AANA Journal Course

Update for Nurse Anesthetists

Evidence-Based Anesthesia: Fever of Unknown Origin in Parturients and Neuraxial Anesthesia

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The safety of neuraxial analgesia in febrile patients is controversial. We performed an evidenced-based project in an effort to establish a guideline for our active obstetric clinical practice.

Neuraxial anesthesia is generally safe for parturients, and complications are rare; however, serious adverse outcomes can result. Because of the devastating nature of the morbidity, the decision to proceed with a neuraxial anesthetic in the face of infection may be contentious.

Fever and sepsis are considered relative contraindications to regional anesthesia; however, epidural anesthesia is a superior method of management of pain during labor. One must also consider that 30% to 40% of patients with chorioamnionitis require cesarean delivery. Because of the increased morbidity and mortality of general anesthesia in this population, it may be reasonable to proceed with regional anesthesia.

Based on a review of the literature, it is difficult to estimate the risk of an infrequently occurring event. We recommend evaluation of each individual to determine the risks and benefits of the anesthetic. However, it is prudent to administer antibiotics before the regional anesthetic and adhere to strict aseptic technique. Post-procedure monitoring is essential for early detection and treatment of complications.

Keywords: Chorioamnionitis, epidural, infection, neuraxial, regional.

Objectives

At the completion of this course the reader should be able to:
1. Describe the anesthesia implications of chorioamnionitis.
2. Discuss the risk of complications of neuraxial anesthesia.
3. Discuss the weight of evidence for regional anesthesia in a febrile patient.
4. Describe antibiotic management for suspected chorioamnionitis.
5. Understand the recommendations for caring for an obstetric patient with suspected chorioamnionitis.

Introduction

A 20-year-old pregnant, gravida 1, para 0, woman at 39 weeks' gestation was admitted to the labor and delivery unit with spontaneous rupture of membranes, with clear, but foul-smelling fluid. The patient was febrile (temperature, 102°F) and had been experiencing generalized fatigue and aches for 1 day. The patient was admitted for labor with a diagnosis of chorioamnionitis. The anesthesia provider was consulted for labor pain management.

This clinical vignette demonstrates an area of controversy for anesthesia providers because they are often conflicted as to whether it is safe to proceed with neuraxial analgesia in a febrile patient. Some clinical practice guidelines are present, but none offer clear guidance for neuraxial analgesia in a febrile patient. Based on this lack, we performed an evidenced-based project in an effort to establish a guideline for our active obstetric clinical practice.

Epidural anesthesia is a widely used method to manage labor pain, with an estimated 2.4 million epidural anesthetics administered during labor annually in the United States.[1] Overall, neuraxial anesthesia has contributed to the quality of care in the obstetric population; it has been shown to decrease postoperative mortality of patients undergoing cesarean delivery by approximately one-third when compared with general anesthesia.[2,3]

Neuraxial anesthesia is generally safe for parturients, and complications are exceedingly rare; however, serious adverse outcomes can result.[1,4,5] Because of the devastating nature of the morbidity, however rare, the decision to proceed with a neuraxial anesthetic in the face of infection may be contentious. Because the incidence of complications is low, the evidence available in the literature is limited to retrospective medical record reviews and case reports. Hence, the development of specific guidelines is hampered by the lack of controlled randomized clinical trials on which to base decisions. This course attempts to highlight the reported incidence rates and findings of retrospective medical record reviews and discuss the considerations that are influential in the choice of anesthesia for an obstetric patient with chorioamnionitis.

Review of the Literature

The literature search for this review was performed by using the MEDLINE (1966-2007) and EMBASE (1980-2007) nationwide medical databases. Using the search terms "anesthesia," "analgesia," "epidural," "chorioamnionitis," intrapartum fever," "intra-amniotic infection," "adverse effect," "danger," and/or "adverse reaction" yielded 68 relevant articles. The articles were reviewed for relevance, and a total of 13 articles were chosen for in-depth investigation (Table).[1-13]

