Perioperative Anaestheisa

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Abstract

Anaphylaxis is a severe, life-threatening hypersensitivity reaction. The pathophysiology of anaphylaxis can be described as immunologic and non-immunologic. Every drug used in anaesthesia reported to cause a reaction, and no premedication has proven to prevent it. NMBAs represent the most frequently incriminated substances followed by latex and antibiotics. Dyes, hypnotic agents, local anaesthetics, opioids, colloids, aprotinin, protamine, chlorhexidine, or NSAIDs are less frequently involved. The clinical presentation of anaphylaxis is a frequent event to all ED and requires prompt recognition and immediate management. Common symptoms and signs include: generalized hives, pruritus, flushing swollen lips-tongue-uvula, periorbital oedema, conjunctival swelling, nasal discharge, nasal congestion, change in voice, choking sensation, stridor, wheeze, cough, shortness of breath. Anaphylaxis may present as mild and resolve spontaneously or it may be severe and may progress within minutes to death. Anaphylaxis always should be considered if immediate hypotension develops following parenteral administration of a therapeutic agent or the induction of anaesthesia. The prevention of peri-anaesthetic anaphylaxis is difficult. A careful medical history that focuses on previous adverse reactions is most important. The basic principles of treatment are the same for all age groups. The ABCDE approach is used to recognize and treat an anaphylactic reaction. Early administration of adrenaline immediately benefits the patient which increases the heart rate, blood pressure, and diverts blood to the essential organs such as the heart and brain by dilating their blood vessels and constricting those vessels of less essential organs, such as the skin or peripheries and the renal system.

Key words: perioperative – anaesthesia – anaphylaxis

Introduction:

Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction. It is characterized by rapidly developing, life-threatening problems involving the airway (pharyngeal or laryngeal oedema) and/or breathing (bronchospasm with tachypnea) and/or circulation (hypotension and/or tachycardia). In most cases, there are associated skin and mucosal changes **(1).**

Anaphylaxis is an allergic reaction to a chemical that has become an allergen. An allergen is a substance that can cause an allergic reaction. After being exposed to a substance such as bee sting venom, the person's immune system becomes sensitized to it. When the person is exposed to that allergen again, an allergic reaction may occur. Anaphylaxis happens quickly after the exposure. The condition is severe and involves the whole body. Tissues in different parts of the body release histamine and other substances. This causes the airways to tighten and leads to other symptoms. Some drugs (morphine, x-ray dye, aspirin, and others) may cause an anaphylactic-like reaction when people are first exposed to them. These reactions are not the same as the immune system response that occurs with true anaphylaxis. But, the symptoms, risk of complications, and treatment are the same for both types of reactions **(2).**

Materials and methods:

This is a review article, The search was performed in MEDLINE, Embase, Pubmed and CINAHL Plus in the same date range with the following mediacl terms: “perioperative – anaesthesia – anaphylaxis.”, including articles from 2000 to 2019, Excluded articles from review are those of language other than English.

Definition of Anaphylaxis:

It is an acute, potentially lethal, multisystem syndrome resulting from the sudden release of mast cell- and basophil-derived mediators into the circulation. It most often results from immunologic reactions to foods, medications, and insect stings, although it can also be induced through non-immunologic mechanisms by any agent capable of producing a sudden, systemic degranulation of mast cells or basophils **(3).**

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allergic reaction. After being exposed to a substance such as bee sting venom, the person's immune system becomes sensitized to it. When the person is exposed to that allergen again, an allergic reaction may occur. Anaphylaxis happens quickly after the exposure. The condition is severe and involves the whole body. Tissues in different parts of the body release histamine and other substances. This causes the airways to tighten and leads to other symptoms. Some drugs (morphine, x-ray dye, aspirin, and others) may cause an anaphylactic-like reaction when people are first exposed to them. These reactions are not the same as the immune system response that occurs with true anaphylaxis. But, the symptoms, risk of complications, and treatment are the same for both types of reactions **(2).**

Classification:

The pathophysiology of anaphylaxis can be described as immunologic and non-immunologic. Classification can be based on the time course of the anaphylactic reaction which may be uniphasic, biphasic or protracted**.**

