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REVIEW ARTICLE

What's new in obstetric anesthesia in 2017?

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ABSTRACT
The Gerard W. Ostheimer lecture is delivered every year at the annual meeting of the Society for Obstetric Anesthesia and Perinatology. The lecture aims to provide the anesthesiologist who provides obstetric anesthesia care with a review of the most relevant articles that were published in the preceding calendar year. This article highlights the literature published in 2017 related to maternal mortality, maternal cardiac arrest, cesarean delivery and labor analgesia.

Introduction

Every year, the Board of Directors of the Society for Obstetric Anesthesia and Perinatology selects one individual to review the prior calendar year's literature and identify articles that are most relevant to the anesthesiologist who provides obstetric anesthesia care. The literature surveyed covers the domains of obstetric anesthesia, obstetrics, perinatology and health services research. This review is presented at the annual meeting of the Society for Obstetric Anesthesia and Perinatology in the Gerard W. Ostheimer Lecture entitled "What's New in Obstetric Anesthesia". This article summarizes some of the content of the lecture that was delivered at the 2018 annual meeting in Miami, Florida. It has a focus on maternal mortality, maternal cardiac arrest, cesarean delivery, complications of neuraxial analgesia and remifentanil for labor analgesia.

Maternal mortality in the USA and UK

There has been increasing concern about the rate of maternal mortality in the United States of America (USA). Specifically, the rate of maternal death is higher than that of other developed countries and appears to be rising. Concerns have been raised, however, about the quality of the USA data, casting doubts on whether mortality is actually increasing or whether this rise is an artifact resulting from better case ascertainment. In fact several changes have been implemented that may improve surveillance, including the introduction of the pregnancy check-box on the 2003 version of the death certificate, the use of record linkage and the introduction in 1999 of a new International Classification of Diseases, 10th Revision (ICD-10) codes for underlying causes of death.

Joseph et al.[1] performed a retrospective cohort study using data from the National Center for Health Statistics and the Wide-ranging Online Data for Epidemiologic Research (WONDER) database from the Centers for Disease Control and Prevention (CDC). The database provided information on maternal deaths and live births from 1993 to 2014. According to these data the maternal mortality ratio (MMR) increased from 7.55 per 100 000 live births in 1993 to 28.2 per 100 000 live births in 2014. However, when examining the underlying causes of deaths between 1999 and 2014, the reported increase in maternal deaths was mainly from the introduction of two new ICD-10 codes (O26.8: primarily renal disease; and O99: other maternal diseases classifiable elsewhere). Exclusion of deaths from those codes abolished the temporal increase in mortality between 1999 and 2014 [relative risk (RR): 1.09, 95% CI 0.94 to 1.27]. A regression analysis adjusting for improvement in surveillance also abolished the temporal increase in MMR [adjusted relative risk (aRR) 2013 compared with 1993: 1.06, 95% CI 0.90 to 1.25].

MacDorman et al.[2] also used data from the CDC WONDER database to examine trends in maternal mortality between the years 2008–2009 and 2013–2104 in the 27 states and the District of Columbia that had adopted the pregnancy check-box on USA death certificates by 2008. There was a 23% increase in maternal mortality rate from 20.6 deaths per 100 000 live births in 2008–2009 to 25.4 deaths per 100 000 live births in

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2013–2014. Using a number of sensitivity analyses, they suggested two possible data quality issues that could incorrectly inflate the MMR. The first related to possible over-reporting of deaths for women ≥40 years-of-age, with maternal mortality rates increasing by 90% for this age group despite no significant change for those ≤40 years. In fact, the increased mortality in the older cohort of women accounted for the overall rise in maternal mortality between the two time periods. The second potential data quality issue related to a 48% increase in maternal mortality from non-specific causes of death, when there was no increase in mortality from specific causes.

Davis et al.[3] evaluated the impact of the pregnancy check-box and increasing maternal age on changes in MMR from 1978 to 2012. They found a 15% increase in MMR between 1998 and 2002 in the 11 states that had not adopted the pregnancy check-box by the end of 2012 (from 8.6 to 9.9 deaths per 100 000), compared to more than doubling of MMR (from 9.0 to 22.4 death per 100 000; 150% increase) in the 23 states that had adopted the pregnancy check-box. Women ≥40 years-of-age had a 528% relative increase in MMR (from 31.9 to 200.5), accounting for approximately one-third of the overall increase within states that had adopted the pregnancy check-box, whereas there was no change in MMR in women of the same age group in states that had not adopted the check-box. The increase in MMR was due to increase in age-specific mortality rather than an increase in maternal age. Assuming that the true increase in maternal deaths resulting from improved identification was reflected by the relative percentage increase in deaths in women <40 years-of-age and applying this observed increase to women ≥40 years-of-age, the authors calculated the expected deaths in the ≥40 years age group. The difference between observed and expected deaths revealed that 28.8% of the observed change was potentially due to maternal death misclassification among women ≥40 years-of-age.

