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

- Understand the relationship between the density of epidural labor analgesia and the outcome of vaginal delivery.
- Explain how the mode of drug delivery into the epidural space (bolus vs. infusion) affects characteristics of neuroblockade.
- Explain the reasoning behind choice of vasopressors (epinephrine 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 the etiology and risk factors associated with neuraxial anesthesia-associated infections (meningitis and epidural abscess) and the new ASA guidelines for prevention of neuraxial-procedure related infections.
- Understand the current knowledge regarding the association between neuraxial labor analgesia and fetal bradycardia.

LABOR ANALGESIA AND MODE OF VAGINAL DELIVERY

Multiple randomized, controlled studies comparing epidural to systemic opioid analgesia have also assessed the rate of instrumental vaginal delivery (forceps or vacuum) as a secondary outcome variable. Interpretation of these results is clouded by the fact that most studies did not assess that quality of second stage analgesia. Additionally, the “triggers” for instrumental vaginal delivery vary widely among obstetric providers, and may not be well controlled. Many randomized controlled trials and meta-analysis have concluded that epidural analgesia is associated with an increased risk of instrumental vaginal delivery compared to systemic analgesia (Fig. 1). \(^1,^2\) In contrast, impact studies (comparing mode of delivery before and after initiation of widespread availability of neuraxial labor analgesia) how generally not found a change in the rate of instrumental vaginal delivery (Fig. 2). \(^3,^4\) These findings were confirmed in a systematic review of impact studies including 26,443 women: there was no increase in instrumental vaginal delivery rate after the institutional initiation of neuraxial labor analgesia (1.1% change, 95% CI -1.5 to 3.7%). \(^5\)

Several investigators have randomized women with 1st stage epidural analgesia to receive continued epidural analgesia or epidural saline during the 2nd stage of labor. \(^6-^10\) In an editorial review, Chestnut concluded that effective 2nd stage analgesia likely increases the risk of instrumental vaginal delivery. \(^11\) A meta-analysis of available studies concluded that 1) there is insufficient evidence to support the hypothesis that discontinuing epidural analgesia...
Figure 2: Impact study of epidural analgesia on mode of delivery.

During the 2nd stage of labor reduces the rate of instrumental vaginal delivery rate, but that a larger study was needed, and 2) there is evidence that this practice increases the rate of inadequate pain relief in the 2nd stage of labor.\(^\text{12}\)

The effect of neuraxial analgesia on the outcome of the 2nd stage of labor may be influenced by the density of neuraxial analgesia. High concentrations of epidural local anesthesia may cause maternal motor blockade, causing relaxation of pelvic and pelvic floor musculature, which in turn may interfere with fetal rotation during descent. Abdominal muscle relaxation may decrease the effectiveness of maternal expulsive efforts. A recent multi-center study in over 1000 nulliparas found that the rate of instrumental vaginal delivery was higher in women who received traditional epidural analgesia with bupivacaine 0.25% compared to women who received low-concentration bupivacaine epidural techniques (bupivacaine 0.1% and fentanyl)(37% vs. 29%).\(^\text{13}\)

Similarly, in another study, women randomized to receive CSE analgesia (maintained with bupivacaine 0.0625% plus fentanyl) had a lower rate of instrumental vaginal delivery compared to women who received epidural analgesia (initiated with bupivacaine 0.25% and maintained with bupivacaine 0.125% with fentanyl).\(^\text{14}\)

In summary, the current evidence suggests that effective 2nd stage neuraxial analgesia may cause an increased risk of instrumental vaginal delivery, particularly dense analgesia with motor blockade. Anesthesia providers can minimize this risk by using low-dose epidural techniques, but this may be associated with less effective analgesia.

**MAINTENANCE OF EPIDURAL LABOR ANALGESIA**

The ideal labor analgesic technique would provide constant pain relief of long duration, minimize undesirable side effects, not interfere with the progress of labor, and minimize physician involvement. Local anesthetic solutions that provide complete analgesia during the whole of labor are often associated with motor blockade and an increased incidence of instrumental vaginal delivery.

The method of delivering the anesthetic solution to the epidural space influences the degree of motor block. Given the same concentration of local anesthetic, analgesia maintained by infusion compared to intermittent boluses results in greater drug utilization, a greater degree of motor blockade,\(^\text{15,16}\) and a higher incidence of instrumental vaginal delivery.\(^\text{17}\) However, intermittent manual bolus administration by the anesthesiologist results in more breakthrough pain, decreased patient satisfaction, and more work for the anesthesiologist. Hence, in recent years, maintenance of epidural analgesia with continuous infusions has been the norm. This requires a decrease in local anesthetic concentration in order to avoid an increased incidence of motor blockade.

Another method of administering bolus doses while minimizing breakthrough pain and anesthesiologist workload is patient controlled epidural analgesia (PCEA). Studies have compared continuous infusions to PCEA. A meta-analysis of these studies concluded that women who had PCEA had fewer interventions by the anesthesiologist (risk difference 27% (95% CI: 18 to 36%)) (Fig. 3), used less local anesthetic, and had less motor blockade compared to women with continuous infusion epidural analgesia.\(^\text{18}\) Ropivacaine and levobupivacaine may be associated with less motor blockade compared to equipotent doses of bupivacaine,\(^\text{19-21}\) although this was not associated with a decreased rate of instrumental vaginal delivery.\(^\text{21}\)