- Immunologic anaphylaxis includes the following:

  a. IgE-mediated reactions

  b. IgG-mediated reactions

  c. Immune complex/complement-mediated reactions

- Non-immunologic anaphylaxis is caused by agents or events that induce sudden, massive mast cell or basophil degranulation in the absence of immunoglobulins **(4).**

Chemical Mediators of Anaphylaxis:

The chemical mediators of immunoglobulin E (IgE)-mediated anaphylaxis in humans include biologically active products of mast cells, basophils, and eosinophils, as well as serum components of the complement, coagulation, and kallikrein-kinin pathways. In addition, cytokines that alter the sensitivity of various target cells to these mediators are believed to influence the severity of anaphylaxis**.**

The degranulation of mast cells and basophils results in the systemic release of various biochemical mediators and chemotactic substances, including the following:

a) Histamine, tryptase, chymase, and heparin, which are preformed substances associated with intracellular

granules.

b) Histamine-releasing factor and other cytokines (tumour necrosis factor [TNF], interleukin-4 [IL-4], interleukin-13 [IL-13]).

c) Newly-generated lipid-derived mediators such as prostaglandin D2, leukotriene B4, PAF, and the cysteinyl leukotrienes, LTC4, LTD4, and LTE4. **(5).**

Causative Agents:

Most anaphylactic reactions are iatrogenic therefore, there is a clear need for practitioners to be able to assess, make a working diagnosis, plan, implement a plan of care with specific outcome identification, and evaluate the care of patients presenting with this condition **(6).**

Anaphylaxis can be precipitated by various triggers most commonly identified include food, drugs and venom.

Allergen triggers (IgE-dependent mechanism) Foods and additives like walnuts, peanuts, shellfish, fish, milk, eggs, strawberries, spices.

- Insect stings (Hymenoptera venom) and insect bites (mosquitoes, horse flies, ants).
- Medications (e.g. b-lactam antibiotics-penicillin, cephalosporin, vancomycin, non-steroidal anti-inflammatory drugs (NSAIDs)).
- Contrast media (iodinated, technetium, fluorescein). Anaesthetic drugs (suxamethonium, atracurium).
- Occupational allergens (natural rubber latex, hair dye).

Immunologic triggers (IgE-independent mechanism) Coagulation system activation. IgG-dependent reactions (e.g. reactions to dextran, infliximab).

Idiopathic anaphylaxis Possibility of mastocytosis or clonal mast cell disorder. Possibility of previously unrecognized trigger.

Non-immunologic triggers (direct activation of mast cells and basophils) Medications (like opioids, some NSAIDS), alcohol and Physical factors (e.g. cold, heat, exercise, sunlight) **(7).**

All NMBA can elicit anaphylaxis and there is an agreement that the short-acting depolarizing succinylcholine poses the greatest risk, despite its close structural homology to acetylcholine **(8).**

The muscle relaxants are used to

facilitate endotracheal intubation or to optimize surgical exposure**.** Rocuronium and succinyl-choline were the most frequently incriminated muscle relaxants in a French study **(7).**

Commonly implicated agents include atracurium, pancuronium, rocuronium, succinylcholine (aka, suxamethonium), tubocurarine (no longer available in the United States and Canada, but used elsewhere), and vecuronium, although this may largely reflect the frequency with which these agents are used. **(9).**

Natural rubber latex sensitivity is the second most common cause of perioperative anaphylaxis in the general population **(10).**

Antibiotics are commonly administered peri-operatively and can cause allergic reactions **(7).**

The most commonly implicated antibiotics resulting in reactions are b-lactam antibiotics and vancomycin **(11).**

Hypnotics commonly used in anaesthesia are thiopental, propofol, midazolam, etomidate, ketamine, and inhaled anaesthetics. Allergic reactions involving these drugs appear to be relatively rare **(12).**

Intravenous barbiturates were previously widely used in anaesthesia, and as a class, they account for most reactions to induction agents. Women are affected three times more often than men. Most reactions caused by barbiturate induction agents are IgE-mediated, although direct mast cell activation has also been described. There is some immunologic cross-reactivity among the barbiturates **(13).**