Chorioamnionitis

Chorioamnionitis is an acute intra-amniotic infection that occurs in 0.5% to 10.5% of normal deliveries[4,7-9,14] but can occur in as many as 28% with prolonged rupture of membranes (>24 hours).[9] Accurate diagnosis of chorioamnionitis can be difficult because the symptoms lack specificity and subclinical chorioamnionitis can occur.[9] Histological evidence from the placenta is required for definitive diagnosis of subclinical chorioamnionitis. Fever is considered to be the most significant clinical marker, although it lacks specificity because maternal fever during labor is common.[9] Conversely, symptoms such as foul-smelling discharge and abdominal tenderness are also possible indicators but are less sensitive because they are frequently absent.[12-15] Clinical diagnosis of chorioamnionitis is typically made based on the presence of 2 or more of the following symptoms: elevated temperature (>38ºC) on 2 or more occasions, maternal leukocytosis (white blood cell count, >20,000/µL), tachycardia (pulse, >120/min), premature or prolonged rupture of membranes, foul-smelling amniotic fluid, and uterine tenderness.[7,9]

Fever is a common symptom during labor and has complex causes that can pose a challenge for diagnosing an infection.[7,15] Although fever is common, the incidence of bacteremia in a laboring parturient is low (3.1%-7%).[7,8] Additional infection rates in pregnancy include the following: septicemia, 0.07%; asymptomatic bacteriuria, 10%; and pyelonephritis, 1% to 2%.[7] It is difficult to know with certainty whether the presence of a fever is indicative of a systemic infection in a parturient in labor; hence, the best approach for achieving adequate pain control with anesthesia in these cases remains an important question.

Approximately 30% to 40% of patients with chorioamnionitis undergo cesarean delivery.[9] Therefore, the decision to administer an epidural anesthetic should be based on a careful evaluation of the risk-benefit ratio for the patient.[2,7,9] Patients who have increased risk factors for general anesthesia, such as morbid obesity, or airway anatomy not favorable for direct laryngoscopy, require additional evaluation of risk vs benefit.[16,17]

Complications of Neuraxial Anesthesia

Retrospective medical record reviews and case studies provide some evidence of the incidence of complications of neuraxial anesthesia. The following discussion highlights some examples of the reviews. However, few of the articles are from the United States, which may be related to the difficulty in obtaining potentially litigious data.

Phillips et al[6] reviewed 2,401 medical records from 1993 to 1998 of patients in the United Kingdom who received epidural anesthetics for nonobstetric procedures. The incidence of epidural abscess in this general postoperative population was 0.125%. A prospective, 1-year survey by Wang et al[11] reviewed 17,372 nonobstetric epidural anesthetics administered to patients in Denmark. The incidence of spinal abscess was 1:5,661, and the incidence of epidural abscess was 1:1,930.

Mixed results are reported in the incidence of spinal vs epidural complication rates. A retrospective review performed in Sweden from 1990 to 1999 evaluated the complication rate of neuraxial anesthetics.[3] The complication rate of epidural anesthesia was higher than for spinal anesthesia (1:3,600 compared with 1:20,000-1:30,000), but it was also significantly lower in the obstetric population compared with all others (1:25,000 compared with 1:3,600). The review considered 1.26 million spinal and 450,000 epidural anesthetics. Of the 450,000 epidural anesthetics, 200,000 were for obstetric cases. There were 127 major complications including the following: 33 spinal hematomas, 32 cauda equina syndromes, 29 meningitis, and 13 epidural abscesses (20 were miscellaneous).[3]

Ruppen et al[1] recently conducted a meta-analysis of complications of neuraxial anesthesia that provides insight to the risk in the obstetric population. The risk of

