Obstetric Anesthesia Update: The New Decade

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OBJECTIVES:

By the end of this lecture, participants should be able to

- Understand current knowledge regarding use of oxytocin for postpartum hemorrhage prophylaxis, including dose and side effects.
- Understand current knowledge regarding treatment of postdural puncture headache after unintentional dural puncture.
- Explain the reasoning behind choice of vasopressors (ephedrine and phenylephrine) for the treatment of neuraxial-anesthesia induced hypotension during cesarean delivery.
- Understand the benefits and limits of crystalloid and colloid administration for the prevention of hypotension during spinal anesthesia for cesarean delivery.
- Understand current knowledge regarding risk of neuraxial infections associated with neuraxial procedures, and recommended techniques to minimize the risk of infection.
- Understand current evidence regarding neuraxial anesthesia/analgesia for external cephalic version of breech presentation.

OXYTOCIN FOR POSTPARTUM HEMORRHAGE PROPHYLAXIS

Recent studies of oxytocin for the management of the third stage of labor have focused on the adverse side effects of oxytocin and the appropriate dose. Oxytocin administered as a bolus (5 or 10 IU) is associated with transient hypotension, as well as ST-segment depression, and occasionally chest pain and shortness of breath.[1-3] Carvalho et al.[4] used a biased coin up-down sequential allocation technique to estimate the ED_{90} of oxytocin administered as a bolus to patients undergoing elective cesarean delivery. The primary outcome was satisfactory uterine tone as assessed by the obstetrician. The ED_{90} was 0.35 IU (95% CI 0.18 – 0.52). Butwick et al.[5] used a random dose allocation method (0, 0.5, 1, 3, 5 IU) to estimate the ED_{50} and ED_{95} of oxytocin in the same patient population. They were unable to estimate these values because of high prevalence of satisfactory uterine tone after all doses of oxytocin, including placebo. The highest dose (5 IU) was associated with a greater incidence of hypotension. Given these results, the investigators stated that high doses of oxytocin should no longer be given and recommend doses between 0.5 and 3 IU.

In an *in vitro* model using rat myometrium, pretreatment of the muscle strips with oxytocin increased the amount of oxytocin required for myometrial contraction in a concentration-dependent manner.[6] Similarly, the ED_{90} for oxytocin [2.99 IU (95% CI 2.32 – 3.67)] was higher in women who underwent cesarean delivery for arrest of labor who had been exposed to oxytocin during labor compared to the ED_{90} without prior exposure to oxytocin.[7]

In the United States, oxytocin administered as part of active management of the third stage of labor is most often administered as an *infusion*, not a bolus. George et al.[8] used a biased-coin up-down sequential allocation technique to estimate the ED_{90} of an oxytocin infusion. The primary outcome was satisfactory uterine tone 3 minutes after delivery as assessed by the obstetrician. The ED_{90} was 0.29 IU/min (95% CI 0.15 – 0.43). If one uses the upper end of the 95% confidence interval, the ED_{90} for an oxytocin infusion is approximately 25 IU/h.

In summary, recent studies suggest high dose oxytocin results in significant hypotension and ST-segment depression. High bolus doses (> 5 IU) are not indicated. Women with previous exposure to oxytocin during labor may require higher doses than those without prior exposure.

PREVENTION OF POSTDURAL PUNCTURE HEADACHE AFTER UNINTENTIONAL DURAL PUNCTURE

The incidence of unintentional dural puncture with an epidural needle during neuraxial procedures in obstetric patients is about 1.5%, and the incidence of postdural puncture headache (PDPH) after unintentional dural puncture is approximately 52%.[9] Techniques to prevent PDPH after dural puncture would be welcome. A recent meta-analysis of possible techniques in the general patient population (including obstetrics) has been published.[10]

Several studies have assessed whether a prophylactic blood patch decreases the incidence of PDPH,[11-14] although most of the studies have methodologic concerns. After unintentional dural puncture, an epidural catheter is placed and used for analgesia/anesthesia. After delivery, autologous blood is injected into the catheter, and the catheter is removed. Scavone et al.[14] performed a double-blind trial in parturients (n = 64) with unintentional dural puncture with a 17-gauge Tuohy needle. Twenty milliliter autologous blood was injected through the epidural catheter after delivery. There was no difference in the incidence of PDPH between the treatment and sham groups (56% in each group, 95% CI of difference (-25% to +25%), nor in the need for therapeutic blood patch (44% vs. 28%, 95% CI of difference -10% to 39%; P = 0.08).

