Review Article

Emergencies in obstetric anaesthesia: a narrative review

C. H. Prior,[1] **C. E. G. Burlinson**[2,3] and **A. Chau**[2,4,5]

1 Consultant, Department of Anaesthesia, West Middlesex University Hospital, London, UK
2 Consultant, Department of Anesthesia, BC Women´s Hospital, Vancouver, BC, Canada
3 Clinical Instructor, Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, BC, Canada
4 Clinical Associate Professor, Department of Anesthesiology, Pharmacology and Therapeutics, University of British Columbia, Vancouver, BC, Canada
5 Consultant, Department of Anesthesia, St. Paul´s Hospital, Vancouver, BC, Canada

Summary

We conducted a narrative review in six areas of obstetric emergencies: category-1 caesarean section; difficult and failed airway; massive obstetric haemorrhage; hypertensive crisis; emergencies related to neuraxial anaesthesia; and maternal cardiac arrest. These areas represent significant research published within the last five years, with emphasis on large multicentre randomised trials, national or international practice guidelines and recommendations from major professional societies. Key topics discussed: prevention and management of failed neuraxial technique; role of high-flow nasal oxygenation and choice of neuromuscular drug in obstetric patients; prevention of accidental awareness during general anaesthesia; management of the difficult and failed obstetric airway; current perspectives on the use of tranexamic acid, fibrinogen concentrate and cell salvage; guidance on neuraxial placement in a thrombocytopenic obstetric patient; management of neuraxial drug errors, local anaesthetic systemic toxicity and unusually prolonged neuraxial block regression; and extracorporeal membrane oxygenation use in maternal cardiac arrest.

Correspondence to: A. Chau
Email: anton.chau@ubc.ca
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Twitter: @CharliePrior11; @Intrathecalcat; @antonchau1

Introduction

Anaesthetists play an essential role during obstetric emergencies, contributing knowledge and skills in resuscitation, human factors and critical care medicine to optimise maternal and fetal outcomes. In this review, we aim to provide a focused overview of the recent evidence and developments surrounding six key areas of obstetric emergencies: category-1 caesarean section; difficult and failed airway; massive obstetric haemorrhage; hypertensive crisis; emergencies related to neuraxial anaesthesia; and maternal cardiac arrest. Where possible, we have included practical clinical recommendations that anaesthetists can use in everyday practice, emphasising new data published within the last 5 y.

Methods

The search strategy is available in online Supporting Information (Appendix S1).

Category-1 caesarean delivery

The 2021 National Institute for Health and Care Excellence (NICE) caesarean birth guideline recommends a decision-to-delivery interval of within 30 min for category-1 caesarean sections, defined as emergency operative

delivery due to immediate threat to the life of the woman or fetus [1]. However, there is significant heterogeneity in how decision-to-delivery intervals are defined and measured. One proposed definition is to mark the start time as when the senior obstetrician decides that surgery is required and the end time as the time when the fetus (or first in the case of multiples) is delivered [2]. Using standardised interprofessional communication of the decision for surgery can improve team response and minimise medicolegal risks.

Failed neuraxial technique

Clear communication of the urgency of an emergency caesarean section is critical, as it can influence the decision to initiate general anaesthesia. One large prospective cohort study of 3115 women who received general anaesthesia for caesarean section in the UK found the most common reason for general anaesthesia was perceived threat to the life of the mother or neonate (52.1%), followed by failed neuraxial block (25.7%) and contraindications to neuraxial anaesthesia (14.9%) [3]. In a subset of patients with failed neuraxial block, conversion to general anaesthesia may potentially be avoidable. A systematic review of 54 randomised controlled trials found the overall prevalence of failed neuraxial anaesthesia requiring general anaesthesia conversion was 0.06% (95%CI 0.0–0.2%). Importantly, spinal or combined spinal–epidural anaesthesia was associated with a lower failure rate compared with epidural anaesthesia as a solo technique (10.2% vs. 30.3%) [4]. Given the time pressure associated with category-1 caesarean section and the potential lack of agency a woman may experience in voicing their concerns, the true prevalence may be higher. This highlights the importance of proactive management of labour epidurals, as well as careful testing of the block before incision [5]. Poor management of a failed neuraxial block resulting in pain is currently the most common successful medicolegal claim against obstetric anaesthetists [6]. Expert recommendations for the prevention and management of intra-operative pain during caesarean section under neuraxial anaesthesia have recently been published [6]. When neuraxial blocks fail to meet the patient's expectations, you should acknowledge the patient's concerns, stop the surgery if feasible and be ready to convert to general anaesthesia without delay. Failure to do so may lead to significant psychological trauma [7].