Data from the CDC Pregnancy Mortality Surveillance System indicate that the MMR in the USA has increased from 7.2 deaths per 100 000 live births in 1987 to 16 deaths per 100 000 live births in 2006–2010.[4] This ratio was unchanged in the most recent report of maternal deaths in 2011–2013,[5] with 2009 pregnancy-related deaths identified for a MMR of 17 deaths per 100 000 live births. Each individual in the USA is classified as having one of the following ethnicities: Hispanic or non-Hispanic: and one of the following racial groups: American Indian/Alaskan native, Asian, Native Hawaiian or Other Pacific Islander, Black or African American, White, or more than one race. The profound racial-ethnic disparities and socio-economic inequalities that were highlighted in previous reports (1987–2010) were still evident in 2011–13, with non-Hispanic black women having a 3.4 times higher risk of death compared to non-Hispanic white women. More than half of Hispanic women (53.9%) and those of other races (55.5%) who died from pregnancy complications were born outside the USA, compared to 3.1% of non-Hispanic white women and 8.2% of non-Hispanic black women. Mortality increased with maternal age, with 30% of women who died from pregnancy-related complications being ≥35 years-of-age despite the fact that only 15% of births were to women in this age group. Obesity was also a factor, with one in six women who died having a pre-pregnancy body mass index (BMI) in the obese range (≥30 kg/m^2). Similar to data from 2006 to 2010, cardiovascular conditions (15.5%) and non-cardiovascular medical conditions (14.5%) were the leading causes of death, followed by infection (12.7%), hemorrhage (11.4%) and cardiomyopathy (11%). Therefore, cardiovascular conditions, including cardiomyopathy, accounted for 26.5% of all maternal deaths. Compared to data from prior to 2006–2010, death from hemorrhage, hypertensive disorders of pregnancy and anesthesia complications declined, while mortality from cardiovascular disease, cerebrovascular accidents and other medical conditions increased. The above studies thus suggest that better case ascertainment has contributed, at least in part, to the reported rise in maternal mortality. They also highlight concerns about the quality of data, suggesting possible misclassification of maternal deaths that artificially inflate the MMR, particularly in women ≥40 years of age.

In the United Kingdom (UK), the maternal death rate in the most recent MBRRACE-UK (Mothers and Babies: Reducing Risk through Audit and Confidential Enquiries in the UK) report covering the years 2013–2015 was 8.76 per 100 000 maternities,[6] which was unchanged from the rate for 2010–2012. There was a statistically significant 23% decrease in maternal mortality from indirect causes compared to 2010–2012, mainly due to a decrease in death from influenza and maternal sepsis. Similar to the USA, cardiac disease remained the leading cause of maternal deaths at a rate of 2.34 per 100 000 maternities. Thromboembolic complications remained the leading cause of direct maternal deaths. Hemorrhage was the second most common cause of direct maternal death with a small, but not statistically significant, increase related to hemorrhage in association with abnormal placentation.

While trauma among pregnant women is common, little is known about the impact of trauma on maternal mortality, since accidental and incidental causes of death are not included in the World Health Organization (WHO) or CDC definitions of maternal mortality. In a retrospective study including 1148 trauma events among pregnant females and 43 608 trauma events among non-pregnant females of reproductive age (14–49 years), and using the Pennsylvania Trauma Outcome Study database from 2005 to 2015, Desphande et al.[7]

reported that pregnant females were twice as likely to experience violent trauma and had a 1.6-fold higher risk of death compared to non-pregnant controls. They were 2.3 times more likely to be dead on arrival and 1.8 times more likely to die during hospitalization compared to non-pregnant women. Pregnant women from an ethnic minority and those without health insurance were more likely to experience violent trauma, which was associated with 3.14-fold higher mortality compared to non-violent trauma. The authors calculated that trauma-related deaths would comprise 18.3% of all maternal deaths in Pennsylvania if included in the vital statistics for the state. The anatomical and physiological changes of pregnancy, in addition to system level factors, may be responsible for the increased trauma-related mortality and this underscores the importance of multidisciplinary training in the care of obstetric trauma patients. Possible system level factors include lack of organizational protocols or structure for rapid availability of experienced providers and inadequate training or unfamiliarity of emergency room providers with obstetric trauma patients. Obstetric anesthesiologists, with their expertise in airway and hemodynamic management of the pregnant woman, should play a key role as members of the obstetric trauma teams.

