What's New in Obstetric Anesthesia: The 2009 Gerard W. Ostheimer Lecture

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This article summarizes the most relevant publications in obstetric anesthesiology from 2008. Forty-two articles were selected from a pool of several thousand in >70 English-language journals that were deemed as having the most impact on the practice of obstetric anesthesia.

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LABOR ANALGESIA

Ultrasound-assisted peripheral nerve blockade has substantially changed the practice of regional anesthesia. Several investigators are now exploring the application of this technology to neuraxial techniques in obstetric anesthesia. Two teams of investigators published studies using ultrasonography to confirm that vertebral interspace assessment by palpation is inaccurate and emphasized the importance of this awareness particularly when using techniques involving dural puncture.[1,2] The use of ultrasound assistance for neuraxial techniques may hold promise particularly in patients with obesity, scoliosis, or in other settings with predicted difficult placement.

Patient-controlled epidural analgesia (PCEA) has the advantages of reducing local anesthetic consumption and anesthesiologist workload and increasing patient satisfaction, but the optimal combination of PCEA variables (background infusion rate, bolus dose, and lockout interval) is not clear. A randomized controlled trial demonstrated that the presence of a background infusion compared with a pure PCEA technique without a background infusion reduced breakthrough pain, although total local anesthetic dose increased as did the duration of the second stage of labor.[3] The authors concluded that, in using ropivacaine 0.1% with fentanyl 2 μg/mL, an intermediate background infusion rate (5 mL/h) combined with a 5-mL bolus, 12-min lockout, and 20-mL maximum allowable hourly dose provided a balance between optimal analgesia and unfavorable second-stage outcomes.

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A randomized trial evaluated the dural puncture epidural (DPE) technique for labor analgesia compared with traditional epidural analgesia.[4] DPE is similar to combined spinal-epidural analgesia in that the dura is punctured with a small needle before placing an epidural catheter, but no drug is administered into the intrathecal space. DPE in this trial, using a 25-gauge pencil-point spinal needle, was associated with less sacral sparing and better early analgesia without an increase in the rate of postdural puncture headache, although the study was underpowered to determine the latter secondary outcome. However, more instrumental deliveries were observed in the DPE group. Both this article and the previous one addressing PCEA establish a concerning pattern of improved neuraxial labor analgesia being provided at a cost of a higher rate of instrumental vaginal deliveries.

Two additional articles addressed the relationship between labor analgesia and second-stage outcomes.[5,6] The first was a retrospective study demonstrating that there is an association between women whose obstetricians requested reductions in their epidural infusion rates in the second stage of labor and higher instrumental delivery rates.[5] It is not clear whether this association reflects a causal relationship (i.e., dense motor blockade leading to increased risk of instrumental vaginal delivery) or is merely a marker for an obstetrician's dissatisfaction with the progress of obstructed labor. The second article, a secondary analysis of a previously published prospective study, reported that women with suboptimal analgesia in the second stage had a higher risk of difficult delivery (defined as cesarean and instrumental deliveries, and third- and fourth-degree perineal tears).[6] In contrast to the first article, however, improvement of analgesia in women with initial suboptimal second-stage analgesia was not associated with a further increased risk of difficult delivery.

Intrathecal microcatheters were removed from the United States market in 1992 because of concerns about permanent neurologic side effects. A multicentered, premarket, safety trial that compared intrathecal opioid analgesia administered via microcatheters

(n = 329) to traditional epidural analgesia (n = 100) demonstrated no permanent neurologic deficits in either group.[7] The postdural puncture headache rate was 9% for the intrathecal catheter group and 4% for the epidural group. The study was not powered to find a difference in this outcome between groups, and it was not large enough to definitively establish the safety of intrathecal microcatheters. At the time of publication, the study sponsor was not intending to pursue Food and Drug Administration approval for their use in the United States.

IV remifentanil has been suggested as an excellent alternative to neuraxial labor analgesia because of its short duration and predictable metabolism. A randomized controlled trial of remifentanil versus epidural analgesia in early labor, however, demonstrated that remifentanil was inferior in analgesic efficacy and had a higher rate of side effects, specifically sedation and nausea.[8]

Two groups of investigators studied the clinical impact of genetic variation on opioid analgesia responsiveness; they specifically examined a single nucleotide polymorphism at the 304 position of the μ-opioid receptor (*ORPM1*) gene.[4,5] One study demonstrated a difference in the ED_{50} of intrathecal fentanyl in women in early labor based on genotype[9] and a second study reported a difference in 24-h IV morphine consumption (administered via patient-controlled analgesia) after intrathecal morphine for cesarean delivery.[10] Noteworthy is that the genotype most sensitive to intrathecal opioid was not consistent between these 2 studies.

