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Original Article

A comparative analysis on the effectiveness of ropivacaine and bupivacaine in combined spinal and epidural analgesia for labor pain and their impact on maternal and neonatal outcomes

Fen Li[1], Jinyu Duan[2]

[1]Department of Anesthesiology, Yulin No.2 Hospital, Yulin City, Shaanxi Province, China; [2]Department of Anesthesiology, 4th (Xing Yuan) Hospital of Yulin, Yulin City 719000, Shaanxi Province, China

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Abstract: Objective: To discuss the effectiveness of ropivacaine and bupivacaine in combined spinal and epidural analgesia (CSEA) for labor pain and their impacts on maternal and neonatal outcomes. Methods: Three hundred pregnant women admitted by Yulin No.2 Hospital from February 2016 to March 2017 with full-term pregnancy and without any contraindications were enrolled in this study and randomly divided into the study group (n=150) and the control group (n=150). The study group received 10 ml of 0.15% ropivacaine combined with 0.2 μg/ml sufentanil in CSEA, and the control group received 10 ml of 0.125% bupivacaine combined with 0.2 μg/ml sufentanil in CSEA. Satisfaction rate, analgesic effect (based on visual analogue scale (VAS)), total administered dose of epidural analgesics and the number of times laboring women pressing patient-controlled epidural analgesia (PCEA) pump of the two groups were compared; duration of labor, usage rate of oxytocin, delivery mode, postpartum blood loss, motor block score after analgesia, postpartum vitals, lactation quantity within 24 hours and cases of neonatal asphyxia were recorded. Results: No statistical significance was found in the differences between the two groups in terms of general indicators such as age, weight, gravidity and parity as well as gestational age (all P>0.05). Overall satisfaction rate of the study group was 94.67%, obviously higher than the 84.00% of the control group (P=0.002). No statistical significance was found in the difference of the VAS results between the two groups before analgesia (P>0.05), whereas there was statistical significant difference in the VAS results between the two groups 10 min, 30 min and 60 min after analgesia and when the cervix was fully dilated in both group (all P<0.05), remarkably, the study group clearly showed better results than the control group (all P<0.001). No statistical significance was found in the difference between the two groups in total administered dose of epidural analgesics, the number of times puerperae using PCEA, duration of labor, delivery mode, usage rate of oxytocin and postpartum blood loss as well as postpartum vitals of puerperae and their lactation quantity within 24 hours, and neonatal asphyxia based on 1 min, 5 min and 10 min Apgar score (all P>0.05). While newborns from the study group scored higher than the control group in modified Bromage score (P<0.05). Conclusion: Compared to bupivacaine, ropivacaine takes effect more rapidly and is more effective when used in CSEA for labor pain, moreover, there was no evidently difference in side effects and impact on maternal and neonatal health between the two groups. Therefore, ropivacaine, which is safe and effective as a labor pain analgesic, is the first choice.

Keywords: Ropivacaine, bupivacaine, combined spinal and epidural analgesia, pregnant women

Introduction

Labor pain is experienced when pregnant women who carried to terms undergoing spontaneous vaginal delivery, which is caused by the fetus pushing and stretching of surrounding tissues when passing through the birth canal as the uterus contracts powerfully [1]. Labor pain brings negative emotions, including anxiety and fear, to women in labor and induces stress responses in them, which increases the morbidity of perinatal complications [2, 3]. The pain simultaneously causes the uterus to contract powerfully, which leads to intrauterine hypoxia, a severe consequence [4, 5]. Therefore, administering analgesia for laboring after ensuring

the safety of mothers and children greatly reduces the negative impact of pain on both of them.

The techniques for labor analgesia are improving. Combined spinal and epidural analgesia (CSEA) has advantages including less time to take effect, small dosage being required and a minor motor nerve block, which makes it a preferred labor analgesia solution in recent years [6, 7]. As labor analgesic techniques keep improving, advances are being made in the field of analgesics as well, among which, low-concentration ropivacaine is the best anesthetic and analgesic currently and is chosen in a variety of clinical applications, due to its advantages including separate sensory and motor blockade and low toxicity [8]. Nogueira et al. compared the analgesic effect for labor between ropivacaine and bupivacaine and based on visual analogue scale (VAS) and Apgar scores, proved ropivacaine to be superior in providing labor analgesia without severe side effects, such as cardiotoxicity and nerve block, whereas there was no significant difference between ropivacaine and bupivacaine in terms of maternal and neonatal health [9]. Based on previous research, this study further evaluates the effectiveness of ropivacaine and bupivacaine and serves as a guide to clinical application.

