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Vasoconstrictors: indications and precautions

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Since 1901, when Braun first combined cocaine and epinephrine, vasoconstrictors have been added to local anesthetic solutions to increase the quality and duration of anesthesia, to aid in hemostasis, and, presumptively, to reduce toxicity of the local anesthetic. With the exception of cocaine, all local anesthetics are potential vasodilators, and vasoconstrictors are combined with them to counteract this effect. Epinephrine (Adrenaline®) and levonordefrin (Neo-Cobefrin®) are the most widely used vasoconstrictors in the United States. Felypressin, a noncatecholamine vasoconstrictor, is also available in Canada and many other countries [1–3].

Mechanism of action

Epinephrine and levonordefrin stimulate adrenergic receptors (also referred to as adrenoceptors) that are responsible for their vasoconstrictive and other properties. There are two basic categories of adrenergic receptors: α, which usually have excitatory actions, and β, which stimulate the heart but otherwise are mostly inhibitory. The α and β adrenoceptors have been further divided into α_1 (α_{1A}, α_{1B}, α_{1D}) and α_2 (α_{2A}, α_{2B}, α_{2C}), and β_1, β_2, and β_3 subtypes, respectively. Some important actions subserved by these adrenoceptors are listed below (Table 1) [2].

Vasoconstrictors differ in their affinity for adrenergic receptors (Table 2) [2]. One might assume that a vasoconstrictor added to a local anesthetic would ideally have only α-agonistic activity, because it is this activity that

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Table 1
Adrenergic receptor activities

Effector organ or function	Receptor[a]	Response
Cardiovascular system		
Heart rate	β_1, β_2	Increased[b]
Contractile force	β_1, β_2	Increased
Coronary arterioles	α_1, α_2/β_2	Constriction/dilation[c]
Automaticity	β_1, β_2	Increased
Conduction velocity	β_1, β_2	Increased[b]
Peripheral resistance	α_1, α_2/β_2	Increased/decreased
Capacitance veins	α_1/β_2	Constriction/dilation
Respiratory system		
Bronchial smooth muscle	β_2	Relaxation
Bronchial glands	α_1/β_2	Decreased secretion/increased secretion
Pulmonary arterioles	α_1/β_2	Constriction/dilation[c]
Gastrointestinal tract		
Motility and tone	α_1, α_2, β_1, β_2	Decreased
Sphincters	α_1	Contraction
Visceral arterioles	α_1/β_2	Constriction/dilation
Liver		
Glucose metabolism	α, β_2	Glycogenolysis, gluconeogenesis
Arterioles	α_1/β_2	Constriction/dilation
Fat		
Lipolysis	α, β_1, β_3	Lipolysis
Arterioles	α_1/β_2	Constriction/dilation
Pancreas		
Insulin secretion	α_2/β_2	Decreased/increased
Genitourinary system		
Urinary bladder sphincter	α_1	Contraction
Detrusor muscle	β_2	Relaxation
Trigone muscle	α_1	Contraction
Uterine tone	α_1/β_2	Contraction/relaxation[d]
Renal arterioles	α_1, α_2, β_1, β_2	Constriction/dilation
Skeletal muscle		
Neuromuscular transmission	α, β_2	Increased
Arterioles	α/β_2	Constriction/dilation
Salivary glands		
Secretion	β	Mucous secretion
Arterioles	α_1, α_2	Constriction
Skin and mucosa		
Arterioles	α_1, α_2	Constriction

[a] Primary receptors mediating pharmacologic response. Receptors separated by commas yield complementary actions; receptors separated by a slash have differing or opposing actions.

[b] Direct effects on the heart may be blocked or reversed by compensatory vagal reflex activity.

[c] Local regulatory processes largely govern blood flow.

[d] Effect depends on stage of menstrual cycle, sexual hormone concentrations, and other factors.

