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Neuraxial Analgesia and its Effects on Neonatal and Maternal Outcomes

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Abstract

Neuraxial analgesia is one of the most popular and effective forms of pain relief for labor and childbirth used by more than 50% of women in North America. Despite the standard use of the procedure, there is much that is still inconclusive about the side effects on mother and baby. Current studies show it has an impact on some outcomes and seemingly no effect on others. While the extent of the impact is still unclear, there are some adverse side effects of neuraxial analgesia, which include instrumental deliveries, respiratory distress and lower Apgar scores. Further research is required to conclude how and to what extent neuraxial analgesia impacts mother and baby.

Introduction

Labor and childbirth are known to be extremely painful experiences. Over the years there have been multiple methods developed which provide pain relief. Neuraxial analgesia, known colloquially as 'epidural', is one of the most popular forms of pain relief and is used by 50-70% of women in North America. It became a standard form of labor analgesia during the 1970s (Silva and Halpern 2010).

When neuraxial analgesia is administered, a small amount of anesthetic is inserted into the epidural space of the spine to prevent pain signals from traveling from the spine to the brain (Schrock and Harraway-Smith 2012). The drugs used most often in North America are bupivacaine and ropivacaine (Silva and Halpern 2010). There are few forms of epidurals used. For the epidural procedure, a catheter is inserted directly into the epidural space of the spine and the patient receives a continuous flow or multiple injections of local anesthetic. Spinal anesthesia refers to local anesthesia inserted into the subarachnoid space and one injection is usually sufficient. Combined spinal-epidural analgesia includes an initial spinal intrathecal injection as well as an epidural catheter for additional drugs. Neuraxial analgesia is an umbrella term which includes all three methods: epidural, spinal and combined spinal-epidural.

This text includes all three types of neuraxial analgesia used in labor. When using the term 'epidural', it refers to any of the three forms.

During labor and delivery, the primary concern is the safety and health of the mother and neonate.

Despite the longevity and standardized use of the procedure, there is much that is still unknown about the side effects of epidural analgesia and its impact on labor progress and maternal and neonatal outcomes. This text aims to explore if there are any adverse effects of epidural on the process of labor and delivery and on the health of the mother and neonate.

Methods

Original studies and scientific papers found through TouroLib access to databases such as PubMed, Proquest, and EBSCO were used for this review. Google scholar was also used. Many of the studies are retrospective since readily available data greatly increases the population sample size. To ensure the research included pertains to current techniques, most studies used were published within the last ten years.

Oxytocin Augmentation

There are several ways in which epidural may have an effect on the mother during labor. Epidural has been linked to increased need for oxytocin augmentation during labor and delivery. Oxytocin is a hormone secreted by the pituitary gland. During labor, it stimulates uterine contractions and dilates the cervix. Oxytocin is continually secreted during labor through a positive feedback loop. Contractions push the fetal head towards the cervix which stimulates additional oxytocin to be produced. If labor does not progress at a proper rate, synthetic oxytocin can be administered intravenously to strengthen the contractions. This process helps progress the labor; however, it increases the risk of multiple adverse outcomes for the neonate (Bell et al. 2014).

A retrospective case-control study was done using clinical records of all mothers admitted to Riga hospital between January 1, 2013, and December 31, 2013. Infants included in the study were singleton pregnancies, at least 37 weeks of gestation, in cephalic position and vaginally delivered.

Epidural analgesia was given on demand, and the birth had to occur more than one hour after the epidural analgesia was used. Eight hundred and thirty-two women were included in the study, 304 who received epidural and 528 in the control group. Women who had epidural analgesia had higher rates of augmentation of their first stage of labor with oxytocin than women who did not receive epidural analgesia (Krievina et al. 2015). These findings are consistent with a study which also found increased oxytocin use in women receiving epidural analgesia (Decca et al. 2004).

Another study of 160 women, 80 receiving epidural analgesia and 80 in the control group found no difference in the percentage of patients who received oxytocin, but the maximum rate of oxytocin infusion was significantly higher in the epidural group, compared to the control group [$P=0.001$] (Mousa et al. 2012).

These studies have exhibited an increase in the relationship between epidural and the need for synthetic oxytocin administration, which increases the risks for complications during labor and delivery.

