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.

Reaction(s) to anesthesia may present in many different ways and the signs and symptoms, which do not vary from those of systemic reaction or anaphylaxis, may be masked by hypovolemia, light, deep anesthesia or extensive regional blockade. Cutaneous symptoms such as flushing or urticaria are common, but during anesthesia they are usually not visible due to surgical drapery. On the other hand, different causes of hypotension or difficulty in ventilation, for instance a misplaced tracheal tube or equipment failure, should be excluded.

The majority of systemic reactions occur during anesthesia within minutes of induction - up to 90% reported in one study (1) - and are mainly linked to agents given intravenously (2, 3). However, agents administered through the skin or mucosa, in the urethra, in contact with the peritoneum or subcutaneously take some time to be absorbed and therefore cause reactions after more than 15 minutes. This is the case, for example, with latex, chlorhexidine and day patent blue.

For diagnostic purposes and to aid prompt decision-making, both perioperative allergies and reactions are classified according to severity (Table 1).

TREATMENT (TABLE 2)

In the event of perioperative allergic reactions, there is a wide spectrum of severity and combinations of clinical features. Although management should be tailored to an individual patient, there is consensus that adrenaline should be given as soon as possible. In addition to having α-agonist activity, adrenaline is a valuable β-agonist which is inotropic and a bronchodilator and further reduces mediator release (4).

Immediate management

a) Remove all potential causative agents (including colloids, latex and chlorhexidine) and maintain anesthesia, if necessary, with an inhaled agent.

b) Keep the airways open and administer 100% oxygen. Intubate the trachea if necessary and ventilate the lungs with oxygen.

c) Elevate the patient's legs if there is hypotension.

d) Administer adrenaline intravenously using appropriate dosages either for children or adults: several doses may be required.

Key words: Anesthesia; Anaphylaxis; Adrenaline; Cardiopulmonary function; Fluid therapy; Corticosteroids; Bronchodilator agents.

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Table 1.

Classification of clinical manifestations of anaphylaxis during anaesthesia.

Class	Clinical manifestations
I	Generalised cutaneous signs: erythema, urticaria with or without angioedema
II	Moderate multiorgan involvement with cutaneous signs, hypotension and tachycardia, bronchial hyperreactivity (cough, ventilatory impairment)
III	Severe life-threatening multiorgan involvement that requires specific treatment: collapse, tachycardia or bradycardia, cardiac arrhythmias, bronchospasm; the cutaneous signs may be absent or occur only after the arterial blood pressure recovers
IV	Circulatory or respiratory arrest

e) If appropriate, start cardiopulmonary resuscitation.

f) Administer 0.9% saline or lactated Ringer's solution; large volumes may be required.

Secondary management

a) Administer chlorphenamine in appropriate doses either for children or adults.

b) Administer hydrocortisone in appropriate doses.

c) If the blood pressure does not return to normal despite infusion of adrenaline, consider giving an alternative intravenous vasopressor such as dopamine.

d) Treat bronchospasm with salbutamol nebulizer. If necessary, consider infusing the drug.

e) Arrange to transfer the patient to an appropriate Critical Care unit.

f) Take blood sample for mast cell tryptase.

The cornerstones of treatment for severe perioperative allergies are adrenaline and fluid therapy. Adrenaline is highly potent and an efficient treatment in most case of severe systemic reactions or anaphylaxis. It should be administered as soon as possible and titrated carefully to response. Its α–agonist property reverses vasodilation and edema and its β-agonist property dilates the airways, increases cardiac output and suppresses the release of inflammatory mediators such as leukotrienes and histamine (5). If administered early, doses of 10-25 μg intravenous adrenaline in children and 10-50 μg in adults are sufficient to reverse anaphylaxis (6). The relatively rare fatalities in anaphylaxis are usually caused by delayed or no administration of adrenaline.

Fluid therapy is important to counteract the great changes in the bloodstream associated with vasodilation and capillary leakage; in severe cases it may be necessary to give repeated infusions.