Three hundred cases of women in labor were administered with ropivacaine or bupivacaine in CSEA from February 2016 to March 2017 in Yulin No.2 Hospital to discuss the effective of ropivacaine for labor pain and its impact on maternal and neonatal outcomes.

Materials and methods

General data

The collection of general materials was approved by the ethics committee of Yulin No.2 Hospital. Patients and their families agreed and signed consent forms.

Three hundred pregnant women admitted by Yulin No.2 Hospital with full-term pregnancy from February 2016 to March 2017 that didn't have any contraindications were enrolled and randomly divided into two groups, 150 in the study group and 150 in the control group. General materials of subjects including age, weight, gestational age and gravidity and parity were collected and analyzed.

Inclusion criteria: Pregnant women who had full-term pregnancy and had a single fetus with cephalic presentation; patients who voluntarily participated in the study and signed consent form; age from 22 to 30; the subjects must have satisfactory pelvic structure for spontaneous vaginal delivery; no contraindications of intraspinal analgesia; the obstetrician and midwife confirmed upon checks that a trial of vaginal delivery was viable and the cervix had dilated to around 3 cm wide.

Exclusion criteria: Patients with hepatorenal insufficiency; patients with a combination of gestational hypertension, gestational diabetes and severe anaemia; patients with mental or neurologic diseases; laboring women that couldn't cooperate with analgesic procedures due to personal reasons.

Methods of analgesia

The study group used ropivacaine in CSEA and the control group used bupivacaine in CSEA. When subjects from both groups had a cervical dilatation of 2-3 cm, venous access was established and vitals were monitored. When laboring women progressed to the active phase of the first stage of labor, a combined spinal and epidural tap was performed and a catheter placed. A total of 3-5 ml of 1% lidocaine was administered as a test dose; if no adverse reactions were observed, the next steps of analgesia were carried out.

The laboring women lied on their left side, and a spinal needle inserted to the subanachroid space between L3 and L4. 0.15% ropivacaine (Astra Zeneca) combined with 5 ml sufentanil was injected to the subanachoid space of laboring women in the study group for analgesia, and 0.125% bupivacaine combined with 5 ml sufentanil in the control group. Three minutes later, laboring women lay on their back and an epidural catheter was inserted 3-4 cm deep towards the head. Level of anaesthesia was below T10 and patient-controlled epidural analgesia (PCEA) was connected. The study group used 100 ml solution prepared with 10 ml of 0.15% ropivacaine combined with 0.2 μg/ml sufentanil; the control group used 100 ml solution prepared with 10 ml of 0.125% bupivacaine combined with 0.2 μg/ml sufentanil; the amount of analgesia was the same in both groups [10]. The solution was fed to epidural catheter via PCEA pump with maintenance dose at 6-7 ml/h, self-administration dose at

Table 1. Comparison of general situation between two groups of postpartum women

Group	Age (years)	Weight (kg)	Gestational week (week)	Pregnancy time
Study group	26.82 ± 3.76	65.86 ± 4.86	38.94 ± 1.93	1.81 ± 0.30
Control group	27.59 ± 3.32	65.71 ± 5.17	38.72 ± 2.11	1.69 ± 0.85
t	-1.871	0.259	0.942	1.630
P	0.062	0.796	0.347	0.104

4-5 ml and loading dose at 4 ml. The lockout interval was 30 min. Analgesic was stopped after full cervical dilatation. If adequate analgesia was not achieved 15 min after using PECA (VAS >3), manual administration was carried out until VAS ≤3 and dosage of which was recorded.

Both groups of laboring women had midwives closely monitoring the delivery. Timely and correct treatments were provided when abnormal situation occurred, such as fetal distress. Laboring women were instructed to hold their breath when the cervix was fully dialed.