Table 2
Relative receptor potencies of adrenergic vasoconstrictors

	α_1	α_2	β_1	β_2
Epinephrine	+++	+++	+++	+++
Levonordefrin	+	++	++	+

Symbols indicate the relative potency: +++ = high, ++ = intermediate, + = low.

causes vasoconstriction. But epinephrine, the most commonly used vasoconstrictor, is also the least selective, exerting both strong α and β actions. Epinephrine is a highly effective vasoconstrictor for intraoral use in concentrations of 1:200,000–1:50,000 (5–20 μg/mL) because of the predominance of α adrenoceptors in the oral mucosa, submucosa, and peridontium.

Levonordefrin is relatively specific for the α_2 receptor. It has about one sixth the vasoconstrictor potency of epinephrine and is therefore marketed in a 1:20,000 concentration (50 μg/mL) [1]. Felypressin, a nonsympathomimetic vasoconstrictor, is a synthetic analogue of vasopressin, otherwise known as antidiuretic hormone. Felypressin stimulates V_{1a} receptors on vascular smooth muscle. Because it does not significantly influence the heart directly and invokes other effects that limit increases in peripheral resistance (eg, by inhibiting sympathetic neurotransmitter release), felypressin in standard doses has little effect on blood pressure, heart rate, or cardiac rhythm. It may, however, cause clinically significant coronary vasoconstriction in patients with heart disease. Felypressin is relatively ineffective as a hemostatic agent [2,3].

Indications

Several benefits accrue from adding vasoconstrictors to local anesthetic solutions. Most important for dentistry is the enhancement of local anesthesia in quality and duration. Vasoconstrictors have also been used to assist in hemostasis. Finally, it has been suggested that inclusion of a vasoconstrictor increases local anesthetic safety.

Enhancement of local anesthesia

Most local anesthetics cause vasodilation clinically, and the addition of a vasoconstrictor opposes this effect [4]. The vasodilating properties of local anesthetics increase local blood flow and their own absorption into the systemic circulation. These effects are especially true in dentistry, where local anesthetics are injected into highly vascular tissues. Lidocaine produces unreliable pulpal anesthesia without a vasoconstrictor. With the addition of epinephrine, however, at a concentration of 1:100,000, 2% lidocaine blocks pulpal nerve fibers for 60–90 minutes, depending on the site of injection [2,3,5]. Procaine is similarly ineffective for pulpal anesthesia without a vasoconstrictor.

Several local anesthetics, most notably mepivacaine and prilocaine, are available without a vasoconstrictor. These two local anesthetics cause less vasodilation than lidocaine or procaine and can be used without a vasoconstrictor for short procedures. A maxillary tooth can be reliably blocked for about 20 minutes after supraperiosteal injection. But with the addition of a vasoconstrictor, the duration of pulpal anesthesia rises to 40 minutes with prilocaine and 50 minutes with mepivacaine. The effect durations of clinically available local anesthetics with and without vasoconstrictors after inferior alveolar nerve block are listed below (Table 3).

Bupivacaine, a long-acting local anesthetic, is also a powerful vasodilator. Because it is highly lipid-soluble (or hydrophobic) and tends to be sequestered in nerve membranes for a prolonged period, it is capable of providing protracted pulpal anesthesia without a vasoconstrictor. Even so, the addition of a vasoconstrictor increases its duration of anesthesia [6].

Hemostasis

Intraoperative hemostasis is important for optimal results when performing surgical procedures in the oral cavity. Infiltration of a local anesthetic containing epinephrine can help reduce blood loss during surgery and improve visualization of the operative field [7,8]. For local hemostasis, an epinephrine concentration of 1:50,000 with 2% lidocaine is more effective than a 1:100,000 strength [9]. Unfortunately, lidocaine partially counteracts the vasoconstrictive effect of epinephrine and enhances its systemic absorption [10]. A more rational, if less convenient, approach to control bleeding may be to inject less concentrated solutions of epinephrine without local anesthetic. Practitioners should also be aware that rebound hyperemia can occur (primarily from tissue ischemia and the accumulation of vasodilatory metabolites) once the vasoconstriction has dissipated, which can accentuate postoperative blood loss [3].