Although episiotomy is controversial, it is still frequently practiced outside the United States and is associated with moderate acute pain in most patients and chronic pain in 13%–23% of patients. A randomized controlled study of the use of unilateral, transperineal nerve stimulator-guided pudendal nerve blockade demonstrated a substantial reduction in acute postpartum pain and may offer hope in reducing chronic pain associated with episiotomy.[11]

CESAREAN DELIVERY

Prophylactic antibiotic timing has received increased attention because it is an easily measured intervention that may serve as a marker of the quality of care. A retrospective cohort study evaluating the effect of a change of a single institution's policy from administering antibiotics after cord clamping to preincision for cesarean delivery showed that the overall surgical site infection rate decreased from 6.4% to 2.5% after the institution of the new policy.[12] Almost all of the effect was attributable to a decreased incidence of infection in nonelective cases.

The optimal vasopressor regimen for treating hypotension after spinal anesthesia continues to be studied. The first randomized controlled trial evaluating various dose ratios of ephedrine combined with phenylephrine showed more fetal acidemia with larger proportions of ephedrine, leading the authors to conclude that there was no advantage to combining phenylephrine and ephedrine over using phenylephrine alone.[13]

Several investigations highlighted concerns about the rapid administration of oxytocin. One study of hemodynamic stability after spinal anesthesia during cesarean delivery used a new monitor capable of accurately measuring continuous cardiac output without central venous access.[14] The technology involves evaluation of radial arterial pulse wave forms using a computer algorithm after calibration by lithium dilution. The study confirmed that spinal anesthesia in severe preeclampsia is associated with relatively stable cardiac output, but it was noteworthy that a 2.5-U bolus of oxytocin had a profound negative impact on hemodynamic variables (increased heart rate and cardiac output with decreased systemic vascular resistance and mean arterial blood pressure). Another group of investigators compared oxytocin (10-U bolus) with IV methylergometrine (200 μg) and also administered oxytocin to a control group of nonpregnant volunteers.[15] They showed that this dose of oxytocin was associated with electrocardiogram ST segment elevation to a degree consistent with myocardial ischemia. This finding was observed in both pregnant patients during cesarean delivery and nonpregnant volunteers. Both of these studies support the cautious administration of oxytocin by slow IV infusion.

Intubation fails more often in pregnant compared with nonpregnant patients. The degree of difficulty of direct laryngoscopy in pregnant patients is likely not static over the course of labor. Mallampati classification increased and oral-pharyngeal volume, as measured by acoustic reflectometry, decreased significantly in patients between the onset and end of labor.[16] There was no correlation observed between these changes and either duration of labor or total fluids administered. An observational study of 1095 general anesthetics for cesarean delivery conducted over a 20-mo period at 13 hospitals in Australia and New Zealand confirmed that the rate of difficult and failed intubations in this population is 3.3% and 0.4%, respectively.[17]

In a secondary analysis of the same 1095 general anesthetic cases, 2 patients were confirmed to have experienced awareness.[18] This corresponds to a rate of 0.26% (95% confidence interval 0.03%–0.9%), which is consistent with previous reports of cesarean deliveries. The confidence interval overlaps with the rate previously reported in general surgery cases of 0.1%–0.2%. It is controversial whether greater use of depth of anesthesia monitors reduces the rate of awareness and whether appropriate values in parturients differ from those in nonpregnant patients. Investigators from Korea administered sevoflurane–nitrous oxide anesthesia to parturients and monitored bispectral index values.[19] Parturients who had labored before receiving general anesthesia were observed to have lower values

(greater depths of anesthesia) as compared with women who had not labored. Elevated levels of maternal norepinephrine measured in patients who had labored were implicated as a possible factor for this observation.

The transversus abdominus plane blockade has become an area of great interest for postoperative pain management after abdominal surgery. The block is simple to perform because of the anatomical relationship between the anterior rami of segmental spinal nerves (T9–T11) and the plane between the transversus abdominus and internal oblique muscles. In a randomized placebo-controlled trial, 48-h IV morphine patient-controlled analgesia consumption was decreased by 70% after cesarean delivery in patients who received a transversus abdominus plane blockade with ropivacaine, suggesting that this block has utility as part of multimodal management of postcesarean delivery pain.[20]

Moderate or severe pain at the incision site has been reported in 7% of respondents 2 yr after cesarean delivery in a survey of 866 patients.[21] On examination of this subset of patients, the pain was classified as neuropathic in 53% and believed to be related to entrapment of the iliohypogastric or ilioinguinal nerves. One-third of this small series of patients received long-term relief after diagnostic/therapeutic nerve blockade. Hyperalgesia has been described as a marker of central sensitization and the development of chronic pain. In a separate investigation, the addition of intrathecal clonidine (75 and 150 μg) to a standard spinal anesthetic regimen resulted in a reduction in both the incidence and extent of peri-incisional hyperalgesia.[22] Further study is required to determine whether clonidine can be used to decrease the risk of chronic pain after cesarean delivery.