Observation indicators

The observation indicators were as follows. (1) Analgesic effect: VAS of pre-administration, 10 min, 30 min and 60 min post-administration and full cervical dilation [11]. VAS scored from 0 to 10: 0, no pain; 1-3, minor pain, tolerable; 4-6, moderate pain that affected sleep but still tolerable; 7-10, severe pain beyond toleration, affecting appetite and sleep. Overall satisfaction rate was based on VAS scores: 0, satisfying; 3-4, satisfying in general; 5 and above, not satisfying. (2) Total administered dose of epidural analgesic. (3) Number of times using PCEA. (4) Duration of the active phase, the second stage of labor, the third stage of labor and the total stage of labor. (5) Postpartum blood loss. (6) Delivery mode: spontaneous vaginal delivery, induced vaginal delivery and caesarean delivery. (7) Usage rate of oxytocin. (8) Postpartum heart rate, blood pressure, oxygen saturation and body temperature were monitored and axillary temperature exceeding 37.3°C was recorded as fever. (9) Postpartum lactation quantity within 24 h; score: 3, hand express yielded splattering breast milk, which was not emptied after lactation; 2, hand express yielded flowing breast milk, nursed newborn ≥ 6 times, the newborn urinated ≥ 6 times, uninterrupted sleeping duration of the newborn after being nursed ≥ 3 h; 1, hand express yielded milk but not sufficient to nurse the newborn and formula was needed; 0, hand express yielded no milk [12]. (10) Modified Bromage score was used to assess level of postpartum motor block in both groups: 0, hips, knees and ankles mobile; 1, hips immobile, knees and ankles mobile; 2, hips and knees immobile, ankles mobile; 3, hips, knees and ankles immobile [13]. (11) Neonatal asphyxia was assessed based on Apgar score [14]. The scores of newborns 1 min, 5 min, 10 min after being delivered were compared, with the full score of 10 and score less than 7 indicted asphyxia.

Statistics processing

The statistics software SPSS 20.0 was used to conduct data analysis. Measurement data was expressed in mean ± SD, a t-test of two individual samples were conducted for data at a particular time point from both groups; The repeated measures analysis of variance (ANOVA) combined with Bonerroni correction was conducted for data from multiple time points, such as VAS. Count data was expressed in percentage and chi-square tests were conducted for intra-group comparisons. $P<0.05$ indicated a statistical significance in the difference.

Results

General information

No statistical significance was found in the difference of general materials between the two groups of laboring women (all $P>0.05$). See **Table 1**.

Comparison of labor analgesia at different time points before and after maternal analgesia

VAS scores of the study group and the control group before administering analgesics and 10 min, 30 min and 60 min after administration as well as when cervix was fully dilated were analyzed with the repeated measures ANOVA. VAS results of the two groups showed difference ($F=33.28$; $P<0.001$); so did VAS of a given patient at different time points ($F=970.94$;

Table 2. VAS pain scores at different time points before and after labor analgesia in the two groups

Group	Before analgesia	10 min after analgesia	30 min after analgesia	60 min after analgesia	Full cervical dilatation	F	P
Study group	9.9 ± 0.52	2.8 ± 0.52	3.2 ± 0.61	3.5 ± 0.40	3.1 ± 0.55	Different time points: 970.94	<0.001
Control group	9.93 ± 0.56	3.9 ± 0.59	4.1 ± 0.17	4.4 ± 0.46	4.0 ± 0.53		
Bonferroni t	1.04	-17.13	-17.41	-18.08	-14.43	Between groups: 33.28	<0.001
P	0.300	<0.001*	<0.001*	<0.001*	<0.001*		

Note: Compared with the control group, *P<0.05.