Corticosteroids and antihistamines are used for Class I clinical manifestations like generalized cutaneous signs, erythema, urticaria and angioedema (Table 1). However, both drugs are valid as secondary treatment for systemic reactions and anaphylaxis, and they help to prevent edema, cutaneous symptoms and a relapse of the systemic reactions that can occur up to 24 h after the initial reaction (7 -8). Early recognition of the clinical features of perioperative allergies is pivotal in order to start prompt, adequate treatment to improve symptoms, avoid both anaphylaxis and myocardial ischemia and therefore achieve resolution of severe symptoms.

PRINCIPAL DRUGS IN CHILDREN: DOSES

Adrenaline

Intramuscular: >12 years: 500 μg IM (0.5 ml of a 1: 1000 solution). 300 μg IM (0.3 ml of a 1:1000 solution) if

Table 2. Guidelines for treating anaphylactic reactions during anesthesia.

Primary treatment	**Dosage**
Stop administration of suspected substance	
Call for help and inform the surgeon	
Trendelenburg position	
Maintain airways and give oxygen	F_iO_2 1.0
Adrenaline	Adults:
Use diluted adrenaline i.v. maximum concentration 0.1 mg/ml	Mild to moderate reaction: 0.01-0.05 mg i.v.
Titrate dose to response	Circulatory collapse: 0.1-1.0 mg i.v.
If large doses are needed, use i.v. infusion	i.v. infusion starting at: 0.05-0.1 µg/kg/min
	Without i.v. access: 0.5-0.8 mg i.m.
	Children:
	Mild to moderate reaction: 0.001-0.005 mg/kg/min
	Circulatory collapse:0.01mg/kg i.v.
	Without i.v. access :0.005-0.01 mg/kg i.m.
Fluid Therapy	Adults:
NaCl 9 mg/ml, Ringer's acetate or colloids	20 ml/kg, more may be needed
	Children:
	20 ml/kg, more may be needed
Secondary Treatment	Adults:
Corticosteroids	Hydrocortisone 250 mg i.v. or Methylprednisolone 80 mg i.v.
	Children:
	Hydrocortisone 50-100 mg i.v. or Methylprednisolone 2 mg/kg i.v.
Anthihistamines	Adults:
	H_1 antagonist, e.g. Clemastin 2 mg or Clorphenamine 10 mg or Promethazin 50 mg given i.v.
	H_2 antagonist: consider Ranitidine 50 mg i.v.
	Children:
	H_1 antagonist e.g. Clemastin 0.0125-0.025 mg/kg or Clorphenamine 5 mg or Promethazin 0.3-1.0 mg/kg given i.v./i.m.
Nebulised β_2-agonist may be used for symptomatic treatment of bronchospasm, but it is not first-line treatment	

i.m.- intramuscularly; i.v.- intravenously.

the child is small - 6–12 years. Up to 6 years: 150 µg IM (0.15 ml of a 1:1000 solution).

Intravenous: Intravenous adrenaline may be used in children in specific areas such as operating rooms or intensive care units by clinicians familiar with its use and if IV access is already available. Great care should be taken to avoid dosage errors when preparing drug dilutions. Prepare a syringe containing 1 ml of 1:10,000 adrenaline for each 10 kg of body weight (0.1 $ml.kg^{-1}$ of 1:10,000 adrenaline solution = 10 $\mu g.kg^{-1}$). Titrate

to response, starting with a dose equal to one-tenth of the contents of the syringe, i.e., 1 μg.kg $^{-1}$. Often a child will respond to as little as 1 μg.kg $^{-1}$. In smaller children, further dilution may be needed to allow dose titration (check carefully for decimal point and concentration errors). The intramuscular route is preferred if there is no venous access or if establishing a venous access would cause a delay in drug administration.

Hydrocortisone: >12 years: 200 mg IM or IV slowly; 6 to 12 years: 100 mg IM or IV slowly; 6 months to 6 years: 50 mg IM or IV slowly; < 6 months: 25 mg IM or IV slowly.

Chlorphenamine: >12 years: 10 mg IM or IV slowly; 6 to 12 years: 5 mg IM or IV slowly; 6 months to 6 years: 2.5 mg IM or IV slowly; < 6 months: 250 μg. kg $^{-1}$ IM or IV slowly.

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