Maternal cardiac arrest

Using the UK Obstetric Surveillance system, Beckett et al.[8] performed a prospective descriptive study to identify women who had a cardiac arrest during pregnancy in the UK from 2011 to 2014. They reported details about perimortem cesarean delivery in this cohort. All women who underwent basic life support in pregnancy were included and the study identified 66 cases of cardiac arrest for an incidence of 1 in 36 000 maternities. Fifty-eight percent of mothers and 71% of babies survived. Perimortem cesarean delivery was performed in 49 of the 66 cases, with the time to performance being significantly shorter in women who survived compared with those who died [median (IQR) 3 (0, 39) vs 12 (0, 67) min, P=0.01]. Survival was more likely when women were not moved from the site of collapse and for inpatient arrests (compared with those occurring outside the hospital). This was likely related to the delay in performance of a perimortem cesarean delivery when cardiac arrest occurred at home. This study therefore provides strong evidence in support of current recommendations for the timely performance of perimortem cesarean delivery within 5 minutes of cardiac arrest if there is no return of spontaneous circulation. Anesthetic complications were the most common cause of cardiac arrest, accounting for 24% of cases in this report, but all those women were successfully resuscitated. Seventy-one percent (14/17) of the women who had an anesthetic-related cardiac arrest were obese and the causes of death were problems with tracheal intubation (n = 3), cardiovascular collapse after an epidural top-up (n = 3), total spinal after a spinal anesthetic (n = 10), or other causes (n = 1). This highlights the known challenges of airway management in obese parturients as well as the need for careful dosing of neuraxial techniques in this patient population. Following anesthetic causes, the three most common causes of cardiac arrest in the study were amniotic fluid embolism, hypovolemia, and thrombo-embolic complications.

Balki et al.[9] performed a retrospective population-based cohort study to describe the epidemiology of cardiac arrest among pregnant women hospitalized for delivery, using data from the Canadian Institute for Health Information Discharge Abstract Database from April 1, 2002 to March 31, 2015. There were 286 cases of maternal cardiac arrest among 3 568 597 hospitalizations for delivery, for an incidence of 1:12 500 deliveries. This is comparable to the incidence reported in the USA[10] but higher than that reported in the UK study mentioned previously.[8] The percentage of women who survived to hospital discharge was 71.3%, which is comparable to the 70% survival reported in the UK study. The most common etiologies of cardiac arrest were postpartum hemorrhage, heart failure, amniotic fluid embolism and complications of anesthesia. Anesthetic complications were reported in 28 women (10%), of whom three had aspiration pneumonia, and three had failed or difficult tracheal intubation. Similar to the UK study, all women experiencing a cardiac arrest due to an anesthetic complication were successfully resuscitated. The most common diagnoses associated with cardiac arrest included pregnancy-related medical conditions such as hypertensive disorders of pregnancy and gestational diabetes, as well as obstetric conditions such as abnormal placentation.

Cesarean delivery

Anesthesia for emergency cesarean delivery in women with a difficult airway

The choice of anesthetic technique for women needing emergency (category I) cesarean delivery for non-reassuring fetal status is challenging. General anesthesia in the parturient carries the risk of difficult tracheal intubation, which is associated with the complications highlighted in the above-mentioned studies of cardiac arrest during pregnancy. On the other hand, prolonged attempts at establishing neuraxial anesthesia increase the risk of neonatal morbidity and mortality. Krom et al.[11] performed a decision analysis study to quantify the time taken to establish anesthesia for emergency cesarean delivery in a parturient with a difficult airway who does not have an existing epidural catheter and to estimate probability of failure of three possible anesthetic approaches, namely rapid sequence induction of general anesthesia using rocuronium and video-laryngoscopy, awake fiberoptic intubation and rapid

spinal anaesthesia. Their analysis showed a shorter mean (95% CI) time to establishing anesthesia with rapid sequence induction compared with awake fiberoptic intubation [1.7 (1.5–1.9) min vs 9 (7–11) min, $P<0.0001$] or spinal anaesthesia [6.3 (5.4–7.2) min, $P<0.0001$]. They estimated the risk of a failed airway after rapid sequence induction to be 21 (0–53) per 100 000 cases or 1 in 4761 cases. While this analysis is based on a comprehensive and systematic review of the literature, several assumptions had to be made and the analysis does not consider the context of stress in the setting of a category I cesarean delivery. Since no randomized controlled trials will ever be conducted to answer this question, this analysis does provide useful guidance for the practicing obstetric anesthesiologist dealing with this challenging scenario.

