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Original Article

Feasibility of epidural injection of ropivacaine and dexamethasone for labor analgesia in women with preeclampsia

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Abstract: Objective: This study aimed to investigate the feasibility of epidural injection of ropivacaine (Rop) and dexamethasone (Dex) for labor analgesia in women with preeclampsia. Methods: A total of 80 women with preeclampsia delivered in our hospital were enrolled, and were divided into a study group (n=41, Rop + Dex) and a control group (n=39, Rop alone). The changes in pain level, sedation, catecholamine hormone levels and vital signs were compared between the two groups after intervention. The motor blockade score and the incidence of adverse reactions after administration of anesthesia were compared in both groups. Results: Pain level [visual analogue scale (VAS) score], sedation (Ramsay score), adrenaline (AD), norepinephrine (NE), heart rate (HR), and mean arterial pressure (MAP) did not differ significantly between the two groups at pre-analgesia (T0) (P>0.05), and Ramsay score in the study group was significantly higher than that in the control group at 30 min (T1), 60 min (T2), 120 min after analgesia (T3), and cessation of analgesia (T4), and VAS score, AD, NE, HR, MAP in the study group were significantly lower than those in the control group during all stages of labor. Conclusion: The epidural injection of Rop + Dex in women with preeclampsia can play a better analgesic and sedative effect, stabilize maternal hemodynamic index and improve postpartum motor blockade.

Keywords: Epidural injection, Rop, Dex, preeclampsia, labor analgesia, safety, feasibility

Introduction

Gestational hypertension is a form of hypertension during pregnancy [1] and may cause some adverse reactions to pregnancy outcomes. It was found that fetal asphyxia and placenta previa were significantly higher in women with gestational hypertension than in healthy parturients, which significantly increased the maternal risk factor in the perinatal period [2]. Epidemiology survey shows that the prevalence of gestational hypertension is about 9.4% in China and about 7%-12% in other parts of the world, which is currently the main cause of maternal and perinatal miscarriage, preterm birth, and neonatal death [3, 4]. Preeclampsia falls under the category of gestational hypertension, which is specific to pregnancy and has also been shown to be the leading cause of maternal and perinatal mortality. Such condition may lead to maternal hypertension and proteinuria, and may also affect fetal growth and development, leading to adverse outcomes such as growth restriction, fetal distress, and stillbirth [5, 6]. Termination of pregnancy is one of the effective measures for the treatment of preeclampsia. However, women with preeclampsia often experience complications, increasing the complexity of surgery and anesthesia [7]. A study found that women with preeclampsia could not tolerate intra-vertebral anesthesia, and are at higher risk of complications such as heart failure, pulmonary edema, and coagulation dysfunction, thus the mode of anesthesia should be chosen more carefully for these women [8].

Ropivacaine (Rop) is a new type of long-acting amide local anesthetic, with low lipid solubility and better sensory-motor dissociation with motor blockade, and is therefore more suitable for patients with cesarean section [9]. However,

clinical practices have found that low concentration of Rop alone has poor sedative effect by self-control, and higher dose Rop also increases the incidence of anesthesia complications, thus combined anesthesia has become a hot research direction [10]. It has been reported that epidural application of dexamethasone (Dex) can significantly prolong the analgesic duration of Rop, and the mechanism may be related to the more complex spatial structure of Dex, which affects the release and absorption of Rop [11].

The aim of this study was to investigate the safety and efficacy of Rop combined with Dex analgesia in women with preeclampsia, thereby providing a clinical reference for improving the prognosis.

Materials and methods

Baseline data

Eighty women with preeclampsia admitted to our hospital from April 2019 to October 2020 were included and divided into a study group (Rop + Dex intervention, n=41) and a control group (Rop intervention alone, n=39).

Inclusion criteria: (1) all women enrolled met the diagnostic criteria for preeclampsia [12] and presented with typical symptoms; (2) patients were conscious and cooperated with the study; (3) the study was approved by the ethics committee of Yichun People's Hospital; (4) the clinical data of the subjects were complete; (5) ASA classification I-III; (6) the study subjects agreed and signed the informed consent; and (7) vaginal delivery.