Table 3. The total amount of epidural analgesia during delivery and the number of active press of analgesic pump

Group	Total dosage			Active press times (times)		
	The first stage of delivery	The second stage of delivery	The third stage of delivery	The first stage of delivery	The second stage of delivery	The third stage of delivery
Study group	19.8 ± 1.74	30.7 ± 3.48	22.8 ± 4.21	1.7 ± 0.73	1.9 ± 0.97	2.1 ± 0.67
Control group	19.6 ± 1.63	31.3 ± 3.25	23.6 ± 3.98	1.6 ± 0.68	1.8 ± 0.81	2.2 ± 0.73
t	1.03	-1.54	-1.69	-1.25	1.082	-1.24
P	0.305	0.124	0.092	0.211	0.280	0.217

Table 4. Comparison of the duration of delivery, the amount of postpartum hemorrhage and the Bromage score in two groups

Group	Duration of delivery (min)				The amount of postpartum hemorrhage	Modified Bromage score
	Active stage	The second stage of delivery	The third stage of delivery	Total stage of delivery		
Study group	180.2 ± 20.63	41.5 ± 15.56	6.2 ± 2.87	401.2 ± 77.47	127.5 ± 24.43	0.09 ± 0.01
Control group	184.7 ± 19.98	47.2 ± 14.74	6.3 ± 2.56	411.2 ± 92.37	131.8 ± 22.66	0.03 ± 0.01
t	-1.91	-1.371	-0.318	-1.016	-1.580	51.96
P	0.056	0.171	0.750	0.31	0.115	0.000*

Note: Compared with the control group, *P<0.05.

P<0.001); interaction effect existed between groups and time (F=4.30; P=0.057). Although average VAS results of 10 min, 30 min and 60 min post-administration and full cervical dilatation from both groups of patients were higher than pre-administration (all P<0.05), the VAS results of the study group were lower than the control group at 10 min, 30 min and 60 min post-administration and full cervical dilatation (all P<0.001). See **Table 2**. No statistical difference of pre-administration VAS results between the two groups was found (P=0.300).

Total administered dosage of epidural analgesia and number of times using PECA

Between the study group and the control group, no statistical significance was found in the difference of total administered dosage of epidural analgesia and number of times using PECA in the first, second and third stages of delivery (all P>0.05). See **Table 3**.

Comparison of delivery duration between the two groups

No statistical significance in the difference of active phase, the second, third and total stage of delivery between the study group and the control group (all P>0.05). Postpartum blood loss of the study group and the control group were 127.5 ± 24.43 ml and 131.8 ± 22.66 ml respectively, with no statistical significance in the difference (all P>0.05). See **Table 4**.

Comparison of delivery mode

No statistical significance was found in the difference between the study group and the control group in terms of spontaneous vaginal delivery rate, Caesarean delivery rate and induced vaginal delivery rate (all P>0.05). No statistical difference was found between the two groups in the usage of oxytocin (P=0.056). Overall satisfaction rate of the study group and

Table 5. Two groups of delivery methods, oxytocin usage and total satisfaction rate

Group	Spontaneous vaginal delivery rate (%)	Instrument induced midwifery rate (%)	Cesarean delivery rate (%)	Oxytocin usage (%)	Total satisfaction rate (%)
Study group (n=150)	108 (72.00)	10 (6.67)	32 (21.33)	28 (18.67)	94.67
Control group (n=150)	102 (68.00)	13 (8.67)	35 (23.33)	32 (21.33)	84.00
X^2	0.571	0.424	0.173	0.333	8.955
P	0.450	0.515	0.678	0.056	0.002*

Note: Compared with the control group, *P<0.05.

Table 6. Comparison of general indicators of postpartum women

Group	Heart rate (beats/min)	Systolic pressure (mmHg)	Diastolic pressure (mmHg)	Blood oxygen saturation (%)	24 h postpartum lactation score	Fever rate (%)
Study group	88.7 ± 13.45	138.5 ± 15.74	83.9 ± 10.26	98.6 ± 1.96	1.69 ± 0.73	15.33
Control group	86.3 ± 12.67	140.1 ± 14.83	84.8 ± 11.39	98.3 ± 1.83	1.57 ± 0.81	27.33
t/X^2	1.591	-0.906	-0.719	1.370	1.348	6.435
P	0.113	0.366	0.473	0.172	0.179	0.011*

Note: Compared with the control group, *P<0.05.

Table 7. Newborn Apgar score

Group	Newborn Apgar score			F	P
	1 min	5 min	10 min		
Study group	8.96 ± 0.25	8.97 ± 0.28	8.97 ± 0.21	Different time points: 0.043	0.958
Control group	8.92 ± 0.33	8.93 ± 0.27	8.94 ± 0.24		
Bonferroni t	1.08	1.26	0.99	Between groups: 0.083	0.777
P	0.282	0.209	0.323		

the control group were 94.67% and 84.00%, and the difference showed statistical significance (P=0.002). See **Table 5**.