Length of Second Stage Labor

Epidural has also been studied in association with its effect on the second stage of labor. The second stage of labor is also known as the pushing stage. Prolonged second stage labor has been associated with adverse effects on neonatal outcome, including

an increased relative risk of birth-asphyxia related complications and increased chances of NICU admission (Sandstrom et al. 2017). The longer the second stage of labor, the lower the infants one-minute Apgar score was and the higher the incidences of asphyxia. Prolonged second stage labor also has adverse effects on the mother. Li et al., discovered that the longer the second stage of labor progressed, the higher the incidences of cesarean section and postpartum hemorrhaging (Li et al. 2011). A study conducted across Washington state found that in nulliparous women, there was a two-fold increase in the median duration of second stage labor in women who received epidural analgesia when compared to those who did not. It also recorded a two-hour increase in second stage labor in the 95th percentile for women who received epidural analgesia (Souter et al. 2018).

A similar retrospective analysis was performed on all live, singleton, full term, vaginal deliveries in a university hospital between the years 2012-2014. Exclusion criteria included operative deliveries due to fetal distress, major fetal anomalies and chromosomal abnormalities. The inclusion criteria were met by 15,499 deliveries. In this sample, women delivering with epidural analgesia were associated with an additional 82 minutes of second stage labor in the 95th percentile for both nulliparous and multiparous women. The study examined the effects of epidural analgesia on both nulliparous and multiparous women, and within each of those groups, there were women who received oxytocin augmentation were compared to those who did not. There was a significant effect found in all four groups. This study found epidural analgesia to be overall associated with over a one-hour increase in second stage labor (Shmueli et al. 2016).

A retrospective cohort study done on all live, singleton births in the University of California, San Francisco between 1976 and 2008 studied the effects of epidural on labor length. The study excluded pregnancy complications and cesarean sections that took place during the first stage of labor. The study included 42,268 women, where 49.9% had received epidural analgesia and 50.1% did not. Statistical analysis showed that women in the 95th percentile of the second stage of labor who received epidural analgesia had an average difference of more than two hours in duration of second stage labor when compared to women who did not receive an epidural. This number was statistically significant in both nulliparous and multiparous women (Cheng et al. 2014).

Instrumental or Operative Vaginal Delivery

Epidural has also been studied in its association with the need for instrumental or operative vaginal delivery. Instrumental or operative vaginal delivery is when forceps or vacuum extraction is used to extract the fetus from the vagina. This has been associated with adverse neonatal outcomes.

One study conducted on 2052 women in San Diego studied the risk of instrumental vaginal deliveries and cesarean sections

in nulliparous and multiparous women when epidural analgesia is administered during the first stage of labor. The study excluded multiple births, inducements and preterm births. In nulliparous women, the relative risk of operative vaginal delivery was 2.5 when compared to women without an epidural. For multiparous women, the crude relative risk was 11.5 for operative deliveries (Nguyen et al. 2010).

A retrospective study on 350 female patients who received epidural analgesia and 1400 controls showed that vacuum extraction and cesarean sections were more frequently performed in the epidural group than the control group [$p < 0.001$]. The epidural analgesia slowed down the progress of labor, which led to an increased rate of instrumental deliveries. The instrumental delivery appeared to affect the neonatal outcome more than the epidural analgesia itself (Hasegawa et al. 2013).

A study conducted on 100 neonates born with epidural analgesia and 100 without had results consistent with other studies regarding epidurals and instrumental deliveries. Instrumental delivery, which included both forceps and vacuum extraction, had taken place during 13 births, 11 of which were from the epidural group [$p < 0.10$], making this a statistically significant study (Shrestha et al. 2014).

Krievina et al. 2015, whose population size was 832, discovered no difference between epidural analgesia groups and the non-epidural groups in regards to the use of vacuum extraction. The study recorded vacuum extraction only used in first-time mothers (Krievina et al. 2015).

While not indisputably conclusive, there is evidence in the research of a correlation between epidural analgesia and an increased need for instrumental deliveries.

Cesarean Section

A few studies noted the association between epidural analgesia and increased rate or risk of cesarean sections. Nguyen et al., (2010) conducted a study showing that administration of epidural analgesia during the first stage of labor increased cesarean section rates (Nguyen et al. 2010). Hasegawa et al., (2013) also recorded that cesarean sections were more frequently performed on the group of women receiving epidural analgesia than the control group [$p < 0.001$] (Hasegawa et al., 2013). Mousa et al. and Decca et al. both recorded no increased cesarean section rates (Mousa et al. 2012) (Decca et al. 2004). The results of the studies disagreed but both Nguyen et al. and Hasegawa et al. studies consisted of significantly larger populations than either Mousa et al. or Decca et al.

Maternal Fever

Epidural is known to increase maternal temperature. Maternal temperature during labor and delivery is associated with effects on the neonate. Intrapartum fever is related to infectious and noninfectious etiology. It is a well-known risk factor for adverse

Neuraxial Analgesia and its Effects on Neonatal and Maternal Outcomes

neonatal outcomes including neonatal sepsis, seizures, asphyxia and mortality (Petrova et al. 2001). It is also known to effect obstetric outcomes; intrapartum fever significantly increases the rates of cesarean sections and operative vaginal deliveries (Lieberman et al. 1999). Whether increased fever related to epidural has the same adverse effects as other intrapartum fever is a question that has been studied.