Epinephrine-impregnated gingival retraction cord is still used by some practitioners as a hemostatic agent. Such retraction cord may contain racemic epinephrine in amounts up to 1 mg/inch. When the retraction cord is placed in the gingival sulcus, especially in abraded, inflamed tissue, the potential exists for systemic uptake of large quantities of epinephrine [11,12].

Table 3
Effect of catecholamine vasoconstrictors on the duration of pulpal anesthesia after inferior alveolar nerve blockade

Local anesthetic	Duration (min)
2% Lidocaine	40 (unreliable)
2% Lidocaine with 1:100,000 epinephrine	85
3% Mepivicaine	40
2% Mepivicaine with 1:20,000 levonordefrin	75
4% Prilocaine	55
4% Prilocaine with 1:200,000 epinephrine	60

Increased safety

It has been suggested that the addition of a vasoconstrictor can protect against systemic local anesthetic toxicity [13]. By decreasing blood flow in the injected tissues, a vasoconstrictor slows the rate at which the local anesthetic enters the circulation. It is presumed that metabolic inactivation of the local anesthetic is more able to keep pace with absorption, and that the resulting smaller peak plasma concentrations of drug elicit fewer adverse effects. These presumptions are reflected in the fact that the maximum manufacturer's recommended dose of lidocaine is 4.5 mg/kg up to a maximum of 300 mg without a vasoconstrictor but 7 mg/kg up to a maximum of 500 mg with epinephrine [2].

Peak plasma concentrations of lidocaine are reduced by about 30–40% when it is coadministered intraorally with epinephrine [14–16]. Levonordefrin, however, has little significant effect on mepivacaine concentrations [15,16]. In neither case is there evidence of a reduction in local anesthetic toxicity with vasoconstrictor use [17–19]. Animal studies suggest that vasoconstrictors increase the relative distribution of large doses of local anesthetics into the brain even as they retard drug absorption from the injection site [20]. Thus, there is little direct proof that the addition of a vasoconstrictor makes a local anesthetic safer by retarding systemic absorption.

Even though the addition of a vasoconstrictor may not moderate maximum plasma concentrations of a local anesthetic, it may be useful in reducing the amount of local anesthetic needed for adequate pain relief. In the case of mepivacaine, a 2% solution is highly effective when combined with levonordefrin, but a 3% solution—representing 50% more drug—is needed in the absence of a vasoconstrictor. Furthermore, because a local anesthetic solution with vasoconstrictor often provides a longer duration of effect, there is a diminished need for reinjection and less likelihood for drug accumulation.

Precautions

As with any medication being considered for use, the potential risks of vasoconstrictors must be weighed against their expected benefits. For adrenergic vasoconstrictors, the greatest potential for adverse effects resides in patients with cardiovascular disease and who are taking certain interacting drugs. Concerns are also sometimes expressed about vasoconstrictor usage during pregnancy and in patients with sulfite intolerance.

Cardiovascular disease

There has been enduring debate about the potential risks of epinephrine and related vasoconstrictors to patients with cardiovascular disease. Arguments have been expressed that the amounts of catecholamines released

endogenously in response to inadequate pain relief and/or the stress of dental treatment are much greater than those commonly injected for dental procedures [13,21]. It has also been suggested that a local anesthetic with vasoconstrictor is desirable in patients with cardiovascular disease because of the greater pain relief afforded by the combination [22].

Historical progression of this issue is reflected in several official pronouncements. In 1955, a special committee of the New York Heart Association (AHA) recommended 0.2 mg as the maximum dose of epinephrine that should be used in local anesthesia for patients with heart disease [23]. In 1964, the American Dental Association and the AHA jointly stated that vasoconstrictors were not contraindicated for patients with cardiovascular disease when administered carefully, slowly, and with preliminary aspiration to avoid intravascular injection [24]. The maximum strength of epinephrine that should be used was 1:50,000. Lastly, in 1986, the AHA emphasized safety by concluding, "Vasoconstrictor agents should be used in local anesthesia solutions during dental practice only when it is clear that the procedure will be shortened or the analgesia rendered more profound. When a vasoconstrictor is indicated, extreme care should be taken to avoid intravascular injection. The minimum possible amount of vasoconstrictor should be used" [25].