Anaphylaxis to non-barbiturate induction agents is uncommon. Propofol is a non-barbiturate induction agent that was initially solubilized in

Benzodiazepines are also non-barbiturate induction agents. Hypotension following intravenous administration is a known adverse effect of these agents, although anaphylactic reactions are rare. Benzodiazepines may be capable of activating mast cells in vitro and skin testing has been reported, although the mechanism of this interaction is not well studied. Cross-reactivity between propofol and benzodiazepines has not been reported **(14).**

OPIOIDS, Reactions to morphine, codeine phosphate, meperidine, fentanyl, and its derivatives are uncommon **(13).**

Opioids used in anaesthesia/analgesia are a common cause of flushing and urticaria

following intravenous administration, although opioids rarely cause life-threatening reactions. Typically, opioids cause limited cutaneous symptoms that are non IgE-mediated. Morphine or meperidine can cause degranulation of dermal mast cells, resulting in release of histamine and other mediators and leading to flushing and urticaria, although rarely angioedema **(15).**

Local anaesthetics include amine (lidocaine, mepivacaine, prilocaine, bupivacaine, levobupivacaine, ropivacaine), and ester derivatives of benzoic acid (chloroprocaine, procaine, tetracaine). Allergic reactions to local anaesthetics are very rare despite their frequent use. It is estimated that less than 1% of all reactions to local anaesthetics have an allergic mechanism. Inadvertent intravascular injection leading to excessive blood concentrations of local anaesthetics, systemic absorption of epinephrine added to the local anaesthetic, or vaso-vagal near syncope are by far the most common causes of adverse reactions associated with these drugs.

Colloids and plasma expanders, such as dextran or hetastarch (hydroxyethyl starch, HES), accounted for about 3 percent of identifiable causes of perioperative anaphylaxis. These agents are capable of causing both IgE-mediated and non IgE-mediated immunologic reactions. Reported rates of anaphylaxis were <0.1 percent of administrations for each of several preparations **(16).**

With the increase in consumption of **NSAIDs** used in multimodal postoperative analgesia, these are likely to be among the most common drugs inducing hypersensitivity reactions as bronchospasms, urticaria, angioedema, and anaphylaxis **(17).**

Aprotinin is a naturally occurring serine protease inhibitor that has found widespread application either by the intravenous route or as a component of biologic sealants **(18).**

Heparin is a strongly acidic, anionic, sulphated mucopolysaccharide, and it has a large molecular weight. It is derived from bovine or porcine lung or intestine and is antigenic in humans. Type I IgE mediated hypersensitivity reactions to heparin are exceedingly rare and skin tests are used for their diagnosis. Although there are no reported cases of anaphylaxis to low-molecular-weight heparin, low-molecular-weight heparin has in vitro and in vivo cross-reactivity with unfractionated heparin **(18) .**

Protamine sulphate is a strongly alkaline,

polycationic, small molecule extracted from salmon sperm and used to reverse the anticoagulant effects of heparin. Exposed patients (0.4%–0.76%) can develop an allergic reaction to protamine, and the risk is increased in patients previously exposed to protamine Some forms of insulin, such as neutral protamine hagedorn and protamine-zinc insulin, contain protamine, and there is an increased risk for a protamine reaction in diabetic patients exposed to neutral protamine hagedorn and protamine-zinc insulin. There is a theoretical risk that patients allergic to fish or those who are infertile or vasectomized are more likely to develop an allergic reaction to protamine (**19) .**

Anaphylaxis or angioedema in response to recombinant tissue-type plasminogen activator or urokinase have been reported in only a few isolated cases. Both agents are endogenous proteins and thus considered non-antigenic. Activation of fibrinolysis may per se facilitate anaphylactoid reactions by pathophysiologic pathways that are not well understood **(20) .**

Allergic reactions to blood transfusion are common and usually mild. The majority is due to the presence of foreign proteins in donor plasma and is IgE-mediated. Pruritus and urticaria, with or without fever, are the most common features. The transfusion should be stopped and antihistamines administered. If symptoms resolve in less than 30 min and there is no cardiovascular instability, the transfusion may be restarted. If the symptoms recur then administration of that particular unit of blood should be abandoned **(21).**