Study	No.	Study Design	Findings	Comments/Conclusions
Bader et al[4] (1992)	10,047 cases	Retrospective review	319 patients with chorioamnionitis; no complications associated with anesthesia	Risks of neuraxial anesthesia unsubstantiated, especially considering risk of general anesthesia
Carp and Bailey[12] (1992)	40 rats	Animal study	Meningitis resulted after cisternal puncture in rats intentionally infected with *Escherichia coli.*	Gentamicin-treated group had no cases of meningitis; cisternal puncture much more invasive than epidural administration in humans
Beilin et al[10] (1996)	177	Survey	Practice patterns of US anesthesiologists	Majority (74%-89%) would place CLE if temperature <101°F and antibiotic therapy initiated
Goodman et al[9] (1996)	517 epidural and 14 spinal anesthetics	Retrospective review	No reports of anesthetic infection, epidural abscess, or meningitis	Lumbar puncture in the face of infection does not seem to increase risk of meningitis.
Wang et al[11] (1999)	17,372	Survey	9 spinal epidural abscesses, none in obstetric cases; overall incidence of complications: 1:1,930 in SAB; 1:5,661 in CLE	Spinal epidural abscess associated with long duration of anesthesia, immunosuppression, and use of low-molecular-weight heparin
Bajwa et al[13] (2002)	1 case	Case report	Diskitis and osteomyelitis after cesarean delivery with spinal anesthesia	No cases of infectious diskitis associated with pregnancy and spinal anesthesia are reported.
Phillips et al[6] (2002)	5,000 in 5 y	Retrospective review	No case of epidural abscess	Low incidence of epidural abscess makes it difficult to show positive effect of prophylactic antibiotics.
Kuczkowski and Reisner[7] (2003)	Review	Review article	Chorioamnionitis incidence, 0.5%-10%	The presence of infection and fever in labor does not always contraindicate the administration of regional anesthesia.
Wlody[2] (2003)	Review	Review article of complications of regional obstetric anesthesia	Anesthetic mortality 17 times greater in cesarean deliveries performed under general anesthesia compared with regional anesthesia	Stresses the importance of risk-benefit analysis and use of sterile technique
Moen et al[3] (2004)	1990-1999: 1,260,000 SAB cases; 450,000 CLE cases	Retrospective review	Complications of obstetric CLE, 1:20,000-30,000	Greater complication rate of CLE compared with SAB; obstetric patients had a lower risk
Schroeder et al[5] (2004)	1 case	Case report	Spinal epidural abscess in postpartum patient after epidural anesthesia	Surgical decompression resulted in no neurological deficits.
Baer[8] (2006)	Review	Review of postdural puncture meningitis	Postdural puncture meningitis most often results from exogenous inoculation, not hematological spread.	Antibiotic prophylaxis is advised and postoperative follow-up is necessary; sterile precautions emphasized.
Ruppen et al[1] (2006)	27 studies	Meta-analysis of epidural complications	Hematoma formation, 1:168,000; deep epidural infection, 1:145,000; persistent neurological injury, 1: 240,000; transient neurological injury, 1:6,700	Provides some best-estimate information for complications; risk-benefit analysis should guide decision to proceed with regional anesthesia

Table. Literature of Chorioamnionitis and Neuraxial Anesthesia
SAB indicates subarachnoid block; CLE, continuous lumbar epidural.

neurological injury may be slightly inflated because it is difficult to determine causation, and there are many other possible obstetric neurological injuries. The risk of epidural infection was 9 cases in 1.2 million (1:110,000), but in cases performed after 1990 it was 7 per million (1:145,000).[1] The authors used estimates for the number of births per country and the overall adverse events to determine the estimated risk for individual countries. The US estimates are calculated as 4,019,280 births per year and an epidural rate of 59%, equating to a risk of 13 epidural hematomas, 22 deep epidural infections, 9 persistent neurological injuries, and 603 transient neurological injuries per year.[1] The relative risks were determined by tabulation of the reported outcomes in the literature and comparison of these results to the number of events (per million) based on the estimated number of epidurals.

Animal Studies on the Use of Neuraxial Anesthesia in the Setting of Chorioamnionitis

There is little evidence of neuraxial anesthesia infection risk in animal studies. Carp and Bailey[12] demonstrated an association between meningitis and dural puncture in rats that were intentionally infected with *Escherichia coli* (12 of 40 rats). However, the cisternal puncture used in this study is significantly more invasive than an epidural procedure in a human subject, making it difficult to extrapolate findings to obstetric cases. It is important to note that the risk of meningitis was eliminated with 1 preprocedure dose of gentamicin.[12]

Human Studies on the Use of Neuraxial Anesthesia in the Setting of Chorioamnionitis

