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Combined spinal-epidural versus epidural analgesia during labor: fetal effects and delivery outcomes

Analgesia espinal-epidural combinada versus epidural durante la labor de parto: efectos sobre el feto y el parto

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ABSTRACT

Pain during labor may elicit different responses that can be detrimental both to the mother and the fetus. Among the different methods used to relieve pain during childbirth, neuraxial analgesia has proven to be the most effective. The epidural technique and the combined spinal-epidural are the most common techniques for administrating neuraxial analgesia. Several studies have analyzed the adverse reactions of these techniques, by comparing their effects on uteroplacental perfusion measured by uterine contractions, fetal heart rate and the need to perform an emergency cesarean delivery due to these alterations. Comparing the results in these studies, it was demonstrated that, even though patients that had received a combined spinal-epidural presented greater fetal heart rate alterations, this did not increase perinatal complications significantly. These alterations have shown to be transient and, if recognized and treated promptly, do not increase maternal or fetal morbidity and mortality.

KEYWORDS: anesthetics; analgesia; heart rate; opioids; parturition

RESUMEN

El dolor durante la labor de parto puede provocar diferentes respuestas que pueden llegar a ser perjudiciales tanto para la madre como para el feto. La analgesia neuroaxial ha demostrado ser el método más efectivo para el control del dolor durante el parto. La epidural y la combinación espinal-epidural son las técnicas más comunes de administración de analgesia neuroaxial. Múltiples estudios han analizado las reacciones adversas de estas técnicas, comparando sus efectos sobre la perfusión uteroplacentaria mediante la medición de contracciones uterinas, frecuencia cardíaca fetal y la necesidad de realizar una cesárea de

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emergencia debido a estas alteraciones. Al comparar los resultados obtenidos en estos estudios se pudo demostrar que, a pesar de que las pacientes a las que se les administró analgesia mediante combinación de espinal-epidural presentaron mayores alteraciones en la frecuencia cardíaca fetal, esto no aumentó de manera significativa las complicaciones perinatales. Se ha demostrado que estas alteraciones son transitorias y que, si se reconocen y se tratan oportunamente, no aumentan la morbimortalidad materna ni fetal.

PALABRAS CLAVE: anestésicos; analgesia; frecuencia cardíaca; opioides; parto.

INTRODUCTION

During labor, there are several cortical and physiological responses that are going to be received and interpreted differently, depending on individual emotional, motivational, cognitive, social and cultural factors. Throughout the first stage of labor, pain is caused by uterine contractions and cervical dilation. It is transmitted through visceral afferent sympathetic nerves that enter the spinal segments from T10 to L1. In the second stage of labor, when the cervix is fully dilated, pain is caused by perineal stretching and is transmitted through the pudendal nerve and sacral nerves from S2 through S4 (1,2).

There are various maternal physiological responses to labor pain. For example, release of stress hormones like cortisol, sympathetic nervous system response, increased oxygen consumption, hyperventilation, increased blood pressure, cardiac output and vascular resistance and delayed gastric emptying. These alterations are usually tolerated by both, the mother and the fetus, but they can also affect their well-being and the progress of labor. When a patient is not able to tolerate adequately labor pain, physiological effects such as increased oxygen consumption and hyperventilation may produce hypocarbia and respiratory alkalosis and the release of stress hormones such as cortisol and catecholamines that can have a detrimental effect on uterine activity and uteroplacental blood flow. These responses can be attenuated by effective analgesia (1,2).

There are several methods of pain relief in childbirth. Neuraxial labor analgesia has proven to be the most effective method of intrapartum pain relief. The American College of Obstetricians and Gynecologists (ACOG) established that a woman's request for labor pain relief is a sufficient medical indication for its provision. The Epidural Technique and the Combined Spinal Epidural (CSE) are the most practiced methods of neuraxial analgesia; nevertheless, their effects are not yet completely elucidated.

The purpose of this review is to describe these techniques and to analyze recent studies in order to compare their effects on the fetus and the outcome of the delivery and to provide effective ways to prevent and treat alterations that may occur after these procedures (1).

METHODS

A systematic electronic literature search was performed in the databases PubMed and Science Direct. The search terms included “neuraxial analgesia”, “labor pain”, “pain relief during childbirth”, “epidural technique” and “combined spinal-epidural”.

NEURAXIAL ANALGESIA

The use of neuraxial analgesia has demonstrated to be not only effective but also beneficial for the mother and the fetus. It attenuates the sympathetic response to anxiety and pain by diminishing sympathetic nervous activity and reduces the risk of lower limb thromboembolism. It also permits women to have skin-to-skin contact with their babies immediately after birth which improves bonding, as recommended by The Royal College of Obstetrics and Gynaecology (3).