A number of retrospective studies have assessed whether the presence of an intrathecal catheter decreases the risk of PDPH. In this technique, an intrathecal

catheter is threaded through the dural puncture after unintentional dura puncture, and used of analgesia/anesthesia. It is hypothesized that the presence of the catheter in the dural rent initiates an inflammatory reaction, resulting in faster healing. In a retrospective study, the incidence of PDPH was reduced from 81% in the control group (no intrathecal catheter) to 31% if the intrathecal catheter was removed after delivery and 3% if the intrathecal catheter was removed after 24 hours.[15] However, this study suffers from a number of methodologic flaws. Other observational studies have not found that the presence of an intrathecal catheter is protective for the development of PDPH, nor did a meta-analysis (RR 0.21, 95% CI 0.02 – 2.65).[10]

Two single-institution randomized controlled trials have assessed the efficacy of epidural morphine (3 mg shortly after delivery and 24 h later)[16] and intravenous cosyntropin (1 mg)[17] for the prevention of PDPH. Both techniques reduced the incidence of PDPH. However, neither study was powered to address side effects; larger studies are needed to confirm safety before these techniques can be recommended.

In summary, the best technique for avoiding PDPH is avoiding dural puncture with a large-bore needle. Evidence is currently not available to support use of specific interventions to avoid PDPH once dural puncture occurs.

EPHEDRINE VS. PHENYLEPHRINE FOR SPINAL ANESTHESIA-INDUCED HYPOTENSION

Ephedrine was the drug of choice for the treatment of hypotension during neuraxial anesthesia for cesarean delivery for many years. Studies in pregnant ewes suggested that ephedrine better maintained uterine blood flow compared to direct acting alpha-adrenergic agonists.[18] Recent evidence, however, no longer supports this practice. A number of human studies in the last 15 years have demonstrated that phenylephrine is equally effective for treating maternal hypotension. More importantly, in studies of spinal anesthesia for elective cesarean delivery, fetal acid-base status is actually improved with phenylephrine compared to ephedrine. A meta-analysis found no differences in maternal blood pressure, although bradycardia was more likely after phenylephrine treatment.[19] Umbilical artery pH was higher after treatment with phenylephrine (weighted mean difference of 0.03; 95% CI, 0.02-0.04), however there was no difference in the number of neonates with umbilical artery pH < 7.2 (RR 0.78; 95% CI, 0.16-3.92) or Apgar score < 7 at 1 and 5 min.

The adverse effect of ephedrine compared to phenylephrine on fetal pH is likely a direct effect of ephedrine on the fetus (increased fetal metabolic activity).[20] Ngan Kee et al.[21] found an increased rate of placental transfer of ephedrine vs. phenylephrine, as well as a decreased rate of fetal metabolism. It is unlikely that these drugs have any clinically significant adverse effect on the healthy fetus. It is unclear whether there is an adverse effect on fetuses with decreased reserve (e.g., intrauterine growth restriction, non-reassuring fetal status during labor).

Maintaining maternal blood pressure close to baseline decreases the incidence of fetal acidosis and maternal nausea and vomiting. Initiation of spinal anesthesia results in an acute decrease in systemic vascular resistance (SVR) and an increase in cardiac output (CO).[3,22] Phenylephrine treats the decrease in SVR and prevents the increase in CO and heart rate. There is no advantage to combining ephedrine and phenylephrine in terms of blood pressure control.[23] Two recent dose-response studies of prophylactic phenylephrine infusions to prevent hypotension after induction of spinal anesthesia in elective cesarean delivery patients concluded that there is no advantage of high dose infusion rates (75 – 100 µg/min) compared to lower rates (25 – 50 µg/min) for blood pressure control, number of interventions necessary to maintain blood pressure or fetal outcome.[24,25] Higher infusion rates are associated with a higher total drug dose.

CRYSTALLOID AND COLLOID ADMINISTRATION TO PREVENT HYPOTENSION DURING SPINAL ANESTHESIA

Factors associated with an increased risk for hypotension after spinal anesthesia include dose of local anesthesia (and maximum cephalad extent of blockade), low baseline blood pressure, high interspinous level of dural puncture, lack of labor (e.g., elective procedure), and increased baseline sympathetic tone.[26] Traditional preloading with crystalloid prior to the induction of spinal or epidural anesthesia does not significantly decrease the incidence of hypotension. In the presence of euvolemia, crystalloid solution is rapidly redistribution from the intravascular to interstitial space.[27] This may explain the ineffectiveness of preload (administered *prior* to the initiation of anesthesia, when the patient is euvolemic) in preventing hypotension. Dyer and colleagues[28] hypothesized that crystalloid administration may be more effective when administered immediately following the initiation of spinal anesthesia (termed coload), during the development of relative hypovolemia. Indeed, the incidence of hypotension was lower and need for ephedrine less, in a group of parturients randomized to coload (20 mL/kg) compared to a preload 20 min prior to induction.

Several groups of investigators have compared crystalloid preload to colloid (starch) preload and found that the incidence of hypotension after induction of spinal anesthesia is lower after colloid preload.[29-31] This conclusion is supported by a meta-analysis.[32] Several randomized controlled trials have compared colloid preload to colloid coload, and found no advantage of colloid preload compared to coload.[33,34] In any case, without the use of vasopressors, the incidence of hypotension remains greater than 20%, despite use of colloids or manipulation of timing of fluid administration.[32]

Ngan Kee[35] demonstrated that the combination of crystalloid coload with a prophylactic phenylephrine

infusion decreased the incidence of hypotension to 1.9% (95% CI 0.3-9.9%) compared to a group who received minimal fluids with phenylephrine (28.3% (95% CI 18.0 to 41.6%)).