Exclusion criteria: (1) patients with concurrent psychiatric disorders; (2) those with multiple births; (3) women in active labor; (4) those allergic to the investigational drugs; (5) those with severe cardiopulmonary disorders; (6) those with placenta abruptio or placenta praevia; (7) those with <28 weeks of gestation; and (8) those with intermediate cesarean delivery.

Intervention methods

All subjects underwent L2-L3 epidural puncture and 3 mL of 0.7% lidocaine was applied before anesthesia. If the subjects showed no signs of total spinal anesthesia, the tube was placed 3 cm towards the head. The control group was injected with 10 mL 0.125% Rop (Manufactured by AstraZeneca AB, Sweden, Specification: 75 mg/10 mL, registration number of imported drugs: H20140763) using the epidural catheter, while in the study group, 0.125% Rop (as above) and Dex (Manufactured by Sinopharm Rongsheng Pharmaceutical Co., Ltd., Specification: 0.2 mg/mL, approval number: H4102-0035) were injected. Nursing staffs monitored the women regularly and recorded the changes in the indicators of maternal parameters.

Outcome measurement

Analysis of maternal analgesia and sedation: The pain level and sedation of the two groups were assessed before analgesia (T0), 30 min after analgesia (T1), 60 min after analgesia (T2), 120 min after analgesia (T3), and at the cessation of analgesia (T4), respectively. The visual analogue scale (VAS) scale [13] is composed of a 0-10 cm straight line, with 0 indicating no pain and 10 indicating severe pain, and the subjects chose a mark on the scale according to the pain level, which is more intuitive and convenient. Ramsay scale [14] is six dimensions of 1-6, with 1 point representing anxious and agitated or restless, 2 points representing co-operative, oriented, and tranquil, 3 points representing responds to commands only, 4 points representing brisk response to light glabellar tap or loud auditory stimulus, 5 points representing a sluggish response to light glabellar tap or loud auditory stimulus, and 6 points representing no response.

Comparison of changes in stress indicators: Venous blood samples (5 mL) were collected from both groups at T0 and T2, centrifuged and stored at -80°C. The enzyme-linked immunosorbent assay (ELISA) was used to measure adrenaline (AD) and norepinephrine (NE) levels in both groups. Vital signs monitoring was performed in both groups and heart rate (HR) and mean arterial pressure (MAP) were recorded from T0-T4 in both groups, and inter-group and intra-group comparisons were performed.

Analysis of maternal labor and neonatal conditions: The first, second and third stages of labor were compared between the two groups of parturients, and Apgar scores were determined for the newborns at 1 min, 5 min and 10 min after birth.

Table 1. Comparison of baseline data (χ ± s)/[n (%)]

Clinical information		Study group (n=41)	Control group (n=39)	t/X^2	*P*
Mean age (years)		30.23±1.11	30.18±1.21	0.193	0.847
Mean weight (kg)		72.38±5.44	72.49±5.10	0.093	0.926
Average gestational weeks (years)		38.11±0.26	38.02±0.41	1.179	0.242
ASA grading	I	15	13	0.879	0.234
	II	20	21		
	III	6	5		

Analysis of motor block after anesthesia: The Bromage scale was used to assess post-intervention motor block in both groups. The Bromage scale [15] was scored on a 0-3 scale, with a score of 0 represening no motor block, 1 representing just able to flex knees with free movement of feet, 2 representing the inability to flex the knee and only the ability to move the ankle, and 3 representing complete block of the lower extremity.

The incidence of adverse reactions after anesthesia: The incidence of adverse reactions such as hypotension, bradycardia, nausea and vomiting were counted separately in the two groups.

Statistical methods

SPSS22.0 statistical software was selected to analyze the data. The measurement data were expressed as (mean ± standard deviation), and t-test was used for comparing data meeting normal distribution. Approximate t-test was applied for data with uneven variance. F-test was used for comparison between multiple groups. Chi-square test was used for differences in count data between groups. Graphpad Prism 8 was used to plot the graphics. *P*<0.05 was considered as statistically significant difference [16].