Comparison of general indicators of postpartum women

Postpartum heart rate, blood pressure (systolic and diastolic), oxygen saturation and body temperature of the study group and the control group were measured. No statistical significance was found between two groups except fever rate (P=0.113, P=0.366, P=0.473, P=0.172, P=0.011). When it comes to the fever rate, the study group had 15.33% and the control group 27.33%, which constituted a statistical significance in the difference (X^2=6.435, P=0.011). See **Table 6**.

Lactation quantity 24 h after the delivery and modified Bromage score for motor nerve block

The study group scored (1.69 ± 0.73) in 24 h lactation quantity while the control group scored (1.57 ± 0.81), showing no statistical significance in the difference (P=0.179), See **Table 6**. Modified Bromage score was used to test postpartum women from both group, and the difference between the results showed statistical significance. (P=0.000). See **Table 4**.

Newborn Apgar score

The repeated measures ANOVA showed no statistical significance in the difference of Apgar scores between the two groups of newborns (F=0.083; P=0.777); the difference of Apgar scores at different time points of all patients showed no statistical significance (F=0.043; P=0.958); there was interaction effect between groups and time points (F=0.001; P=0.999); no statistical significance was found between newborns from the two groups in the difference of Apgar scores of 1 min (P=0.282), 5 min (P=0.209) and 10 min (P=0.323) after being born. See **Table 7**.

Discussion

Laboring women experience pain caused by nervous impulses arising from pushing and stretching in vagina and uterus as fetus is be-

ing delivered [15]. Labor pain causes negative emotions and physical agony; powerful contractions wear laboring women out, leading to uterine inertia, incongruous contractions, even shock [16]. Currently, intraspinal analgesia is considered to be the most dependable by scholars all over the world, the analgesia effective rate of which is more than 90%. New advances are constantly being made in the field of analgesics as PCEA and CSEA emerges. Ropivacaine improves the effectiveness of labor analgesia and gradually relieves laboring women of negative effects caused by labor pain. Ropivacaine, when combined with synthetic opioid analgesics such as sufentanil, is long-acting and safe, takes effect quickly and has a limited impact on breathing.

Ropivacaine CSEA was used in this study and intra-group comparison of pre- and post-administration proved the effectiveness of this analgesic; in addition, VAS score of two groups was compared, which further indicated ropivacaine takes effect more quickly. The overall satisfaction rates of the two groups were also compared, which showed overall satisfaction rate in study group to be higher than the control group, indicating superior analgesic effectiveness of ropivacaine. However, the study conducted by Nogueira et al. concluded that ropivacaine scored higher than bupivacaine in VAS, which is the opposite of this study's conclusions [9]. That is because the Nogueira study used 0.2% ropivacaine and 0.25% bupivacaine to compare their analgesic effectiveness for labor pain, and produced such results that 0.25% bupivacaine scored lower on VAS but was superior to ropivacaine in nerve block; whereas this study used 0.15% ropivacaine and 0.125% bupivacaine which was of equivalent concentration, excluding the difference in analgesic effectiveness caused by non-equivalent concentrations.

Ropivacaine is a new long-acting long-acting local anaesthetic that has a high plasma protein binding rate and takes effect quickly. Its optimum anaesthetic effect can be achieved with a low concentration, whereas a higher concentration is not only less effective, but causes side effects associated with analgesia [17]. Therefore, a low concentration of ropivacaine is the most effective at providing analgesia and comfort for laboring women, a conclusion consists of our study's findings. A higher concentration of bupivacaine, on the other hand, provides more analgesia; however, the nerve block is also more severe. Therefore, ropivacaine is the better choice for labor analgesia.