Colloid is expensive, and some patients may have an allergic reaction. Whether routine colloid administration to all healthy women undergoing spinal anesthesia will contribute to improved outcomes is questionable; however, its use may be justified in women at increased risk of hypotension, or in women for whom hypotension or decrease in preload may be associated with clinically adverse outcomes. Taken together, these studies suggest that crystalloid should be administered rapidly at the time of induction of spinal anesthesia, and the use of colloid should be considered in women considered at high risk for hypotension.

NEURAXIAL ANESTHESIA-ASSOCIATED INFECTIONS

Spinal-epidural abscesses and meningitis are rare complications of neuraxial procedures. In a review of 38 case reports of postpartum meningitis, Reynolds[36] concluded that all cases were associated with neuraxial procedures (no cases occurred in the absence of a neuraxial procedure). Although there is no denominator, review of the reports suggests that labor and dural puncture are risk factors for meningitis.

In contrast to community acquired meningitis, iatrogenic meningitis is usually caused by streptococcal viridans species;[36] these organisms are commonly found in the upper airway. Case reports of meningitis following lumbar puncture procedures tend to occur in clusters rather than sporadically, and the offending bacteria have been linked to identical organisms in the airway of the proceduralist.[37] This suggests that meningitis is due to a break in sterile technique, and is not secondary to hematogenous spread.

Of significant concern is the January 2010 report by the Centers for Disease Control (CDC) of 5 obstetric patients in whom spinal or combined spinal-epidural labor analgesia was complicated by postpartum meningitis.[38] Three procedures from one hospital were linked to a single anesthesiologist, and 2 from a second hospital were linked to a second anesthesiologist. *Streptococcus salivarius* was the confirmed cause in 4 of the cases. One patient died. The CDC concluded that *S. salivarius* was likely transmitted directly from the anesthesiologist to the patients, either by droplet transmission directly from the oropharynx (one anesthesiologist did not wear a mask during the procedure), or contamination of sterile equipment. The CDC,[39] the American Society of Regional Anesthesia and Pain Medicine (ASRA),[40] and the American Society of Anesthesiologists (ASA)[41] all recommend that practitioners wear masks while performing neuraxial procedures.

In contrast to meningitis, epidural abscesses are more likely to be caused by skin flora (e.g., *Staph aureus*). Studies have suggested that chlorhexidine[42] and povidone iodine with alcohol[43] produce better skin antisepsis than povidone iodine. The ASRA,[40] the ASA,[41] and the Association of Anaesthetists of Great Britain and Ireland (AAGBI)[44] recommend an alcohol based chlorhexidine solution be used for skin asepsis before regional nerve block procedures. Other recommendations include removal of all jewelry (including rings and watches), handwashing with an alcohol-based antiseptic solution, sterile gloves, individual packets of antiseptics for skin preparation (not multidose bottles), sterile draping of the patient, and the use of sterile occlusive dressings.[40,41,44]

NEURAXIAL ANALGESIA/ANESTHESIA FOR EXTERNAL CEPHALIC VERSION OF BREECH PRESENTATION

A major indication for primary cesarean delivery is malpresentation. The American College of Obstetricians and Gynecologists (ACOG) states that the "cesarean delivery will be the preferred mode of delivery for most physicians because of the diminishing expertise in vaginal breech delivery."[45] However, the ACOG also states that "obstetricians should offer and perform external cephalic version whenever possible."[45] Successful external cephalic version (ECV) decreases the risk of cesarean delivery. A number of small randomized controlled trials have assessed whether neuraxial analgesia/anesthesia increases the likelihood of ECV compared to intravenous or no analgesia. The most recent trial in multiparous women found neuraxial anesthesia (bupivacaine 7.5 mg) resulted in improved success of ECV attempt compared to no analgesia (87 vs. 58%, 95% CI of difference 7.5% to 48%).[46] A meta-analysis (trials = 7, n = 681) also suggests that neuraxial anesthesia/analgesia may improve the rate of successful ECV compared to control (RR 1.44 (95% CI 1.16 – 1.79)).[47] The overall risk of adverse events was low and not different between groups. Several authors have noted that studies which employed *analgesic* doses of neuraxial local anesthetics had less favorable results compared to studies which employed *anesthetic* doses of local anesthetics.[47,48] A head-to-head comparison of neuraxial analgesia vs. anesthesia for ECV is warranted.

Given that the overall rate of cesarean delivery continues to climb, and that cesarean compared to vaginal delivery is associated with a higher incidence of morbidity and mortality, practices that improve the chance of successful ECV, and therefore decrease the rate of cesarean delivery, should be encouraged. A recent editorial by Caughey and El-Sayed[49] suggests that the evidence now supports offering neuraxial analgesia/anesthesia for this procedure.

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