Results

Comparison of the differences in baseline data

A total of 80 subjects were included in this study, aged 22-39 years, with an average age of (30.19±1.10) years, gestational age of 37-42 weeks, and an average gestational age of (38.04±0.43) weeks. Baseline data, such as age, weight, gestational age and ASA grade, were compared between the two groups, and the results showed that baseline data did not differ significantly between the two groups (*P*>0.05), suggesting that the two groups were comparable (**Table 1**).

Analysis of maternal analgesia and sedation

At T0, the VAS and Ramsay scores did not differ significantly between the two groups (*P*>0.05), while from T1-T4, the VAS scores of the study group were significantly lower and the Ramsay scores of the study group were significantly higher than those of the control group (*P*<0.05). Maternal VAS scores at T1-T4 were significantly lower in both groups than at T0 (*P*<0.05), Ramsay scores were significantly higher in the study group at T1-T4 than at T0 (P<0.05), and Ramsay scores did not change significantly in the control group before and after treatment (*P*>0.05) (**Figure 1**).

Changes in maternal stress indicators

There was no significant difference between the two groups in NE and AD levels at T0 (*P*>0.05), and both NE and AD levels in the study group were significantly lower than those in the control group at T2 (*P*<0.05), and within-group pre-post comparisons showed that NE and AD levels were lower in both groups at T2 than at T0 (*P*<0.05) (**Figure 2**). Fom T1-T4, MAP and HR in the study group were lower than those in the control group, and a pre-post comparison within the group showed that MAP and HR were lower at T1-T4 than at T0 (*P*<0.05) (**Figure 3**).

Comparison of maternal delivery and neonatal conditions

It was calculated that the first, second and third stages of labor in the study group were significantly shorter than those in the control group (*P*<0.05), while the 1 min, 5 min and 10 min Apgar scores of the newborns in the study

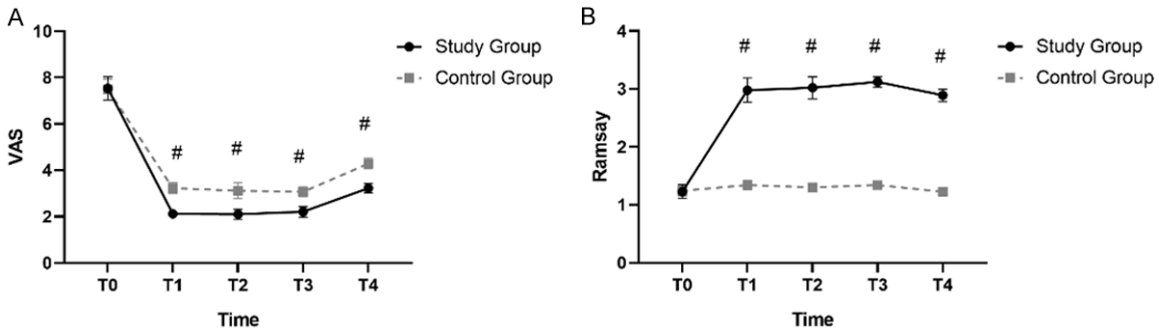

Figure 1. Analysis of analgesia and sedation in the two groups. (A) VAS scores and (B) Ramsay scores. #*P*<0.05.