ANESTHETIC COMPLICATIONS

Several publications addressed complications of epidural analgesia/anesthesia. Epidural blood patch is the standard of care for the treatment of moderate to severe postdural puncture headache. In a randomized placebo-controlled study, epidural morphine administration reduced the incidence of headache and need for epidural blood patch.[23] The safety of this technique has not, however, been adequately evaluated. There is concern over the theoretical risk of translocation of epidural morphine to the cerebrospinal fluid via a large hole in the dura, potentially increasing the risk of respiratory depression.

Infection associated with neuraxial techniques has received recent scrutiny. Among the areas of active investigation include identifying patients at increased risk for serious infection and the optimal aseptic skin preparation. An observational study of trainees placing labor epidural blocks suggested that lack of learning proper aseptic technique may be contributing to this problem.[24] Appropriate aseptic technique scored by observers did not improve with increasing resident experience, unlike general technical skills, and the authors hypothesized that there may be a major gap in either teaching or resident understanding of aseptic technique.

OBSTETRIC COMPLICATIONS

Preeclampsia is associated with an increase in long-term cardiovascular morbidity. An epidemiologic study from Norway using the Medical Birth Registry of Norway and the Norwegian Renal Registry determined that women with a history of preeclampsia had a higher relative risk for developing renal failure than women without preeclampsia, albeit a low absolute risk.[25]

The relationship between the number of prior vaginal births after cesarean (VBAC) delivery and the probability of successful vaginal delivery and uterine rupture were more clearly defined in a secondary analysis of a large, previously published trial.[26] Overall VBAC success was 73% with a risk of uterine rupture of 0.7%. In women with a history of 1 or more successful VBAC deliveries, the success rate increased to approximately 90%, whereas the uterine rupture rate decreased to approximately 0.4%–0.5%.

A large, 6-yr retrospective study of maternal mortality at the largest private health care system in the United States confirmed an increased risk of death associated with cesarean compared with vaginal delivery.[27] Most deaths occurred in women without preexisting risk factors and were deemed to be due to nonpreventable causes including hypertensive disorders, amniotic fluid embolism (AFE), hemorrhage, and cardiac disease. The authors advocated for the development of stronger practice guidelines to support the use of mechanical sequential compression devices to reduce thromboembolism, the one leading cause that was deemed preventable. Other investigators studying maternal mortality attempted to more accurately estimate the incidence of AFE.[28] Analyzing a health care database of nearly 3 million births, they reported 227 cases of AFE, an incidence of 7.7 cases per 100,000 births and a case fatality rate of 21.6%. These rates agree with those reported in 2 previous large-scale studies of AFE that estimated the incidence to be between 5 and 15 cases per 100,000 births with case fatality rates ranging from 13% to 26.4%.

MATERNAL COMORBIDITIES

The prognosis for patients diagnosed with peripartum cardiomyopathy, including the impact of future pregnancy, was more clearly delineated in a prospective study of 70 patients.[29] Regardless of presenting severity of cardiomyopathy, subsequent pregnancy was associated with a higher rate of progression of heart failure. In addition, presentation with a left ventricular ejection fraction of <25% at the index

pregnancy was associated with very unfavorable outcomes: 16 of 28 subjects received or were wait-listed for cardiac transplantation during the 3.4-yr average follow-up period (range 1–6 yr) as compared with 0 of 42 who presented with an ejection fraction >25%.

With regard to peripartum infective endocarditis, the American College of Obstetricians and Gynecologists published a practice bulletin adopting the 2007 American Heart Association guidelines. These guidelines reduced the number of surgical procedures for which prophylactic antibiotic administration are indicated, so that currently antibiotics are only indicated for genitourinary procedures.[30] Prophylactic antibiotics are no longer recommended for routine vaginal or cesarean deliveries. Only patients who have infections associated with bacteremia and are at highest risk for adverse outcomes with endocarditis (those with prosthetic cardiac material, a history of endocarditis, and unrepaired, recently repaired, or partially repaired cardiac lesions) should receive prophylactic antibiotics in addition to an antibiotic regimen to treat the underlying infection.