Left lateral tilt during cesarean delivery

It is currently recommended that women undergoing cesarean delivery be placed in a left lateral tilt position to avoid the supine position that could lead to aorto-caval compression with subsequent maternal hypotension and a reduction in utero-placental perfusion.[12] Some studies reported improved neonatal acid base status with the tilt position compared to the supine position.[13,14] However, those older studies predated the current practice of using a prophylactic phenylephrine infusion and a fluid co-load for the management of spinal anesthesia-induced hypotension. Therefore, Lee et al.[15] randomized 100 healthy women with uncomplicated pregnancies to be placed in a 15 °C left lateral tilt or the supine position. All patients received a standardized spinal anesthetic including a prophylactic phenylephrine infusion titrated to maintain systolic blood pressure at baseline. The primary outcome of the study, umbilical artery base excess, was not significantly different between the supine and left lateral tilt groups (mean $\pm$ SD -0.5 ± 1.6 vs -0.6 ± 1.5 mM). However, during the 15 min after spinal injection, systolic blood pressure and cardiac output were significantly lower in the supine group compared to the left lateral tilt group, despite the supine group receiving 29% more phenylephrine. Therefore, while neonatal acid base status was not negatively impacted in the supine position in this study, maternal hemodynamics were significantly better in the left lateral tilt group. The results might also not be applicable to high-risk pregnancies such as women with obesity or utero-placental insufficiency, so more studies are needed in those patient populations.

Enhanced recovery after cesarean delivery

There has been an increased interest in enhanced recovery after cesarean delivery protocols. Many components of those enhanced recovery protocols were investigated in studies published in 2017, including delayed cord clamping, antibiotic prophylaxis and postoperative analgesia.

Delayed cord clamping

While in 2012 the American College of Obstetricians and Gynecologists (ACOG) stated that there was insufficient evidence to recommend delayed cord clamping in term infants,[16] the committee opinion was updated in 2017[17] and now recommends delayed cord clamping for all vigorous term and preterm infants unless there are maternal or fetal indications for immediate clamping such as hemorrhage or need for resuscitation. The document notes the benefits to term infants, including higher hemoglobin levels at birth and increased iron stores in the first few months of life, but also states that there might be a small increase in the risk of jaundice requiring phototherapy. In preterm infants, benefits include improved transitional circulation, reduced blood transfusion requirement and decreased risk of necrotizing enterocolitis and intraventricular hemorrhage. The document also states that delayed cord clamping does not increase the risk for postpartum hemorrhage and should not interfere with the management of the third stage of labor or administration of uterotonics after delivery. However, the optimal timing of uterotonic agents in relation to umbilical cord clamping needs further study according to the opinion of this committee. Delayed cord clamping is now included in many of the protocols for enhanced recovery after cesarean delivery. Whether this specifically impacts mortality in preterm infants is, however, not clear. Tamow-Mordi et al.[18] performed a large multicenter randomized controlled study involving 1566 newborns who were born before 30 weeks' gestation, to assess if delayed cord clamping would confer benefits in preterm infants with respect to mortality and major morbidity. There was no significant difference in the incidence of the primary outcome (death or major morbidity by 36 weeks of postmenstrual age) between delayed (60 s or more after delivery) and immediate (within 10 s of delivery) clamping groups (37.0% vs 37.2%). The mortality was 6.4% in the delayed-clamping group and 9.0% in the immediate-clamping group ($P=0.03$ in unadjusted analyses; $P=0.39$ after post hoc adjustment for 13 secondary outcomes). There were also no significant differences between the two groups in the incidence of chronic lung disease or other major morbidities, but peak hematocrit levels were higher by 2.7% in the delayed clamping group.

Wound infection

Obesity is a known risk factor for surgical site infection in women undergoing cesarean delivery, despite timely pre-incisional antibiotic prophylaxis. Valent et al.[19] performed a single center randomized double-blind placebo-controlled study investigating the impact of postoperative administration of oral cephalexin 500 mg and metronidazole 500 mg vs placebo 8 hourly, for

48 hours following cesarean delivery, in 404 obese women who had received intravenous preoperative prophylaxis with 2 g cephazolin (a first-generation cephalosporin). Randomization was stratified by whether membranes were intact or ruptured prior to delivery. The primary outcome of surgical site infection was significantly lower in the intervention group compared with the placebo group (6% vs 15%, P=0.01, number needed to treat 12). Exploratory subgroup analysis suggested a reduction in surgical site infection with the intervention in those who had prior rupture of membranes, constituting about 31% of patients in both groups, but not in those with intact membranes. The study however was a single center study and the impact of this strategy on breastfed neonates, development of resistant microorganisms, as well as its cost-effectiveness, need to be studied before wide-spread adoption is considered. Furthermore, some centers use additional prophylaxis with azithromycin in those with ruptured membranes or use a higher dose of cephazolin (3 g) for prophylaxis in morbidly obese women, which could impact the infection rate.