Several factors affect the extent, duration and density of the block, these include the anesthetic agents used, the dose of these agents, the position of the patient and the baricity, which determines how the solution will spread in the intrathecal space (1).

To prevent neurological injury, all neuraxial procedures must be performed below the conus medullaris, which usually can be found at the lower border of L1 vertebral body or sometimes it can end around L2. For this reason, the epidural/spinal needle is regularly inserted at the L3-L4 or L4-L5 intervertebral space (4,5).

There are relative and absolute contraindications for neuraxial analgesia. The absolute contraindications are lack of consent from the patient, a condition that produces an elevated intracranial pressure and infection on the site of the procedure. Among the relative contraindications are preexisting neurological disease, coagulopathy or thrombocytopenia, severe mitral and aortic stenosis, left ventricular outflow obstruction and severe dehydration (5).

Effective neuraxial analgesia should provide pain relief while reversing the adverse maternal physiological responses during childbirth. Among the benefits of neuraxial analgesia are reduced maternal stress hormones, reduced hyperventilation, uterine vasodilation with increased placental perfusion and fewer episodes of hemoglobin desaturation (1).

The most common maternal side effects of neuraxial analgesia are hypotension, sedation, pruritus, nausea and vomiting, urinary retention, fever and shivering. They are caused by the neuraxial block itself or by direct effects of the local anesthetics and the opioids used to relieve the pain (6,7).

- **Epidurall technique**

The epidural technique consists in the insertion of a catheter into the epidural space through the epidural needle with the subsequent administration of local anesthetic solutions. No dural puncture is required. Once the catheter is in place, a test dose of the anesthetic agent is injected to ensure the catheter is not in a vessel or in an intrathecal location. Administrating the test dose prior to the actual doses is important because the quantities of medication used for epidural analgesia are approximately 10 times larger than the ones used for a spinal block. The epidural catheter allows a

constant administration of medication, which usually consists of a combination of long-acting anesthetics with short-acting opiates, by continuous infusion, boluses or a combination of both (4).

An epidural provides a more gradual onset of action, usually 15-20 minutes, and gives less neuromuscular blockade than spinal anesthesia. This slower onset is advantageous in situations in which a rapid onset of sympathetic blockade may cause hemodynamic alterations like in the case of cardiac or respiratory comorbidities (4,8).

- **Combined spinal-epidural technique**

The CSE is a procedure that combines the spinal injection of an analgesic agent to provide a rapid dense neuraxial block with the placement of an epidural catheter to prolong this block (6).

In the combined spinal-epidural technique, a spinal needle, usually 25–27 gauge, is passed through the epidural needle. It punctures the dura-arachnoid membrane and enters the subarachnoid space. Then, in this space, it is administered a local anesthetic agent, an opioid, or both. After that, a catheter is inserted into the epidural space to provide ongoing analgesia. With the CSE technique, lower doses of anesthetic medications are required (3).

The CSE has advantages from both techniques. It provides a rapid onset of blockade, compared with the epidural technique. It also produces a symmetric block and allows the anesthesiologist to extend both the duration and the level of the block. The disadvantages of this technique are that the recovery time is longer than that of an epidural and that it carries a higher risk of postdural-puncture headache and medication errors that could cause a high spinal block (1,3).

FETAL EFFECTS

There are direct and indirect effects of neuraxial analgesia on the fetus. It may affect the fetus directly when local anesthetics or opioids are transferred to the maternal circulation and indirectly through the placenta, via maternal physiological and biochemical effects (6).

- **Uterine blood flow and placental perfusion**

During pregnancy, cardiac output is redistributed, increasing the uterine blood flow that supplies the myometrium, endometrium and the placenta. At term, the uterine blood flow represents approximately 10% to 15% of maternal cardiac output, nearly 750 mL/min (9).

The placenta is an organ that does not regulate itself. Near term, it receives almost 90% of total uterine blood flow. This blood flow redistribution may be subject to short-term regulatory influences and, therefore, hypotension caused by the sympathectomy produced by the neuraxial block can cause a reduction in placental perfusion. This may lead to alterations in the fetal heart rate pattern and even to a transient decrease in fetal oxygenation (9).

- **Effects on the fetus and the outcome of labor**

The administration of neuraxial analgesia may be followed by fetal heart rate abnormalities. These alterations may include bradycardia, reduced variability and late decelerations (1).

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One of the theories that explain the mechanism that causes these fetal heart rate alterations is that, after the administration of neuraxial analgesia, there is a significant reduction of plasma epinephrine and a minor increase in plasma norepinephrine levels. Epinephrine has a tocolytic effect via β-2 adrenergic agonism, therefore, when epinephrine is reduced, there is an unopposed increase in uterine tone that leads to a decrease in placental blood flow and results in fetal bradycardia. Another theory proposes that the increases of norepinephrine levels may lead to vasoconstriction of uterine arteries, which may produce a reduction in placental perfusion that may also cause fetal bradycardia (8).