Hyaluronidase is a proteolytic enzyme that is sometimes used as a spreading factor in order to improve diffusion of other drugs. Topical applications are as an adjunct to local anaesthesia, especially in nerve blocks and ophthalmic anaesthesia. Hypersensitivity reactions towards hyaluronidase comprise local acute or delayed reactions as well as more generalized anaphylactic reactions. Diagnosis of IgE-mediated allergy to hyaluronidase can be confirmed by skin tests, quantification of sIgE or flow cytometry **(22).**

Povidone-iodine (betadine) is the most common topical antiseptic solution used and there are only a few reports in the literature of anaphylaxis to this drug . A positive skin prick test to povidone-iodine and povidone extract and the presence of serum-specific IgE to povidone demonstrate a Type I IgE-

mediated hypersensitivity. Allergic contact dermatitis, a Type IV cell-mediated hypersensitivity reaction, is more common with povidone-iodine. Patch testing to diagnose this type of reaction is best done with dried 10% povidone iodine solution, because long exposure to povidone iodine in the aqueous state may yield a false-positive result due to direct skin irritation **(23).**

Oxytocin is a synthetically manufactured hormone that stimulates contractions of uterine smooth muscle and is indicated for induction and augmentation of labour as well as in abortions. Anaphylaxis from oxytocin is rare and diagnosis is generally based upon skin tests. Note that oxytocin can produce hypotension through a pharmacodynamical mechanism when given in larger intravenous boluses, an interesting differential diagnosis that could be mentioned **(24).**

Sugammadex, a chemically modified -cyclodextrin, has been developed specifically for the reversal of the action of the aminosteroid neuromuscular blocking drug (NMBD) rocuronium and to a lesser extent the structurally related vecuronium. It has been claimed that sugammadex is well tolerated and is viewed as a relatively 'safe' drug with only a documented hypersensitivity reaction being an absolute contraindication. Sugammadex has the capacity to induce allergic type reactions in susceptible patients but it is not yet clear whether sugammadex is more allergenic than other commonly used agents in anaesthesia **(25).**

Various other potential causes or mimics of anaphylaxis during the peri-anaesthetic period are present. Such as:

Chymopapain, bisulphites or other medication preservatives, Immune reaction to IgA, Chlorhexidine, Chymopapain sensitivity (used for herniated disc surgery), Ethylene oxide (used for sterilization), Isosulphan blue dye (used for sentinel lymph node biopsy), Methylmethacrylate (bone cement), Insulin
(24).

Incidence:

General anaesthesia is a unique situation described as a reversible state of unconsciousness, amnesia, analgesia, and immobility as a result of administering several drugs in a short period **(26)**.

Uniphasic anaphylaxis is the most common type accounting for 80%-90% of all episodes. Its response peaks within 30-60 minutes after exposure to allergens and

tends to resolve either spontaneously or with treatment within the next 30-60 minutes.

Biphasic anaphylaxis has an estimated incidence of 1-23% of all anaphylactic reactions. These reactions are characterized by a uniphasic response, followed by an asymptomatic period of an hour or more and the subsequent recurrence of symptoms without re-exposure to the antigen. These reactions can occur at any age **(4).**

Pathophysiology:

The immune system is an integral part of human protection against disease, but the normally protective immune mechanisms can sometimes cause detrimental reactions in the host. Such reactions are known as hypersensitivity reactions, and the study of these is termed immunopathology. The traditional classification for hypersensitivity reactions is that of Gell and Coombs and is currently the most commonly known classification system **(27).**

The pathophysiology of anaphylaxis can be described as immunologic and non-immunologic. Classification can be based on the time course of the anaphylactic reaction which may be uniphasic, biphasic or protracted **(4).**

Immunologic reactions:

There are four mechanisms of hypersensitivity, which are classified according to the components of the immune system involved.

Type one, hypersensitivity reactions/anaphylactic reactions: This occurs in individuals who have inherited very high levels of a type of antibody called immunoglobulin E (IgE). When exposed to an antigen, these high levels of antibodies activate mast cells and basophils, which release their granular contents.