Post cesarean delivery analgesia

In order to optimize pain relief after cesarean delivery, a multimodal analgesic regimen incorporating neuraxial morphine is currently considered the gold standard. There is, however, significant interindividual variability in pain experience and analgesic needs following cesarean delivery. There is also heterogeneity in women's sensitivity to opioids and desire to avoid opioid related side-effects. Those factors are, however, rarely considered in current practice when planning for postoperative analgesia. Carvalho et al.[20] performed a randomized controlled study to assess whether the patients' choice for the intrathecal morphine (ITM) dose would be reflective of their postoperative opioid consumption and pain scores. One-hundred-and-twenty women undergoing elective cesarean delivery were randomized to a (perceived) choice or no choice group. In the perceived choice group, women were given a choice of 100 or 200 μg ITM, after the investigators explained the tradeoff between analgesia and side effects of the two morphine doses. The study however involved deception, in that all women in the study were randomized to 100 or 200 μg ITM irrespective of their choice. Those who chose the higher morphine dose had 36% higher postoperative opioid consumption (25 vs 16 mg morphine equivalents, P<0.001), and higher pain scores on movement (P=0.0008) that those choosing the lower dose, regardless of the dose actually received. Interestingly, those who chose the lower dose required more rescue antiemetics for the treatment of postoperative nausea and vomiting (20% vs. 9%, P=0.01). Those results suggest that women could correctly predict their postoperative analgesic requirements and sensitivity to side effects of ITM, since the main reason for choosing the higher dose was fear of pain, while concern about side effects was the main driver for choosing the lower dose. Future studies should establish whether patients' choice could help improve their postoperative analgesia and provide the optimal balance between analgesia and side effects.

Pain relief following cesarean delivery is sometimes inadequate despite multimodal analgesia and neuraxial morphine. A few randomized controlled trials were published in 2017 investigating interventions to optimize postoperative analgesia in this patient population. Patel et al.[21] investigated intraperitoneal administration of 20 mL lidocaine 2% in epinephrine 1:200 000 or saline before peritoneal or fascial closure. They included 204 women scheduled for elective cesarean delivery under spinal anesthesia with 100 μg ITM and receiving a standardized multimodal postoperative analgesic regimen with acetaminophen and non-steroidal anti-inflammatory drugs (NSAIDs). There were no differences between the groups in pain scores on movement (primary outcome) or at rest at 24 hours. Pain scores on movement and at rest were, however, significantly lower at two hours in the lidocaine group. While there was no difference in opioid consumption between the groups, the number of patients needing opioids was lower in the lidocaine group compared with the saline group (40% vs 65%, P=0.001). Peritoneal closure was not standardized in the study and a subgroup analysis suggested a benefit of intraperitoneal lidocaine on the primary outcome of pain score on movement in women who underwent peritoneal closure (n = 64), but not in those without peritoneal closure. Further studies with a standardized peritoneal closure technique are therefore needed.

Lui et al.[22] investigated the analgesic efficacy of rectus sheath block (20 mL bupivacaine 0.25% in epinephrine 5 μg/mL per side) performed by the surgeon in 144 women undergoing elective cesarean delivery under spinal anesthesia. Patients were randomly assigned to receive either ITM 100 μg or rectus sheath block, or a combination of both. ITM improved postoperative analgesia in the combination and the ITM groups compared with the rectus sheath block only group. There was no additional analgesic benefit from rectus sheath block among women who received ITM in this study. There was, however, no group comparing rectus sheath block versus a control group not receiving ITM.

There are limited data about the efficacy of local anesthetic wound infiltration in the setting of a multimodal analgesic regimen. Lalmand et al.[23] performed a prospective randomized clinical trial including 182 women undergoing elective cesarean delivery. Women were randomized to ITM 100 μg or continuous wound infiltration of 0.2 % ropivacaine at 10 mL/h for 30 hours delivered via a subfascial catheter, or to a control group.

All women received a multimodal analgesic regimen with regular NSAIDs and acetaminophen. An intravenous (IV) patient-controlled analgesia (PCA) with morphine was provided for breakthrough pain. Compared with the control group, median (IQR) analgesia duration, defined as time from completion of spinal anesthesia to first PCA request (primary outcome), was significantly longer with ITM [247 (182–338) vs 380 (215–1527) min, P=0.002], and ropivacaine wound infusion [351 (227–594) min, P=0.006), with no difference between the morphine and ropivacaine groups. Morphine consumption [median (IQR)] was also significantly lower in the morphine [4 (1–10) mg], and ropivacaine groups [8 (4.5–19) mg], compared with the control group [20.5 (10–30.5) mg, P<0.001 for both comparisons], and lower in the morphine group compared to the wound infusion group (P=0.02). The study, however, did not include a group receiving both wound infusion and ITM, so it is not clear if this modality confers additional benefit in patients receiving ITM in the context of a multimodal postoperative analgesic regimen. However, it does suggest that ropivacaine wound infusion might be a useful alternative when ITM is not used. It is important to note that the infusion rate used in this study is higher than that utilized in previous studies investigating local anesthetic wound infusion for post cesarean delivery analgesia, but there are no studies to date that investigated the optimal infusion rate for local anesthetics in this patient population.