Epinephrine is normally released from the adrenal medulla at a basal rate of 2.5–7.5 ng/kg per minute [21] This endogenous amount may rise twenty- to fortyfold in times of stress [21]. The plasma concentrations of epinephrine associated with several injected doses and various physical activities are depicted here (Fig. 1) [2]. The data represented suggest that a single cartridge of 2% lidocaine with 1:100,000 epinephrine significantly increases plasma epinephrine over resting values, and that two cartridges yield a concentration equivalent to that of mild physical exertion. It is logical to conclude that ambulatory patients, including those with cardiovascular disease, should be able to tolerate these doses of vasoconstrictor because they are already doing so during the course of daily life.

Unfortunately, certain individuals have special risk for cardiovascular problems during dental treatment. These patients include those with unstable angina pectoris (chest pain without exertion), a recent heart attack or stroke (within 6 months), severe untreated or uncontrolled hypertension, and uncontrolled or untreated congestive heart failure. The American Society of Anesthesiologists' (ASA) physical status score classifies patients from ASA I (healthy patients with no systemic disease) to V (moribund patients with little chance of survival over the next 24 hours). The patients listed above would mostly be ranked as ASA IV, having severe systemic disease that is constantly life-threatening. Patients in this category should not receive invasive dental treatment until they have been stabilized medically [12]. Even then, vasoconstrictors should be avoided if at all possible because of the threat posed by accidental intravascular injection or rapid systemic absorption of the drug.

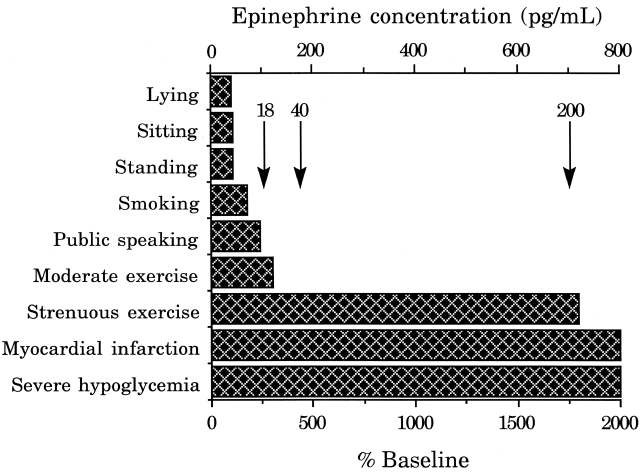

Fig. 1. Influence of various activities and conditions on venous plasma epinephrine concentrations. (*From* Jastak JT, Yagiela JA, Donaldson D. Local anesthesia of the oral cavity. Philadelphia: WB Saunders; 1995; with permission.)

Heart transplants have created a special group of patients who are supersensitive to injected catecholamines. When a heart is transplanted, it is of necessity surgically denervated. The loss of sympathetic nerves to the heart eliminates the adrenergic nerve terminals that both release norepinephrine and take it back up for later reuse (by a transport system known as uptake$_1$) [4]. This reuptake process is also the principal means by which the actions of epinephrine and levonordefrin molecules reaching the cardiac adrenoceptors are terminated [26]. The resulting increased exposure to these drugs magnifies cardiac stimulation in these patients [27]. Though there are no published recommendations regarding vasoconstrictors in these patients, the dentist should be cautious in their use, administering local anesthetic solutions in small divided doses and monitoring the heart for any changes in rate or rhythm.

Pregnancy

Prudence dictates that elective dental procedures be deferred when a patient is pregnant. When delay is not possible, necessary treatment—including the administration of local anesthesia for pain relief—must be provided in an optimally safe manner for both mother and fetus. Occasionally, the use of vasoconstrictors in this regard has been questioned. Potential concerns regarding epinephrine involve the drug's effects on uterine muscle tone and blood flow.

Experimentally, stimulation of α_1-adrenergic receptors causes contraction of uterine muscle strips. But the principal effect of clinically used doses of

epinephrine during pregnancy is uterine relaxation during the third trimester, a β_2-adrenoceptor effect. Because it only weakly stimulates α_1 and β_2 adrenoceptors, levonordefrin probably has little effect on uterine tone.