In this study, no statistical significance was found in the difference of total administered dose of epidural analgesics, number of times using PCEA, duration of labor, postpartum blood loss, delivery mode and how oxytocin was used between the two groups. After analgesics were administered, laboring women were able to wait for the delivery process to happen without suffering, which preserved their stamina for the following stages and limited the duration of labor. Ropivacaine and bupivacaine, when used to reduce labor pain, could ensure the successful progression of stages of delivery and meet clinical standards for a safe delivery. Such findings are consistent with conclusions from the study conducted by Wang et al. [18]. According to the study of Roomruangwong el al., negative emotions brought about by labor pain cause a surge of endogenous and exogenous stress response matter in laboring women, which leads to a decrease of oxygen delivery to the placenta [19]. After analgesia is administered, placenta blood flow is effectively improved and laboring women produce less catecholamine, which allows them to preserve stamina and work with midwives while maintaining a normal rate of contractions. In our study, no statistical significance was found in the difference between the groups in terms of postpartum heart rate, blood pressure, oxygen saturation and lactation quantity within 24 hours, which proves that ropivacaine and bupivacaine do not affect postpartum vitals and ensure the safety of postpartum women; however, the comparison of body temperature between the study group and the control group showed difference of statistical significance, at 15.33% and 27.33% respectively, which was insignificantly different in other studies. It might be due to the fact that the sample in this study was small. Further studies with larger samples are needed to prove whether there is a statistical difference between the two.

Results from modified Bromage score showed ropivacaine had less motor nerve block effect than bupivacaine, which could result from the former's lower lipid solubility. Physiological

changes occurred after inferior vena cava of laboring women were pressured, including increased blood flow in vertebral venus plexus, dilation of epidural veins, caused the analgesics to be absorbed more quickly, which posed risks of cardiotoxicity and convulsions. However, ropivacaine has lower cardiotoxicity and high convulsion threshold. This is because ropivacaine is a single enantiomer that is effective in blocking pain but has a weak effect on motor tissue. It has a short duration of effect, which poses less interference on the circulation. That makes the separation of sensory and motor tissue blockade possible, allowing patients to walk while feeling the amount of pain reduced, which is why the side effects and inhibition of central nervous system of ropivacaine are significantly lesser than that of bupivacaine [20]. No statistical significance was found when comparing the 1 min, 5 min and 10 min of newborns' Apgar socre of the study group with the control group. That proved both ropivacaine and bupivacaine ensure the safety of fetus. A large amount of studies showed that ropivacaine does not pass easily through placental barrier, thus does not create more risks for fetus.

That is because ropivacaine bonds with α-acid glycoprotein (AAG), a glycoprotein that weakly alkaline drugs mainly bond with in plasma. AAG concentration decrease in plasma leads to lower drug-protein binding rate, which in turn increases the risk of local anesthetic poisoning. When the absolute concentration of AAG in a newborn's plasma is around a fifth of the mother's, the child is at risk of being poisoned when ropivacaine is administered. Calder et al. fed ropivacaine into the epidural space continuously, which increased the absolute concentration of AAG in plasma and reduced free ropivacaine concentration below the threshold, therefore fetal heart beat would not be affected and thus fetus was kept safe [21, 22].

Most pregnant women choose Cesarean delivery to replace spontaneous vaginal birth, which is why C-section rate continues to surge in China [23]. Although C-section reduces labor pain, risks are still involved: more traumas on the mother's body, slow post-surgical recovery, serious complications that might lead to hysterectomy [24]. Therefore, it's crucial to choose labor analgesia that laboring women are willing to use, that has limited impact on duration of delivery and contractions and that is safe for both the mother and the child.

This study observed multiple indicators and conducted comprehensive evaluation of laboring women and newborns. These were its strengths. However, due to the small sample and limited duration of follow-up on mothers and their newborns, complications that might arise from analgesia weren't observed to a full extent, which could be improved in future experiments.

In conclusion, by comparing the effectiveness of ropivacaine and bupivacaine as labor analgesics, we found that ropivacaine CSEA is an effective and safe solution for labor pain, which deserved to be promoted for clinical application.

Disclosure of conflict of interest

None.

Address correspondence to: Jinyu Duan, Department of Anesthesiology, 4th (Xing Yuan) Hospital of Yulin, No.33 West Renmin Road, Yulin City 719000, Shaanxi Province, China. Tel: +86-13720445035; E-mail: duanjinyudjy63@163.com

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