Preparation for safe general anaesthesia

In preparation for rapid sequence induction and intubation, there may be inadequate time for pre-oxygenation to reach the desired end-tidal oxygen fraction. Although studies on the use of high-flow nasal oxygen in the obstetric population have not demonstrated significant benefits over traditional facemask for pre-oxygenation (see Table 1) [8–12], there is likely to be a benefit during the apnoeic phase, which is logistically more difficult to study. A clinical surrogate of desaturation was explored in a study using high-fidelity computer simulated models of pregnant patients [13]. The findings illustrated a significant prolongation in time to onset of apnoea to SaO_2 90% of > 60 min in lower BMI 24 $mg.kg^{-1}$, even when the starting end-tidal oxygen fraction was at 60%. Moreover, the extent of the improvement is markedly attenuated during labour and with increasing BMI [13]. Since pre-oxygenation to end-tidal oxygen fraction > 90% may be difficult to achieve in patients during an emergency, this study provided valuable simulated information. Furthermore, computational modelling found only marginal improvement with this technique in high BMI parturients.

The increasing availability of sugammadex has led to some anaesthetists substituting succinylcholine with rocuronium as the primary neuromuscular block during obstetric general anaesthesia. Muscle relaxation has been shown to facilitate facemask ventilation [14] and front-of-neck airway access [15] in the event of difficult intubation. However, further research is needed to define the role of rocuronium in obstetrics. The use of opioids has traditionally been avoided due to concerns around neonatal respiratory depression, but a recent meta-analysis of 17 trials suggested that opioids are effective sympatholytic drugs. Those with shorter duration of action such as remifentanil 0.5–1 $mcg.kg^{-1}$ and alfentanil 7.5–10 $mg.kg^{-1}$ are safe and devoid of clinically significant adverse effects on the neonate. However, fentanyl 0.5–1 $mcg.kg^{-1}$ may cause a significant reduction in 5 min Apgar scores [16].

Accidental awareness during general anaesthesia (AAGA)

The largest multicentre prospective cohort study of obstetric general anaesthesia patients in the UK revealed an incidence of 1 in 212 (95%CI 122–147) for accidental awareness in caesarean deliveries, with one-third of patients meeting the criteria for post-traumatic stress disorder at 12 months. The study found a 42-fold increase in the odds of post-traumatic stress disorder after AAGA compared with non-AAGA controls [17]. Approximately 75% of the cases occurred during induction or emergence with risk factors including high BMI (25–30 $kg.m^{-2}$); low BMI (< 18.5 $kg.m^{-1}$);

Table 1 Summary of evidence for the use of high-flow nasal oxygen (HFNO) for pre-oxygenation in obstetric general anaesthesia.

Study	Study characteristics	Primary outcome	Result	Comment
Shippam et al. [8]	- Prospective, randomised, non-inferiority, physiological study - n = 40 healthy term parturients - HFNO 30–70 l.min^{-1} vs. tight facemask 15 l.min^{-1}	EtO_2 after pre-oxygenation via 2 methods: a) 3 min tidal volume breathing; b) 30 s tidal volume breathing then 8 vital capacity breaths	a) (estimated marginal means): - HFNO 87.4% (95%CI 85.5–89.2%) - facemask 87.4% (95%CI 85.5–89.2%) (p = 0.02) b) (estimated marginal means): - HFNO 85.9% (95%CI 84.1–87.7%) - facemask 91.8% (95%CI 90.1–93.4%) (p = < 0.0001)	HFNO performed worse than standard flow rate facemask
Tan et al. [9]	- Prospective, observational study - n = 73 healthy term parturients - 3 min tidal volume breathing with HFNO protocol (30 l.min^{-1} for 30 s, then 50 l.min^{-1} for 150 s)	Proportion of participants who achieved ETO_2 > 90% for the first expired breath after HFNO protocol	ETO_2 > 90% achieved in 60% of participants (95%CI 54–66%)	HFNO 30 l.min^{-1} for 30 s, then 50 l.min^{-1} for 150 s is inadequate for pre-oxygenation in pregnant women
Au et al. [10]	- Prospective, randomised, biased-coin up-down sequential allocation trial - n = 80 healthy term parturients - HFNO 50–70 l.min^{-1} (+/– simple facemask) vs. tight facemask 15 l.min^{-1}	Effective time-interval in 90% of subjects (EI90) to achieve an ETO_2 > 90% with tidal volume breathing	- EI90 facemask – 3.6 min (95%CI 3.3–6.7 min) - EI90 HFNO – not reached within 8 min Participants reaching ETO_2 > 90% after 4 min: facemask group – 100% HFNO alone – 67% HFNO + simple facemask – 80%	HFNO performed worse than standard flow rate facemask
Al-Sulttan et al. [11]	- Prospective, up-down sequential allocation study - n = 20 healthy term parturients - Pre-determined number of vital capacity breaths with HFNO 50 l.min-1 (with mouth open and closed) - Number of vital capacity breaths with facemask required to achieve ETO_2 > 90% recorded for each participant	Number of vital capacity breaths using HFNO to achieve ETO_2 > 90% in 90% of parturients (EN90) - EN90 for facemask pre-oxygenation was a secondary outcome	- Estimation of EN90 not achievable using HFNO – study terminated at 20 patients - With up to 20 vital capacity breaths, rate of achieving ETO_2 > 90% significantly better with facemask pre-oxygenation than with HFNO (p = 0.006 for mouth closed, p = 0.001 for mouth open)	HFNO performed worse than standard flow rate facemask
Tan et al. [12]	- Prospective, randomised, controlled, non-inferiority, crossover study - n = 62 patients, pregnancy>36 weeks - Simulated pre-oxygenation protocols with facemask and HFNO sequentially, order randomised - Both protocols for 3 min, HFNO up to 70 l.min^{-1}, facemask 10 l.min^{-1}	First EtO_2 concentration with a chosen non-inferiority margin of 5%	First EtO_2 concentration after HFNO protocol non-inferior to first EtO_2 concentration after facemask protocol (p = 0.025)	HFNO may be a suitable alternative to facemask oxygen for pre-oxygenation in late pregnancy