Physiologically the most important substance released is histamine, which constricts smooth muscle within the bronchioles, activates vasodilation and increases vascular permeability (leading to exudation of fluid and proteins into tissues). The IgE-mediated reaction is classically initiated by the antigen (allergen) interacting with the allergen-specific IgE bound to the receptor Fc on the mast cells and/or basophils. The B cells differentiate into IgE-producing cells via the activity of CD4 Helper T cells (Th2 cells). This occurs in the peripheral lymphoid tissues. The cytokines interleukin-4 and interleukin-13 along with their receptors contribute to the

IgE response. Once produced, allergen-specific IgE diffuses into the tissues and vasculature and occupies the receptors on the mast cells and basophils.

When the allergen diffuses into the proximity of a mast cell or basophil, it interacts with the surface bound IgE that is specific for that allergen. This interaction causes the receptors to initiate intracellular signalling. Certain allergens are able to interact on two or more surface receptors of IgE and thus are capable of cross-linking. If signalling is robust enough it will activate mast cells and basophils and cause degranulation. The result is the release of preformed mediators, enzymes and cytokines (tryptase, histamine and tissue necrosis factor) and the production of additional mediators, cytokines and enzymes. These mediators either act directly on tissue or indirectly by activating eosinophils to cause the symptoms of allergy. Examples of type 1 reactions include allergic rhinitis (hay fever), allergic asthma and penicillin induced anaphylaxis **(4).**

A good, general example of IgE-mediated anaphylaxis is an allergic reaction to peanut ingestion **(24).**

IgG-mediated anaphylaxis has not been demonstrated in human beings. However, human IgG receptors are capable of activating macrophages and neutrophils to secrete platelet activating factor (PAF), which activates mast immune complex/complement mediated. This type of anaphylaxis has been implicated in life threatening reactions to many drugs like protamine**.**

Type two, hypersensitivity reactions/cytotoxic hypersensitivity: when an antibody reacts with an antigen on a cell surface, that cell is marked for destruction via a number of mechanisms, for example: phagocytosis, or destruction by lytic enzymes.

This is the usual procedure in the elimination of bacteria. If antibodies are directed against self-antigens the result is destruction of the body's own tissues (autoimmune destruction).

Conditions of particular concern within this area are blood transfusion reactions and haemolytic disease of the new-born.

Type three, hypersensitivity reactions/immune complex mediated hypersensitivity: Antibody-antigen complexes are usually cleared efficiently

from the blood by phagocytosis. If this process fails; the complexes can be deposited within the body's tissues, where upon an inflammatory response is initiated.

The kidneys are often affected because they receive a large proportion of the cardiac output, and filter the blood. Immune complexes block the glomeruli, impairing renal function (glomerulonephritis).

Penicillin sensitivity can also lead to a type three reaction; the body's antibodies bind to penicillin, which is the offending antigen, the symptoms are the result of deposition of immune complexes in the tissues.

Examples include rashes, joint pains and haematuria. Infectious diseases such as malaria and viral hepatitis can lead to a type three hypersensitivity reaction.

This form of hypersensitivity has been implicated in causing systemic lupus erythematosus (SLE).

Type four, hypersensitivity reactions/delayed hypersensitivity: unlike the earlier mentioned reactions, type four reactions do not involve antibodies. The reaction is mediated by T-lymphocytes, which overreact to an antigen. When an antigen is detected in the blood it provokes clonal expansion of the T-lymphocyte cells and large numbers of cytotoxic T-lymphocytes are released to terminate the antigen.

If the T-lymphocytes are over stimulated and the response becomes inappropriate the aggressive cytotoxic T-lymphocytes will damage normal body cells/tissues.

Examples include contact dermatitis, and organ rejection **(4).**

It is important to note that all of the above hypersensitivity reactions have the potential to induce a state of physiological shock to the individual affected by them **(28).**

Non-immunologic reactions:

An anaphylactoid reaction produces a very similar clinical syndrome to anaphylaxis, but is not immune-mediated **(4).**

In contrast, nonallergic anaphylaxis indicates the lack of a specific antibody or immune response. The exact aetiology for nonallergic anaphylaxis is unknown**.** The potential pathogenic mechanisms of nonallergic anaphylaxis include idiosyncratic events **(24).**

Anaphylactoid reactions are caused by activation of mast cells and the release of the

same mediators as an anaphylactic reaction, but without the involvement of IgE antibodies.

