Management of Allergy and Anaphylaxis During Oral Surgery

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KEYWORDS

• Allergy • Anaphylaxis • Anaphylactoid • Epinephrine

KEY POINTS

- Minor and major allergic reactions occur during oral and maxillofacial treatment.
- Immediate diagnosis and pharmacologic intervention are imperative.
- Signs and symptoms may be variable.
- The early administration of epinephrine is critical.

Allergic reactions can and do occur during routine oral and maxillofacial surgery and dental treatment.[1] These reactions can vary from mild to life threatening, and the clinical manifestations of a reaction to an antigen may vary from mild (with minor skin manifestations occurring over time) to those requiring immediate diagnosis and aggressive treatment to prevent ultimate respiratory and cardiovascular collapse, leading to death.

MILD ALLERGY

Mild allergic reactions that are slow in onset and consist primarily of itching, hives, and/or rash and are not associated with respiratory or cardiovascular issues are usually initiated by the body's histamine release response. As with any medical emergency, consciousness should be ascertained and vital signs monitored. Treatment is symptomatic and involves the administration of a histamine blocker, such as diphenhydramine by the intramuscular (IM), intravenous (IV), or oral route. Because drugs given via the oral route are slow in onset, the parenteral route is preferred for immediate relief. It is imperative to appreciate that even after initial treatment, histamine may continue to circulate for 3 or more days and an oral prescription of diphenhydramine should be prescribed to manage this time period. A verbal and written warning of the sedating effects of histamine blocking drugs must be given to the patient.

SEVERE ALLERGY (ANAPHYLAXIS/ ANAPHYLACTOID REACTIONS)

Anaphylaxis is an acute life-threatening systemic reaction with varied mechanisms, clinical presentations, and involvement of multiple organ systems. It has recently been defined "as a serious allergic reaction that is rapid in onset and may cause death."[2] Anaphylaxis occurs when antigen-specific IgE molecules, which are bound to mast cells and basophils, are cross-linked by the specific antigen and on antigenic re-exposure causes these cells to degranulate. It takes an extremely small

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amount of antigen to trigger the releases of a combination of biochemical mediators, such as histamine, neutral proteases, prostaglandins, leukotrienes, and other chemokines and cytokines.[3] These mediators are responsible for the signs and symptoms of anaphylaxis. Anaphylactoid reactions are not IgE related, but they release similar mediators and can cause identical symptoms and pathology. Symptoms usually occur with 20 minutes to an anaphylactic or anaphylactoid reaction, but the time course may be variable.

Although many drugs and substances (**Table 1**) can trigger acute hypersensitivity reactions, the most commonly involved substances and drugs during perioperative anaphylaxis are neuromuscular blocking agents, antibiotics, and latex.[4] Data concerning the incidence and severity of anaphylaxis are limited; the estimated incidence during anesthesia ranges from 1 in 10,000 to 1 in 20,000 anesthesia cases.[5] Anaphylaxis reactions triggered by antibiotics are of special concern to oral and maxillofacial surgeons and primarily involve penicillins and cephalosporins, which contain a β-lactam ring. Reactions from the rapid IV administration of vancomycin are rare and should be differentiated from red man syndrome that is a nonallergic phenomenon.[6] Publication of the Federal Drug Administration medical alert on this documented the increasing number of allergic reactions to medical products composed of latex during the perioperative period.[1]

Certain subsets of patients have a higher risk of latex allergy and can exhibit any of the 3 types of reactions to natural rubber products. The first type is a nonallergic irritant dermatitis; the second is a type IV T cell-mediated delayed hypersensitivity reaction, is due to the chemicals added to the latex during manufacturing, and is usually a delayed localized dermatitis; and the most serious one—type I—is an immediate hypersensitivity reaction mediated by IgE antibodies specifically toward low molecular weight antigens in latex and can range from mild to severe. Populations at risk include (1) patients with histories of myelodysplasia, bladder extropy, and multiple surgeries; (2) health care workers; (3) atopic individuals (those with asthma, rhinitis, eczema, or food allergies, especially tropical ones); and (4) workers in the rubber industry.[7] There is a growing trend in creating latex-free oral surgical environments to reduce the incidence of latex issues relating to both the surgical team and patients.[8]