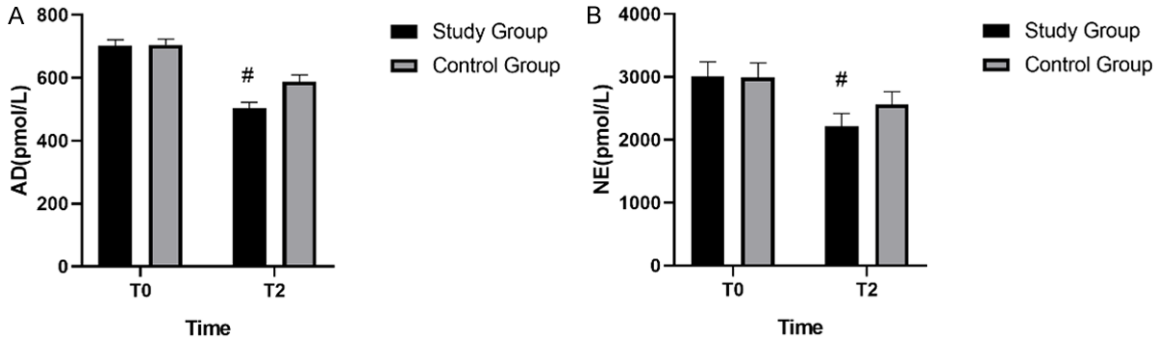

Figure 2. Analysis of the changes in AD and NE levels. Comparison showed that there was no significant difference in AD and NE levels between the two groups at T0 (*P*>0.05); AD and NE levels in the study group were significantly lower than that in the control group (*P*<0.05). #*P*<0.05.

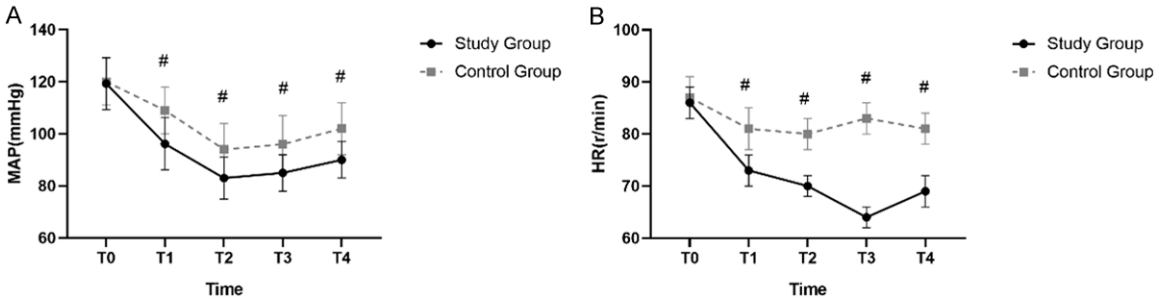

Figure 3. Differences in hemodynamic indices between the two groups. The differences between groups in MAP and HR were not statistically significant (*P*>0.05) at T0 and were significantly lower (P<0.05) in the study group than in the control group at T1-T4. #*P*<0.05.

group were higher than those in the control group (*P*<0.05) (**Figure 4**).

Comparison of post-anesthetic motor block

The Bromage scale was used to evaluate the motion block of the two groups after anesthesia, and the difference between the two groups was compared. After anesthesia, the study group had 40 cases (97.56%) of grade 0 and 1 case (2.44%) of grade 1, while the control group had 33 cases (84.62%) of grade 0, 5 cases (12.82%) of grade 1, and 1 case (2.56%) of grade 2. The percentage of grade 0 in the study group was significantly higher than that in the control group (*P*<0.05) (**Table 2**).

Comparison of the incidence of maternal adverse reactions

The incidence of adverse reactions after anesthesia, such as hypotension, bradycardia, nau-

Figure 4. Comparison of delivery and neonatal conditions. The first, second and third stages of labor in the study group were significantly shorter than those in the control group ($P<0.05$) and the 1 min, 5 min and 10 min Apgar scores in the study group were higher than those in the control group ($P<0.05$). $^{\#}P<0.05$.

Table 2. Comparison of maternal and neonatal Apgar scores ($\chi \pm s$)

Group	n	Grade 0	Grade 1	Grade 2
Study group	41	40 (97.56)	1 (2.44)	0 (0.00)
Control group	39	33 (84.62)	5 (12.82)	1 (2.56)
X^2	-	4.195	3.105	1.065
P	-	0.041	0.078	0.302

sea and vomiting, were recorded in the two groups, and the differences between the two groups were compared. The results showed that the study group had 3 cases of hypotension, 2 cases of bradycardia and 1 case of nausea and vomiting, with the total incidence of 14.63%, while the control group had 2 cases of hypotension, 2 cases of bradycardia and 1 case of nausea and vomiting, with the total incidence of 12.82%. The difference in the incidence of adverse reactions was not statistically significant between the two groups ($P>0.05$) (**Table 3**).