EtO_2, end-tidal oxygen.

out-of-hours procedures (20.00–08.00); and use of ketamine or thiopental for induction. Interestingly, only three out of 12 cases of AAGA were in patients undergoing category 1 caesarean section.

Recommendations to reduce the risk of AAGA include the use of propofol at ≥2.5 $mg.kg^{-1}$ for induction, with care not to under-dose at extremes of BMI, as well as the addition of a short-acting opioid adjunct at induction if readily available. When lower intravenous doses are used before paralysis, there is a risk of AAGA during the time interval before sufficient depth of inhalational anaesthesia is reached. If reduction of the volatile agent is required, ensure depth of anaesthesia using propofol or opioids. The use of an amnestic drug such as midazolam has also been suggested [18], but evidence of efficacy is lacking and the appropriate dose to prevent AAGA remains unknown so recommendations cannot be made. Recovery of neuromuscular function before waking should be confirmed routinely. In addition, direct screening questions for AAGA should be used routinely after general anaesthesia, given the high incidence, risk of psychological harm and likelihood of under-reporting [17].

Difficult and failed airway

A multicentre retrospective cohort study of patients undergoing caesarean section under general anaesthesia in the USA between 2004 and 2019 found the incidence of difficult intubation was 1 in 49 (95%CI 1:55–1:44) and the frequency of failed intubation of 1 in 808 (95%CI 1:1276–1:511) [19]. The UK data from 2017–2018 reported a frequency of difficult intubation of 1 in 19 (95%CI 1 in 16–22) and failed intubation of 1 in 312 (95%CI 1 in 169–667). Although heterogeneity in the definitions used makes it difficult to directly compare frequencies across different studies, both studies indicate that the incidence of difficult airway remains consistent and continues to be a significant concern. Failed intubations can lead to maternal mortality due to aspiration or hypoxaemia secondary to obstruction or oesophageal intubation [20]. The low rate of obstetric general anaesthesia in many centres has reduced exposure to difficult and failed intubation. Regular multidisciplinary participation in difficult airway simulations and designation of a local airway lead to implement current guidelines are strategies that could promote patient safety [21, 22].

`Can't ventilate, can't oxygenate´

A retrospective review of closed malpractice cases related to obstetric anaesthesia in the USA between 2005 and 2015 found failed intubation was among the top three most common causes of maternal death or brain injury, along with high neuraxial blocks and embolic events [23]. In the analysis of difficult and failed intubations, documentation on the use of videolaryngoscopy or other advanced airway devices was absent. A prospective, multicentre study in the UK also found that the use of videolaryngoscopy in obstetric units was low in comparison with other subspecialties [3]. While evidence from randomised controlled trials favouring videolaryngoscopy over direct laryngoscopy is lacking in obstetric anaesthesia [24], data from the non-obstetric population suggests that access to videolaryngoscopy as the first line for intubation should be prioritised [25, 26].

During a `can't ventilate, can't oxygenate´ scenario, persistence with tracheal intubation and failure to perform timely emergency front-of-neck airway access are common ingredients for catastrophic patient outcomes. Every obstetric anaesthetist should be skilled in performing emergency front-of-neck airway via a midline vertical incision using a scalpel-bougie-tube technique [27]. In patients with impalpable neck landmarks, there is evidence from a small observational study that pre-procedural airway ultrasound can assist in greater accuracy and speed in locating the cricothyroid membrane. During an emergency caesarean section, waking the patient is not always feasible or practical. One novel approach using supraglottic airway-guided flexible bronchoscopic intubation has been proposed as an alternative rescue technique for failed intubation in obstetrics [28]. However, this is not currently incorporated into national guidelines and is not recommended without experience.

Massive obstetric haemorrhage

Postpartum haemorrhage (PPH) is a leading cause of maternal morbidity and mortality worldwide, and its incidence is increasing [29, 30]. Uterine atony is implicated in 30–80% of all cases of PPH, but less common causes such as morbidly adherent placentas, uterine inversion and uterine rupture are also significant. Many cases occur in the absence of recognised risk factors, highlighting the constant need for systemic vigilance and preparedness [31].