The clinical signs of an anaphylaxis/anaphylactoid reaction usually occur within minutes after the agent is injected IV. The clinical signs can be varied and either cascade from one system to another or appear simultaneously in many organs. The primary target organs are the skin, mucous membranes, gastrointestinal tract, and cardiorespiratory systems. Clinical cutaneous-mucous signs may include erythema, pruritus, and edema, with or without angioedema. Moderate multivisceral signs include hypotension, tachycardia, dyspnea, and gastrointestinal disturbances. The most serious manifestations involve swelling of the airway, severe bronchospasm, cardiac dysrhythmias, and cardiovascular collapse (**Table 2**).

The appearances of signs can also be classified and graded on a clinical severity scale:

Grade I, involving cutaneous-mucous features
Grade II, having cutaneous-mucous features with accompanying cardiovascular and/or respiratory signs
Grade III, cardiovascular collapse with multivisceral signs
Grade IV, cardiac arrest[9]

The rapid, initial diagnosis of an anaphylactic/anaphylactoid reaction is critical and early intervention is the key to successful management. The immediate removal or discontinuing of the triggering agent, early administration of epinephrine, maintenance of the airway and ventilation with 100% oxygen, and calling for help are fundamental. Epinephrine is the primary and first drug of

Table 1
Triggering agents of anaphylactic and anaphylactoid reactions

Common	Food (eg, peanuts, fish, shellfish, milk, eggs, bisulfites) Insect stings Medications: antibiotics, nonsteroidal anti-inflammatory drugs, aspirin, opioids, general anesthetic agents, radiocontrast dye, protamine, neuromuscular blocking agents Latex Exercise
Uncommon	Local anesthetics
Rare	Nitrous oxide, benzodiazepines, antihistamines

Table 2
Clinical characteristics of anaphylaxis/anaphylactoid reactions

System	Signs	Symptoms
Pulmonary	Increased respiratory rate Laryngeal edema Bronchospasm Pulmonary edema	Wheezing, stridor, coughing, dyspnea, chest tightness
Cardiovascular	Hypotension, tachycardia, cardiac Dysrhythmias, cardiac arrest	Chest tightness and pain
Mucocutaneous	Urticaria, flushing, diaphoresis, Periorbital and gingival edema	Itching, burning
Neurologic	Altered mentation Unconsciousness	Dizziness, loss of orientation, fatigue
Gastrointestinal	Vomiting, diarrhea	Nausea, cramping
Renal	Decrease in urine output	
Hematologic	Disseminated intravascular coagulation	Bleeding from mucosal surfaces

choice in the treatment of anaphylaxis due to its α_1 effects of supporting the blood pressure while its strong β_2 effects provide bronchial smooth muscle relaxation. In addition, epinephrine also effectively blocks the deleterious effects of circulating mediators.[10] If epinephrine is administered via an autoinjector or needle and syringe IM, absorption is more rapid and plasma levels are higher when in the thigh (vastus lateralis) than when injected IM into the arm (deltoid). IM injection into the thigh (vastus lateralis) is also superior to IM or subcutaneous injection into the arm (deltoid).[11,12]

No established dosage or regimen for IV epinephrine in anaphylaxis is recognized. Because of the risk for potentially lethal arrhythmias, epinephrine should be administered IV only during cardiac arrest or to profoundly hypotensive patients who have failed to respond to IV volume replacement and several injected doses of IM epinephrine. Poor outcomes during anaphylaxis are often associated with late, absent, inadequate, or excessive doses of epinephrine. When anaphylaxis is suspected, however, early intervention is the key to a successful outcome. The American Academy of Allergy, Asthma and Immunology practice parameter on the diagnosis and management of anaphylaxis is an excellent reference and should be reviewed.[2] If the reaction is severe, the patient has lost, or soon will lose, consciousness and laryngeal edema may occur. The patency of the airway should be immediately verified and basic airway rescue techniques used, beginning with basic head tilt and chin lift and escalating, if unsuccessful, to positive pressure ventilation via a bag-valve-mask device, advanced airway adjuncts (eg, supraglottic airways, endotracheal intubation, and, in rare exceptional cases, a surgical airway (**Box 1**).[13]