**Figure 3: PCEA vs. continuous infusion**

<table>
<thead>
<tr>
<th>Study (first author)</th>
<th>PCEA (n/N)</th>
<th>Infusion (n/N)</th>
<th>Risk difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sia(^\text{511})</td>
<td>17/20</td>
<td>16/20</td>
<td></td>
</tr>
<tr>
<td>Boutros(^\text{253})</td>
<td>42/48</td>
<td>34/50</td>
<td></td>
</tr>
<tr>
<td>Gambling(^\text{254})</td>
<td>34/55</td>
<td>5/13</td>
<td></td>
</tr>
<tr>
<td>Purdie(^\text{257})</td>
<td>38/75</td>
<td>16/84</td>
<td></td>
</tr>
<tr>
<td>Collis(^\text{256})</td>
<td>27/44</td>
<td>12/46</td>
<td></td>
</tr>
<tr>
<td>Curry(^\text{255})</td>
<td>29/30</td>
<td>17/30</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>187/272</td>
<td>100/243</td>
<td></td>
</tr>
</tbody>
</table>

There are conflicting data as to whether PCEA should include a background infusion. Bupivacaine consumption is higher with background infusions compared to a pure PCEA technique without a background infusion.\(^\text{22}\) In a review of the topic, Halpern and Carvalho\(^\text{23}\) concluded that a background infusion of one third to one half the total hourly dose (2 to 10 mL) improves analgesia and may be helpful.
in selected parturients (e.g., nulliparas with long labors).

As discussed above, the bolus administration of epidural anesthetic solution appears to result in improved analgesia with a lower total drug dose. There may be more wide-spread distribution of anesthetic solution within the epidural space when large volumes are injected as a bolus compared to a slow infusion. Investigators have demonstrated that programmed (automated) intermittent boluses (PIEB) administered via a programmable pump results in improved patient satisfaction, less drug use, longer duration of analgesia, and less breakthrough pain compared to a continuous infusion of the same mass of drug per unit time. The maintenance dose is administered as a bolus at regular intervals, instead of as a continuous infusion (i.e., 5 mL q 30 min instead of 10 mL/h). Commercial pumps that allow easy utilization of this mode of anesthetic solution delivery are not yet currently available.

Ephedrine vs. phenylephrine for treatment of neuraxial 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. 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. 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 min instead of 10 mL/h). Commercial pumps that allow easy utilization of this mode of anesthetic solution delivery are not yet currently available.

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. 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 euolemia, crystalloid solution is rapidly redistributed from the intravascular to interstitial space. This may explain the ineffectiveness of preload (administered prior to the initiation of anesthesia, when the patient is euolemic) in preventing hypotension. Dyer and colleagues 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.\textsuperscript{43,45} This conclusion is supported by a meta-analysis.\textsuperscript{46} Several randomized controlled trials have compared colloid preload to colloid coload, and found no advantage of colloid preload compared to coload.\textsuperscript{47,48}

Ngan Kee\textsuperscript{49} 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 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 of hypotension. Phenylephrine is no longer contraindicated for the treatment of hypotension and may be the drug of choice.

**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\textsuperscript{50} 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; 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.\textsuperscript{51} 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.\textsuperscript{52} 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\textsuperscript{53} the American Society of Regional Anesthesia and Pain Medicine (ASRA)\textsuperscript{54} and the American Society of Anesthesiologists (ASA)\textsuperscript{55} all recommend that practitioners were masks while performing neuraxial procedures.

In contrast to meningitis, epidural abscesses are more likely caused by skin flora (e.g., Staph aureus). Studies have suggested that chlorhexidine\textsuperscript{56} and povidone iodine with alcohol\textsuperscript{57} produce better skin antisepsis than povidone iodine. The ASRA\textsuperscript{54} and the ASA 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\textsuperscript{54,55}

**NEURAXIAL LABOR ANALGESIA AND FETAL BRADYCARDIA**

Fetal bradycardia not associated with maternal hypotension occurs after the initiation of neuraxial labor analgesia. Although unproved, current information suggests that uterine tachysystole (hypertonus) is responsible. Circulating epinephrine levels are markedly elevated during labor. Levels drop precipitously after the initiation of neuraxial labor analgesia.\textsuperscript{58} Epinephrine is a tocolytic, and an acute decrease may temporarily “unbalance” the equilibrium between tocolytic and uterotonic activity.\textsuperscript{59} Fetal bradycardia seems to occur earlier after initiation of CSE (15 min) than epidural (<30 min) analgesia. There is some disagreement as to whether it occurs more commonly after CSE.\textsuperscript{60-62} In a randomized controlled trial fetal bradycardia and uterine tachysystole were more common after CSE than epidural analgesia.\textsuperscript{63} However, fetal heart rate was only monitored for 15 min after initiation of analgesia, so that fetal bradycardia after epidural analgesia may have been missed.\textsuperscript{64}

The results of a systemic review suggest that fetal bradycardia is more common after intrathecal opioid analgesia compared to any other neuraxial labor analgesia technique.\textsuperscript{65} Data are inconsistent was to whether there is a intrathecal opioid dose response of fetal bradycardia.\textsuperscript{66-68} Patient selection bias for the CSE technique may play a role in that women in advanced labor more often receive a CSE compared to epidural technique, and these women are at higher risk of fetal heart rate decelerations and bradycardia.\textsuperscript{69} The emergency cesarean delivery rate secondary to fetal bradycardia was not different.
between parturients who received CSE vs. systemic analgesia in a large observational study,\textsuperscript{70} and in several large randomized controlled trials.\textsuperscript{71,72} In contrast, another randomized study did find an increased incidence of emergency cesarean delivery in subjects randomized to CSE vs. systemic analgesia (2% vs. 0%).\textsuperscript{73} Discontinuing oxytocin administration, administration of terbutaline, IV or sublingual NTG, and a fluid bolus are effective treatments of uterine tachysystole.

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