A retrospective study of 40,000 patients by Goodman et al[9] of spinal and epidural anesthetics used for cesarean delivery and vaginal delivery did not report any cases of meningitis or spinal epidural abscess. Of note, 531 patients had chorioamnionitis confirmed by evaluation of the placenta, and in addition, 24% of patients had fever and 76% had leukocytosis before the epidural anesthetic was administered. Also, only 24% of patients received antibiotics before the epidural was administered. However, one of the major flaws noted by the investigators was that the patients who had a complicated clinical picture of chorioamnionitis may not have been considered appropriate candidates for neuraxial anesthesia. These authors concluded that neuraxial anesthesia may be safely administered without antibiotics to nonbacteremic obstetric patients with chorioamnionitis.[9]

A meta-analysis of 267 articles conducted by Ruppen et al[1] concluded that there was no evidence that regional anesthesia should be contraindicated in parturients with chorioamnionitis. There were no studies that could delineate a causal relationship between regional anesthesia and complications such as meningitis and epidural hematoma

formation in bacteremic patients.[1] However, the authors pointed out that estimation of complications is somewhat flawed because most reports of serious complications are in the form of case reports or observational studies, so it is possible that these reports were missed by the literature search. In addition, it is possible that owing to potential litigation, these events may not be reported. The incidence rates given by Ruppen et al[1] are as follows: deep epidural infection, 1:145,000; persistent neurological injury, 1:240,000; and transient neurological injury, 1:6,700.

In 1992, Bader et al collected information via a retrospective medical record review of all obstetric deliveries for a 1-year period.[4] They identified 319 cases of chorioamnionitis from a total of 10,047 deliveries. Bacteremia was found in 8 (2.5%) of 319 patients identified with chorioamnionitis. Of the 319 patients, 293 (91.8%) received antibiotics during labor and delivery. However, only 43 (15.4%) of the 279 patients who actually received a regional anesthetic received antibiotics before the administration of the anesthetic and none of the bacteremic patients who received a regional anesthetic received antibiotics before the administration of the anesthetic. The consensus of the study was that none of the bacteremic patients had infectious complications that could be directly associated with regional anesthesia.[4] Philips et al[6] conducted a retrospective review of 5,000 labor epidural cases in a 5-year period that revealed no cases of epidural abscess.

In a recent review, Wedel and Horlocker[18] found that reported complications of neuraxial and infection to be extremely rare. These authors concluded that it may be safe to proceed with neuraxial anesthesia in a patient with appropriate antibiotic therapy, but there is a theoretical risk of neuraxial infection. These authors recommended making the decision on an individual basis after reviewing the risks and benefits. Furthermore, they recommended discontinuing any catheter with evidence of erythema and/or discharge. Finally, these authors also stressed the importance of early diagnosis of a complication because the neurological outcomes are related to the time from symptom onset to initiation of treatment.

Antibiotic Management

Infection usually results from bacteria ascending from the parturient's genital tract into the uterus to infect the membranes (chorion and the amnion) and the amniotic fluid; occasionally, infection may result from hematogenous spread. The most common causative organisms include *E coli*, group B streptococcus, anaerobes, *Mycoplasma* organisms, and *Listeria* species.

For parturients with a fever and the possibility of chorioamnionitis, cultures should be obtained, including 2 sets of blood cultures, a urine culture, and an amniotic fluid culture, if fluid is readily available. A positive Gram stain, leukocyte esterase activity, and a low glucose (<15

mg/dL) in the amniotic fluid support the diagnosis of an intra-amniotic infection.

Antibiotics should be initiated for cases of suspected chorioamnionitis for preventing maternal bacteremia and for the initial treatment of the fetus.[19] Studies that have compared intrapartum and postpartum antibiotic administration have shown that intrapartum therapy is associated with improved maternal and fetal outcomes.[20,21] Antimicrobial therapy should treat the most likely causative organisms and be able to transverse the placental barrier to reach the fetus. The antibiotics of choice include ampicillin (2 g intravenously every 4-6 hours) and gentamicin (5 mg/kg daily).[19-22] If a cesarean delivery is performed, the addition of clindamycin (600-900 mg intravenously every 8 hours) is recommended.[23] If indicators of a continued, active infection are present despite antibiotic treatment, other unusual infections should be suspected; novel cases of chorioamnionitis caused by methicillin-resistant *Staphylococcus aureus* have been reported but are rare.[24] The duration of maternal antibiotic therapy is debatable; however, because the nidus of the infection (ie, the placenta) is removed on delivery, long-term antibiotic therapy is not usually necessary, and 1 study suggested that a single additional dose postpartum is sufficient in an immunocompetent woman.[25]