Although the injection of epinephrine usually reverses systemic vasodilation and inhibits the release of mediators from mast and basophil cells, there are episodes where the circulatory system function continues to deteriorate. The use of vasopressin, in cases where patients seem refractory to epinephrine and where fluid therapy is unable to counteract profound hypotension, has been put forward as a possible intervention.[4,14]

PATIENT EVALUATION FOR LOCAL ANESTHETIC REACTIONS

Although adverse reactions to local anesthetics are frequently reported, true documented immune-mediated reactions to local anesthetics are rare.[15] Often the allergic response is not even reproduced with subsequent testing/challenge.[16,17] There are also many confounding factors in these reactions, such as the presence of epinephrine, latex, and other possible triggers often found in environments where local anesthetics are used.[18] As a result, the mechanism behind local anesthetic reactions is poorly understood, and there is often confusion about the safety of using local anesthetics in patients who previously experienced a reaction. Patients with a suspected history of local anesthetic allergy must be thoroughly questioned to determine the nature of the response. The vast majority of patients labeled as allergic to local anesthetics have experienced adverse reactions related to a direct pharmacologic effect of the local anesthetic and/or vasoconstrictor, suffered an acute anxiety reaction, or experienced syncope. In a

Box 1
Pharmacologic management of anaphylaxis/ anaphylactoid reactions

Primary Treatment

IV fluids (25–50 mL/kg of crystalloid solution)

Epinephrine Intramuscular

Autoinjection of 1:1000 solution

Weight 10–25 kg: 0.15 mg epinephrine IM (deltoid or vastus lateralis) autoinjector or needle

Weight >25 kg: 0.3 mg epinephrine IM (deltoid or vastus lateralis) autoinjector or needle

Repeated doses of epinephrine may be needed every 5–15 minutes

Epinephrine Intravenous

(for profound bronchospasm or hypotension)

Use epinephrine 1:10,000 in prefilled syringe for IV use

Begin at dose of 50–200 μg IV (0.5–2 mL), increase as needed

Secondary Treatment

Bronchodilator (β_2-agonist)

Albuterol (90 μg per inhalation puff)

H_1-blocker (antihistamine)

Diphenhydramine (Benadryl) (IV 0.5 mg/kg), requires dilution to avoid vein damage

Optional H_2-blocker

Famotidine (Pepcid) (20 mg IV)

(Optional) steroids

Hydrocortisone (1–2.5 mg/kg)

Methylprednisolone (1 mg/kg)

Data from Refs.[2,4,21]

review of 5018 patients receiving local anesthetics, 25 experienced an adverse reaction. Two were determined to have possible allergic reactions, which were later ruled out by intradermal and challenge testing.[19,20]

Most commonly, patients screened for local anesthetic allergy are tested solely with intradermal local anesthetic injections. Unfortunately, this testing may produce false results, and patients do not have the knowledge that receiving a local anesthetic is safe.

A multimodal testing approach has been used for local anesthesia evaluation/screening at the University of Cincinnati Medical Center to permit patient screening to rule out agent sensitivity, anxiety leading to syncope, amide tachyphylaxis, catecholamine sensitivity, and possible poor technique for injection; patients with known allergy to local anesthetics have been screened over a 20-year period.

This program involved testing patients in a controlled setting at the medical center due to potential adverse reaction requiring immediate emergency medical care. Patient monitoring for local anesthetic screening included pulse, ECG, blood pressure, pulse oximeter, and respirations. An IV line was started before local anesthetic screening. No alcohol or antiseptic was applied to the skin before start of the IV.

There were 3 parts to the evaluation protocol: intradermal screening, IV lidocaine challenge, and right and left posterior superior alveolar (PSA) nerve blocks.

