Acute management of anaphylaxis in pregnancy

CPD

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Background
Anaphylaxis in pregnancy is rare but can potentially be associated with significant morbidity and mortality for the mother, fetus and neonate. With appropriate and timely management, even severe anaphylaxis can be managed with excellent maternal and fetal outcomes.

Objective
The aim of this article is to provide an illustrative case and highlight current recommendations for diagnosis and management of acute maternal anaphylaxis, which have recently been reviewed and developed into a guideline by the Australasian Society of Clinical Immunology and Allergy.

Discussion
An understanding of management of anaphylaxis in pregnancy is essential knowledge in the general practice setting. The recommended dosage and administration of adrenaline (epinephrine) for anaphylaxis is the same in pregnant and non-pregnant patients: 0.5 mg adrenaline intramuscularly in the mid-outer thigh (or dose of 0.01 mg/kg if <50 kg). The use of adrenaline in maternal anaphylaxis is supported by various international guidelines.

CASE

A woman aged 27 years with a known history of anaphylaxis to peanuts presented to the emergency department following accidental exposure to peanuts after ingestion of a kebab containing satay sauce. The patient was 14+5 weeks pregnant with her third child. Within minutes of ingestion, she had developed facial and lip angioedema, the sensation of throat swelling, difficulty breathing, generalised urticarial rash and nausea. She self-administered her EpiPen (0.3 mg adrenaline autoinjector, intramuscular [IM]) and administered a second EpiPen five minutes later because of persistent symptoms. On initial review by paramedics, she was hypotensive with a systolic blood pressure of 68 mmHg, which improved to 105 mmHg with intravenous (IV) fluid resuscitation. Her angioedema and dyspnoea resolved. On review in the emergency department her airway was patent, with observations – including blood pressure – remaining within normal limits. An urticarial rash was the only persisting sign found on examination. Adjunctive IV and oral corticosteroids were administered, and obstetric ultrasonography performed in the emergency department confirmed the presence of a healthy fetus. The patient was discharged after a four-hour observation period with subsequent review by her obstetrician the same day. She gave birth to a healthy baby boy at 39 weeks' gestation via caesarean section with no further complications during the antenatal period.

The purpose of this article is to highlight current recommendations for management of acute anaphylaxis in pregnancy. This is in the context of the recent development of the first consensus Australian guidelines for acute management of anaphylaxis in pregnancy by the Australasian Society of Clinical Immunology and Allergy (ASCIA).

Maternal anaphylaxis is rare, with a reported incidence of between 1.6 and 2.7 cases per 100,000 deliveries.[1,2] The majority of cases occur in the intrapartum or postpartum period, with β-lactam antibiotics identified as the most common cause.[1–4] Antibiotic exposure in pregnancy is increasing, with guidelines recommending intrapartum antibiotic prophylaxis for group B streptococcal carriage to prevent neonatal transmission, and for antibiotic prophylaxis prior to caesarean section.[1] Other causes of anaphylaxis in the intrapartum period include latex and medications such as neuromuscular blocking agents or

components of spinal anaesthesia.[1,2,5] Maternal anaphylaxis in the antepartum period is less common, and causes of anaphylaxis in this period are similar to those in the general population, such as foods, medications and insect venom.[1,4] Rarely, vaccines that are recommended during pregnancy and routinely administered by general practitioners, including influenza and pertussis-containing vaccines, can also cause anaphylaxis.[6,7]

As per the ASCIA anaphylaxis guidelines, anaphylaxis is defined as:[8]

> *Any acute onset illness with typical skin features (urticarial rash or erythema/flushing, and/or angioedema), plus involvement of respiratory and/or cardiovascular and/or persistent severe gastrointestinal symptoms; or*

> *Any acute onset of hypotension or bronchospasm or upper airway obstruction where anaphylaxis is considered possible, even if typical skin features are not present.*

Signs and symptoms of maternal anaphylaxis include sudden onset and rapid progression of typical airway, respiratory, gastrointestinal and cardiovascular signs associated with anaphylaxis. Additional features may include less specific signs such as persistent hypotension, lower back pain, uterine cramps and evidence of fetal distress.[3,4] In pregnancy, differential diagnoses for hypotension include neuraxial block, aortocaval compression, venous thromboembolism, haemorrhage, amniotic fluid embolus (AFE), sepsis, magnesium toxicity or local anaesthetic toxicity.[5] Bronchospasm may be attributable to pulmonary oedema, pulmonary aspiration or adverse effects of synthetic prostaglandin analogues.[5] Signs and symptoms that are more suggestive of anaphylaxis as the underlying cause include acute-onset urticaria, angioedema, pruritis or wheeze along with hypotension, as well as absence of an associated coagulopathy that may be seen in AFE or sepsis.[4,5] However, anaphylaxis should be suspected even in the absence of cutaneous signs and/or symptoms.