One study was performed to investigate the relationship between combined-spinal epidural and increased maternal intrapartum temperature. Seventy women were included in the study, 35 receiving combined spinal-epidural anesthesia and 35 who did not receive any pharmacological form of pain relief. At the start of the study, the median temperature of the women was the same in both groups; after the first hour, there was an increase of intrapartum maternal temperature in the women receiving epidural analgesia. The difference in temperature between the two groups remained until the sixth hour and onward, where no statistically significant difference was found.

Five of the 35 women receiving combined-spinal epidural developed intrapartum fever while no fever was found in the group receiving non-pharmacological pain relief ($P=0.027$). However, there were no statistically significant differences in neonatal outcome. None of the infants born to mothers who had intrapartum fever developed neonatal sepsis, required antibiotic treatment, nor were they evaluated for neonatal infection. This study showed that combined-spinal epidural had an impact on intrapartum maternal temperature and can cause fever. It does not, however, have any adverse effects on neonatal or maternal outcome (de Orange et al. 2011).

A statewide study was conducted in Colorado on the association between epidural analgesia, maternal fever and neonatal antibiotics. Antibiotic administration to neonates who are at risk of infection is essential in preventing neonatal sepsis. However, unnecessary exposure to antibiotics is associated with significant risks.

There was no difference found between epidural and non-epidural groups in the administration of antibiotics to newborns born to mothers with fever. Women who received epidural analgesia were 5.4 times more likely to develop intrapartum fever. However, the infants had antibiotics administered equally in all cases of fever, regardless of what the cause was. This indicates that infants born to mothers who received epidural analgesia are more at risk of receiving unnecessary antibiotic treatment (White et al. 2017). While epidural-related fever did not seem to have a physiological effect on the neonate, the fever did lead to unnecessary antibiotic exposure.

Apgar Scores

One of the first assessments performed on a neonate is the Apgar score. The Apgar scoring system is a rapid method of assessing the clinical status of a newborn at one and five minutes of age. The Apgar score comprises of five components: 1. Color

2. Heart rate 3. Reflexes 4. Muscle tone and 5. Respiration. Each component is given a score of 0, 1, or 2. This is an accepted and standard method for reporting the status of an infant immediately after birth. While the Apgar score cannot be used to predict outcomes or diagnose alone, it is a useful tool in assessing the newborn. Because this is the standard test performed on all infants born in Western countries, it is simple data to collect and study and is one of the foremost things to examine when determining a baby's status (acog.org). Since most studies are conducted retroactively and all infants are scored on the Apgar system, it is an easy and commonly studied component.

A study was conducted in Spain on all full-term infants excluding inductions, elective cesarean sections and major pregnancy complications. The mean Apgar scores at one and five minutes were slightly but statistically significantly lower in the group of infants exposed to epidural analgesia [$p=0.001$] (Herrera-Gomez, 2015).

A different study conducted by Krievina et al. had a similar infant population, however with only singleton infants included. There was no statistically significant difference in the Apgar scores of infants whose mothers received epidural analgesia and those whose mothers did not. In this case, the birth had to be at least one hour after the epidural analgesia was administered. Although the outcome was different than in the previous study, the population size was much smaller in this study than in the study conducted by Herrera-Gomez (Krievina et al. 2015).

Another study recorded the Apgar scores were significantly lower in neonates who were delivered via vacuum extraction when compared to those delivered via spontaneous vaginal delivery and cesarean sections, regardless of whether the mother had an epidural or not. However, this study also found that epidural analgesia significantly increased the incidences of operative delivery. This leads to an indirect association between epidural analgesia and lower Apgar scores (Hasegawa et al. 2013).

Respiratory Distress

One of the variables that is observed when a child is born is the respiratory state of the newborn. A case-control study discusses the effects that epidural analgesia can have on the respiratory state of newborns in the immediate neonatal period. The case consisted of newborns who had gone into respiratory distress. The control group was comprised of site matched neonates of similar gestational age who did not go into respiratory distress. Infants included were late preterm or term. Exclusion criteria for this case group were major congenital malformations associated with newborn respiratory distress, culture-proven sepsis within 72 hours of birth or elective cesarean sections. Two hundred and six infants and 206 matched controls were included in the study. Seventy percent of infants who experienced respiratory distress had mothers who were exposed to epidural analgesia. In the control group 63% of infants had mothers who were exposed

to epidural analgesia. After statistical adjustments, the difference between the two groups was statistically significant [$P=.04$]. This study shows an association between epidural use and subsequent respiratory distress in the infant (Kumar et al. 2014).