Estimation of blood loss

Early recognition and management of PPH rely on accurate, real-time measurement of blood loss. Even with protocol-driven management in a high-resource setting, a response will only be triggered when visual estimated blood loss, or quantitative blood loss, using gravimetric or colourimetric methods, reaches a pre-determined threshold volume. At present, it is uncertain whether it is the use of quantitative

blood loss alone, or its inclusion within a dedicated PPH bundle, that leads to improved outcomes [32, 33]. Nevertheless, there is agreement that quantitative blood loss is more accurate and objective than visual estimation and that it can also increase the rate of PPH detection and earlier care escalation [34, 35]. The inaccuracy of estimated blood loss increases with increasing volume loss [36], making quantitative blood loss especially useful in an evolving, massive PPH.

Transfusion triggers and protocols

Blood transfusion is required in 0.5–3% of PPH and accounts for 1% of transfused blood products in high-income countries [37]. Transfusion decisions can be guided clinically by massive transfusion protocols which utilise a ratio-based transfusion that resembles that of whole blood. However, there are no high-quality trial data to support the use of fixed ratio transfusions in obstetrics and the empiric use of this approach might expose patients to unnecessary transfusion of plasma and platelets [38]. Early use of plasma is rarely required and may be harmful, including the risk of adverse reactions such as transfusion-related acute lung injury, a major cause of transfusion-related death [39]. Placental abruption is a risk factor for requiring early platelet transfusion, which is otherwise reserved until > 5000 ml of blood loss has occurred [38]. Institution-specific transfusion protocols are useful when the rate of blood loss is so rapid that it outpaces any attempt to request and administer blood products in an individualised manner.

Alternatively, transfusion decisions can be guided by laboratory results or point-of-care viscoelastic haemorrhage assays such as thromboelastography or rotational thromboelastometry. Viscoelastic testing can provide a quicker and more current snapshot of the coagulation profile for guiding plasma and coagulation product therapy during an evolving PPH [40, 41]. Some institutions have developed specific PPH transfusion protocols guided by viscoelastic assays [38, 41] but larger studies demonstrating the effectiveness of thromboelastography- or rotational thromboelastometry-guided treatment algorithms for PPH are needed to support their widespread clinical adoption.

Tranexamic acid

The use of tranexamic acid (TXA) was found to reduce death from bleeding in women with PPH in the World Maternal Antifibrinolytic (WOMAN) multicentre randomised trial involving 20,060 women from 23 countries (see Table 2) [42]. Based on this trial, the World Health Organization recommended all women with PPH after vaginal or caesarean delivery receive TXA 1g intravenously within 3 h of delivery. The borderline statistical significance of the primary outcome and the generalisability of the WOMAN trial data to high-income countries, where rates of death from haemorrhage are around 40 times lower than in low-income countries, remain in question [39]. However, there is evidence demonstrating its cost-effectiveness [43] and several national guidelines have recommended its use as part of the first response bundle for the treatment of PPH. Prophylactic TXA, in addition to prophylactic oxytocin administration for the prevention of PPH (i.e. administration after delivery, but before PPH is declared) has been investigated in two multicentre randomised placebo-controlled trials [44, 45], during vaginal and caesarean deliveries, respectively. In vaginal delivery, the study by Sentilhes et al. found the risk of PPH was similar between groups [44]. In caesarean delivery, the other study by Sentilhes et al. found the risk of PPH was significantly lower in the TXA group; however, there was no significant impact found on haemorrhage-related secondary outcomes including blood or iron transfusion, ICU admission or death [45]. Overall, current evidence supports the early administration of TXA 1g intravenously as an adjunct to aid control of PPH during caesarean section [45, 46], particularly in developing countries, with minimal adverse events. A higher TXA dose (4 g loading then 1 $g.h^{-1}$ for 6 h) has been studied but more safety data are needed [47]. The use of prophylactic TXA during vaginal delivery is not currently recommended [48]. Data from currently ongoing trials will provide insight into the impact of TXA in preventing PPH in women with anaemia [49, 50].

Fibrinogen concentrate

Fibrinogen levels during PPH are predictive of outcomes [38]. A fibrinogen level < 2 $g.l^{-1}$ early in PPH has a positive predictive value of 100% for a > 4 U of packed red blood cell transfusion [51]. Levels tend to fall below 4 $g.l^{-1}$ after 2 l blood loss and below 2 $g.l^{-1}$after 4 l loss [38]. Hypofibrinogenaemia can develop well before prolongation of the activated partial thromboplastin time/prothrombin time and thrombocytopenia, particularly after placental abruption [52–55]. Despite this, trials of empiric fibrinogen concentrate administration without laboratory testing in PPH > 1500 ml have been disappointing (Table 3) [56–58]. Using point-of-care viscoelastic assays during PPH to guide fibrinogen concentrate administration did not reduce transfusion rates or blood loss [56]. Overall, fibrinogen < 2 $g.l^{-1}$ is suggested as a cut-off for replacement with fibrinogen concentrate or cryoprecipitate as < 1.5 $g.l^{-1}$ is likely to be inadequate [38, 39].