Discussion

Epidemiology shows that the global incidence of preeclampsia is about 3%-5%, with moderate to severe preeclampsia ranging 1%-2%, which most often occurs after 20 weeks of gestation. It is a leading cause of maternal and perinatal mortality [17]. Preeclampsia is characterized by contraction of the arterioles. Treatments of preeclampsia include spasmolysis, volume expansion, and blood pressure reduction. Punctual pregnancy is a more effective intervention for women with preeclampsia during labor, and proper anesthesia is a basis to ensure the smooth of operation [18]. Epidural injection anesthesia has the advantages of low drug consumption, rapid onset, good nerve block, and controllability, and is now a commonly used anesthetic during labor in women with preeclampsia [19].

In this study, the results showed that the study group with Dex + Rox had lower post-intervention pain levels and sedation scores, lower VAS scores and higher Ramsay scores than the control group with Rop alone. A previous study of women with postoperative transversus abdominis plane block after cesarean delivery showed that compared with women anesthetized with Rop alone in R group, women in the DR group treated with Dex + Rop had significantly lower resting and active pain during the 2-10 h postoperative period, but the difference between the groups was not significant after 24 h. Meanwhile, women in the DR group had significantly lower analgesic drug consumption during the 4-24 h postoperative period than women in the R group, which suggested that Dex could significantly prolong the duration of action of local anesthetics and improve postoperative analgesia [20]. Another study conducted on 200 women who delivered by cesarean section indicated that Dex combined with Rop had an excellent analgesic effect of up to 98%, significantly higher than 90% for Rop alone [21], which were similar to the results of the present study. We believe that on the one hand, glucocorticoids are able to cause local vasoconstriction in individuals, thus slowing down the absorption of local anesthetic drugs. On the other hand, Dex has a complex spatial structure, and the combination of Rop and Dex can prolong the release process of this drug, bringing better analgesic and sedative effects [22, 23]. This was also supported by the significant reduction in NE, AD, MAP and HR in the study group, which may be related to the fact that

Table 3. Comparison of the incidence of adverse reactions [n (%)]

Group	Number of cases	Hypotension	Bradycardia	Nausea and vomiting	Total incidence rate
Study group	41	3 (7.32)	2 (4.88)	1 (2.44)	6 (14.63)
Control group	39	2 (5.13)	2 (5.13)	1 (2.56)	5 (12.82)
X^2	-	-	-	-	0.055
P	-	-	-	-	0.814

good analgesia and sedation relieved the adverse experience of the patients, affecting secretion of catecholamine hormone and hemodynamic indices.

This study showed that the maternal duration of labor in the study group was significantly shorter than that in the control group, the postnatal Apgar score of the neonate in the study group was significantly higher than that in the control group, and the maternal postanesthetic motor block in the study group was significantly better than that in the control group. A retrospective study of 200 women in spontaneous labor has shown that the third stage of labour was (6.61±2.93) min in group A with Rop + Dex and (7.53±3.09) min in group B with ropivacaine alone, while the percentage of women with a score of 0 for motor block was 100% in group A and 96% in group B, similar to the results of the present study [24]. The reason may be that Rop alone can block the sacrococcygeal nerve, which leads to a reduced sensation and affects the correct exertion and prolongs labor. Dex may alter the arrangement of molecules on the surface of the cell membrane, which in turn blocks the membrane and leads to a blocked migration of substrates and metabolites. Dex may also act synergistically with Rop to improve maternal sensation and speeds up labor without affecting motor sensation [25, 26]. In our study, Rop + Dex could reduce the incidence of adverse reactions caused by anesthesia, which may be related to the ability of Dex in improving the retention of Rop in the epidural as well as in the bloodstream, thus reducing the incidence of adverse reactions.

However, this study also has some shortcomings. On the one hand, the included sample source is from single center, leading to high sample repeatability, which may have a certain impact on the research results; on the other hand, the included sample size is small, which may affect the accuracy of the research results.

In conclusion, epidural injection of Rop + Dex can bring better analgesic and sedative effect, stable hemodynamic indices, and improve postpartum motor block with high safety.

Disclosure of conflict of interest

None.

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