Anaphylactic Reactions Associated with Anesthesia

An Essay

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List of Abbreviations

ACT: Activated clotting time

BAT: basophil activation test

CABG: coronary artery bypass graft

CD4: cluster differentiation 4

CPB: cardiopulmonary bypass

Da: dalton (Mathematics & Measurements / Units) another name for atomic mass unit[named after John Dalton (1766-1844), English chemist and physicist]

DTH: delayed (type) hypersensitivity

EAACI: European Academy of Allergology and Clinical Immunology

EF : Ejection fraction

ELISA: enzyme-linked immunosorbent assay

Fc : Fragment Crystallizable

FcRε : Fragment Crystallizable receptor epsilon

HES: hydroxyethyl starch

Hev b: Hevea brasiliensis

IDTs: intradermal tests

Kd: Kilodalton

KIU: kallikrein inhibitor units

NMBAs: Neuromuscular Blocking Agents

NPH : neutral protamine Hagedorn

NRL : natural rubber late

PF4: Platelet factor 4

POD: postoperative day

PTs: prick tests

QAI: Quaternary ammonium ions

RAST: Radioallergosorbent Test

RIA: Radioimmunoassay

rPF4: Recombinant PF4

Introduction

Introduction

Anaphylaxis, is severe type I hypersensitivity reaction, it is an acute multiorgan system reaction, potentially fatal, caused by the release of chemical mediators from mast cells and basophils. The most common organ systems involved include the cutaneous, respiratory, cardiovascular, and gastrointestinal systems.(Kemp et al.,2008) .

Between 1% and 15% of the population of the world can be considered "at risk" for having an anaphylactic reaction if they are exposed to one or more allergens. Of those people who actually experience anaphylaxis, up to 1% may die as a result. Anaphylaxis results in approximately 1,500 deaths per year in the U.S. In England, mortality rates for anaphylaxis have been reported as up to 0.05 per 100,000 population, or around 10-20 a year (Simons ,2008).

Based on the pathophysiology, anaphylaxis can be divided into "true anaphylaxis" and "pseudo-anaphylaxis" or "anaphylactoid reaction." The symptoms, treatment, and risk of death are the same; however, "true" anaphylaxis is caused by degranulation of mast cells or basophils mediated by immunoglobulin E (IgE), and pseudo-anaphylaxis occurs without IgE mediation (Pascale ,2009).

Perioperative anaphylaxis may be a life-threatening clinical condition and is typically a result of drugs or substances used for anesthesia or surgery. After anaphylaxis, immunologic assessment is essential to identify the offending agent and prevent recurrences, because no preemptive therapeutic strategies exist. Pascale seeks to identify the clinical diagnostic pathway necessary to distinguish anaphylaxis from confounding clinical diagnoses, discuss the more common allergens that cause anaphylaxis during anesthesia, discuss a rational approach to the identification of the offending allergen through blood and skin testing that allows for the safe future clinical management of patients experiencing

perioperative anaphylaxis, and discuss new therapeutic perspectives for the management of patients whose hemodynamic collapse is unresponsive to catecholamines, the initial recommended pharmacologic intervention (Pascale ,2009).

Chapter 1:

Immune mechanisms associated with anaphylaxis

Immune mechanisms associated with anaphylaxis

◉ *Overview on hypersensitivity reactions*

Excessive or inappropriate immune responses sometimes lead to host tissue damage resulting from prolonged or repeated antigen exposure. These reactions, called hypersensitivity reactions, cause tissue injury by the release of chemical substances that attract and activate cells and molecules resulting in inflammation. These reactions are classified into four hypersensitivity types (Thao et al., 2007) depending upon the mechanism(s) that underlie the tissue damage. The first three types involve antigen-antibody reactions, while the fourth is antibody-independent, involving cell-mediated immune responses only:-

- Type I (also called immediate hypersensitivity) reactions are rapid, occurring within minutes of exposure to an antigen, and always involve IgE-mediated degranulation of basophils or mast cells.
- Type II reactions are initiated by the binding of antibody to a cell membrane or to the extracellular matrix.

Mechanism: IgM or IgG antibody binds to epitopes on cells or other tissue components promoting phagocytosis, antibody dependent cell-mediated cytotoxicity, antibody-mediated function disruption (receptor blocking), or complement mediated lysis.

- Type III hypersensitivity reactions involve the interaction of antibodies with soluble molecules to make soluble antigen-antibody complexes that become deposited in tissues.

Mechanism: serum activate complement and attract neutrophils that release lytic molecules.

- Type IV hypersensitivity reactions are those in which cells of the immune system directly attack host cells in the absence of antibody. These reactions include contact dermatitis (also called contact sensitivity);

delayed type hypersensitivity (DTH); and, occasionally, cytotoxic T lymphocyte responses.

Mechanism: Release of mediators by sensitized cluster differentiation 4 (CD4+) T cells provoke tissue destruction by mononuclear cells. CD8+ T cells known as cytotoxic T lymphocytes may kill chemically modified host cells and cells that display disparate major histocompatibility complex molecules.