The management of anaphylaxis during pregnancy is similar to management of anaphylaxis in the general population, with a few key differences in maternal positioning and consideration of timing of delivery as discussed in the remainder of this article.

Positioning

Pregnant patients over 20 weeks' gestation should be placed in the left lateral position to minimise impaired venous return due to compression from the gravid uterus.[4,9–14] Alternatively, manual left uterine displacement with the patient in the supine position can be performed in the setting of cardiac arrest to facilitate effective cardiopulmonary resuscitation.[4,9–12,14]

Adrenaline

The current recommended dose of adrenaline for pregnant patients with anaphylaxis is 0.5 mg (or a dose of 0.01 mg/kg if <50 kg) IM, with repeated doses of 0.5 mg IM every five minutes if signs or symptoms of anaphylaxis persist. This is the same dose used to treat anaphylaxis in non-pregnant patients. Prior to 2019, the ASCIA anaphylaxis management guidelines for health practitioners recommended administration of a dose of 0.3 mg of adrenaline IM in pregnant women experiencing anaphylaxis.

Practitioners may be reluctant to administer adrenaline to pregnant patients because of concerns regarding safety of adrenaline to the fetus and the theoretical potential negative impact of vasoconstriction on uteroplacental blood flow secondary to α-adrenergic effects.[1,3] Importantly, however, the key determinant of uteroplacental perfusion (and therefore fetal oxygenation) is maternal blood pressure.[4] Adrenaline increases maternal systemic vascular resistance, cardiac output and uteroplacental perfusion.[1,3] Favourable outcomes for both mother and fetus have been shown with appropriate doses of adrenaline administered via IM injection (including at doses of 0.5 mg or more), with repeated doses if signs or symptoms of anaphylaxis persisted.[3,15–17] There is no evidence in the literature of harm to the mother or fetus from a dose of 0.5 mg adrenaline IM for treatment of anaphylaxis in pregnancy.[3] Several case reports describe adrenaline administered in IV boluses or continuous infusions in the setting of maternal anaphylaxis with concurrent continuous electronic fetal monitoring (CEFM). During the administration of adrenaline, CEFM showed no evidence of fetal distress, and good fetal outcomes have resulted.[18–20] Conversely, poor neonatal outcomes, such as fetal hypoxic ischaemic encephalopathy or death, may occur with inadequate adrenaline administration and delayed caesarean section.[3,21]

Various international guidelines recommend the same dosing of adrenaline in pregnant patients as in non-pregnant patients in cases of anaphylaxis and during management of cardiac arrest.[9,10,14,22,23] Therefore – as for all adults and children experiencing anaphylaxis – adrenaline should be the first-line treatment for anaphylaxis in pregnancy and can be given at a dose of 0.5 mg IM (or at a dose of 0.01 mg/kg if <50 kg).

In 2019, ASCIA sought to develop guidelines for acute management of maternal anaphylaxis, intended for medical practitioners, midwives, nurses and paramedics providing first responder emergency care. Worldwide there are no randomised controlled trials regarding the management of anaphylaxis in pregnancy. The evidence regarding treatment of anaphylaxis is predominantly observational and based on physiological principles. Therefore, guideline development was based on review of the existing literature focusing on maternal anaphylaxis management and outcomes[1–5] and review of existing guidelines addressing management of anaphylaxis and/or cardiac arrest in pregnancy.[8–12,14,22,24–26] The ASCIA guideline for the acute management of anaphylaxis in pregnancy was subsequently endorsed by the Australasian College of Emergency Medicine, The Royal Australian and New Zealand College of Obstetricians and Gynaecologists, the College of Intensive Care Medicine of Australia and New Zealand and the Australian and New Zealand Anaesthetic Allergy Group.