A study conducted in Spain with 2399 infants studied the association between epidural analgesia and need for resuscitation. From the infants born to mothers who used epidural analgesiac, resuscitation was required in 28.7% versus 17.6% in the infants whose mothers did not have epidural analgesia [$p=.001$]. This study shows a correlation between epidural analgesia and the risk of resuscitation in newborns (Hererra-Gomez 2015).

Breastfeeding

The benefits of breastfeeding both on infant and mother have been well documented. In infants, breastfeeding is associated with reduced incidences of respiratory and gastrointestinal tract infections. Breastfeeding is also shown to reduce the long-term risk of diseases, obesity and diabetes. Maternal benefits include reduced bleeding after delivery, more rapid involution of the uterus and lower risks of future diseases (Eidelman 2012).

A study was conducted on the relationship between epidural analgesia during labor and onset of lactation in healthy women. Those included in the study were all singleton, full-term, vaginal deliveries and pregnancies that had no other pathological conditions. Women who experienced complications during labor were excluded. Only healthy babies with Apgar scores of greater than eight and those that did not require intensive care were included. All the women who participated in the study intended to breastfeed. There were 209 women who received epidural analgesia and 157 who did not. There was a five and twenty day follow up with the mother. There was no difference found in the onset of lactation between the two groups. Onset of lactation was determined as the time between birth and the peak intensity of the three major symptoms of lactation: breast tension, heat, and pain. At 20 days postpartum, more mothers who received epidural analgesia were formula feeding their babies than the mothers who did not receive epidural analgesia (Mauri et al. 2015).

Conflicting results were obtained in a retrospective study conducted by Herrera-Gomez et al. 2015 on all full-term infants born in San Juan de la Cruz Hospital between March 2010 and March 2013. Exclusion criteria included induced labors, elective cesarean sections and high-risk pregnancy factors. The study included 2399 infants. One of the variables studied was the onset of early breastfeeding, which was defined as within the first two hours of birth. Early breastfeeding onset was observed in 82.4% of infants in the epidural group and in 91.1% of infants in the non-epidural group, a significant difference with the odds ratio (OR) factor of 1.96 (Herrera-Gomez et al. 2015).

A study by Dozier et al. (2013) which observed the relationship between epidural analgesia and breastfeeding cessation, found similar results to Mauri et al. 2015. This study included

722 full term, singleton vaginal deliveries in which the mother-initiated breastfeeding. A significant crude relationship was found between epidural analgesia and breastfeeding cessation within 30 days [$p<.01$]. It was also found that the overall interaction between epidural analgesia and intravenous oxytocin negatively affected breastfeeding (Dozier et al. 2013).

Another study conducted on 100 women who received epidural analgesia and 100 women who did not. Exclusion criteria were cesarean sections, preterms, low birth weight and other complications. The timing of the initiation of breastfeeding was divided into three groups: within six hours of birth, six to 24 hours postpartum and after 24 hours. In the epidural and non-epidural group, 96 and 98 infants in each group respectively had started breastfeeding within six hours. Only one in each group established breastfeeding between six to twenty-four hours. Two newborns in the epidural group and one in the non-epidural group started breastfeeding after 24 hours. The P value was .06 not a statistically significant value (Shrestha et al. 2014).

Most studies show no significant difference in the onset of lactation between mothers who had epidurals and those who did not. Women who did not have epidurals were more likely to be breastfeeding for a longer period. However epidural analgesia was not the primary factor in predicting the duration of breastfeeding.

Conclusion

The research discussed in this paper covered a variety of topics such as oxytocin, length of labor, increased need for instrumental-assisted deliveries, Apgar scores and breastfeeding. There are, however, many other areas of impact that have not been covered, such as hypertension, NICU admission and urine passage. The exact impact that epidural analgesia has on maternal and neonatal outcomes is not conclusive. However, studies show that neuraxial analgesia is associated with increased risk of some maternal and neonatal outcomes such as instrumental deliveries, respiratory distress and lower Apgar scores, while having less of an effect on variables such as breastfeeding. Due to the considerable number of variables that determine maternal and neonatal health, it is difficult to identify which outcomes are due solely to epidural analgesia. Most of the research focuses on whether neuraxial analgesia causes side effects, but there is less research on the reasons why it does. Perhaps if the mechanism could be better understood, then more may be understood as to who is at greater risk for experiencing side effects and clinicians can then have the possibility and tools to better treat and educate mothers to be.

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Neuraxial Analgesia and its Effects on Neonatal and Maternal Outcomes

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