EFFECTS ON MOTHER AND FETUS OF EPIDURAL AND COMBINED SPINAL-EPIDURAL TECHNIQUES FOR LABOR ANALGESIA

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SUMMARY
Objective. Epidural (EA) and combined spinal-epidural (CSE) techniques have both been utilized for labor analgesia. This study compared the effects on the mother and newborn of these techniques in labor analgesia and anesthesia.
Methods. Forty pregnant women received epidural analgesia with 15 mL of 0.125% ropivacaine (EA group) and 5 μg of sufentanil plus 2.5mg bupivacaine in the subarachnoid space (CSE group). Pain intensity, sensory blockade level, latency time, motor block intensity, labor analgesia duration, epidural analgesia duration, maternal hypotension, and pruritus were evaluated. The newborns were evaluated by Apgar and the neurological and adaptive capacity score (NACS) developed by Amiel-Tison.
Results. There were no significant statistical differences between groups for pain scores, latency time, sensory blockade level, and Apgar score. Motor block, labor analgesia duration, and epidural analgesia duration were greater in the CSE group, whose seven mothers had mild pruritus. The NACS were greater in the EA group after half, two, and 24 hours. Ninety five percent of EA group newborns and 60% of CSE group newborns were found to be neurologically healthy at the 24 hour examination.
Conclusion. EA and CSE analgesia relieved maternal pain during obstetric analgesia, but CSE mothers had pruritus and a longer labor. Newborns of mothers who received epidural analgesia showed the best NACS.

Key words: Obstetric analgesia. Local anesthetics. Sufentanil. Newborn.

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Introduction

Epidural analgesia (EA) has been extensively used to provide pain relief in labor. The use of ropivacaine for EA in labor has increased, in part because it has been considered less cardiotoxic and neurotoxic than bupivacaine[1] and because it has been associated with lower incidence of motor block[2, 3] and better outcome for the newborn.[4, 5]

Recently, the combined spinal-epidural technique has gained popularity in labor analgesia. This technique offers some benefits including faster onset of analgesia, decreased incidence of motor blockade, more reliable technique, higher level of patient satisfaction, and decreased incidence of accidental dural puncture.[6]

Spinal addition of opioids, alone or in combination with bupivacaine, has been associated with high levels of pruritus (>80%),[7] hypotension (20%), and respiratory depression.[8] It also may cause fetal bradycardia.[9] Placental transfer is rapid whether the opioid is given by intravenous (5 min), epidural (>15 min), or intrathecal bolus (>15 min).[10] The ideal dose of intrathecal sufentanil in addition to a low dose of local anesthetic (LA) varies between 1.5μg and 5μg.[3, 11] With Neurological and Adaptive Capacity Scores (NACS), the effects of intrapartum drugs on the neonate can be observed.[12]

The aim of this study was to use a randomized trial to compare analgesia and anesthesia with CSE and EA on women in labor and their newborns.

Methods

This study was approved by the Clinical Research Ethics Committee of the Botucatu School of Medicine and written informed consent was obtained from parturients before labor analgesia. All patients had a single healthy pregnancy and were ASA grade I or II. Parturients who had received opioids, had a history of hypersensitivity to LA, or whose fetus showed signs of possible distress or neurological deficit were excluded from the study.

Forty women, without ruptured membranes and inductions, requesting analgesia for labor were randomly (conducted by means of drawing lots) assigned to one of two study groups: EA group (n=20) receiving 15mL 0.125% ropivacaine (18.75mg)

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epidurally; or CSE group (n=20) receiving an intrathecal injection of 0.5ml 0.5% bupivacaine (2.5mg) plus 1ml 0.0005% sufentanil (5μg). Maternal monitoring included noninvasive arterial blood pressure, heart rate, and oxygen saturation. An intravenous infusion of 500mL of lactated Ringer's solution was administered before epidural and CSE techniques were performed. In the EA group, with the patient in a sitting position, an epidural catheter was inserted into the L3-L4 interspace using the loss of resistance to air technique; 2-3cm of catheter were left in the epidural space. With the patient supine, a test dose of LA (30mg of 1% lidocaine with 15μg of epinephrine) was administered followed by ropivacaine. For the CSE group, the same technique was performed to locate the epidural catheter and the same test dose was administered. Using a 25-G Quincke needle at the L2-L3 level, the intrathecal space was confirmed by free flow cerebrospinal fluid and sufentanil with bupivacaine were administered.