Approach to Patients with peri Anaesthetic Anaphylaxis:

Clinical Picture of Anaesthesia-related Anaphylaxis:

The clinical presentation of anaphylaxis is a frequent event to all emergency departments (ED) and requires prompt recognition and immediate management **(28).**

The diagnostic criteria for anaphylaxis were published by a group of experts in 2005 and 2006 to aid clinicians in the recognition of the full spectrum of signs and symptoms.

Anaphylaxis is highly likely if ONE of the following criteria is fulfilled:

1 - Acute onset (minutes to several hours) involving skin, mucosal tissue or both (generalized hives, urticaria, pruritus and flushing, swollen lips-tongue-uvula) and at least one of the following: Respiratory compromise (bronchospasm, wheeze, stridor, hypoxaemia, reduced peak expiratory flow).

Reduced blood pressure (BP) or associated symptoms and signs of end-organ dysfunction (collapse, syncope, incontinence).

2 - Two or more of the following that occur rapidly after exposure to a likely allergen for that patient (minutes to several hours): Involvement of skin and mucosal tissue as described above.

Respiratory compromise as described above, Reduced BP or associated signs and symptoms of reduced BP.

Persistent gastrointestinal signs and symptoms (crampy abdominal pain, nausea, vomiting).

3 - Reduced BP after exposure to a known allergen for that patient (minutes to several hours): Reduced BP in adults is defined as a systolic BP (SBP) of less than 90 mmHg or 30% decrease in that patient's baseline. In infants and children, reduced BP is defined as low systolic BP (age specific) or greater than 30% decrease in SBP **(4).**

Signs of anaphylaxis include flushing or urticaria, hypotension, difficulty with intubation caused by laryngeal oedema, and the requirement of increased ventilatory

pressure or the inability to ventilate because of bronchospasm.

Diagnosis of peri-anaesthesia anaphylaxis may be hampered by the limited ability of the affected subject to describe symptoms of pruritus, shortness of breath, or angioedema. Also skin manifestations may be masked by surgical drapes. The early signs often are unrecognized, and cardiovascular collapse may be the sole presentation, occurring in about 50% of cases.

Anaphylaxis always should be considered if immediate hypotension develops, with or without bronchospasm, following parenteral administration of a therapeutic agent or the induction of anaesthesia.

The clinical diagnosis of anaphylaxis can sometimes be supported by the elevated concentrations of serum tryptase or plasma histamine **(24).**

Future tests e a laboratory test for mature b-tryptase, a better marker of mast cell activation than total serum tryptase has been developed, although is not widely available. The diagnosis is challenging because of the multiple drugs administered, concurrently or sequentially, and the effects of anaesthesia itself.

Serum complement assays may be valuable if complement activation is suspected. An elevated serum tryptase level 1 to 6 hours after suspected anaphylaxis suggests mast cell degranulation and supports the diagnosis of anaphylaxis in the presence of a typical history and clinical findings.

Additional diagnostic testing for the agent responsible for mast cell degranulation, usually by measuring specific IgE, would be advisable if the serum tryptase was elevated.

Skin tests may be difficult to interpret with agents used during anaesthesia, because many drugs cause direct mast cell histamine release in the absence of specific IgE.