The study "Elevation of Uterine Basal Tone and Fetal Heart Rate Abnormalities After Labor Analgesia" evaluated 77 low-risk laboring patients. They were randomly assigned to receive one of two labor analgesia techniques: traditional epidural or CSE. They were monitored for 15 minutes before and 15 minutes after the administration of the analgesia with an intrauterine pressure transducer and with an external transducer for fetal heart rate (10).

All women received 10 mL/Kg Lactated Ringer's solution or normal saline. Patients in the epidural group received an epidural injection of 12.5 mg of 0.125% bupivacaine and 10 mcg of sufentanil. Patients in the CSE group received intrathecal solution of 2.5 mg 0.5% bupivacaine and 2.5 mcg sufentanil. Both procedures were followed by the placement of an epidural catheter with needle-through-needle technique. Analgesia was maintained with subsequent epidural boluses upon patient request, with doses according to cervical dilatation: 0.125% until 7 cm, 0.25% between 8 and 9 cm, and 0.5% in the second stage and no epidural boluses were administered in the first 20 minutes of analgesia induction (10).

The study evaluated the alterations in fetal heart rate by testing the occurrence of prolonged decelerations (15 beats per minute or more for more than 2 minutes) or bradycardia (<100bpm) and the alterations in basal uterine tone by measuring the increase of 10 mmHg or more after the administration of a CSE compared with the traditional epidural. The analysis was performed for the first 15 minutes of analgesia induction.

The incidence of hypertonus and fetal heart rate alterations was greater in the CSE group than in the epidural group. There were 17 women that presented hypertonus in the CSE group, compared with 6 in the epidural group (P=0.018). 13 patients experienced fetal heart rate abnormalities in the CSE group compared with 2 on the epidural group (P<0.01). Both events presented simultaneously in 11 patients of the CSE group compared with 1 in the epidural group (P<0.01) (10).

In all cases both hypertonus and nonreassuring fetal heart rate were treated with general measures such as hydration, suspension of oxytocin and oxygen supplementation. There was no need for administration of tocolytic agents or to perform an emergency cesarean delivery. These findings exemplify that the faster the pain relief, as in the case of the combined spinal-epidural group, the higher the probability of uterine hypertonus and fetal heart rate changes (10).

In a prospective, randomized and double-blind study conducted at the Royal Free Hampstead NHS Trust in London, 115 parturients were recruited and randomly assigned to either CSE or epidural labor analgesia. They compared the two neuraxial techniques by assessing neonatal outcome based on Apgar scores and umbilical artery and vein pH and base excess and the obstetric outcome. They analyzed base excess under the premise that it may be a better indicator of neonatal metabolic status than pH because the latter may be affected by maternal breathing. Based on the results of this study, no difference was found in neonatal and obstetric outcomes between both neuraxial techniques (7).

How neuraxial analgesia affects the progression of labor and the delivery outcome has been subject to multiple trials. Several modifications have been made through the years in the choice of anesthetics and the doses of administration to prevent adverse effects. Some of the most concerning aspects are whether or not neuraxial analgesia increases the need for cesarean delivery, how it affects the duration of labor and its association with increased risk of instrumental delivery (11).

A 2018 Cochrane systematic review compared the effects of epidural with non-epidural or no analgesia for pain management in labor. They analyzed the association between neuraxial analgesia and the requirement of cesarean delivery in 33 trials involving 10,350 women. No difference was found in cesarean section rates between both groups (12).

The “Update on Modalities and Techniques for Labor Epidural Analgesia and Anesthesia” analyses different neuraxial techniques and their effects on the mother, the fetus and the outcome of labor. They compared the results of various previous studies and concluded that the incidence of uterine tachysystole was greater with CSE than with the epidural technique and that the incidence of fetal bradycardia was also greater with CSE technique. Nevertheless, there was no difference observed in emergency cesarean delivery rates caused by fetal bradycardia between the two groups (8).

The effect of neuraxial analgesia on the duration of labor has been widely studied. Several randomized trials have compared epidural or intrathecal analgesia with systemic opioid analgesia. They have measured the time from the analgesia administration to complete dilation of the cervix and they have found that this time is significantly shorter after neuraxial analgesia, demonstrating that either epidural or CSE may reduce the duration of the first stage of labor (11).

Studies have determined that neuraxial analgesia may prolong the duration of the second stage of labor when being compared with other types of analgesia. However, the effect of neuraxial analgesia on the duration of this stage is still unclear, not only because the measurement of the time from the full cervical dilation to delivery is difficult to assess, but also because randomized trials have shown that this duration depends on the local anesthetic being administered and its concentration. Higher concentration neuraxial local anesthetics tend to cause a greater prolongation of the second stage than lower concentration solutions (11).