Intradermal Screening Protocol

For the intradermal screening, 27-gauge needles with fixed volume of 0.05 mL of agent were used. Scratch test and progressive challenge were not used. Skin sites were evaluated 5 minutes after injection using the HollisterStier grading system (Allergy Skin Test Guide/HollisterStier - Sliding Guide Miles [www.hsallergy.com]). Grading included evaluation of erythema and weal by size in centimeters and regular versus irregular wheal shape. This screening provided background information on potential patient agent sensitivities and likelihood of a vasovagal syncope response to injection being the reason for the prior "allergic reaction".

Agents used for intradermal testing included

1. Normal saline (control)
2. 1% Lidocaine
3. 2% Mepivacaine
4. 0.5% Bupivacaine
5. 1% Lidocaine with 1:100:000 epinephrine
6. 4% Articaine with 1:100,000 epinephrine
7. 5% Diphenhydramine (Benadryl)
8. 1% Lidocaine with methylparaben
9. 3% 2-Chloroprocaine (Nesacaine)
10. 1% Tetracaine/procaine

- With no skin reaction to intradermal lidocaine, IV lidocaine 30-mg challenge was given 15 minutes after the last intradermal skin weal. This screening permitted patients to observe that the most commonly used local anesthetic in health care was safe for them.
- Actual injection/block using local anesthetic agents was performed 15 minutes after the IV lidocaine challenge. Right and left PSA nerves were blocked using 3 mL of different local anesthetics, each at 15-minute

intervals. The choice of local anesthetics for the PSA blocks was based on patient response to the intradermal testing and IV challenge: 2% lidocaine with 1:100,000 epinephrine and 0.5% bupivacaine with 1:200,000 epinephrine were used most often for the PSA blocks

Initial Results

1. One patient demonstrated a 4+ irregular weal and 4+ erythema to lidocaine. This patient did not receive the lidocaine IV challenge.
2. All patients screened, including the patient who that reacted to intradermal lidocaine, were found able to receive at least one amide local anesthetic per the PSA block screening.
3. Diphenhydramine (Benadryl) has not been recommended as a local anesthetic because the injection is painful and gives a poor response of limited duration.

Long-Term Results

In 2012, this group of 55 patients (tested from 1981 to 2003) was contacted to verify that ongoing use of the screened and recommended local anesthetic was acceptable: 13 patients were successfully contacted; 41 patients were not able to be reached for follow-up; 3 of the 13 patients (23%) answered "no" when asked whether they had been exposed to local anesthetics since their screening at the medical center; 10 of the 13 patients (77%) stated they had subsequent exposure to local anesthetics; 8 of these patients denied having a subsequent reaction to local anesthetics; 2 of the 10 patients with subsequent local anesthetic exposure stated they had a reaction to the local anesthetic; and 1 patient stated the reaction consisted of pain in her chest and throat, but she could not recall if this was the same reaction that she had experienced with her previous exposure—she stated the medication was Novocaine, which is unlikely given that Novocaine is not commonly available and used. The second patient with a subsequent reaction experienced an "increased heart rate." This was the same reaction that the patient had experienced with her initial exposure. This patient recalled that the reaction was to either lidocaine or bupivacaine.

Even after patients have been screened and found to safely tolerate a particular local anesthetic or anesthetic, significant anxiety about re-exposure may persist. To effectively maximize the subsequent exposure to a local anesthetic for an oral surgical procedure, sedation may be beneficial in treatment planning.

SUMMARY

Anaphylaxis and anaphylactoid reactions can be life threatening even to healthy patients during oral and maxillofacial procedures done with or without sedation and/or anesthesia. With such a rapid onset and the potential for a rapid dangerous cascade to respiratory compromise and cardiac arrest, especially when medications are administered IV, immediate diagnosis and treatment is imperative. Although these conditions can arise suddenly and without warning, a meticulous history focusing on drug reactions and allergies and latex exposure assists in identifying atopic individuals. Anaphylaxis/anaphylactoid reactions are uncommon and their courses may be unpredictable, but luckily most episodes respond to treatment to epinephrine and fundamentals of basic life support.

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