As with many vascular beds, epinephrine can cause vasoconstriction and decrease uterine blood flow. This effect has been examined in pregnant women receiving epidural local anesthesia for labor. Most studies have shown that uterine and umbilical blood flow are not compromised by epinephrine [28–31]. A possible exception includes women whose pregnancies are complicated by hypertension [32]. In this case, epinephrine may increase vascular resistance in the uteroplacental circulation, indicating impaired blood flow. Even so, there is no evidence of increased deleterious effects. Because the use of a vasoconstrictor can reduce the amount of local anesthetic administered and concomitantly reduce fetal drug exposure [31], it has been argued that vasoconstrictors are appropriate when local anesthesia is administered to a pregnant woman [33].

Drug interactions

With the growing variety and number of drugs patients are taking, and the rising use of multiple medications, drug interactions are of increasing concern. The most important and best characterized interactions with vasoconstrictors include the tricyclic antidepressants, nonselective β-adrenergic blocking agents, certain general anesthetics, and cocaine. These and other drug interactions that have been discussed in the dental/medical literature are listed below (Table 4).

Tricyclic antidepressants (TCAs) such as imipramine (Tofranil®), amitriptyline (Elavil®), and doxepin (Sinequan®) are now second-line agents for the treatment of depression as well as for orofacial and other chronic pain disorders. These drugs act on the central and peripheral nervous systems by blocking the reuptake of certain neurotransmitters, most notably norepinephrine and 5-hydroxytryptamine. The affected neurotransmitters are thus free to interact more effectively with their receptors, augmenting their physiologic effects. Epinephrine and levonordefrin are subject to the same uptake process and, therefore, the same potentiation. Significant increases in blood pressure and disturbances of the normal cardiac rhythm may occur [34–36].

The potentiation of epinephrine with TCAs is about threefold, at least early in TCA therapy. The potentiation is six- to eightfold with levonordefrin. It is recommended that levonordefrin not be used with patients on TCAs because of the acute hypertension and cardiac dysrhythmias that might occur after an accidental intravascular injection [36]. Epinephrine-impregnated gingival retraction cord is also contraindicated because of the large amounts of epinephrine available for absorption. If a local anesthetic with epinephrine is to be used, it should have no more than 1:100,000 epinephrine, and the maximum recommended dose should be reduced by one-third [34,36].

β-Adrenergic antagonists (also referred to as β-adrenoceptor blockers or β blockers) are prescribed for numerous conditions: essential hypertension, angina pectoris, myocardial infarction, hyperthyroidism, cardiac dysrhythmias, and disorders with excessive sympathetic nervous system activity. Some β blockers affect β_1 and β_2 receptors similarly; others are selective for β_1 receptors. Both types attenuate epinephrine's stimulation of the heart but only the nonselective forms prevent the ability of epinephrine to stimulate β_2 receptors and dilate skeletal muscle blood vessels. When epinephrine is administered to a patient with nonselective β blockade, unopposed α-adrenergic stimulation may lead to a serious rise in blood pressure and reflex bradycardia [34,36]. Therefore, patients taking nonselective β blockers should receive a minimal initial dose such as one half of a cartridge of local anesthetic with 1:100,000 epinephrine and then be monitored for systemic effects at 5 minutes before additional drug is administered [36] Special care should also be taken to avoid intravascular injection. This interaction is not evident in patients receiving selective β_1 blockers.

Certain general anesthetics are known to potentiate dysrhythmias associated with the administration of vasoconstrictors. The inhalation agent halothane (Fluothane®) has the greatest potential of all currently available inhalation anesthetics to elicit this reaction, and epinephrine should not be administered in single doses over 2 μg/kg when used with halothane [36]. (For a 70-kg [154-lb] man, 2 μg/kg would equal 14 mL of a 1:100,000 epinephrine solution.) The intravenous anesthetic thiopental (Pentothal®) is likewise capable of enhancing the dysrhythmic activity of adrenergic drugs. Thiopental may be used as an induction agent, and when given concomitantly with halothane the recommended maximum dose of epinephrine is reduced to 1 μg/kg [36]. Gingival retraction cord containing epinephrine is best avoided in all patients receiving general anesthesia.

