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REVIEW ARTICLE

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Allergic reactions during labour analgesia and caesarean section anaesthesia

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ABSTRACT
Allergic reactions in the parturient are challenging for the anaesthetist who is dealing with both mother and baby, often in circumstances when there is a need for delivery. While most previous reviews have focused on specific substances in individual cases, this review focuses on allergic reactions during the peripartum period, the differential diagnosis and specific treatment options. Immunoregulation and susceptibility to allergic reactions may change during pregnancy. Compared with non-pregnant patients, in whom neuromuscular blocking drugs are the most common triggering substances, allergic reactions in parturients mostly occur following contact with latex, injection of antibiotics and uterotonics, and infusion of colloids. With the exception of latex, where patient history may raise suspicion, allergic reactions may occur without prior exposure to triggering agents. Most drugs used for resuscitation of the non-pregnant patient are suitable for the parturient. Some substances, such as H_2-receptor antagonists for aspiration prophylaxis or corticosteroids for prematurity, may have been given before the event. Although fetal outcome is important, the mother is the primary focus of care.

Keywords: Anaesthesia; Allergy; Anaphylaxis; Labour; Caesarean section

Introduction

Anaphylactic reactions during anaesthesia are rare in the general population.[1] Management of the parturient is challenging since the welfare of both mother and fetus must be considered. There have been many reviews on anaphylaxis during anaesthesia in general,[2–4] but other than case reports, only a few reviews have been written specifically about obstetric patients. Haemodynamic changes are common during obstetric anaesthesia which may delay the diagnosis of an allergic reaction. The present review aims to increase awareness of possible allergic reactions and highlight the different triggering agents and treatment options.

Epidemiology

There is large variability in the reported incidence of intraoperative anaphylactic reactions, ranging from 1:10 000 to 1:20 000 in Australia to 1:6000 in Norway.[5,6] Recently, the estimated annual incidence of allergic reactions during anaesthesia in France was reported to be 100.6 per million procedures (1:9940).[4] In contrast, a retrospective study at a large United States centre reported approximately one referral per 34 000 anaesthetics.[7] Associated mortality rates range from 3.4% to as high as 6%.[1,8] A significant female predominance has been observed, independent of the causal agent.[3,4,9]

An IgE-mediated reaction is involved in approximately 50–70% of cases.[4,7] French epidemiological surveys revealed neuromuscular blocking drugs (NMBDs) to be involved in 54–58% of cases, followed by latex (19.6–22.3%) and antibiotics (12.8–14.7%).[3,4] Whereas a Norwegian study reported NMBDs as the responsible allergen in 93.2%, the United States report found NMBDs to be causative in only 11.1%.[7,10] These discrepancies may be caused by the potential of NMBDs to produce positive skin tests, as demonstrated in volunteers, independent of mast cell degranulation, which may explain the high but probably false incidence of alleged allergic reactions.[11–13] In addition, exposure to certain drugs, such as pholcodine in Norway, may presensitize patients for cross-reactivity to NMBDs.[14]

Stephens analyzed intensive care unit (ICU) admissions from an obstetric hospital.[15] Of 24 161 anaesthetics in 10 years, five cases involved an allergic reaction. As

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only cases requiring ICU admission were included, the true incidence may have been underestimated. Prospective surveys of 'near-accidents' in the UK revealed five cases in the period 2003–2005, giving an incidence of 3 in 100 000 pregnancies.[16] Similarly, Mulla et al.[17] reviewed the hospital discharge data of Texan parturients during 2004–2005 and noted an incidence of maternal anaphylaxis of 2.7 per 100 000 deliveries. No maternal deaths were reported and 14 out of 19 parturients presenting with anaphylaxis (74%) were delivered by caesarean section. Antibiotics were the trigger in 68%.[17] Draisci et al, however, reported an incidence as high as 1:310 of latex anaphylactic reactions in caesarean section patients.[18]