During labor analgesia, the following parameters were assessed: 1) pain using the visual analog scale (VAS) (0=no pain and 10=worst possible pain) (before analgesia and after installation of sensory block), 2) height of the sensory blockade determined up to 20 min after LA administration, 3) latency time between drug administration and installation of highest sensory blockade level determined at one minute intervals, and 4) motor blockade determined by testing the abdominal rectus muscles - ARM[13] (100% power, able to rise from a supine to sitting position with hands clasped behind the head; 80%, only able to extend the arms; 60%, only able to lift the scapulae from the bed; 40%, only able to lift the shoulders; 20%, only an increase in tension during effort) after installation of sensory blockade. The duration of labor analgesia was also assessed and is defined as the time between first LA administration and LA administration for delivery (for episiotomy or cesarean section) and the duration of epidural analgesia, defined as the time from beginning of analgesia to childbirth. If a supplementary LA dose was needed (when the pain score was > 3) for labor analgesia, 6mL of epidural 0.125% ropivacaine was always administered. For vaginal delivery, 8mL and for cesarean section 20mL of epidural 0.5% ropivacaine were administered.

Delivery mode and Apgar scores at one, five, and 10 min were recorded. Gestational age (in days) was determined by date of the last menstrual period and in accordance with ultrasonography performed until 20 weeks of gestation age. In the nursery, newborns were again evaluated, always by the same anesthesiologist in a well-lit and heated environment without much noise, at 30 min, 2h, and 24h after birth according to the Amiel-Tison method.[12] It uses scores from the evaluation of five criteria - adaptive capacity (response to sound, habituation to sound, response to light, habituation to light, consolability), passive tone (scarf sign, recoil of elbows, popliteal angle, recoil of lower limbs), active tone (active contraction of neck extensors - from leaning forward position -, palmer grasp, response to traction - following Palmer grasp -, supporting reaction - upright position), primary reflexes (automatic walking, Moro reflex, sucking), and overall vision (alertness, crying, motor activity) (0, 1 or 2 for each sub-item) that were summed to give the final NACS. A total score [3] of 35 is indicative of a neurologically vigorous newborn. The evaluating anesthesiologist was blinded.

Table 1 - Maternal data

Variable	CSE	EA	Significance
Age (yr)*#	21.4 ± 4.4	19.9 ± 3.6	p = 0.27
BMI kg.(m^2)$^{-1}$*#	27.4 ± 3.1	28.3 ± 3.8	p = 0.59
Dilation (cm)*#	7.0 ± 1.1	7.4 ±0.9	p = 0.22
Initial VAS**€	10 (8, 10)	10 (6, 10)	p = 0.41

*Mean ± SD; ** Median (inferior, superior values); BMI = body mass index; VAS = visual analog scale; # Student's t test; € Mann Whitney test

Maternal blood pressure, heart rate, ECG, hemoglobin saturation, and fetal heart rate were monitored at regular intervals. Maternal hypotension was defined as systolic arterial pressure <100mmHg or <30% from baseline, and was treated by increasing the intravenous infusion rate, positioning the patient on her left side, and if necessary, administering ephedrine.

Patients complaining of pruritus were assessed on a scale where 0 represented no pruritus and 10 represented the worst pruritus imaginable.

Statistical analysis

Data were analyzed: 1) for categorical variables, proportions of the variances in the two groups were compared by the Chi-square test calculating the c^2 statistic and P value, or by Fisher's exact test; 2) group semiquantitative variables (Apgar scores etc.) were compared by the Mann-Whitney test; 3) group quantitative variables (measurements) were compared by the t test for independent samples. Level of significance was $P<0.05$ for all tests.

The number of subjects in each group was determined considering the difference in time of labor analgesia and NACS between the two groups with a power of 0.8 and $p<0.05$.

Results

Demographic data for each group was similar (Table 1). In the EA group, 18 were nulliparous, and in the CSE group, 15. The remaining parturients in both groups had had one previous pregnancy.

In each group, one parturient received a supplemental bolus for analgesia (epidural ropivacaine), after 30 min and 15 min after the beginning of analgesia.

The CSE group presented significantly higher motor blockade, labor analgesia duration and epidural analgesia duration. There was no difference between groups for onset time, levels of analgesia, and analgesia evaluation (Table 2). There was no instrumental delivery.