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A 2017 meta-analysis studied the effect of epidural labor analgesia with low concentrations of local anesthetics on obstetric outcomes in ten trials that included 1809 women. They analyzed the effect on cesarean delivery rate in nine studies with a total of 1681 women and found that there was no significant difference between women with epidural and non-epidural analgesia.

For the effect on the duration of the first stage of labor they analyzed four trials with 438 women and for the effect on the duration of the second stage of labor, eight studies with a total of 1445 women. These studies showed no significant difference between both groups. The effect on the instrumental delivery birth rate was also studied. They included eight trials involving 1442 women. No difference in the instrumental birth rate was found whether or not rescue analgesia was used (13).

Neuraxial analgesia may be administered at any moment during labor. A 2014 Cochrane systematic review compared the effects of early versus late initiation of epidural analgesia in nine trials with a total of 15,752 women. They reported no difference in cesarean delivery rate, instrumental delivery, duration of second stage of labor and fetal outcomes between patients that received the analgesia with less than 4cm cervical dilation or later during labor. The results analyzed in this study have shown that, if the patient is in labor, there is no need to wait for a specific degree of cervical dilation (11,14).

MANAGEMENT OF ADVERSE EFFECTS

Hemodynamic alterations caused by neuraxial analgesia are usually transient and must be recognized promptly in order to treat them and prevent perinatal complications. There are several pharmacological and non-pharmacological methods to prevent and treat these adverse effects.

The first recommendation is to discontinue intravenous oxytocin, if being used. This because oxytocin produces vasodilation that, in addition to the hypotension produced by the induced sympathectomy, may produce a decrease in cardiac output which can lead to a reduction in uterine blood flow and fetal bradycardia (11).

Then, the parturient should be placed in lateral decubitus position immediately after the administration of the analgesia to relieve aortocaval compression. Other options to displace the uterus are a lateral table tilt of >15° or a lumbo-pelvic wedge. Lower limb compression stockings or elastic bandages may be used to increase venous return (15, 16).

Pregnant women present a reduction in functional residual capacity and an increase in oxygen demand of nearly 20%, which may cause early desaturations. Therefore, supplemental oxygen should be administered to prevent maternal desaturation and fetal hypoxemia (15).

Neuraxial anesthesia-induced hypotension causes several clinical manifestations. The mother may experience nausea, vomiting or syncope. These adverse effects may affect the overall birth experience and, if untreated, may be associated with fetal hypoxia and acidosis (16).

Symptomatic hypotension may be treated with vasoconstrictor agents and IV fluids. The ideal vasoconstrictor should be effective and able to improve maternal

blood pressure and uteroplacental blood flow with minimal placental transfer and adverse effects. It should also be easily titrated and should have a fast onset and a short duration of action. The most common agents used to treat hypotension after the administration of neuraxial analgesia are ephedrine and phenylephrine. Small repeated IV doses of these agents should be administered until hypotension is corrected (11,17).

Ephedrine stimulates α-adrenergic receptors in blood vessels, producing vasoconstriction and increasing maternal blood pressure. Its β-adrenergic metabolic effect increases maternal heart rate and cardiac output. However, there is evidence that this β-adrenergic effect may lead to tachyarrhythmias and fetal acidosis (16).

Phenylephrine is an α-adrenergic agonist that counteracts the reduction in systemic vascular resistances caused by the neuraxial analgesia while producing a decrease in heart rate, that is usually elevated due to reflex tachycardia. In the absence of bradycardia, phenylephrine has shown to maintain maternal blood pressure and umbilical artery pH better than ephedrine and to reduce maternal adverse symptoms (16).

CONCLUSIONS

If not tolerated adequately, pain during childbirth may be detrimental for the fetus and the progression of labor. Neuraxial analgesia is the most effective method of intrapartum pain relief. The most used techniques of neuraxial analgesia are the traditional epidural and the combined spinal-epidural. Both may produce maternal and fetal hemodynamic alterations. These alterations are more common after the intrathecal administration of local anesthetics or opioids, therefore, the incidence of hypertonus and fetal heart rate abnormalities is greater after the combined spinal-epidural technique. Studies have shown that hemodynamic alterations produced by both epidural and CSE are usually transient and that when recognized promptly and treated with adequate measures, they do not increase maternal or fetal morbidity and do not affect delivery outcomes; nevertheless, is recommended to monitor the patient's blood pressure, heart rate, oxygen saturation and the fetal heart rate, during and at least 15 minutes after the administration of any method of neuraxial analgesia to be able to detect and correct these alterations.

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