Labor analgesia

Complications of neuraxial labor analgesia

Intrapartum fever

Fever occurs at a higher rate in women receiving labor epidural analgesia compared to those delivering without a neuraxial technique. The mechanism of this fever is unclear, but could possibly be related to an inflammatory rather than an infectious process. Intrapartum fever may be associated with adverse neonatal outcomes and there is concern about its impact on the developing brain. Segal et al.[24] developed a rat model of non-infectious fever, where 24 pregnant Sprague-Dawley rats at 20 days gestation (term is 22 days) were injected at 90-minute intervals with rat recombinant IL-6 or vehicle, then delivered by cesarean delivery eight hours after the first treatment. Maternal temperatures were significantly higher in the IL-6 group compared with the vehicle group, with a mean difference of 0.52°C (95% CI 0.10 to 0.93). The pups of rats treated with IL-6 developed signs of neuroinflammation in the hippocampus, septal areas and caudate nucleus. The mechanism of elevation of IL-6 with epidural analgesia is, however, not clear. This model also does not address placental involvement in the inflammatory process, which is believed to be associated with epidural fever. While the study does not assess any possible consequences of the neuroinflammation reported, it provides a promising model for future work in this area.

Magnesium sulfate is used for neuroprotection, seizure prophylaxis and as a tocolytic agent in the obstetric patient population. It has also been shown to attenuate IL-6 mediated fever in a rat model. Therefore, Lange et al.[25] evaluated the association between intrapartum fever and magnesium sulfate use in a retrospective single center study involving all deliveries from 2007 to 2014 (n = 58,541). Intrapartum fever, defined as a temperature ≥38.0°C any time between admission and delivery, occurred in 5924 (10.1%) patients. Those who received magnesium were less likely to develop a fever (aOR: 0.42, 95% CI 0.31 to 0.58). Neuraxial labor analgesia was also identified as being associated with intrapartum fever in the multivariable model (aOR = 4.17, 95% CI 3.48 to 5.05), in addition to nulliparity, obesity, intrapartum administration of prostaglandins or systemic opioids, chorioamnionitis, prolonged labor and cesarean delivery. While the study reports interesting findings, it was retrospective and did not account for dose or duration of magnesium administration.

Risk of epidural hematoma in thrombocytopenic parturients

There are limited data about the safety of neuraxial techniques in thrombocytopenic parturients. Lee et al.[26] retrospectively reviewed data from 1524 parturients who received neuraxial techniques and had a platelet count <100 000 mm^{-3} within 72 hours of block placement. Those cases were identified from the Multicenter Perioperative Outcomes Group database, which were then combined with data from 14 studies obtained through a systematic review of the literature. No cases of epidural hematoma requiring decompressive laminectomy were identified. Of the cases included in this study, 84% (n=1286) had platelet counts of 70 000–100 000 mm^{-3}, with the upper bound of the 95% CI of the incidence of epidural hematoma calculated as 0.2%; 6% (n=89) had platelet counts of 50 000–69 000 mm^{-3} with the upper bound of the 95% CI of the incidence of epidural hematoma calculated as 3%; and 2% (n=27) had platelet counts of 0–49 000 mm^{-3} with the upper bound of the 95% CI of the incidence of epidural hematoma calculated as 11%. The etiology of thrombocytopenia was not specified and the number of patients with a platelet count <70 000 mm^{-3} was small. The study, however, provides the largest series to date of neuraxial procedures performed in thrombocytopenic parturients.

Remifentanil

The role of remifentanil for labor analgesia is controversial. While, theoretically, its pharmacokinetic properties could be advantageous in this setting, concerns have

been raised about its safety. There are also no clear guidelines about the optimum administration regimen or monitoring requirements for women receiving remifentanil for labor analgesia. Aaronson[27] performed a survey of remifentanil use in 126 academic centers in the USA and obtained a response rate of 67% (May–July 2015). The survey revealed that remifentanil was used infrequently, with most centers (87%) only considering its use when there is a contraindication to neuraxial techniques, and only 36% using it in the year preceding the survey, mostly less than five times. There was also significant variability in the dosing regimens used and monitoring standards applied among the respondents. Serious complications were reported including nine cases of maternal respiratory depression, two of which resulting in maternal cardiac arrest. There were also five cases of neonatal complications attributed to remifentanil. This survey highlights the lack of consensus on the optimal regimen of remifentanil for labor analgesia among academic centers in the United States, the potential for significant safety issues associated with its current use and the need to develop guidelines to enhance the safety of its administration.