Mild hypotension occurred in one parturient of each group during delivery. Both were successfully treated with additional fluid and 10mg ephedrine IV. Seven patients in the CSE group had mild pruritus (35%) - two had pruritus score 2 in a score of 1 to 5 , and none needed treatment.

Newborns did not differ in weight or gestational age. Apgar score in the CSE group at one minute was higher than in the EA group, but the 5 and 10 min scores were similar in both groups (Table 3).

Results for criteria of the Amiel-Tison method were presented as a median of the scores, with the lower and higher values

Table 2 - Labor analgesia characteristics

Variable	CSE (n=20)	EA (n=20)	Significance
Latency time (min)*#	10.7 ± 4.4	8.8 ± 4.9	$p = 0.19$
Sensory blockade level**€	T6 (T2, T10)	T7 (T4, T10)	$p = 0.10$
ARM (%)**€	60 (20, 100)	80 (40, 100)	$p = 0.02$
Analgesia evaluation (NVS)**€	0 (0, 5)	0 (0, 9)	$p = 0.95$
Duration of labor analgesia (min)*#	89.4 ± 56.3	52.2 ± 37.3	$p = 0.02$
Duration of epidural analgesia (min)*#	112.1 ± 63.2	74.9 ± 45.2	$p = 0.04$
Delivery¥			$p = 0.72$
Vaginal (%)	70	75	
Cesarean section (%)	30	25	

*Mean ± SD; ** Median (inferior, superior values); ARM = abdominal rectus muscles testing; # Student's t test; € Mann Whitney test; ¥ $\chi 2$

Table 3 - Newborn characteristics

	CSE (n=20)	EA (n=20)	Significance
Weight(**)(g)#	3130.3±254.1	3341.3±530.6	$p = 0.11$
Gestation age(**)(days)#	276.3±9.3	278.3±8.3	$p = 0.56$
1st min Apgar score(*)€	9 (7, 10)	8 (2, 9)	$p = 0.10$
5th min Apgar score(*)€	10 (8, 10)	10 (8, 10)	$p = 0.83$
10th min Apgar score(*)€	10 (9, 10)	10 (9, 10)	$p = 0.97$
Adaptive capacity(*)€ (score)			
½ h	6 (3, 8)	7 (2, 10)	$p = 0.13$
2 h	6 (3, 10)	8 (6, 10)	$p = 0.001$
24 h	10 (6, 10)	10 (8, 10)	$p = 0.05$
Passive tonus(*)€(score)			
½ h	4 (2, 7)	6 (1, 8)	$p = 0.02$
2 h	4 (2, 7)	6 (4, 8)	$P = 0.001$
24 h	8 (6, 10)	8 (4, 8)	$P = 0.68$
Active tonus (*) € (score)			
½ h	4 (2, 7)	6 (3, 9)	$p = 0.001$
2 h	5 (2, 9)	7 (4, 10)	$P = 0.01$
24 h	8 (6, 10)	9 (5, 10)	$p = 0.32$
Primary reflex(*) € (score)			
½ h	3 (2, 5)	4 (1, 5)	$p = 0.49$
2 h	3 (2, 6)	5 (2, 6)	$p = 0.02$
24 h	5 (3, 6)	5 (4, 6)	$p = 0.04$
Overall vision (*) €(score)			
½ h	4 (2, 6)	6 (2, 6)	$p = 0.09$
2 h	3 (2, 6)	6 (4, 6)	$p = 0.0008$
24 h	6 (5, 6)	6 (5, 6)	$p = 0.78$
NACS(*)€(score)			
½ h	22 (12, 26)	29 (17, 34)	$p = 0.005$
2 h	23 (17, 28)	33 (21, 36)	$p = 0.00001$
24 h	35 (29, 38)	38 (34, 39)	$p = 0.0063$

(*)Median (inferior, superior values); (**) Values reported as mean ± SD; # Student's t test; € Mann Whitney test

between parentheses. Adaptive capacity score for newborns during the two and 24h exams were statistically higher in the EA than in the CSE group. No significant difference was seen between groups at 30 min. Passive and active tonus at 30 min and 2h were significantly greater in the EA than in the CSE group while at 24h the groups did not differ. Primary reflexes at 30 min were statistically the same in both groups, but at two and 24h they were higher in EA. Statistically, the overall vision at the two hour exam was better in the EA group, but at 30 min and 24h exams results were the same for both groups. At the times of all three analyses, NACS were statistically higher in the EA group than in the CSE (Table 3).

