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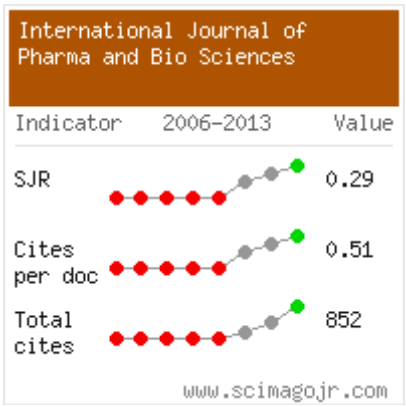

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MANAGEMENT OF ANAPHYLAXIS IN DENTAL OFFICE – AN UPDATE

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ABSTRACT

Anaphylaxis is an acute, life threatening systemic reaction, which can be triggered by any commonly used or prescribed agents in dentistry. Dental practitioners must have adequate knowledge about this medical emergency, to diagnose at its earliest onset and provide prompt treatment for the patients. This article reviews about the epidemiology, etiology, pathophysiology, clinical features and differential diagnosis of anaphylaxis. An up-to-date information for assessment and management of anaphylaxis as given by World allergy organization [WAO] guildelines and NICE clinical guideline are summarized.

KEYWORDS: Anaphylaxis, epinephrine [adrenaline], anaphylactoid, medical emergency, drug allergy

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INTRODUCTION

Anaphylaxis is an acute life-threatening systemic reaction that can occur during routine treatment procedures in dental office due to any of the most commonly used or prescribed agents in dentistry[1].It is imperative for dentists to have adequate knowledge in identifying and treating anaphylaxis at its earliest onset to prevent mortality. In this article latest literature on anaphylaxis has been reviewed and presented to provide up-to-date knowledge about diagnosis and management of anaphylaxis. The purpose of this article is to give a detailed description for dental practitioners about recent trends in the management of anaphylaxis as per world allergy organization guidelines and NICE clinical guideline 134.

DEFINITION

The term anaphylaxis is derived from the Greek words *a* (against) and phylaxis (immunity, protection). Worldwide, anaphylaxis definitions in common use are:"a serious, life-threatening generalized or systemic hypersensitivity reaction" and "a serious allergic reaction that is rapid in onset and might cause death." [2,3,4] Anaphylaxis is a type I immune-mediated, acute life threatening severe systemic allergic reaction with varied mechanisms, clinical presentations, and involvement of multiple organ systems.[5]

EPIDEMIOLOGY

In USA, Anaphylaxis is conservatively estimated to occur at a rate of 25,000 cases annually [6]. In dental practices, the incidence is between 0.004 and 0.015 cases per dentist annually[7,8,9]. Morbidity occurs in 0.5% to 1.3% of all cases [10,11,12]. In comparison, the incidence during general anaesthesia is between 1 in 4000 to 1 in 25 000.Women are more prone than men.

ETIOLOGY[13,5]

Antibiotics [penicillins and cephalosporins, which contain a b-lactam ring] , Topical skin preparations (povidone-iodine/chlorhexidine), Neuromuscular blocking agents, Latex, Colloids, Opioids, Hypnotics, nonsteroidal anti-inflammatory drugs, aspirin, General anesthetic agents [nitrous oxide], Radiocontrast dye, Protamine, Benzodiazepines, Exercise, Local anesthetics, Food (eg, peanuts, fish, shellfish, milk, eggs, bisulfites), Insect stings, vaccines, venom, parasites, hormones and enzymes, Antihistamines [rare].

HIGH-RISK GROUP OF PATIENT FOR ANAPHYLAXIS

History of anaphylaxis, Multiple allergy to food and drugs, Poor controlled asthma, Pre-existing lung diseases

PATHOPHYSIOLOGY

It is a specific immunoglobulin IgE–mediated, antigen induced reaction to various allergens resulting in mast cell degranulation and basophil activation. The first contact of the allergen with the host results in the production of specific IgE antibodies by plasma cells – a process called sensitization which occurs in 3-5 days.[14,15] The Fc portion of these IgE antibodies then becomes fixed to high affinity cell surface receptors on mast cells and basophils. Subsequent exposure to the allergen causes cross linking of the IgE antibodies and aggregation of their receptors resulting in the release of preformed mediators (such as histamine, tryptase, carboxypeptidase A, proteoglycans, chymase and TNF-a) and newly synthesized mediators (such as leukotrienes, prostaglandins, TNF-a, platelet-activating factor).[16,17,18] Collectively, these mediators are responsible for the clinical manifestations of anaphylaxis. Genetics has an important role to play in the severity of anaphylaxis. Also sensitization to an allergen does not imply that anaphylaxis will occur when the person is exposed to that allergen again. Anaphylactoid reactions (non- allergic anaphylaxis) are not IgE related, but they release similar mediators and can cause identical symptoms and pathology. They do not require previous exposure to the allergen. Mechanisms include direct activation of mast cells and basophils to cause histamine release, as well as

activation of the kallikrein-kinin system and complement and clotting cascades.