Table 2 Studies of tranexamic acid (TXA) in the treatment and prevention of primary postpartum haemorrhage (PPH).

Study	Study characteristic	Primary outcome	Result	Conclusion
WOMAN Trial Collaborators [42]	- International randomised double-blind, placebo-controlled trial - n = 20,021 patients with PPH following vaginal delivery or CS - TXA 1g vs. placebo	Death due to bleeding	1.5% in TXA vs. 1.9% control, RR 0.81; (0.65–1.00, p = 0.045) If TXA given within 3 h of delivery 1.2% vs. 1.7%, RR 0.69; (0.52–0.91, p = 0.008).	TXA significantly reduced death due to bleeding Survival benefit decreased by 10% for every 15 min delay in TXA administration. Hysterectomy not reduced in TXA group
Sentilhes et al. [44]	- Multicentre double-blind randomised, placebo-controlled trial - n = 3891 patients - Vaginal delivery ≥35/40 weeks gestational age - Prophylactic TXA 1g in addition to oxytocin after vaginal delivery vs. placebo	Incidence of PPH ≥500 ml	8.1% in TXA vs. 9.8% control, RR 0.83; (0.68–1.01, p = 0.07)	No significant reduction in rates of PPH > 500 ml. Does not provide evidence for prophylactic TXA in vaginal delivery
Sentilhes et al. [45]	- Multicentre double-blind randomised, placebo-controlled trial - n = 4451 patients - CS before/during labour ≥34/40 weeks gestational age - TXA 1g or placebo	Composite: incidence of PPH > 1000 ml or transfusion within 2 days of delivery	26.7% in TXA vs. 31.6% control, RR 0.84; (0.75–0.94, p = 0.003)	TXA significantly reduced estimated blood loss >1000 ml or red blood cell transfusion within 2 days of delivery
Gungorduk et al. [46]	- Randomised, double-blind, placebo-controlled trial - n = 660 patients having elective CS - prophylactic TXA 1g vs. placebo before surgery	Estimated blood loss following CS	Mean estimated blood loss 499.9 ml in TXA vs. 600.7 ml control, p < 0.001 Estimated blood loss >1000 ml: 2.1% in TXA vs. 5.8% control, RR 2.7; (1.1–6.3, p < 0.03). Use of additional uterotonics 8.5% in TXA vs. 14.5% in control vs. RR 1.7; (1.1–2.6, p = 0.02)	TXA significantly reduced blood loss No significant difference in maternal or neonatal outcomes. No thrombotic events
Ducloy-Bouthors et al. [47]	- Multicentre, open-label randomised, controlled trial - n = 144 patients, inclusion when PPH > 800 ml after vaginal delivery - randomised to high dose TXA (4 g loading then 1 $g.h^{-1}$ for 6 h) vs. none	Total blood loss volume from inclusion (at PPH > 800 ml) until 6 h after inclusion	Median blood loss 173 ml in TXA vs. 221 ml control, p = 0.041; TXA group had reduced evolution to severe PPH, p = 0.028; Hb drop >4 $g.dl^{-1}$, p ≤ 0.001 and number of packed red blood cells transfused before day 42, p ≤ 0.001	High-dose TXA significantly reduced blood loss Not powered to address safety concerns
Ker et al. [49]	- International multicentre double-blind randomised controlled trial - n = 10,000 patients with moderate to severe anaemia (Hb < 100 $g.l^{-1}$ or packed cell volume < 30%) having vaginal delivery - TXA 1g or placebo within 15 min of vaginal delivery	Proportion of women with a clinical diagnosis of primary PPH	Recruiting	ClinicalTrials.gov NCT03364491

(continued)

Table 2 (*continued*)

Study	Study characteristic	Primary outcome	Result	Conclusion
Arribas et al. [50]	- Prospective, randomised, open-label trial - n = 120 patients - Patients with ≥1 risk factor for PPH having CS - 1 g TXA intravenous, 1 g TXA intramuscular, 4 g TXA orally or no TXA 1 h pre-CS	Maternal blood TXA concentrations over time	Recruiting	ClinicalTrials.gov NCT04274335

CS, caesarean section; Hb, haemoglobin; RR, risk ratio; TXA, tranexamic acid.

Cell salvage

In a large pragmatic randomised controlled trial involving 26 obstetric units in the UK, no case of amniotic fluid embolism was identified among the 1517 women who received intra-operative cell salvage for caesarean section. [59] Similarly, observational data over 10 y on 1170 women who had reinfusion of cell salvage blood demonstrated no clinical safety concerns [60]. Evidence on reduction of allogeneic blood transfusion and cost-effectiveness do not support the routine use of cell salvage [61, 62] and many institutions currently reserve the use of cell salvage in high-risk bleeding cases such as morbidly adherent placentas, with or without leukocyte depletion filters. A leukocyte depletion filter is highly effective at removing white blood cells and squamous cells [63]; however, its use is controversial as it has been associated with acute hypotension.