Discussion

Because the level of evidence relating to this topic is limited to retrospective studies, case reports, and expert opinion, it is difficult to provide specific recommendations for the care of a parturient with chorioamnionitis. There are no reported cases of major complications from neuraxial anesthesia in parturients with chorioamnionitis, despite the reported incidence of bacteremia in this population of 3% to 8%.[1,4,5,9] This finding may be related to the fact that the common causes of chorioamnionitis are uncommon causes of bacterial meningitis.

Absolute contraindications to neuraxial anesthesia are patient refusal, infection at the needle insertion site, significant coagulopathy, uncorrected hypovolemia, increased intracranial pressure, and cardiac disease or impairment inconsistent with the regional anesthesia–induced sympathectomy (aortic valve stenosis, mitral valve stenosis, or septic shock).[7,16,26] Comorbidity is also associated with an increased risk of neuraxial complications; thus, an assessment of these factors should be included in the risk assessment: osteoporosis, coagulopathies, diabetes, steroid use, chronic renal failure, and rheumatoid arthritis.[4,17]

Infectious complications after a neuraxial anesthetic are more closely related to failure of pure aseptic technique rather than a hematological spread of an infective agent.[2,4] Infections occur due to contaminated solutions and contaminated catheters.[6] In addition, skin colonization of bacteria and respiratory droplets from the anesthesia provider are other sources of potential infection.[6]

Therefore, sterile technique should be used for all patients, not just febrile patients.

Nonpregnant patients admitted to an emergency department with fever of unknown origin often undergo a diagnostic lumbar puncture to rule out meningitis as part of a sepsis workup, despite the theoretical risk of iatrogenic infection. This type of lumbar puncture is usually performed before administration of antibiotics to prevent skewing culture results. The risk of the procedure is accepted because it is a necessary part of a workup leading to an accurate diagnosis.

The risk of the nonpregnant and pregnant women should be similar; however, there may be a theoretically increased risk to the parturient because of the normal physiologic engorgement of the epidural vasculature that occurs during pregnancy, which may increase the risk of free blood in the epidural space.[5,8]

Overall, the review of the literature does not substantiate the common practice of withholding neuraxial anesthesia from febrile parturients.[1,7,9] However, owing to the rare but potentially devastating morbidity associated with meningitis and abscess, this conservative treatment is difficult to criticize. It is important to emphasize that when faced with this scenario, one must be cognizant of the increased incidence of poor labor pattern and cesarean section in this population, so a full assessment of the risks must include the risk of general anesthesia as well.

Based on the review of literature, we developed a consensus guideline for our obstetric anesthesia practice. We determined that it may be safe to perform a neuraxial pain management technique in a laboring patient with chorioamnionitis; however, we have determined that it is prudent to defer the neuraxial intervention until after the patient has received at least 1 dose of antibiotics.[7,8,10,12,13,15] Our guidelines at this institution were discussed previously in the Antibiotic Management section.

It is important to note that the surveillance of patients with chorioamnionitis includes postpartum assessment and education by an anesthesia provider, which are paramount for the early detection of complications. The earliest possible treatment of epidural abscess is necessary to avoid permanent neurological injury,[19,27] yet this population is likely discharged to home before symptoms arise.

The care for a patient with chorioamnionitis is a relatively common challenge that anesthesia providers face. The evidence to guide clinical decisions is lacking owing to the difficulty of accurately estimating the risk of an infrequently occurring event. Our recommendation is to evaluate each patient individually, with input from obstetric colleagues, keeping in mind the sum of the pertinent risk factors to guide the decision of the safest possible anesthetic for each particular case. Strict sterile technique and close surveillance are also important considerations for amelioration of the risk.

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