CLINICAL FEATURES [19,20,21,5]

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 cardio respiratory systems. The appearances of signs can also be classified and graded on a clinical severity scale:[5]

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

SYSTEM	SIGNS AND SYMPTOMS
MUCOCUTANEOUS	Urticaria, angioedema, erythema/flush, pruritus, conjunctival erythema, tearing, gingival edema
RESPIRATORY	Increased respiratory rate, Laryngeal edema, Bronchospasm Pulmonary edema, Wheezing, stridor, coughing, dyspnea, chest tightness, rhinorrhea, hypoxia, upper airway angioedema (lips, tongue, throat swelling)
CARDIOVASCULAR	Hypotension, tachycardia, cardiac Dysrhythmias, cardiac arrest Chest tightness and pain, syncope
GASTROINTESTINAL	Vomiting, diarrhea, Nausea, cramping
CENTRAL NERVOUS	Altered mentation, Unconsciousness, Dizziness, loss of orientation, fatigue, blurred vision
RENAL	Decrease in urine output
HEMATOLOGIC	Disseminated intravascular coagulation, Bleeding from mucosal surfaces

Though cutaneous signs [urticaria and angioedema] are common in anaphylaxis, their absence does not preclude anaphylaxis. These cutaneous manifestations are also common in other conditions. In anaphylaxis, hypotension is when the systolic blood pressure is less than 90 mm Hg or there is a 30% reduction in the systolic pressure from baseline. Mortality in anaphylaxis is most commonly due to respiratory or cardiovascular collapse.

CLINICAL CRITERIA FOR DIAGNOSING ANAPHYLAXIS[22]

Anaphylaxis is highly likely when any one of the following three criteria is fulfilled

1. Acute onset of an illness (minutes to several hours) with involvement of the skin, mucosal tissue, or both (eg, generalized urticaria, itching or flushing, swollen lips-tongue-uvula) and at least one of the following

A) Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF,hypoxemia)

B) Reduced blood pressure or associated symptoms of end-organ dysfunction (eg.Hypotonia, collapse, syncope, incontinence) OR

2. Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours)

A) Involvement of the skin-mucosal tissue (eg, generalized urticaria, itch-flush, swollen lips- tongue-uvula)

B) Respiratory compromise (eg, dyspnea, wheeze-bronchospasm, stridor, reduced PEF, hypoxemia)

C) Reduced blood pressure or associated symptoms (eg, hypotonia ,collapse, syncope, incontinence)

D) Persistent gastrointestinal symptoms (eg, crampy abdominal pain, vomiting) OR

3. Reduced blood pressure after exposure to known allergen for that patient (minutes to several hours)

A) Infants and children: low systolic blood pressure (age-specific) or greater than 30% decrease in systolic blood pressure

B) Adults: systolic blood pressure of less than 90 mm Hg or greater than 30% decrease from that person's baseline

PEF – peak expiratory flow

DIFFERENTIAL DIAGNOSIS[23]

Faint (vasovagal syncope), Panic attack, Breath-holding episode in child, Idiopathic (non-allergic) urticaria or angioedema, Acute asthma, Adverse reaction to local anesthetics.

TREATMENT[23,24,25,26]

The rapid, initial diagnosis of an anaphylactic/ anaphylactoid reaction is critical and early intervention is the key to successful management. The fundamentals of basic life support form the mainstay of the initial management of anaphylaxis, with rapid evaluation and maintenance of airway, breathing, circulation and disability [level of consciousness]. If anaphylaxis is suspected, the dentist should immediately cease their procedure, clear the airway of any materials and remove any contact of likely triggering agent from the patient. Other staff members should be alerted of the situation. The patient should then be positioned supinely with leg elevation. If breathing is difficult, the patient may be allowed to sit, maintaining leg elevation. The next and most important step is the administration of adrenaline to the patient.

Epinephrine

is the primary and first drug of choice in the treatment of anaphylaxis due to its alpha1effects of supporting the blood pressure while its strong beta 2 effects provide bronchial smooth muscle relaxation. In addition, epinephrine also effectively blocks the deleterious effects of circulating mediators.

Routes of epinephrine administration[23]

Intra-muscular injection [IM] into anterior-lateral thigh [vastus lateralis] is the preferred route than IM into the arm [deltoid] because absorption is more rapid and plasma levels are higher when injected into the thigh. Either an auto-injector [Epipen, or Anapen] or needle and syringe are used for injection. Subcutaneous injection is no longer the preferred route for emergency epinephrine administration. Subcutaneous vasculature contains only alpha receptors, and epinephrine produces vasoconstriction, delaying its absorption. Muscle vasculature is populated with greater numbers of beta-2 receptors, and epinephrine dilates these vessels, thereby speeding absorption. Repeat administrations of adrenaline should be given every five minutes if symptoms are persisting. Given the risk of potentially fatal arrhythmias, intravenous (IV) use of adrenaline is reserved for patients who are profoundly hypotensive, [who have failed to respond to IV volume replacement], refractory to several doses of IM adrenaline or who are in cardiorespiratory arrest.

