

PERIOPERATIVE PERIOD: IMMUNOLOGICAL MODIFICATIONS

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Surgical stress induces complex modifications in the hemodynamic, metabolic, neuro-hormonal and immune response of the individual. The magnitude of these alterations depends on preoperative events leading to surgery, the severity of surgical trauma, and also on post-operative/post-traumatic complications ("multiple hit hypothesis"). As in other conditions of tissue damage, surgery trauma is followed by an immune-inflammatory response, initiated at the site of injury by the innate immune system, followed by a compensatory anti-inflammatory (or immunosuppressive) response (CARS), involving mainly cells of the adaptive immune system, which predispose the host to septic complications. The up-regulated inflammatory response, together with a profound impairment of macrophage and cell-mediated immunity, appear to be the cause for patients' increased susceptibility in developing subsequent sepsis after major surgery.

IMMUNOLOGICAL MODIFICATIONS INDUCED FROM PRODUCTS USED DURING THE PERIOPERATIVE PERIOD

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Anesthetics and other products used during the perioperative period may influence immune function not only merely by reducing the HPA-axis stress response but also by directly modulating innate and adaptive immune responses. Most of the literature on the immune effects of anesthetics has been derived from in vitro or animal studies, due to the number of confounding variables in "real life" surgical settings. These immunosuppressive effects might not normally have clinical consequences for an immune-competent patient, but may act as important modifiers in postoperative morbidity and mortality. Furthermore, some inhibitory effects on neutrophil functions may provide a therapeutically beneficial effect under specific surgical clinical conditions, such as ischemia-reperfusion injury.

PERIOPERATIVE ANAPHYLAXIS: EPIDEMIOLOGY

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The clinical diagnosis of an anesthesia-related immediate hypersensitivity reaction is a difficult task for clinicians. Anaphylaxis may present as cardiovascular collapse or airway obstruction, associated or not with cutaneous manifestations. Drug hypersensitivity reactions that occur during anesthesia are responsible for significant morbidity and mortality and socio-economic costs. Perioperative anaphylaxis is becoming more common, probably because of the more frequent use of anesthesia and the increasing complexity of the drugs used. However, despite increased awareness of anaphylactic reactions to drugs and compounds used in anesthesia, their incidence remains poorly defined. Moreover, current epidemiological data should be carefully evaluated since the various studies published concerned non-homogeneous populations and gave differing definitions of drug hypersensitivity.

PERIOPERATIVE ALLERGY: RISK FACTORS

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Perioperative anaphylactic as well as anaphylactoid reactions can be elicited by drugs, diagnostic agents, antiseptics, disinfectants and latex. In some individuals, allergic reactions occur in the absence of any evident risk factor. Previous history of specific safe exposure to a product does not permit to exclude the risk of having a reaction. We have systematically reviewed characteristics in the patient's history or clinical parameters that affect the risk of developing reactions during anesthesia. Evidence shows that patients with previous unexplained reaction during anesthesia are at risk for perioperative allergic reactions. An allergic reaction to an agent is associated with previous reaction to a product that is related with the culprit agent. Multiple surgery procedures, professional exposure to latex and allergy to fruit are associated with an increased frequency of latex allergy. It has been shown that in some instances, allergic perioperative reactions may be more common in atopic patients and in female.

MUSCLE RELAXANTS ALLERGY

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The most common agents that are responsible for intraoperative anaphylaxis are muscle relaxants. In fact, neuromuscular blocking agents (NMBAs) contribute to 50-70% of allergic reactions during anaesthesia. The main mechanism of hypersensitivity reactions to NMBAs is represented by acute type I allergic reactions and the most severe form is anaphylaxis. The rate of non IgE mediated immediate hypersensitivity reactions usually varies between 20 % and 35% of the reported cases in most large series. In a recent report, non allergic suspected reactions to NMBAs occurred with almost the same frequency as did those with an allergic component. Although the precise mechanisms of these reactions remain difficult to ascertain, they usually result from direct non specific mast cell and basophil activation. After diagnostic procedures, regardless of the specific IgE results, NMBAs are contraindicated if the skin tests were positive. In view of the constantly evolving anesthesiologic practices, and of the complexity of allergy investigation, an active policy to identify patients at risk and to provide any necessary support to anaesthetists and allergologists should be promoted. The high frequency of IgE anaphylactic reactions and the feasibility of skin tests in children justify systematic allergy testing whenever hypersensitivity reaction occurs during general anaesthesia.

ANTIBIOTIC ALLERGY

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Antibiotics are commonly injected during the perioperative period and are responsible of 15% of the anaphylactic reactions. Anaphylaxis triggered by antibiotics primarily involves penicillin and cephalosporin. The management of patients with histories of allergic reactions to antibiotics is a common situation in clinical practice. The confirmation or invalidation of the allergic nature of the reported reaction is not based on in vitro tests, but on a rigorous allergological work-up based on detailed analysis of clinical history, skin tests and drug provocation test. Considering a possible cross-reactivity between penicillins, once an immediate penicillin allergy has been diagnosed, skin testing with the alternative molecule (cephalosporin, carbapenem, aztreonam) is mandatory and, if negative, the relevant drug should be given in an appropriate setting at increasing doses.

PERIOPERATIVE LATEX ALLERGY

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The prevalence of latex allergy varies greatly depending on the population studied and the methods used to detect sensitization. Subjects considered to be at high risk for latex allergy are rubber industry workers, children with spina bifida and urological abnormalities, children undergoing multiple surgical procedures and with urinary catheterization, health care workers and people with food allergy (latex fruit syndrome). In this paper we report a review of latex proteins, the symptoms of latex allergy, diagnosis and management in subjects with latex allergy.