Because the administration of low-molecular-weight heparin (LMWH) has in many circumstances replaced unfractionated heparin in pregnant patients, controversies regarding dosing strategies have arisen. The optimal dose of LMWH in pregnancy is not clear nor is it clear whether antifactor Xa levels should be used to monitor therapy. An observational study of 77 pregnant women receiving weight-based dosing of LMWH found that 26% were subtherapeutic for thrombosis prophylaxis.[31] Future changes in recommended LMWH dosing may lead to more restrictions for neuraxial labor analgesia. The American College of Chest Physicians published the comprehensive eighth edition of guidelines for prophylaxes and treatment of thromboembolism in pregnancy.[32]

Two important recent studies addressed the management of gestational diabetes.[33,34] The first evaluated pregnancy outcomes associated with fasting maternal blood glucose levels that were increased but below the diagnostic threshold for gestational diabetes (75–105 mg/dL).[33] Patients presenting with glucose values in this range in the early third trimester demonstrated a strong, continuous association with increased birth weight, cesarean delivery, and neonatal hypoglycemia. Unfortunately, there was no single blood glucose value at which a substantially increased risk was identified that obstetricians could use as a new threshold to justify initiating antihyperglycemic therapy. The use of oral antihyperglycemics in pregnancy, specifically metformin, has been controversial. A randomized, controlled trial demonstrated that, compared with insulin, patients taking metformin had no difference in the composite outcome of gestational diabetes–related morbidity or other pregnancy outcomes.[34] However, the patients receiving metformin experienced a higher rate of premature birth in this trial.

NEONATAL OUTCOMES

Twelve percent of all births in the United States are preterm, which results in considerable morbidity and resource utilization in our health care system. Several publications in the obstetric literature last year addressed advances in the prevention and treatment of preterm labor and delivery.[35–39] The National Institutes of Child Health and Human Development Consensus Panel has recommended that providers consider corticosteroid administration to mothers at risk for preterm delivery between 24 and 34 wk estimated gestational age (EGA) to reduce the risk of neonatal pulmonary morbidity. However, there is an increasing number of deliveries occurring between 23 and 24 wk gestation, and it is unclear whether these mothers should also be receiving this therapy. In a retrospective study of 181 infants at imminent risk for delivery between 23 and 24 wk EGA, infants whose mothers received a complete dose of steroids had an 82% reduction in the adjusted odds ratio for death.[35] Many women at risk for preterm delivery remain undelivered for several weeks. There seems to be no reduction in perinatal death or morbidity if corticosteroids are repeated every 2 wk beyond the initial single dose administered in the first 2–3 wk.[36] In fact, infants born to mothers who received more than a single dose of corticosteroids had significantly reduced birth weight, length, and head circumference compared with infants whose mothers received a single dose.

Maintenance tocolysis of preterm labor with nifedipine has been a common practice but its efficacy had been questioned, and 2 previous unblinded trials demonstrated conflicting results. In a randomized, double-blind trial, there was no difference in the percentage of patients who remained pregnant at 37 wk EGA among those that received nifedipine (every 4–6 h until 37 wk EGA) versus placebo control.[37] The causes of preterm labor remain unknown but infection is a likely contributing cause. A meta-analysis of 11 randomized trials on the use of antibiotics to prevent preterm delivery demonstrated that antibiotic administration is associated with prolongation of pregnancy with preterm, premature rupture of membranes but not in the setting of preterm labor with intact membranes.[38] Important secondary outcomes associated with antibiotic administration were the reduction of chorioamnionitis in all patients who received antibiotics regardless of membrane status and reduced infection rate in infants born to these mothers. An American College of Obstetricians and Gynecologists committee opinion also advocated the administration of antenatal progesterone (17-hyrdoxyprogesterone caproate) to reduce the likelihood of recurrent preterm labor in women with a history of singleton delivery before 37 wk EGA.[39]

Cerebral palsy is the most common neuromotor developmental disability in childhood affecting 2–3 per 1000 liveborn children. The prevalence is largely

unchanged over the past few decades despite major improvements in clinical care and additional resources dedicated to detecting "fetal distress." Fetal heart monitoring not only lacks specificity in detecting fetal distress but also lacks reproducibility in interpretation. In a secondary analysis of fetal heart rate tracings from a previously published fetal pulse oximetry trial, there was poor agreement among clinicians in classifying tracings as "reassuring" or "nonreassuring," and clinicians were unable to predict which patients subsequently required emergency cesarean deliveries or had acidemic umbilical cord blood gases.[40] In part, to address some of these current limitations, updated definitions and guidelines for evaluating fetal heart rate tracings were published by the National Institute of Child Health and Human Development, which most notably included a new 3-tiered interpretation system with the categories of "normal," "indeterminate," and "abnormal."[41] On a positive note, the use of IV magnesium aimed at reducing cerebral palsy in infants at risk for preterm delivery (between 24 and 31 wk EGA) has gained enthusiasm after the publication of a large, randomized, controlled trial.[42] Although the primary outcome of the study (the combined rate of death and moderate to severe cerebral palsy) was negative, the prespecified secondary outcome of cerebral palsy alone was significantly reduced in children exposed to magnesium as compared with placebo.

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