Anaphylaxis Treatment in Anesthesia

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Patients are exposed to a variety of medications, intravenous fluids, and latex in the operating room. Anaphylaxis or type I hypersensitivity reaction can present during anesthesia as skin redness/rash, bronchospasm, laryngospasm, hypotension, or circulatory collapse. The condition can be life-threatening. Preoperative assessment of allergies, asthma, allergy testing (if possible), prompt diagnosis during anesthesia, and rapid management of the condition are essential to prevent adverse outcomes.

Incidence of Anaphylaxis in Anesthesia

There is significant variation in the reporting of incidences of anaphylactic reactions during surgery. This is due to the difficulty in reporting the total number of cases undergoing anesthesia as well as to the difficulties in diagnosing anesthesia-related anaphylaxis. The incidence rate is reported to vary between 1 in 4,000 to 1 in 20,000 cases, with more adult women than men being affected.

Pathogenesis of Anaphylaxis in Anesthesia

Anaphylaxis means “against protection” and usually occurs when an individual is re-exposed to an antigen. An anaphylactic reaction is a type I hypersensitivity reaction in which IgE is released from mast cells and basophils. This is followed by the release of inflammatory mediators such as histamine, leukotrienes, bradykinin, and platelet-activating factor.

Anaphylactoid reactions, though identical to anaphylaxis, are not IgE dependent. They occur due to the non-immune mediated release of inflammatory mediators.
from the mast cells or basophils, or due to complement activation.

Histamine, or a complement/bradykinin cascade, is initiated with the activation of tyrosine kinase and the influx of calcium into the mast cells and basophils, irrespective of the initial antigen. This leads to the release of histamine, tryptase, chymase, carboxypeptidase A3, and proteoglycans. In addition, there is activation of COXs, lipoxygenases, and phospholipase A2, and the release of prostaglandins, leukotrienes, and platelet-activating factor. Other cytokines such as IL-6, IL-33, and TNF-alpha are also released.

Gq/G11 mediate opening of the vascular endothelial barrier. Histamine, along with other vasodilators, causes vasodilatation with pooling of blood peripherally and increased vascular permeability. This, in turn, leads to reduced systemic vascular resistance, hypovolemia, hypotension, and circulatory collapse. Histamine also causes bronchospasm, while leukotrienes cause peripheral airway spasm leading to airway obstruction, laryngeal edema, and asphyxiation followed by death.

Anaphylaxis can also occur with the first exposure to an antigen. This is due to cross-reactions between various drugs and products administered in rapid succession, or to latex allergy. Adverse reactions to drugs used during anesthesia can be of two types:

- Dose-dependent reactions related to the drug’s pharmacological properties or related to the drug’s metabolites
- Non-dose dependent reactions unrelated to the drug’s properties

Etiology of Anaphylaxis in Anesthesia

Causes of anaphylaxis during anesthesia include, in order of frequency:

- Muscle relaxants: Anaphylactic reactions due to muscle relaxants occur at a rate of 1 in 6,500 cases. Succinylcholine, atracurium, pancuronium, and vecuronium have been reported to cause these reactions.
- Latex: Polypeptides in latex are known to cause a direct IgE-mediated response, especially in susceptible individuals such as those with spina bifida, congenital genitourinary anomalies, or spinal cord injuries.
- Antibiotics: Beta-lactams such as penicillin, cephalosporin, and sulfas are responsible for drug-related anaphylaxis. Vancomycin, which is used for prophylaxis, can cause “red man” syndrome. This condition is characterized by erythema of the upper body, pruritus, and hypotension.
- NSAIDs: Aspirin and other nonsteroidal anti-inflammatory drugs are associated with anaphylaxis as well as anaphylactoid reactions. They inhibit cyclooxygenase with excessive leukotrienes production and hypersensitivity symptoms within 10 minutes of intravenous and within 30 minutes after rectal and 60 minutes after oral administration.
- Colloids: Plasma volume expanders, or colloids, are responsible for approximately 4% of anaphylactic reactions in the operating room. Their effects are visible approximately 20 minutes after starting a colloid infusion and can be severe in approximately 20% of cases.
- Other anesthetic drugs: Thiopental has been reported to cause anaphylaxis in 1 out of 30,000 cases, with women affected more than men. Propofol can stimulate the release of histamine directly, especially when administered with muscle relaxants. Amongst benzodiazepines, midazolam is known to be safer than diazepam. Narcotics, on the other hand, cause an anaphylactoid reaction,
with flushing and urticaria.

- **Antiseptic solutions**: Povidone-iodine is associated with type IV hypersensitivity and not type I reactions. Patients can become sensitized to chlorhexidine, as it is widely used. Chlorhexidine anaphylaxis can occur following its cutaneous, mucosal, or even parenteral usage.

**Diagnosis of Anaphylaxis in Anesthesia**

Identifying the exact cause of the anaphylactic reaction can be difficult, as several drugs are often used in rapid succession during anesthesia. In addition, the patient is draped (therefore not completely visible) and unable to vocalize discomfort. Therefore, it is up to the anesthetist, surgeon, and operating room personnel to look for the following signs:

- **Skin**: urticaria, flushing, facial edema are often immediate reactions.
- **Cardiovascular system**: fall in blood pressure (hypotension) or tachycardia.
- **Respiratory system**: difficulty in ventilation (bronchospasm/laryngospasm), pulmonary edema, hypoxia.

The most common signs are flushing, difficulty ventilating the patient and a rapid fall in blood pressure.

**Management of Anaphylaxis in Anesthesia**

1. As soon as anaphylactic/anaphylactoid signs are noticed, the suspected drug infusion should be discontinued.
2. The patient should be ventilated with 100% oxygen.
3. The patient should be laid flat, and the end of the operating table should be elevated.
4. Intramuscular epinephrine should be administered and can be repeated if necessary.
5. Bronchodilators should be administered to relieve bronchospasm.
6. Antihistamines and corticosteroids can also be administered.

**Prevention of Anaphylaxis in Anesthesia**

1. Detailed patient history should be taken prior to surgery.
2. A skin/prick test/patch test/intradermal test to determine the presence of allergies prior to scheduling surgery should be performed on all patients with a suspected history of allergies.
3. Alternative drugs or products should be used if there is a known history of allergy.

**References**


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