Data are emerging for utilising cell salvage during vaginal delivery. In a large case series describing 64 patients with severe haemorrhage (median quantitative blood loss 2150 ml) who were reinfused with vaginally shed blood, there were no cases of maternal sepsis or severe infectious morbidity. There was one case of suspected amniotic fluid embolism, but symptoms began before reinfusion of vaginally shed blood. Further studies using a randomised design and a control group are needed [64].

Placenta accreta spectrum

Placenta accreta spectrum is a leading cause of major obstetric haemorrhage and the incidence has increased from 0.03 per 1000 pregnancies in the 1950s to 0.79–3.11 per 1000 pregnancies [65]. The most important risk factors are the number of previous caesarean deliveries and placenta previa, the latter increasing the risk by 35–65 fold [66]. However, some cases are unexpected and first recognised during caesarean delivery.

There is no consensus on the optimal anaesthetic technique and multiple clinical and institutional factors may influence these choices [67]. The key to successful management is anticipating the need for rapid and massive transfusion. In a systematic review of 7001 cases of placenta accreta spectrum, peripartum hysterectomy occurred in 52.2% (95%CI 38.3–66.4%), and blood transfusion occurred in 46.9% (95%CI 34.0–59.9%) [68].

There are minimal data on prophylactic placement of vascular occlusion devices such as the resuscitative endovascular balloon occlusion of the aorta (REBOA) technique or internal iliac balloon catheters in obstetrics. Prophylactic placement of REBOA in zone 3 of the aorta can result in significant hypertension (systolic blood

Table 3 Randomised controlled trials of fibrinogen concentrate treatment in postpartum haemorrhage.

Study	Study characteristics	Primary outcome	Result	Conclusion
Collins et al. [56]	- Randomised placebo-controlled trial - n = 663 patients enrolled with postpartum haemorrhage 1000–1500 ml, randomised if Fibtem A5 < 15 mm and continued bleeding - 55 randomised to fibrinogen concentrate 3 g or placebo	Transfusion of packed red blood cells, cryoprecipitate and platelets	58 units in fibrinogen concentrate group (mean transfusion rate 2.07) vs. 75 units in control group (mean transfusion rate 2.78); adjusted Incidence rate ratio 0.72; (0.3–1.7, p = 0.45)	No difference in transfusion rates or blood loss. Fibrinogen concentrate group had trend to reduced bleeding in Fibtem A5 < 12 mm. No thromboembolic events
Wikkelso et al. [57]	- Multicentre, double-blind, parallel randomised controlled trial - n = 249 patients with severe postpartum haemorrhage ≥ 1500 ml randomised to 2 g fibrinogen concentrate pre-emptively at estimated blood loss 1500 ml or placebo	Transfusion of packed red blood cells up to 6 weeks postpartum	Transfusion rate 20% in fibrinogen concentrate vs. 22% control, risk ratio 0.95; (0.58–1.54, p = 0.88) despite significant increased fibrinogen concentration in fibrinogen concentrate group	No significant difference in primary or secondary outcomes Only 2.2% patients had a fibrinogen level < 2 $g.l^{-1}$ - 15% subjects could not be consented due to the severity of bleeding
Ducloy-Bouthors et al. [58]	- Multicentre, double-blind, randomised placebo-controlled trial - n = 437 patients with persistent postpartum haemorrhage after vaginal delivery requiring prostaglandins - 3 g fibrinogen concentrate within 30 min of prostaglandins vs. placebo	Failure as a composite primary efficacy endpoint: at least 4 $g.dl^{-1}$ of Hb decrease and/or transfusion≥2 units of packed red blood cells within 48 h of fibrinogen concentrate	40% in fibrinogen concentrate vs. 42% control group. OR 0.99 (0.66–1.47; p = 0.96)	No significant difference in primary or secondary outcomes No thromboembolic events in fibrinogen concentrate group

pressure > 160 mmHg) at deployment, and hypotension requiring vasopressor at removal [69]. For patients at imminent risk of exsanguination, REBOA by an obstetrician trained in using the device may assist with resuscitation and minimise blood transfusion, although the risk of arterial thrombotic and ischemic complications have limited the use of this technique [70]. By contrast, prophylactic placement of iliac balloon catheters has been associated with a better safety profile but the efficacy in reducing peripartum blood loss is marginal, perhaps due to extensive collateral supply or balloon migration [71, 72].