Cocaine and epinephrine possess a potentially lethal interaction. Cocaine is occasionally applied as a topical anesthetic for mucosal membranes; however, its most prominent use is illicit consumption. Cocaine is a stimulant that blocks the reuptake of norepinephrine, dopamine, and 5-hydroxytryptamine at presynaptic nerve terminals. This action also includes epinephrine and levonordefrin used in local anesthesia. Serious adrenergic stimulation leading to hypertension, myocardial infarction, and even sudden death may ensue in patients actively abusing cocaine [37]. Therefore, patients who are under the influence of cocaine should have elective dental treatment postponed for at least 24 hours after the last drug exposure.

A number of the interactions listed below (see Table 4) are poorly documented clinically or occur in situations not likely to be encountered in dental practice. The monoamine oxidase inhibitors (MAOIs) illustrate a widely mentioned interaction that actually has little clinical relevance for adrenergic vasoconstrictors used in dentistry. The MAOIs include the antidepressants phenelzine (Nardil®) and tranylcypromine (Parnate®), the antiparkinson drug selegiline (Eldepryl®) and the antimicrobial agents

Table 4
Drug interactions involving catecholamine vasoconstrictors

Drug class	Examples	Mechanism	Effect	Recommendation
Tricyclic antidepressants and related drugs	Amitriptyline (Elavil®), doxepin (Sinequan®), imipramine (Tofranil®), maprotiline (Ludiomil®)	TCAs block the uptake of catecholamines by sympathetic nerve terminals, increasing their actions	Potentiation of cardiovascular effects	Use epinephrine cautiously, avoid levonordefrin and gingival retraction cord with epinephrine
Nonselective β-adrenergic blockers	Nadolol (Corgard®), propranolol (Inderal®)	Unopposed α-adrenergic stimulation of catecholamines	Hypertension and reflex bradycardia	Use epinephrine and levonordefrin cautiously; avoid gingival retraction cord with epinephrine
Volatile general anesthetics	Desflurane (Suprane®), enflurane (Ethrane®), halothane (Fluothane®)	Potentiation of the dysrhythmic potential of catecholamines	Ventricular dysrhythmias	Use epinephrine and levonordefrin cautiously after informing anesthesiologist; avoid gingival retraction cord with epinephrine
Intravenous general anesthetics	Thiopental (Pentothal®)	Potentiation of the dysrhythmic potential of catecholamines	Ventricular dysrhythmias	Use epinephrine and levonordefrin cautiously after informing anesthesiologist; avoid gingival retraction cord with epinephrine
Recreational drugs	Cocaine	Cocaine potentiates sympathetic nervous system activity and blocks the uptake of catecholamines by sympathetic nerve terminals, increasing their actions	Hypertension, myocardial infarction, ventricular dysrhythmias	Have patient abstain from cocaine for 48 hours before treatment; avoid catecholamines if emergency dental treatment necessary
COMT inhibitors	Entacapone (Comtan®), tolcapone (Tasmar®),	Metabolism of catecholamines by COMT is inhibited, increasing their actions	Potential of cardiovascular effects	Use epinephrine and levonordefrin cautiously; avoid gingival retraction cord with epinephrine
Antiadrenergic agents	Guanadrel (Hylorel®), guanethidine (Ismeline®), methyldopa (Aldomet®)	Uptake of catecholamines is inhibited and/or target tissue responsiveness is increased	Possible potentiation of cardiovascular effects	Use epinephrine and levonordefrin cautiously; avoid gingival retraction cord with epinephrine