Dosage of epinephrine[23]

Adult	**500 micrograms IM (0.5 mL)**
Child more than 12 years	500 micrograms IM (0.5 mL)
Child 6 - 12 years	300 micrograms IM (0.3 mL)
Child less than 6 years	150 micrograms IM (0.15 mL)

Syringe and needle – 1:1000 adrenaline IM

Auto-injector – 0.3mg IM for people above 5 years, 0.15mg IM for people less than 5 years IV Intravenous titration of 0.1 mg / ml increments using 1: 10,000 concentration. For cardiac arrest, 1.0 mg IV [1: 1000] to be given. Call for help from hospital must be initiated; until ambulance arrives further treatment must proceed in the dental office.

Other measures

supplemental oxygen
should then be delivered, ideally via a one-way valve face mask with oxygen running at a rate

of at least 6–8 L/min, and can be titrated according to pulse oximetry. Nebulized/inhaled beta 2 agonist(bronchodilator) therapy using Albuterol for severe bronchospasm not relieved by epinephrine. salbutamol (albuterol) solution, 5 mg/3 mL (adult), 2.5 mg/3 mL [child]. Whilst awaiting retrieval, at frequent and regular intervals, the dentist should monitor patient's blood pressure, cardiac rate and function, respiratory status and oxygenation and obtain electrocardiograms. If breathing stops, basic life support should be commenced and cardiopulmonary resuscitation must be started immediately. Large volumes of IV fluid 0.9 % isotonic saline[crystalloids], vasopressor therapy [noradrenaline/dopamine] to be given to combat severe hypotension due to anaphylactic shock. Secondary line of drugs include Antihistamines[H1, H2 blockers] and corticosteroids. H1 and H2 blockers are given as an adjuvant therapy orally or parenterally. H1 blockers are very useful when there is mild allergic reactions where only muco-cutaneous manifestations like urticaria (hives), pruritis (itch), and rash, are present. chlorpheniramine 10 mg (adult), 2.5-5 mg (child) IM or slow IV or diphenhydramine 25-50 mg (adult), (1 mg/kg, maximum 50 mg [child]) IM or slow IV. H2 blockers [optional] ranitidine 50 mg (adult) or 1 mg/kg, maximum 50 mg (child) IM or slow IV. Because of slower onset of action, Corticosteroids are not useful in acute phase of anaphylaxis but are used as second line of drugs for preventing biphasic reactions or in protracted cases. eg. As IM or slow IV hydrocortisone 200 mg (adult), maximum 100 mg (child); or methylprednisolone 50-100 mg (adult); 1 mg/kg, maximum 50 mg (child). Meanwhile the patient must be transferred to the hospital for further medical review, treatment and follow up. Airway should be continuously monitored, if compromised an endotracheal intubation or surgical airways must be done.

Observation

The incidence of biphasic reactions varies from 1% to 20% of anaphylactic cases.[27] Anaphylaxis can recur up to 72 hours after the resolution of the initial reaction, although more commonly it occurs within 8 hours. So it is essential to monitor the patients after initial anaphylactic episode. Duration of monitoring should be individualized; for example, patients with moderate respiratory or cardiovascular compromise should be monitored in a medically supervised setting for at least 4 hours and if indicated, 8–10 hours or longer, and patients with severe or protracted anaphylaxis might require monitoring and interventions for days.[28]

Anaphylaxis – confirmation criteria

Once the patient is stabilized, adequate history followed by biochemical analysis of serum Tryptase [mast cell] and plasma and urinary histamine, are done to confirm the condition.[29] The basal tryptase level concentration is 0.8 to 1.5 ng/mL. Tryptase levels greater than 15 ng/mL suggest an anaphylactic reaction. It should be remembered that the diagnosis of anaphylaxis is primarily clinical, and that negative biochemical tests do not preclude the diagnosis. Referral to an allergist or immunologist is important for further work-up and this can involve skin prick and intradermal testing, assays for specific IgE, basophil activation and histamine release, as well as oral challenge tests. True anaphylaxis to local anesthetic agents can occur, but are very rare and must be tested to rule out their possibility.[30] The most likely reason for such an event could be an adverse reaction to local anesthetic due to psychogenic shock or an intravascular injection.[31] After adequate and timely management, recovery from anaphylaxis is usually rapid and complete. Measures must be taken to prevent further anaphylaxis [causative allergen must be identified and avoided] and the patient must be adequately equipped [epinephrine auto-injector] and informed to deal with, in case an episode occurs in the future.

CONCLUSION

Dentists are likely to encounter anaphylaxis at some point in their careers. They must keep themselves updated with the management protocol for anaphylaxis. They must be able to recognize the symptoms and initiate the basic

initial treatment quickly. This includes clearing the airway, removing likely contact with an allergen, administering IM adrenaline, providing oxygenation, and placing the patient in a supine position.[26] Then Anti-histamines, if necessary salbutamol to be administered. It is important to arrange for transport to a medical facility, where the patient can be treated and referred to an allergist or immunologist for follow-up. Dentists must also be able to differentiate anaphylaxis from an adverse reaction to local anesthetics or a vasovagal reaction. Dental offices must be well equipped with the armamentatium and drugs required for managing medical emergencies like anaphylaxis and all dental assistants must be well trained in handling them efficiently.

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