and cardiac insufficiency.³⁻⁵ By far, thyrotoxic crisis, a life-threatening condition, is the most feared complication. It may be precipitated by sepsis, trauma, surgery, or premature cessation of antithyroid treatment.⁶ Clinically it is characterized by extreme irritability, delirium, coma,

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severe hyperthermia, marked tachycardia, arrhythmia, and hypotension.¹⁻³ Several authors⁷⁻⁹ also reported cases of myocardial infarction associated with thyrotoxicosis.

The effects of thyroid hormone on the heart closely resemble those of catecholamines. In fact, thyrotoxicosis is responsible for an hyperdynamic circulatory state leading to tachycardia, hypertension, and an increase in cardiac output. Because of a similar effect on the cardiovascular system, it has been suggested that a synergistic effect might exist between the sympathetic nervous system and the thyroid hormones.^{1, 2, 4, 5} This view has led to numerous debates, and the recent discovery of an increased concentration of adrenergic receptors in hyperthyroid animals has revived the controversy.⁵ For dentists the main reason to avoid local anesthetic with vasoconstrictors in untreated hyperthyroidism has been the possibility that sympathomimetic amines could potentiate the vascular effect of thyroid hormone.

There is disagreement about the possible interaction between sympathomimetic amines and thyroid hormone. Results of both animal and human studies are inconsistent regarding hypersensitivity of catecholamines receptors in hyperthyroidism. Aoki et al.¹⁰ studied five patients and did not observe any significant difference in the increments of systemic blood pressure, mean right atrial pressure, heart rate, cardiac index, and change in total systemic resistance during graded infusion of epinephrine and norepinephrine at dosages of 5.25, 10.5, and 21 $\mu\text{g}/\text{min}$. All their subjects were studied during a hyperthyroid session and again later during an euthyroid session. Another study by Varma et al.¹¹ compared the effect of subcutaneous adrenalin (0.4 mg) and propranolol (40 mg orally) on heart rate and blood pressure on five euthyroid control subjects and four hyperthyroid subjects. Similar changes were observed in both groups, suggesting a lack of hypersensitivity of the cardiovascular system to catecholamines in hyperthyroidism. McDevitt et al.¹² reached the same conclusion when they noted that the heart rate response to isoprenaline sensitivity test did not significantly change in seven patients when they were hyperthyroid and euthyroid. However, these investigators reported isolated cases of catecholamine hypersensitivity among patients with hyperthyroidism. For this reason and because a subclinical cardiac disease is often associated with hyperthyroidism, dentists must be extremely cautious with these patients. Until more data are available, we recommend the use of local anesthetic without vasoconstrictor for non-medically treated hyperthyroid patients.

Uncontrolled diabetes

Traditionally the use of local anesthetic with vasoconstrictor has been considered risky and even contraindicated for patients with diabetes. As a general rule in dentistry, this recommendation is certainly debatable because it has been based on a warning regarding the use of large quantities of epinephrine for regional anesthesia and for the treatment of allergic reactions in medicine.

Like cortisol, thyroxin, and growth hormone, the action of epinephrine directly opposes that of insulin.^{13, 14} Its effect on glycemia occurs through the stimulation of neoglucogenesis and hepatic glycogenolysis. As such, epinephrine is considered an hyperglycemic hormone.¹⁵ The route of administration, the dosage, and very likely the type of diabetes influence the response of the diabetic patient to the administration of epinephrine. In general, chances of metabolic complications after the administration of epinephrine in concentration used in dentistry are much smaller than what they are when used in doses recommended for medical purposes. For example, subcutaneous or intravenous injections of 0.3 to 0.5 mg of epinephrine are routinely used to treat laryngeal edema or anaphylactic shock. These quantities are 15 to 30 times greater than what is contained in 1.8 ml of lidocaine 1:100,000 (0.018 mg). The risk, however, may vary significantly in the diabetic population, which by itself is an heterogeneous group of patients. Thus chances of complications may be greater in patients treated with insulin than in those treated with diet alone or hypoglycemic medications. This is suggested by the findings of Christensen¹⁶ and Berk et al.,¹⁷ who observed a higher level of circulating catecholamines and an increased hyperglycemic response to epinephrine, respectively, in patients insulin-dependent diabetes.