Definition, pathophysiology and alterations during pregnancy

Although there are different types of allergic reactions, clinical symptoms are similar, making them clinically indistinguishable. The classification of allergic reactions has often changed, but since 2001 consensus has been achieved with respect to terminology. 'Anaphylactic' is now the preferred term to describe any reaction, whereas the term 'anaphylactoid' should be abandoned.[19,20] A diagnostic work-up may elucidate whether an event was IgE-mediated, non-IgE-mediated or a non-immunological hypersensitivity reaction. In an IgE-mediated reaction, B-lymphocytes produce IgE antibodies during first exposure to an antigen, which bind to receptors on the surface of mast cells and basophils. On repeated exposure, the antigen bridges two adjacent IgE antibodies resulting in release of mediators such as histamine, tryptase, and chemotactic factors from storage granules, as well as newly synthesized mediators (leukotrienes, prostaglandins, platelet activating factor) from the cell membrane and also cytokines. Other mechanisms involve either immunological (IgG or IgM) or non-immunological complement activation, with the release of complement fragments, known as anaphylatoxins, which induce subsequent release of mediators from mast cells and basophils. Finally, a direct non-immune-mediated hypersensitivity reaction is also possible, causing release of histamine by mast cells in a dose-dependent fashion with symptoms that are usually mild.[1,2]

During pregnancy, hormonal changes may be responsible for alterations of the immune system. Modification of autoimmune diseases during pregnancy, such as systemic lupus erythematosus which tends to develop or worsen, or rheumatoid arthritis which tends to improve, supports an alteration in immunoregulation.[21] Oestrogen and progesterone concentrations are greatly increased during pregnancy and are considered immunomodulating hormones.[21] Progesterone promotes type 2 T helper (Th2) cell polarization by inhibiting type 1 T helper (Th1) cell cytokine production and inducing Th2 cytokines and interleukin 10 production. These alterations serve to prevent rejection of the fetus;[21] however, it is unclear if they predispose the parturient to anaphylaxis or affect its severity.[22]

The placenta plays a role in protecting the fetus against maternal anaphylactic reactions, as it prevents the passage of high-molecular-weight IgE antibodies.[23] Furthermore, the high diamine oxidase activity of the maternal decidua catalyzes oxidative deamination of histamine and other amines released during anaphylaxis.

Maternal hypotension can result in fetal hypoxia causing thalamic and basal ganglia lesions with adverse outcome.[24–27] After anaphylactic shock at 27 weeks of gestation, multicystic bilateral encephalomalacia of both hemispheres and atrophy of the corpus callosum have been reported.[28] Sleth et al.[29] postulated that fetal asphyxia is the result of both maternal cardiovascular collapse and chorio-umbilical vasoconstriction due to release of mediators.

Clinical manifestations

Table 1 summarizes symptoms associated with allergic reactions, some or all of which may occur depending on receptor location, reaction severity and anaesthetic modality.[30] During neuraxial anaesthesia, early signs such as malaise, pruritus, nausea and dyspnoea may be apparent in the awake patient. With general anaesthesia, however, they may be unrecognized and bronchospasm or cardiovascular collapse may be the first recognizable signs.[2] In 90% of cases, symptoms appear within minutes of administration of the triggering substance.[1,31] If the appearance of signs is delayed until after induction or during maintenance of anaesthesia, allergy to latex, antibiotics, disinfectants or local anaesthetics should be suspected.[31] The most common clinical features are cardiovascular symptoms (73.6%), cutaneous reactions (69.6%) and bronchospasm (44.2%).[1,2,30,31] Although a combination usually raises suspicion of an allergic reaction, symptoms may appear in isolation and thus delay the diagnosis.

The severity of clinical manifestations related to allergic reactions can be classified in four grades:

- Grade I: cutaneous symptoms.
- Grade II: measurable but not life-threatening symptoms including hypotension, tachycardia and respiratory disturbance (cough, difficulty to inflate).
- Grade III: life-threatening symptoms including collapse, tachycardia or bradycardia, arrhythmias and bronchospasm.
- Grade IV: cardiac and/or respiratory arrest.[31]

Clinical manifestations appear more severe in patients with true IgE-mediated anaphylaxis in comparison with those suffering what was previously called an