◉*Type I Hypersensitivity*:-

Commonly called allergic or immediate hypersensitivity reactions, type I responses occur within minutes to hours of antigen exposure. This type may be associated with anesthesia due to exposure to anesthetic or nonanesthetic agents. Some individuals develop IgE antibodies in response to relatively harmless environmental antigens or allergens. IgE molecules readily bind to Fragment crystallizable receptors (FcRε or CD23) on the surfaces of mast cells and basophils. Unlike other Fc receptors, FcRεs bind antigen-free immunoglobulin (IgE), and the IgE-CD23 complexes function as antigen-specific cell-surface receptors. Cross- linking of surface-bound IgE molecules generates intracellular signals via CD23, leading to mast cell or basophil degranulation and the release of vasoactive amines (e.g., histamine) and other inflammatory mediators**(Table 1).**

Histamine and other inflammatory mediators cause vascular endothelial cell junctions to loosen (vasodilation) and increase vascular permeability, resulting in fluid accumulation in the tissues (edema). Histamine also induces smooth muscle contraction in arterial and arteriolar walls (vasoconstriction) to accelerate fluid distribution from the central trunk of the body into peripheral tissues. (Thao et al., 2007)**.**

A. Localized reactions

Because mast cells accumulate in respiratory passages, intestinal walls, and the skin, type I reactions are most often pronounced in these tissues. Sites affected are typically those where the initiating antigen is most often encountered.

Antigens that enter the body by inhalation localize primarily to the nasopharyngeal and bronchial tissues, where smooth muscle contraction and vasodilation increase mucous production and the constriction of respiratory passages . In combination, these responses can produce the severe and potentially fatal disorder known as asthma. Allergens that contact other tissues may produce IgE-mediated inflammatory responses, causing rashes, redness, and edema—the classic "wheal and flare" appearance. Food or ingested allergens primarily affect the gastrointestinal tract (Thao et al., 2007).

B. Systemic reactions

In some cases, such as injected allergens (e.g., venom or toxins), antigen may be disseminated by the bloodstream, resulting in systemic inflammation. Termed anaphylaxis, this clinical shock syndrome is characterized by vascular smooth muscle constriction (vasoconstriction) combined with gap formation between adjacent capillary endothelial cells (vasodilation) that results in severe fluid loss and leads to shock (Thao et al., 2007).

◉*Definitions:-*

The term 'anaphylaxis' has been used for all types of acute life-threatening illness triggered by abnormal sensitivity (hypersensitivity) to a trigger agent, and for apparently spontaneous attacks with similar features (idiopathic anaphylaxis). This has made it difficult to define.

The European Academy of Allergology and Clinical Immunology (EAACI) Nomenclature Committee proposed the following broad definition: Anaphylaxis is a severe, life-threatening, generalized or systemic hypersensitivity reaction. Minor, localised or non-systemic reactions are outside the definition of anaphylaxis. Anaphylaxis may be divided into 'allergic anaphylaxis' and'non-allergic anaphylaxis'. The clinical features of allergic anaphylaxis and non-allergic anaphylaxis may be identical (Johansson et al., 2003).

The EAACI committee proposed the term 'allergic anaphylaxis' should be used only when the reaction is mediated by an immunological mechanism (such as IgE, IgG, or complement activation by immune complexes). An anaphylactic reaction mediated by IgE antibodies, such as to amoxicillin, is referred to as 'IgE mediated allergic anaphylaxis'. The term 'anaphylactoid' reaction had been

introduced for non- IgE-mediated anaphylactic reactions but the EAACI committee has recommended this term should no longer be used. This proposal has not been universally accepted.

American Academy of Allergy, Asthma and Immunology & the American College of Allergy, Asthma and Immunology states: Anaphylaxis is defined as a condition caused by an IgE-mediated reaction. Anaphylactoid reactions are defined as those reactions that produce the same clinical picture as anaphylaxis but are not IgE mediated (Phillip et al., 2005).

Anaphylaxis is not a homogeneous process: the pathways, mediators, time course and response to treatment depend on the trigger agent, its route and rate of administration, the nature of the patient's hypersensitivity and the state of health of the patient, including incidental pathology such as respiratory or cardiovascular disease and the effects of concomitant medication such as Beta-blockers and ACE inhibitors. Clinical severity scale of immediate hypersensitivity reactions shown in **(table 2)**.Although anaphylaxis commonly involves respiratory, cutaneous and circulatory changes, variations such as shock with gastrointestinal disturbance or shock alone are possible. Alternatively, reactions may be fatal without significant shock except as the terminal event following respiratory arrest (Pumphrey, 2000).

Angioedema and urticaria may be features of anaphylaxis but commonly result from mechanisms other than anaphylaxis. Intravascular volume redistribution is an important component of anaphylactic shock. Cardiac output may be decreased as a result of reduced coronary artery perfusion pressure as well as impaired venous return. Local release of mediators may cause coronary artery spasm and there may be features of acute left or right ventricular failure. Myocardial ischemia with ECG changes is expected within minutes of anaphylactic shock becoming severe. Asphyxia may be due to upper airway occlusion caused by angioedema, or bronchospasm with mucus plugging of the lower airways; the latter most commonly occurs in patients taking daily treatment for asthma. Both these processes may occur simultaneously in patients reacting to foods, latex, b-lactam antibiotics or aspirin (Harper et al., 2009).