Two hours after birth, no newborn in the CSE group had NACS≥35 versus 30% of newborns in the EA group ($p<0.01$).

Twenty-four hours after birth, 60% of CSE newborns had NACS≥35 versus 95% of EA newborns ($p<0.01$).

Discussion

Combined spinal-epidural for labor analgesia allows for use of smaller doses of local spinal anesthetics because the block can be supplemented at any time. It provides easy identification of the intrathecal space, rapid-onset analgesia, lack of motor blockade, and low exposure of the maternal-fetal unity to drugs. Epidural with catheter, no only prolongs analgesia, but can control its level. Despite the growing and increasing worldwide popularity of this technique,[14] there are complications and side effects, most of them due to intrathecal opioid.

D'Angelo et al.[15] reported higher motor blockade and onset-time by the epidural technique compared to CSE, but 0.25% bupivacaine was used. Researchers using 0.125% bupivacaine plus 50mg sufentanil have found lower motor blockade in epidural than in CSE parturients[16]. In our study, in addition to local anesthetic, decreased motor blockade (ropivacaine) with a smaller dose was found.

The benefits of a limited motor blockade in parturients during labor are well defined. Motor blockade has been associated with lack of maternal satisfaction, prolonged labor and increased number of cesareans[17]. These associations partially coincide with those in this work where the CSE group had longer epidural analgesia duration with increased motor blockade (Table 2), but without presenting an increase of cesarean sections.

A study showed that many factors, such as parity, ruptured membranes, cervical dilation, and others, influence pain intensity. Certain groups of patients would benefit from obstetric analgesia according to this cross-sectional study of one thousand parturients. These include nulliparous patients, young patients, patients who have had labor induced, those with preterm deliveries and those with an assisted vaginal delivery, especially if they are well educated.[18] Our results come from young parturients, mostly primigravida, with no difference in VAS scores before the request for labor analgesia. Both groups benefited from both techniques.

Intrathecal sufentanil is rapidly absorbed into the bloodstream. Lu et al[19] found a statistically significant relationship between intrathecal sufentanil dose and resultant serum sufentanil concentration. In their study, doses of intrathecal sufentanil higher than 12.5mcg did not improve the magnitude or duration of analgesia, but did result in increased serum levels. The authors related that excessive respiratory depression occurred even after small or repeated doses of intrathecal sufentanil, which is consistent with the rapid effect onset. Only 5mg of sufentanil were administered in the subarachnoid space, but decreased NACS was observed in newborns from this group. The significantly greater number of newborns with NACS≥35 at 24h after ropivacaine (EA group) may reflect a difference in the drug's permanence in newborn tissues. Ropivacaine has lower lipid solubility and a shorter half-life than bupivacaine[20]. One can therefore hypothesize that bupivacaine stays in newborn neural tissues longer than ropivacaine and its subtle changes on the neurological function become evident at a time when the effects of ropivacaine have declined. The neurobehavior in EA and CSE groups at 2h were different and NACS in the CSE group were lower. Furthermore, a study undertaken with multiparous patients undergoing induction of labor and receiving a continuous epidural infusion of 0.1% ropivacaine, following an epidural bolus, showed no manifest significant correlation between maternal unbound ropivacaine concentration nor neonatal (cord) ropivacaine concentration, a measure of placental transfer.[21]

Why subarachnoid administration of sufentanil leads to analgesia remains uncertain. Based on studies in humans, Lu et al.[19] observed that 12.5, 25.0, and 50.0mg doses of sufentanil via subarachnoid injection significantly decreased pain. However, together with analgesia, there was an increase in CO_2 arterial blood partial pressure, clearly mediated by opioid distribution in brain receptors. Furthermore, sufentanil plasmatic concentrations after injection were higher than the minimum needed for eliminating postoperative pain in patients when sufentanil was intravenously administered by a Patient Controlled Analgesia pump[22]. Plasmatic distribution of sufentanil after subarachnoid administration has been confirmed, explaining the association between respiratory depression and analgesia which can also be mediated by brain and spinal receptors. Therefore, spinal administration of opioids to the parturient is associated with the same adverse effects brought about by systemic administration. Some analgesic and anesthetic agents administered during labor determine mild to severe neonatal neurological effects remaining after birth. These effects depend on transfer of drugs to the placenta, ability of the newborn to metabolize and excrete the agents, and on central nervous system response. Trauma at birth, perinatal asphyxia and neurological diseases also affect the neurological status, and such effects must be differentiated.