Nonetheless, skin testing has been shown to be valuable in evaluating anaphylaxis to barbiturates, chymopapain, streptokinase, penicillin, insulin, and latex **(24).**

Treatment:

The basic principles of treatment are the same for all age groups. The ABCDE approach is used to recognize and treat an anaphylactic reaction. The specific treatment of an anaphylactic reaction depends on: Location Treating an anaphylactic patient in the community will not be the same as in an acute hospital setting. An ambulance should

be called immediately and the patient transferred to the emergency department. Training of rescuers all clinical staff should be able to call for help and initiate initial treatment in an anaphylactic patient. Number of responders The single responder must ensure that help is coming. If there are several responders appropriate delegation of tasks can be undertaken. Equipment and drugs available Resuscitation equipment and drugs to aid rapid initiation of treatment must be available immediately in all clinical settings**.** Remove trigger agent Removing the trigger agent may not always be possible, for example STOP any drug suspected of causing anaphylaxis like antibiotics, gelatines; remove the stinger after the bee sting. DO NOT DELAY definitive treatment if removing the trigger agent is not possible **(4).**

Acute anaphylaxis is often poorly recognised and treated. The focal point being to facilitate practitioners into providing an evidence-based approach to their practice when treating patients attending with anaphylactic reactions **(29).**

The administration of glucocorticoids can produce profound generalised inhibitory effects on the inflammatory response and a decreased activity of macrophages and fibroblasts involved in the chronic stages of inflammation, this leads to decreased inflammation **(28).**

Results:

Diagnosis of peri-anaesthesia anaphylaxis may be hampered by the limited ability of the affected subject to describe symptoms of pruritus, shortness of breath, or angioedema. Also skin manifestations may be masked by surgical drapes. The early signs often are unrecognized, and cardiovascular collapse may be the sole presentation, occurring in about 50% of cases.

Anaphylaxis always should be considered if immediate hypotension develops, with or without bronchospasm, following parenteral administration of a therapeutic agent or the induction of anaesthesia.

Discussion:

Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction. It is characterized by rapidly developing, life-threatening problems involving the airway (pharyngeal or laryngeal edema) and/or breathing (bronchospasm with tachypnea) and/or circulation (hypotension and/or tachycardia). In most cases, there are associated skin and

mucosal changes**.**

The chemical mediators of immunoglobulin E (IgE)-mediated anaphylaxis in humans include biologically active products of mast cells, basophils, and eosinophils, as well as serum components of the complement, coagulation, and kallikrein-kinin pathways. In addition, cytokines that alter the sensitivity of various target cells to these mediators are believed to influence the severity of anaphylaxis**.**

Factors that determine a specific "shock organ" include variations in the immune response, the location of smooth muscle, and the distribution, rate of degradation, and responsiveness to chemical mediators. The predominant shock organs are the heart, vasculature, and lungs, and fatalities are divided between circulatory collapse and respiratory arrest.

Most anaphylactic reactions are iatrogenic therefore, there is a clear need for practitioners to be able to assess, make a working diagnosis, plan, implement a plan of care with specific outcome identification, and evaluate the care of patients presenting with this condition.

Anaphylaxis can be precipitated by various triggers most commonly identified include food, drugs and venom.

Signs of anaphylaxis include flushing or urticaria, hypotension, difficulty with intubation caused by laryngeal oedema, and the requirement of increased ventilatory pressure or the inability to ventilate because of bronchospasm.

References:

1. **Kate, E.S.; Roisin, F.; Katherine, A.; Alia, B. and Adam, T.F (2016):** The prevention and management of anaphylaxis**:** pediatrics and child health 26:7**.**

2. **Lieberman PL. (2014):** Recognition and first-line treatment of anaphylaxis. Am J Med.; 127: S6-S11.

3. **Sampson HA, Muñoz-Furlong A, Campbell RL (2006):** Second symposium on the definition and management of anaphylaxis: summary report--Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. J Allergy Clin Immunol: 117:391.

4. **Vandana Girotra, Abdul Ghaaliq Lalkhen (2014):** Anaphylaxis. Anaesthesia and Intensive Care Medicine 15:1.

5. **Akin C, Scott LM, Kocabas CN (2007):** Demonstration of an aberrant mast-cell population with clonal markers in a subset of patients with "idiopathic" anaphylaxis. Blood: 110:2331.

6. **Pumphrey R (2004):** Anaphylaxis: can we tell who is at risk of a fatal reaction? Curr Opin Allergy Clin Immunol: 4:285.

7. **Mertes PM, Alla F, Tréchot P, Auroy Y, Jougla E; and the Groupe d'Etudes des Réactions Anaphylactoïdes Peranesthésiques (2011):** Anaphylaxis during anesthesia in France: an 8-year national survey [publishedonline ahead of print.

