Anesthesiology

Anaphylaxis Treatment in Anesthesia

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

Incidence of Anaphylaxis in Anesthesia

There is a great variation in the reporting of incidences of anaphylactic reactions during surgery. This is due to the difficulty in reporting of the total number of cases undergoing anesthesia as well as due to the difficulties in diagnosing anesthesia-related anaphylaxis. The incidence 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. 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 like histamine, leukotrienes, bradykinin and platelet activating factor.

Anaphylactoid reactions, though identical to anaphylaxis, are not IgE dependent. They occur due to 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 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, phospholipase A2, and release of prostaglandins, leukotrienes and platelet activating factor. Other cytokines like IL-6, IL-33 and TNF-alpha are also released.

Gq/G11 mediate opening of the vascular endothelial barrier. Histamine, along with the 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.

It can occur with first exposure to the antigen too. This is due to cross-reaction between various drugs and products administered in rapid succession, or due 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**

The causes for anaphylaxis during anesthesia in order of frequency are:

**Muscle relaxants**: Most of the anaphylactic reactions are due to muscle relaxants with an incidence 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 like those with spina bifida, congenital genitourinary anomalies and spinal cord injuries.

**Antibiotics**: Beta-lactams, e.g., 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 NSAID drugs are associated with anaphylaxis as well as anaphylactoid reactions. They inhibit cyclo-oxygenase with excessive leukotrienes production and hypersensitivity symptoms within ten minutes of intravenous, within 30 minutes after rectal and within 60 minutes of oral administration.

**Colloids**: Plasma volume expanders, or colloids, are responsible for approximately 4% of anaphylactoid reactions in the operation theater. They are noticed about 20 minutes after starting a colloid infusion and can be severe in around 20% of the cases.

**Other anesthetic drugs**: Thiopental has been reported to cause anaphylaxis in 1 out of 30,000 cases with a female preponderance. Propofol is another anesthetic drug which
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 is **not easy** as several drugs are often used in rapid succession during anesthesia. In addition, during anesthesia, the patient is draped (therefore not completely visible) and unable to vocalize discomfort. Therefore, it is the duty of the anesthetist, surgeon and operation room personnel to look for the following signs:

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

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

**Management of Anaphylaxis in Anesthesia**

1. As soon as the 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 with the foot end of the operating table being elevated**.
4. **Intramuscular epinephrine** should be administered and can be repeated if necessary.
5. **Bronchodilators** have to be administered to relieve bronchospasm.
6. **Antihistamines and corticosteroids** can also be administered.

**Prevention of Anaphylaxis in Anesthesia**

1. Detailed patient history prior to surgery.
2. **Skin/prick test/patch test/intradermal test** to determine allergy prior to scheduling surgery in all cases suspected to have a **previous history of allergies**.
3. Use **alternative drugs or products** if there is a previous history of allergy.

**References**


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