Hypertensive crisis

Women with pre-eclampsia are susceptible to hypertensive emergencies, increasing the risk of intracranial haemorrhage and other serious maternal complications such as heart failure [73]. Systolic blood pressure ≥ 160 mmHg or diastolic blood pressure ≥ 110 mmHg on two separate occasions at least 4 h apart is a feature of severe pre-eclampsia [74]. Severe systolic hypertension is more consistently predictive of adverse cerebral events than severe diastolic hypertension [75]. Haemodynamic heterogeneity between those with early and late onset severe pre-eclampsia is increasingly recognised. The use of transthoracic echocardiography may help to identify these distinct phenotypes and guide fluid and pharmacological therapy [76, 77]. When blood pressure is persistently uncontrolled and unresponsive to antihypertensives, expedited delivery is indicated irrespective of gestational age [74].

Neuraxial procedures and pre-eclampsia/HELLP syndrome

Timely planning and provision of neuraxial analgesia may contribute to blood pressure management in patients with pre-eclampsia. However, the development of thrombocytopenia and coagulopathy in severely pre-eclamptic patients can complicate or contraindicate neuraxial placement. Evidence for precise thresholds for safe neuraxial insertion is limited due to a low incidence of adverse events and few cases involving very low platelet counts. Recent practice recommendations from the Society for Obstetric Anesthesia and Perinatology suggest that the risk of epidural haematoma with neuraxial procedures is likely to be low with platelet counts > $70 \times 10^9.l^{-1}$. In patients with HELLP syndrome, verifying platelet counts 6 h before the neuraxial procedure should be considered [78]. Recommendations from the Association of Anaesthetists suggest using a threshold of > $75 \times 10^9.l^{-1}$ and checking the platelet count 6 h before neuraxial procedures for all patients with pre-eclampsia, with the addition of coagulation tests when platelets are < $100 \times 10^9.l^{-1}$ [79]. Determining the risk of epidural haematoma is an inexact science and decisions must be balanced against the risk associated with general anaesthesia on a case-by-case basis. Potential complications of general anaesthesia, including hypertensive surge during laryngoscopy, stroke and intracranial haemorrhage are leading causes of morbidity and mortality in the pre-eclamptic population.

Eclampsia

Eclampsia is caused by vasogenic oedema secondary to acute severe hypertension, resulting in encephalopathy and seizures [73]. The most common symptom preceding seizures is headache, often described as throbbing or pounding. Focal neurological deficits are not usually present [80]. Abrupt loss of consciousness is followed by a generalised tonic–clonic seizure, which may lead to maternal hypoxia and aspiration. Transient fetal bradycardia is common during and immediately after an eclamptic seizure. However, persistent fetal bradycardia may signify an occult placental abruption necessitating immediate delivery [81].

Evidence is well established for the administration of magnesium sulphate in women with eclampsia or pre-eclampsia with severe features; the number needed to treat to prevent one seizure is approximately 50 [82]. The evidence is less clear in asymptomatic cases (number needed to treat approximately 100) [82]. An intravenous bolus of 4 g and infusion of 1 $g.h^{-1}$ is typically used. A recent systematic review and meta-analysis of 10 randomised controlled trials found that a shorter duration (< 12 h) of magnesium sulphate was not associated with an increased risk of eclamptic seizures compared with the standard 24 h regimens [83]. However, external validity is limited due to significant heterogeneity across studies (71%) and data remain underpowered to draw firm conclusions.

Acute neurological complications and neuro-imaging

Severe pre-eclampsia can predispose women to cerebral hypoperfusion (i.e. stroke), vasogenic cerebral oedema (i.e. posterior reversible encephalopathy syndrome) and cerebral vasoconstriction (i.e. reversible cerebral vasoconstriction syndrome). Any acute neurological deterioration constitutes an emergency. Neuro-imaging is an essential part of evaluation regardless of cause, and the appropriate modality based on suspected pathology should be discussed with a neurologist or neuroradiologist. Iodinated computed tomography contrast may be given in pregnancy with minimal risk to the fetus [84]. Gadolinium

contrast is generally avoided in pregnancy due to limited fetal data but there is consensus that its use can be considered if the diagnostic value may significantly improve maternal and fetal outcomes [85].

Emergencies related to neuraxial anaesthesia

Neuraxial drug errors

The incidence of wrong drug errors involving obstetric neuraxial procedures is very low but may be under-reported. Fortunately, most wrong drug neuraxial errors are successfully managed with supportive measures alone and do not result in permanent adverse sequelae. Three notable exceptions for drugs commonly used in obstetrics are thiopentone, chlorhexidine and TXA, which have resulted in cauda equina syndrome, catastrophic irreversible neurological impairment, and death due to refractory ventricular arrhythmias, respectively [86–88]. Recommended interventions to prevent errors include a careful reading of all ampoule and syringe labels, strategically storing the drugs in a way to prohibit errors, proper labelling of all syringes, second person checks and, recently, the use of non-Luer lock devices for all neuraxial procedures [86, 89].