8. **Fisher MM, Doig GS (2004):** Prevention of anaphylactic reactions to anaesthetic drugs. Drug Safe: 27:393–410.

9. **Dong SW, Mertes PM, Petitpain N (2012):** Hypersensitivity reactions during anesthesia. Results from the ninth French survey. Minerva Anestesiol: 78:868.

10. **Lieberman P (2003):** Anaphylaxis and anaphylactoid reactions. In: Middleton's allergy: Principles and practice, Adkinson NF, Yunginger JW, Busse WW (Eds), Mosby, St. Louis, MO. p.1497.

11. **Levy JH, Adkinson NF Jr (2008):** Anaphylaxis during cardiac surgery: implications for clinicians. Anesth Analg: 106(2):392–403.

12. **Clarke RS (1982):** Epidemiology of adverse reactions in anaesthesia in the United Kingdom. Klin Wochenschr: 60(17):1003–5.

13. **Mertes PM, Laxenaire MC(2003):** Allergic reactions occurring during anaesthesia. Eur J Anaesthesiol: 19:240–262.

14. **Palacios Benito R, Domínguez Ortega J, Alonso Llamazares A (2001):** Adverse reaction to tetrazepam. J Investig Allergol Clin Immunol: 11:130.

15. **Veien M, Szlam F, Holden JT (2000):** Mechanisms of nonimmunological histamine and tryptase release from human cutaneous mast cells. Anesthesiology: 92:1074.

16. **Wiedermann CJ (2004):** Hydroxyethyl starch--can the safety problems be ignored? Wien Klin Wochenschr: 116:583.

17. **White PF (2008):** Multimodal analgesia: its role in preventing postoperative pain. Curr Opin Investig Drugs: 9(1):76–82.

18. **Kober BJ, Scheule AM, Voth V (2008):** Anaphylactic reaction after systemic application of aprotinin triggered by aprotinin-containing fibrin sealant. Anesth Analg: 107(2):406–9.

19. **Koch P, Munssinger T, Rupp-John C, Uhl K (2000):** Delayed-type hypersensitivity skin reactions caused by subcutaneous unfractionated and low-molecular-weight heparins: tolerance of a new recombinant hirudin. J Am Acad Dermatol: 42:612–9.

20. **Pechlaner C, Knapp E, Wiedermann CJ (2001):** Hypersensitivity reactions associated with recombinant tissue-type plasminogen activator and urokinase. Blood Coagul Fibrinolysis: 12:491.

21. **Mertes PM, Laxenaire MC, Lienhart A, Aberer W, Ring J, Pichler WJ (2005):** Reducing the risk of anaphylaxis during anaesthesia: guidelines for clinical practice. J Investig Allergol Clin Immunol: 15:91–101.

22. **Ebo DG, Wets RD, Spiessens TK, Bridts CH, Stevens WJ (2005):** Flow-assisted diagnosis of anaphylaxis to patent blue. Allergy: 60:703–704.

23. **Kozuka T (2002):** Patch testing to exclude allergic contact dermatitis caused by povidone-iodine. Dermatology: 204(Suppl 1): 96–8.

24. **Thomas JS, Koh SH, Cooper GM (2007):** Haemodynamic effects of oxytocin given as i.v. bolus or infusion on women undergoing Caesarean section. Br J Anaesth: 98:116–119.

25. **Baldo B.A, McDonnell.N.J (2016):** Sugammadex and anaphylaxis in the operating theatre. Rev Esp Anestesiol Reanim: 61(5):239---245.

26. **Ishizawa Y (2007):** Mechanisms of anesthetic actions and the brain. J Anesth: 21(2):187-199.

27. **Gell PGH, Coombs RRA (1963):** Clinical Aspects of Immunology. 1st ed. Oxford, England: Blackwell.

28. **Cliff Evans, Emma Tippins (2005):** Emergency treatment of anaphylaxis. Accident and Emergency Nursing: 13, 232–237.

29. **Hughes, G., Fitzharris (1999):** Managing acute anaphylaxis. BMJ 319, 1–2.

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