Besides the particular type of diabetes, the quality of medical control is another important predisposing factor. There is little doubt that medically controlled diabetic patients have better tolerance to vasoconstrictors than those with uncontrolled diabetes, who are at higher risk for acid ketosis and hyperglycemic coma.^{13, 14} The study by Hamburg et al.¹⁸ showing that even a small threefold increment in plasma epinephrine level (23 ± 4 pg/ml before infusion to 78 ± 9 pg/ml after infusion) influences glucose tolerance in otherwise healthy subjects supports this observation. During intravenous perfusion of small doses of epinephrine in healthy volunteers, Clutter et al.¹⁹ estimated the plasma epinephrine threshold value at 150 to 200 pg/ml for increments in the plasma glucose concentration and glucose production,

and for decrement in glucose clearance. On the basis of these estimates, the hyperglycemic effect of epinephrine may be well within the range of plasma epinephrine concentration observed after the injection of 1.8 to 5.4 ml of local anesthetic with epinephrine 1:100,000.²⁰⁻²² This could be enough to increase significantly the risk of a complication in patients with unstable diabetes. Because the threshold data reported by Clutter et al.¹⁹ have not yet been retested, firm conclusions regarding the hyperglycemic effect of epinephrine at plasma concentrations within the range observed after dental anesthesia are premature. For now, most investigators agree only that a transient increase in hepatic glucose production occurs, but on the other hand, epinephrine seems to have a more sustained inhibitory effect on glucose uptake.²³

To summarize, we believe vasoconstrictors can be used safely for the majority of diabetic patients treated by diet or hypoglycemic agents as long as their condition is stable. As Munroe²⁴ pointed out, patients with well-controlled insulin-dependent diabetes can also benefit from small quantities of vasoconstrictor. The amount of local anesthetic with epinephrine 1:100,000 should be the smallest doses compatible with profound anesthesia of sufficient duration and should be administered slowly after negative aspiration has been ensured. From what is actually known regarding the hyperglycemic effect of epinephrine, we must recognize that patients with labile or unbalanced diabetes may be at risk for serious complications and therefore the use of vasoconstrictors should be avoided for these patients until their condition is under medical control.

Sulfite sensitivity

Sulfites are widely used in the food and beverage industry as a preservative to reduce or prevent microbial spoilage of foods or to inhibit undesirable organism reactions during fermentation. An excellent review by Blackmore²⁵ gives a list of foods and beverages likely to contain sulfites. Adverse reactions to ingested alimentary sulfites are considered serious because sensitive people can develop severe and prolonged asthmatic crisis or anaphylactoid shock.^{26, 27} These reactions are more likely to happen after ingesting a restaurant-prepared meal, which usually contains from 25 to 200 mg of sulfites.²⁸ Sulfites are also used as antioxidant agents in anesthetic solutions to prevent the breakdown of vasoconstrictors. Sodium metabisulfite, sodium bisulfite, and acetone sodium bisulfite in concentrations of 0.15 to 2.0 mg/ml are currently incorporated in dental local anesthetics.²⁹ Local anesthetics with vasoconstrictor provide a

source of sulfite, and therefore in any cases of proven allergy their administration becomes formally contraindicated.

Recently dentists have been warned to avoid dental anesthetic with vasoconstrictor in patients with asthma.³⁰⁻³² More emphasis has been given to this warning since Huang and Fraser³³ reported a sulfite sensitivity threshold of 0.6 to 0.9 mg. These authors believed the quantity of antioxidant agent found in dental local anesthetic could seriously threaten asthmatic patients because a substantial proportion are potentially sensitive to sulfite.^{28, 34} A thorough review of the immunologic literature, however, shows an altogether different attitude toward the use of vasoconstrictors in asthmatic patients. We recently discussed this specific issue and suggested to restrict this widely publicized recommendation to steroid-dependent asthma patients.³⁵

In a sample of 203 asthma patients, Bush et al.³⁶ reported a 3.9% prevalence of sulfite sensitivity. Approximately 40% of the patients tested in this study were steroid dependent and thus had severe asthma. Such a high proportion of steroid-dependent asthma patients in the general asthmatic population is unlikely, and therefore the estimated prevalence of sulfite sensitivity reported by Bush et al. represents an inflated projection of the real prevalence in the asthmatic population as a whole. This is suggested by their data in which 8.4% of the steroid-dependent group tested positive for sulfite sensitivity as compared with only 0.8% in the non-steroid-dependent group. According to these figures, the risk of sulfite allergy in the non-steroid-dependent asthmatic population appears to be low and should not contraindicate the administration of local anesthetic with vasoconstrictor in all asthmatic patients.