Wrong route errors are more common, typically occurring in the context of an unrecognised intrathecal or subdural catheter. This may lead to high neuraxial block, respiratory depression and hypotension or in the case of total spinal, loss of consciousness, apnoea and cardiovascular collapse, with associated severe fetal compromise. This is a potentially devastating complication, usually necessitating emergency caesarean delivery under general anaesthetic with appropriate cardiovascular support. Where rapidly advancing block due to inadvertent intrathecal injection is immediately recognised, the successful use of emergency cerebrospinal fluid lavage (intermittent aspiration of cerebrospinal fluid and injection of saline) with 40 ml of sterile preservative-free normal saline has been described [90]. Cerebrospinal fluid lavage has also been performed for treatment of inadvertent wrong drug administration [87]. Due to the rarity of these emergency situations, trials to help inform the optimum type of lavage solution, volume and duration to be utilised are difficult to conduct and thus anaesthetists should consider cerebrospinal fluid lavage on a case-by-case basis.

Local anaesthetic systemic toxicity

Physiological changes of pregnancy (i.e. increased cardiac output, reduced plasma levels of α_1-acid glycoprotein, and engorgement of epidural veins) lead to relatively rapid local anaesthetic absorption, high peak free local anaesthetic concentrations and increased risk of intravascular migration of epidural catheters. These changes can predispose parturients to local anaesthetic systemic toxicity [91]. All obstetric anaesthetists should be familiar with therapeutic protocols for local anaesthetic systemic toxicity; the 2020 American Society of Regional Anaestheisa and Pain Medicine version has been published [92]. On recognition or suspicion of toxicity, emphasis should be placed on appropriate airway support followed by rapid administration of 20% lipid emulsion and subsequent seizure control and cardiovascular support. In contrast to earlier guidance that advised the administration of intravenous lipid emulsion therapy at the first sign of rapid deterioration, arrhythmia or prolonged seizure, current guidelines unequivocally recommend early lipid emulsion therapy after airway management in any suspected local anaesthetic systemic toxicity event judged to be potentially serious [93].

Neuraxial block regression

Serious complications including epidural haematoma, abscess or cauda equina syndromes resulting in permanent neurological injuries are rare. However, when they occur, they may require emergency neurosurgical intervention as recovery is time-dependent (e.g. decompression within 8 to 12 h in the case of epidural haematoma) [94]. Timely identification of these complications is challenging as early signs of nerve injury overlap with normal clinical signs of residual block and limited access to imaging out-of-hours. In recognition of these difficulties and the potentially devastating consequences of missed or delayed diagnoses, the Association of Anaesthetists has recently produced practice guidelines for assessment and escalation. As a screening tool, patients who are unable to straight-leg raise at any point after initiation of neuraxial analgesia, or from 4 h after the last neuraxial anaesthetic dose, should be formally assessed by an anaesthetist [94]. Quality improvement initiatives such as the application of an alert bracelet on neuraxial placement that is subsequently removed if patients can perform straight-leg raise but left on for those who cannot, may assist with the implementation of these important recommendations.

Maternal cardiac arrest

Approximately 1 in 12,000 admissions for delivery in the USA ends in cardiac arrest and the incidence appears to be increasing [95]. The prospective descriptive study by Beckett et al., using the UK Obstetric Surveillance System, captured 66 peripartum cardiac arrests over

three years (1:16,000). Almost a quarter (15/66) were precipitated by airway and neuraxial complications. Maternal and neonatal survival rates were 58% and 71%, respectively; a delay in perimortem caesarean section > 5 min was associated with maternal death [96]. A high perimortem caesarean section (74%, 49/66) rate was observed, attributed in part to the influence of obstetric-specific skills programmes, such as the Managing Obstetric Emergencies and Trauma course [96].

Extracorporeal membrane oxygenation (ECMO) is an option in cases of severe cardiac or respiratory failure or cardiac arrest in the peripartum period. In a systematic review of 90 case reports of ECMO use in 97 pregnant or postpartum patients, the maternal and neonatal survival rates were 90.7% (88/97) and 83.3% (80/96, one undocumented), respectively. Haemorrhage was the most frequently reported complication, with others including infections, atrial fibrillation, renal impairment and generalised myopathy. Survival was better for cardiac than respiratory indications [97]. Overall, ECMO is feasible in late pregnancy and has the potential for good outcomes in advanced, severe maternal disease and cardiac arrest. However, more studies are needed due to the likelihood of publication bias towards cases with favourable outcomes.

Conclusion

Emergencies in obstetrics pose a unique challenge to obstetric anaesthetists because they are typically rare, high acuity and dynamic, with the potential for rapid deterioration. The recent publication of the Ockenden report in the UK is a timely reminder of the importance of multidisciplinary teamwork and training in all maternity units, providing an impetus to consolidate and develop the role of obstetric anaesthetists as `peripartum physicians´ [98]. Multidisciplinary training and simulation can improve outcomes in many emergencies and obstetric anaesthetists have a central role within the multidisciplinary team in enhancing a culture of peri-delivery safety.

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Supporting Information

Additional supporting information may be found online via the journal website.

Appendix S1. Search strategy.