The salient points for management are outlined in this article, and the full guidelines are available on the ASCIA website (www.allergy.org.au/hp/papers/acute-management-of-anaphylaxis-in-pregnancy).[27]

Delivery

In the event of anaphylaxis in the community or general practice setting, a plan should be made for hospital transfer via ambulance to allow continuous monitoring and management and/or alerting the relevant obstetric team for possible emergency caesarean section. If indicated, caesarean delivery should occur promptly in conjunction with resuscitative measures. This is recommended if there are signs of fetal distress (eg on cardiotocography or assessment of fetal heart rate) or if anaphylaxis is refractory to treatment.[3,4,9] In the event of cardiac arrest, cardiopulmonary resuscitation (CPR) should be performed in addition to manual left uterine displacement (refer to Australian and New Zealand Committee on Resuscitation CPR guidelines and American Heart Association's *Guidelines for cardiopulmonary resuscitation: Cardiac arrest associated with pregnancy*).[9,12,28] Hospital transfer in this situation should be initiated as early as possible with the aim of performing peri-mortem caesarean delivery (PMCD) with incision achieved at four minutes.[9,12] The primary aim with PMCD is to facilitate resuscitation of the mother.[9,12]

Additional management

Retrospective confirmation of anaphylaxis can be assisted by serial measurement of serum mast cell tryptase (MCT), a serine protease released from activated mast cells.[29] Results are usually delayed several days from collection so are not useful for acute diagnosis of anaphylaxis. Recommended sampling times are immediately after symptom onset, then 1–2 hours later to capture peak MCT concentrations, followed by a third sample at least 24 hours after symptom onset to determine baseline levels.[29,30] An acute rise followed by return to baseline levels is typically seen with anaphylaxis but is not present in all cases.[29] All patients with anaphylaxis should be referred to a clinical immunology/allergy specialist to confirm the history; review MCT results; and access additional testing, such as skin testing and specific immunoglobulin (Ig) E testing, to aid diagnosis and to ensure appropriate patient education and provision of an action plan documenting their anaphylaxis triggers and acute management. The general practitioner has an important role in long-term care of all patients with a history of anaphylaxis, including ensuring that adrenaline autoinjectors (eg EpiPen, Anapen) are up to date and that the patient continues to be confident to self-administer, and that cofactors such as asthma are optimally managed. Notably, systemic mastocytosis increases the risk of anaphylaxis to multiple agents; therefore, pregnant patients with systemic mastocytosis should have input from an allergy specialist to aid in planning of delivery.[4,31] During antenatal review, it should be ensured that pregnant patients with known anaphylaxis have up-to-date anaphylaxis and asthma management plans. An opportunity can be taken to re-educate on adrenaline autoinjector administration and reassure patients that adrenaline is safe to use in pregnancy and is associated with better outcomes for mother and fetus, in comparison to potential adverse effects resulting from delayed first-line treatment for anaphylaxis.

Conclusion

While the majority of cases of maternal anaphylaxis occur in the intrapartum or postpartum period, anaphylaxis during the antepartum period may occur secondary to allergens similar to those in the general population, such as antibiotics, food and insect venom. The recommended dosage and administration of adrenaline for anaphylaxis is the same in pregnant and non-pregnant patients: 0.5 mg adrenaline IM in the mid-outer thigh (or dose of 0.01 mg/kg if <50 kg). The use of adrenaline in maternal anaphylaxis is supported by various international guidelines. Best outcomes for mother and fetus can be achieved with appropriate doses of IM adrenaline, with repeated doses where required, in conjunction with prompt caesarean delivery (within 10–15 minutes) if indicated.

Key points

- Dosage and administration of adrenaline for anaphylaxis is the same in pregnant and non-pregnant patients: 0.5 mg adrenaline (epinephrine) IM in the mid-outer thigh (or dose of 0.01 mg/kg if <50 kg), with repeated doses of 0.5 mg IM every five minutes if signs or symptoms of anaphylaxis persist.
- Placing the patient in the left lateral position or performing manual uterine displacement in the supine position prevents obstruction of the inferior vena cava and reduced cardiac output.
- Prompt caesarean section is indicated if there are signs of ongoing fetal distress in a viable pregnancy or if there is persistent maternal hypotension refractory to treatment.

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