From reports published in the immunologic literature, the estimated sulfite sensitivity threshold reported by Huang and Fraser³³ must be questioned and needs to be reassessed. In 1984 Goldfarb and Simon³⁷ tested six highly sulfite-sensitive asthma patients and none reacted to a subcutaneous challenge test at a concentration of 10 mg/ml. Simon²⁸ reported that only a minority of its most sulfite-sensitive patients reacted to challenge doses smaller than 10 mg/ml through subcutaneous injection. He also pointed out that the most sensitive patients are unlikely to react to doses contained in local anesthetic employed in dentistry. It would take 18 ml of local anesthetic with 0.55 mg/ml of sodium metabisulfite to equal a subcutaneous challenge dose of 10 mg/ml. We must then question the validity of the sulfite sensitivity threshold reported by Huang and Fraser.³³ Despite all

the facts presented by the authors, the symptoms they describe do not seem compatible with a true allergic reaction to sulfite. In their report they mention a history of palmar and plantar pruritus, generalized urticaria, facial and laryngeal edema, abdominal pain, and fulminating diarrhea, but no asthmatic reaction. According to the authors the ingestion of alimentary sulfites was responsible but unfortunately no challenge test was carried out to confirm the diagnosis. So far, there is no proven case of urticaria and angioedema as a result of sulfite sensitivity reported in the medical literature. Furthermore, allergy to sulfites is extremely rare in the nonasthmatic population.³⁴ According to Simon,²⁸ the symptoms described by Huang and Fraser could have been caused by an important accumulation of sulfur dioxide in the stomach and no allergic or immunoallergic mechanism needed to be implied. Although most investigators do not attribute the presence of urticaria and angioedema to sulfite sensitivity,^{28, 34, 37} others³⁸ have debated this issue and suggested the existence of a subgroup of sulfite-sensitive persons whose reaction might not be asthmatic and might be exquisitely sensitive to parenteral exposure.

Because sulfites are abundant in our environment and the majority of sulfite-sensitive persons seem to have a subcutaneous threshold greater than 10 mg, chances for a patient to develop a first major reaction after a dental injection are remote. More likely, a sensitive subject would have already been recognized by a previous untoward reaction to sulfite ingested from foods and beverages. Therefore we believe local anesthetic with vasoconstrictor can be used safely for non-steroid-dependent asthma patients. Until we know more about the sulfite sensitivity threshold, we recommend avoiding local anesthetic with vasoconstrictors in cortico-dependent asthma patients on account of a higher risk of sulfite allergy and the possibility that an accidental intravascular injection might cause a severe and immediate asthmatic reaction in the sensitive patient.³⁹

Pheochromocytoma

Pheochromocytoma is a rare but serious disorder characterized by the presence of catecholamine-producing tumors.^{40, 41} If untreated, it may cause death by pulmonary edema, ventricular fibrillation, or cerebrovascular hemorrhage.^{42, 43} In addition to hypertension, clinical manifestations include headaches, palpitations, and diaphoresis, which may all occur paroxysmally. Because of high level of circulating catecholamines, particular attention should be given to this condition. The use of vasoconstrictors puts these patients at high risk for lethal cardiac or cere-

brovascular complications and should be strictly avoided.

CONCLUSION

The risks of serious medical complications after the injection of local anesthetics with vasoconstrictor or after the use of epinephrine-impregnated retraction cords are not exclusive to patients with severe cardiovascular diseases. There are other instances where dentists should be as concerned and avoid the use of vasoconstrictor. Undoubtedly these substances can be used safely in dentistry in most medically compromised patients, but the possibility of an intravascular injection makes the risk far greater than the benefit of deep anesthesia in patients with uncontrolled or non-medically treated hyperthyroidism, labile or unstable diabetes, steroid-dependent asthma, sulfite allergy, or pheochromocytoma. We should also stress the impression of false security surrounding the intraligamentary injection and the use of impregnated retraction cord on the account of the small quantities of vasoconstrictor. It is now well documented that these techniques lead to immediate systemic reperfusion and are equivalent to an intravascular injection of vasoconstrictor.⁴⁴⁻⁴⁶ To minimize the risk and prevent serious complication, a thorough medical history is mandatory for every dental patient. Only then will dentists be able to rationally use vasoconstrictor in medically compromised patients.

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