Nonselective α-adrenergic blockers	Chlorpromazine (Thorazine®), clozapine (Clozaril®), haloperidol (Haldol®), olanzapine (Zyprexia®)	Unopposed β_2-adrenergic stimulation of catecholamines	No interaction with normal doses of interacting drugs; hypotension with large doses	No special precautions in ambulatory patients; avoid epinephrine when treating hypotensive emergencies
Digitalis glycosides	Digoxin (Lanoxin®)	Additive dysrhythmogenic effects	Potentially dangerous dysrhythmias with large doses of vasoconstrictor	Use epinephrine and levonordefrin cautiously; avoid gingival retraction cord with epinephrine
Thyroid hormones	Desiccated thyroid (Armour Thyroid®), levothyroxine (Synthroid®), liothyronine (Cytomel®)	Additive dysrhythmogenic effects	Potentially dangerous dysrhythmias with large doses	No special precautions in euthryoid patients; use epinephrine and levonordefrin cautiously and avoid gingival retraction cord with epinephrine in hyperthyroid patients
MAO inhibitors	Furazolidone (Furoxone®), linezolid (Zyvox®), phenelzine (Nardil®), selegiline (Eldepryl®), tranylcypromine (Parnate®)	Exogenously administered catecholamines are not inactivated by monoamine oxidase	No interaction	None

COMT, catecholamine-*O*-methyltransferase; MAO, monoamine oxidase; TCAs, tricyclic antidepressants.

furazolidone (Furoxone®) and linezolid (Zyvox®). The package insert for local anesthetics with vasoconstrictors lists MAOIs as interacting drugs. It was once thought that this interaction might be significant because MAOIs block the metabolism of some adrenergic drugs as well as the intraneuronal breakdown of norepinephrine, increasing the pool of neurotransmitter that can be released by indirect-acting adrenergic drugs. A MAOI drug interaction is significant with such drugs as dextroamphetamine, used to treat narcolepsy, and pseudoephedrine found in nasal decongestants. A MAOI interaction is not clinically significant, however, with epinephrine or levonordefrin as used in dentistry [34–36]. These direct-acting, exogenously administered catecholamines are primarily inactivated by the enzyme catechol-*O*-methytransferase (COMT).

Two drugs, tolcapone (Tasmar®) and entacapone (Comtan®), have been recently introduced that inhibit COMT. These medications are used in the management of Parkinson's disease by helping to prevent the breakdown of levodopa, the principal therapeutic agent used for this disorder. Because COMT is directly involved in the metabolism of epinephrine and levonordefrin, care should be taken when using local anesthetics with vasoconstrictors in patients taking these medications. There are little data on the clinical significance of this interaction, possibly because of the short time that the drugs have been on the market, but it is recommended that no more than the equivalent of one cartridge of lidocaine with 1:100,000 epinephrine be administered initially and that the patient's heart rate and blood pressure be checked 5 minutes afterward before giving more local anesthetic [38].

Sulfite intolerance

Numerous reports exist of alleged allergic reactions to local anesthetics. The majority of true allergic reactions to amide local anesthetic solutions are probably responses to the methyparaben preservative used in multidose vials. Reactions have also been attributed to sulfites, most notably, sodium metabisulfite.

Sulfites are found naturally in many common foods and beverages [39]. Sulfites are also added to prevent or delay undesirable changes in the color, taste, or texture of such edibles. Wine, for example, contains about 10 mg/oz sulfites [39]. Sulfites are used in local anesthetic solutions as antioxidants to prevent the breakdown of the vasoconstrictor components. Local anesthetics with vasoconstrictors can contain as much as 2 mg/mL of sulfite salts [40].

Allergic-like reactions to sulfites are most commonly seen in asthmatic adults who react to inhaled or ingested sulfites through a nonimmunologic pathway. These individuals are not particularly sensitive to small amounts of injected sulfites. In fact, documented anaphylactic reactions to sulfites, which would be expected to be more intense with an injected allergen, are quite rare.

Although most patients who describe themselves as being sulfite-sensitive can receive intraoral injections of sulfite-containing solutions safely,

whenever a patient reports a history of "allergy" to a local anesthetic, the treating dentist must include sulfite intolerance in the differential diagnosis. Local anesthetics with adrenergic vasoconstrictors are absolutely contraindicated in the rare patient with a true sulfite allergy.

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