Many depressions or neonatal lesions are apparent and easily diagnosed by a common neurological examination. However, some depressions or mild lesions are not easily detected in neonates. Neonates with higher Apgar scores may display mildly depressed neurological signs due to drugs like mild hypotonia or poor primary reflex responses, etc.[22]

NACS was developed to differentiate newborn drug-induced depression as a result of asphyxia, labor trauma, or neurological disease.[12]

In a review article, Brockhurst et al.[23] criticized the Amiel-Tison test as follows: 1) variability of maternal anthropometric data, 2) exclusion/inclusion factors for neonates, and 3) gestational age. In our study, samples from both groups were homogeneous - young parturient women with similar data (BMI); most were in their first pregnancy and had stated maximum pain evaluation before analgesia (Table 1). The Brockhurst et al.[23] criticism of the Amiel-Tison test would therefore not apply.

Other researchers[24] also assessed NACS reliability with two teams of observers trained to perform the test on healthy, full-term neonates born in vertex presentation. Two tests were carried out: 1) the first team would observe the second performing the test, and separately, both would give NACS to the newborns, and 2) both teams would examine the newborns, but with 30 min intervals between examiners to prevent newborn stress. The test disclosed poor validity, according to the authors. However, some items in the test are subjective, like tone and the authors utilized one examiner to perform and one examiner to observe. They also chose a short time interval, 30 min, between tests; was that sufficient?

The mechanism by which opioids affect fetal heart rate seems to be due to uterine hyperactivity caused by rapid analgesia peaking. Based on laboratory investigations, Segal et al.[25] believed that both increase in myometrial tonus and vascular resistance were determined by epinephrine concentrations associated with the sudden decline in pain. We did not search for uterine hyperactivity in this study. Cited studies showed no evidence of alterations in the newborn condition after high doses of subarachnoid opioids; this is based on Apgar scores, umbilical cord arterial blood gases, or admission to intensive care unit.[26]

Conclusion

EA and CSE analgesia relieved maternal pain during obstetric analgesia, but CSE mothers had pruritus and a longer labor. Newborns of mothers who received epidural analgesia showed the best neurological and adaptive capacity score.

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Resumo

Efeitos maternos e fetais da analgesia de parto pelas técnicas peridural e duplo bloqueio

Objetivo. A peridural (AP) e a técnica de duplo bloqueio (DB) são utilizadas em analgesia para o trabalho de parto. Este estudo comparou os efeitos na mãe e no feto de ambas as técnicas em analgesia e anestesia para o parto.

Métodos. Quarenta parturientes ASA I e II receberam por via peridural 15 ml de ropivacaína a 0,125% (grupo AP) e 5 µg de sufentanil com 2,5 mg bupivacaína por via subaracnóidea (grupo DB). Foram avaliados: intensidade de dor, altura do bloqueio sensitivo, tempo de latência, bloqueio motor, duração da analgesia de parto, tempo para a resolução do parto, hipotensão materna e presença de prurido. Os recém-nascidos foram avaliados pelo índice de Apgar e escore da capacidade adaptativa e neurológica (ECAN), método de Amiel-Tison.

Resultados. Não houve diferenças significativas entre os grupos na intensidade da dor, no tempo de latência, no nível do bloqueio sensitivo e no índice de Apgar. O bloqueio motor, a duração da analgesia e o tempo para resolução do parto foram maiores no grupo DB, do qual sete parturientes apresentaram prurido leve. ECAN foi maior no grupo AP após meia hora, duas horas e 24 horas. Noventa e cinco por cento dos recém-nascidos do grupo AP e 60% do grupo DB foram considerados neurologicamente vigorosos ao exame de 24 horas.

Conclusão. As duas técnicas mostraram-se eficazes para analgesia do trabalho de parto. As parturientes do grupo DB apresentaram prurido e trabalho de parto mais prolongado. Recém-nascidos de mães que receberam analgesia de parto via peridural apresentaram melhor ECAN. [Rev Assoc Med Bras 2009; 55(4): 405-9]

Unitermos: Analgesia obstétrica. Anestésicos locais. Sufentanil. Recém-nascidos.

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