Weiniger et al.[28] performed a secondary analysis of data from 19 laboring women receiving IV PCA with remifentanil to assess if monitoring respiratory variables can provide early warning alerts for apnea, defined as maximal end-tidal carbon dioxide ($EtCO_2$) <5 mmHg for at least 30 seconds. They included four candidate variables, and defined an early warning alert as any drop in a variable value below a prespecified threshold for 15 seconds: respiratory rate (RR) <8 breaths per min, $EtCO_2$ <15, end-tidal CO_2 ($EtCO_2$) <15 mmHg, peripheral oxygen saturation (SpO_2) <92%, and integrated pulmonary index (IPI) ≤4. The latter is generated from a proprietary algorithm using RR, $EtCO_2$, SpO_2, and heart rate parameters, with values ranging from 1 to 10 (10 = healthy patient, ≤4 = immediate attention required, 1 = dire condition). There were 62 apneas among 10 women (52.6%). Alerts for $EtCO_2$, RR, and IPI detected most apneas, whereas SpO_2 alerts missed the majority of apneas. All variables, however, had a low positive predictive value (4.3–35.8%) with many false alarms triggered, demonstrating the limitations of all those respiratory monitors as early warning modalities in women receiving remifentanil for labor analgesia. Most of the $EtCO_2$ alerts occurred just before the onset of apnea, but the median time to reach the SpO_2 threshold was 40 seconds after the apnea occurred. This further highlighted the limited usefulness of SpO_2 as an early warning monitor in this setting.

In an attempt to improve the safety of remifentanil administration for labor analgesia, Leong et al.[29] described the performance of a closed loop feedback system that utilized an algorithm that titrates the bolus dose and basal infusion rate of remifentanil. Titration is based on two inputs: the first is the parturients' pattern of utilization, where dosing is stepped up or down based on use. The second input is through a pulse oximeter coupled with the pump, whereby the pump would temporarily pause and reduce subsequent dosing when predefined critical values of SpO_2 (<95% for >15 s) or heart rate (<60/min for >15 s) were reached. They included 29 parturients in this case series; oxygen saturation <95% for >60 s was detected in 52% of cases and heart rate <60/min for >60 s in 24% of patients. The system automatically responded by reducing the dosages and halting remifentanil administration, preventing further hypoxia and bradycardia. While this system is promising, the limitations of pulse oximetry as an early monitor for apnea highlighted above in the Weiniger study suggest that incorporating other monitors of ventilation in this system might improve safety.[30] Furthermore, this series had only a small sample size.

Those studies reveal that remifentanil use is associated with frequent apneas and desaturations and there are currently no clear guidelines for dosing or monitoring, with significant variability in regimens used in practice. Given the potential for adverse events and limited usefulness of respiratory monitors, one-to-one care is currently recommended for women receiving remifentanil for labor analgesia.[31] Further refinements of the closed loop system and larger studies about its safety are needed.

Conclusions

This review of the 2017 literature shows causes and trends of maternal mortality in the USA and UK, highlighting areas where progress has been achieved, as well as areas that need attention. It also reveals issues with maternal mortality data in the USA and the urgent need for focused efforts to improve the quality of data, and address the causes of mortality and health disparities. The review also highlights areas for future research and identifies new findings with respect to labor analgesia and cesarean delivery, with a focus on several studies that investigated components of enhanced recovery after cesarean delivery protocols. The obstetric anesthesiologist plays a key role in leading and facilitating the implementation of those evidence-based protocols, in order to optimize recovery and increase safety for women throughout the continuum of peripartum care.