PERIOPERATIVE ALLERGY: UNCOMMON AGENTS

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Anesthesia may often be considered as a high-risk procedure and anaphylaxis remains a major cause of concern for anesthetists who routinely administer many potentially allergenic agents. Neuromuscular blocking agents, latex and antibiotics are the substances involved in most of the reported reactions. Besides these three agents, a wide variety of substances may cause an anaphylactic reaction during anesthesia. Basically all the administered drugs or substances may be potential causes of anaphylaxis. Among them, those reported the most in literature include hypnotics, opioids, local anesthetics, colloids, dye, Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), Iodinated Contrast Media (ICM), antiseptics, aprotinin, ethylene oxide and formaldehyde, and protamine and heparins. No premedication can effectively prevent an allergic reaction and a systematic preoperative screening is not justified for all patients; nevertheless, an allergy specialist should evaluate those patients with a history of anesthesia-related allergy. Patients must be fully informed of investigation results, and advised to provide a detailed report prior to future anesthesia.

PERIOPERATIVE ALLERGY: CLINICAL MANIFESTATIONS

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Adverse drug reactions or side effects are usually expected, dose dependent, and occur at therapeutic doses. Anaphylactic and anaphylactoid reactions are unexpected and dose independent and can occur at the first exposure to drugs used during anesthesia. Perioperative anaphylaxis is a severe and rapid clinical condition that can be lethal even in previously healthy patients. The initial diagnosis of anaphylaxis is presumptive. A precise identification of the drug responsible for the adverse reaction is more difficult to establish in the case of anaphylactoid reaction because the adverse reaction could result from additive side effects of different drugs injected simultaneously. The timing of the reaction in relation to events, e.g. induction, start of surgery, administration of other drugs, i.v. fluids, is essential for the diagnosis. Generally, reactions are predominant in the induction and recovery phases, and manifested mainly as cutaneous symptoms. Reactions to drugs coincide with the phases when they are administered. Reactions to antibiotics are more frequent in the induction phase, to neuromuscular agents in the initiation and maintenance phases and to non-steroidal anti-inflammatory agents in the recovery phase. The differential diagnosis of any adverse reaction during or following anesthesia should include the possibility of anaphylaxis.

CLINICAL MODIFICATIONS INDUCED BY DRUGS DURING THE PERIOPERATIVE PERIOD

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Total intravenous anesthesia (TIVA) can be defined as a technique in which general anesthesia is induced and maintained using only intravenous agents. TIVA has become more popular in recent times because of the pharmacokinetic and pharmacodynamic properties of propofol, the availability of short acting synthetic opioids, and the development of delivery systems. Significant differences in anatomy and physiology in adults and children and special needs of younger patients have important consequences on many aspects of anesthesia. Airway and respiratory complications are the most common causes of morbidity during general anesthesia in children. Knowledge of the functional anatomy of airways in children forms the basis in the understanding of the pathological conditions that may occur.

ANESTHESIA IN CHILDREN WITH ASTHMA AND RHINITIS

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The incidence of asthma is increasing worldwide, but morbidity and mortality are decreasing, because of improvements in medical care. Although the incidence of severe perioperative bronchospasm is relatively low in asthmatics undergoing anaesthesia, when it does occur it may be life-threatening. Preoperative assessment of asthma should include a specialized medical history and physical examination as well as pulmonary function testing. Potential trigger agents should be identified and avoided. In many asthmatic patients treatment with systemic corticosteroids and bronchodilators is indicated to prevent the inflammation and bronchoconstriction associated with endotracheal intubation. Nonetheless, acute bronchospasm can still occur, especially at induction and emergence, and should be promptly and methodically managed.

PREVENTION OF ALLERGIC REACTIONS IN ANESTHETIZED PATIENTS

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Hypersensitivity reactions during perioperative period are increasing and may be potentially life-threatening. Therefore, major emphasis is given to prevention. We perform a review to examine which measures should be taken to prevent reactions to products used in elective and emergency surgery. Any patient with a history of previous anaphylaxis or severe reaction during anaesthesia should be referred to allergist for detection of the offending compound. However, the identification of the triggering agent is not always feasible because of the low accuracy of diagnostic tests. In these cases and when emergency surgery is required, it should be considered to replace all drugs administered before the onset of the reaction with alternatives. Furthermore, any cross-reacting agent and latex, especially in patients belonging to populations at-risk for latex allergy should be avoided. In susceptible patients, premedication with antihistamines and corticosteroids might reduce the severity of reaction to drugs or contrast material while it is unclear whether pre-treatment decreases incidence of anaphylactic reactions. There is no evidence that premedication prevents allergic reactions to latex. Overall, physicians should not rely on the efficacy of premedication.

PERIOPERATIVE ALLERGY: THERAPY

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Perioperative allergic reactions manifest in various ways. The majority of systemic reactions occur during anesthesia within minutes of intravenous induction; however, agents which are administered via other routes may cause reactions after more than 15 minutes. Anaphylaxis during anesthesia may present in many different ways and the signs and symptoms, which do not vary from those of anaphylactic reactions in general, may be masked by hypovolemia, light, deep anesthesia or extensive regional blockade. Recommendations for treatment are based on available evidence in the literature. A treatment algorithm is suggested, with emphasis on the incremental titration of adrenaline and fluid therapy as first-line treatment. Increased focus on this subject will hopefully lead to prompt diagnosis and rapid, correct treatment.