Declaration of interest

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References

1. Joseph KS, Lisonkova S, Muraca GM, et al. Factors underlying the temporal increase in maternal mortality in the United States. *Obstet Gynecol* 2017;**129**:91–100.
2. MacDorman MF, Declercq E, Thoma ME. Trends in maternal mortality by sociodemographic characteristics and cause of death in 27 States and the District of Columbia. *Obstet Gynecol* 2017;**129**:811–8.
3. Davis NL, Hoyert DL, Goodman DA, Hirai AH, Callaghan WM. Contribution of maternal age and pregnancy checkbox on maternal mortality ratios in the United States, 1978–2012. *Am J Obstet Gynecol* 2017;**217**. 352 e1–352 e7.
4. Creanga AA, Berg CJ, Syverson C, et al. Pregnancy-related mortality in the United States, 2006–2010. *Obstet Gynecol* 2015;**125**:5–12.
5. Creanga AA, Syverson C, Seed K, Callaghan WM. Pregnancy-related mortality in the United States, 2011–2013. *Obstet Gynecol* 2017;**130**:366–73.
6. Knight M, Nair M, Tuffnell D, et al. Saving Lives, Improving Mothers' Care – Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2013–15. Oxford: National Perinatal Epidemiology Unit, University of Oxford; 2017.
7. Deshpande NA, Kucirka LM, Smith RN, Oxford CM. Pregnant trauma victims experience nearly 2-fold higher mortality compared to their nonpregnant counterparts. *Am J Obstet Gynecol* 2017;**217**(590). 590 e1–590 e9.
8. Beckett VA, Knight M, Sharpe P. The CAPS Study: incidence, management and outcomes of cardiac arrest in pregnancy in the UK: a prospective, descriptive study. *BJOG* 2017;**124**:1374–81.
9. Balki M, Liu S, Leon JA, Baghirzada L. Epidemiology of cardiac arrest during hospitalization for delivery in Canada: a nationwide study. *Anesth Analg* 2017;**124**:890–7.
10. Mhyre JM, Tsen LC, Einav S, et al. Cardiac arrest during hospitalization for delivery in the United States, 1998–2011. *Anesthesiology* 2014;**120**:810–8.
11. Krom AJ, Cohen Y, Miller JP, et al. Choice of anaesthesia for category-1 caesarean section in women with anticipated difficult tracheal intubation: the use of decision analysis. *Anaesthesia* 2017;**72**:156–71.
12. Practice Guidelines for Obstetric Anesthesia: An Updated Report by the American Society of Anesthesiologists Task Force on Obstetric Anesthesia and the Society for Obstetric Anesthesia and Perinatology. Anesthesiology 2016;124:270–300.
13. Crawford JS, Burton M, Davies P. Time and lateral tilt at caesarean section. *Br J Anaesth* 1972;**44**:477–84.
14. Ansari I, Wallace G, Clemetson CA, Mallikarjuneswara VR, Clemetson CD. Tilt caesarean section. *J Obstet Gynaecol Br Commonw* 1970;**77**:713–21.
15. Lee AJ, Landau R, Mattingly JL, et al. Left lateral table tilt for elective cesarean delivery under spinal anesthesia has no effect on neonatal acid-base status: a randomized controlled trial. *Anesthesiology* 2017;**127**:241–9.
16. Committee Opinion No. 543: Timing of umbilical cord clamping after birth. Obstet Gynecol 2012;120:1522–1526.
17. Committee Opinion No. 684 Summary: Delayed umbilical cord clamping after birth. Obstet Gynecol 2017;129:232–233.
18. Tarnow-Mordi W, Morris J, Kirby A, et al. Delayed versus immediate cord clamping in preterm infants. *N Engl J Med* 2017;**377**:2445–55.
19. Valent AM, DeArmond C, Houston JM, et al. Effect of post-cesarean delivery oral cephalexin and metronidazole on surgical site infection among obese women: a randomized clinical trial. *JAMA* 2017;**318**:1026–34.
20. Gupta D, Srirajakalidindi A, Soskin V. Dural puncture epidural analgesia is not superior to continuous labor epidural analgesia. *Middle East J Anaesthesiol* 2013;**22**:309–16.
21. Patel R, Carvalho JC, Downey K, et al. Intraperitoneal instillation of lidocaine improves postoperative analgesia at cesarean delivery: a randomized, double-blind, placebo-controlled trial. *Anesth Analg* 2017;**124**:554–9.
22. Lui MW, Li TKT, Lui F, Ong CYT. A randomised, controlled trial of rectus sheath bupivacaine and intrathecal bupivacaine, without or with intrathecal morphine, vs. intrathecal bupivacaine and morphine after caesarean section. *Anaesthesia* 2017;**72**:1225–9.
23. Lalmand M, Wilwerth M, Fils JF, Van der Linden P. Continuous ropivacaine subfascial wound infusion compared with intrathecal morphine for postcesarean analgesia: a prospective, randomized controlled, double-blind study. *Anesth Analg* 2017;**125**:907–12.
24. Segal S, Pancaro C, Bonney I, Marchand JE. Noninfectious fever in the near-term pregnant rat induces fetal brain inflammation: a model for the consequences of epidural-associated maternal fever. *Anesth Analg* 2017;**125**:2134–40.
25. Lange EMS, Segal S, Pancaro C, et al. Association between intrapartum magnesium administration and the incidence of maternal fever: a retrospective cross-sectional study. *Anesthesiology* 2017;**127**:942–52.
26. Lee LO, Bateman BT, Kheterpal S, et al. Risk of epidural hematoma after neuraxial techniques in thrombocytopenic parturients: a report from the multicenter perioperative outcomes group. *Anesthesiology* 2017;**126**:1053–63.
27. Aaronson J, Abramovitz S, Smiley R, Tangel V, Landau R. A survey of intravenous remifentanil use for labor analgesia at academic medical centers in the United States. *Anesth Analg* 2017;**124**:1208–10.
28. Weiniger CF, Carvalho B, Stocki D, Einav S. Analysis of physiological respiratory variable alarm alerts among laboring women receiving remifentanil. *Anesth Analg* 2017;**124**:1211–8.
29. Leong WL, Sng BL, Zhang Q, et al. A case series of vital signs-controlled, patient-assisted intravenous analgesia (VPIA) using remifentanil for labour and delivery. *Anaesthesia* 2017;**72**:845–52.
30. Weiniger CF, Carvalho B, Landau-Cahana R. Optimising triggers for patient-assisted remifentanil analgesia during labour. *Anaesthesia* 2017;**72**:1155–6.
31. Van de Velde M. Remifentanil patient-controlled intravenous analgesia for labor pain relief: is it really an option to consider? *Anesth Analg* 2017;**124**:1029–31.