Int J Clin Exp Med 2025;18(10):255-261
www.ijcem.com /ISSN:1940-5901/IJCEM0164040

Original Article

Epidural sufentanil decreases intrapartum fever during labor: a controlled randomized trial

Bin Su[1*], Panlian Qian[2*], Zeyong Yang[3], Dong Li[4#], Ying Zhang[5#]

[1]Department of Anesthesiology, Tongxiang Maternity and Child Health Hospital, Jiaxing 314000, Zhejiang, China; [2]Department of Obstetrics and Gynecology, Tongxiang Maternity and Child Health Hospital, Jiaxing 314000, Zhejiang, China; [3]Department of Anesthesiology, International Peace Maternity and Child Health Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, China; [4]Department of Obstetrics, Women and Children's Hospital, Jiaxing University, Jiaxing 314000, Zhejiang, China; [5]Department of Emergency, Coast Guard General Hospital, Jiaxing 314000, Zhejiang, China. [*]Equal contributors. [#]Co-corresponding authors.

Received February 19, 2025; Accepted October 12, 2025; Epub October 15, 2025; Published October 30, 2025

Abstract: Objective: Intrapartum fever is a common complication during epidural labor analgesia. Sufentanil is the most frequently used adjuvant to local anesthetics for epidural analgesia. The purpose of this study was to investigate the effects of Epidural sufentanil on maternal intrapartum fever during labor. Methods: Parturients were randomly assigned to the sufentanil (S) group and the control group. The S group received 0.1% ropivacaine plus sufentanil 0.5 μg/mL for epidural analgesia, while the control group received 0.1% ropivacaine alone for analgesia. The maternal temperature, blood pressure, heart rate (HR), fetal HR, and pain intensity were recorded. The adverse events were also recorded during epidural analgesia. Results: Initially, 420 women were enrolled in this study, then 401 women were randomly assigned to the group S (n=201) and the control group (n=200). The incidence of intrapartum fever was lower in the S group than in the control group (2.5% vs. 7.0%, *P*=0.033). The visual analogue scale (VAS) was lower at 5 to 10 cm of cervical dilatation in the S group than the control group (3.6±0.81 vs. 3.9±0.78, 3.8±0.86 vs. 4.3±0.98, 3.5±0.85 vs. 3.8±0.71, respectively, $P < 0.05$). The incidence of adverse events of the mothers and neonates was similar between the two groups. Conclusions: Epidural sufentanil reduces the incidence of intrapartum fever and improves analgesic effect during epidural analgesia without increasing the adverse events of the mothers and neonates. (Registration number: ChiCTR1800017097).

Keywords: Intrapartum fever, epidural, labor analgesia, sufentanil, neonates

Introduction

Intrapartum maternal fever after epidural analgesia is a common clinical phenomenon. Epidural analgesia (EA) is the most common technique for pain relief during labor [1]. Sufentanil is the most used adjuvant to local anesthetics for epidural labor analgesia. The literature reports that epidural analgesia increases the risk of maternal intrapartum fever during epidural labor analgesia [2, 3]. Maternal fever can bring about adverse effects on the fetus, including increased oxygen consumption, fetal distress and neonatal brain injury and so on [4].

Currently, the exact mechanisms of intrapartum fever are not well known [5]. It is likely to be the result of noninfectious inflammation caused by maternal immune activation, which is characterized as increasing levels of proinflammatory cytokines in the parturient [6, 7]. Local analgesics combined with adjuvants have been widely used in epidural labor analgesia [8]. Wang and colleagues [9] found that the use of epidural dexamethasone alleviated maternal temperature elevation and did not obviously decrease the incidence of maternal intrapartum fever. While Li and colleagues [10] found that epidural dexmedetomidine decreased the incidence of maternal intrapartum fever following labor epidural analgesia from 8.7% to 4.1%. The literature reported magnesium reduced the incidence of fever in parturients from 10% to 6% compared to those who were not administered magnesium [11]. It is unclear whether epidural sufentanil increases intrapartum fever

https://doi.org/10.62347/GJUW9636

during labor analgesia. The purpose of this study was to investigate the effects of epidural sufentanil on intrapartum fever and analgesic effect in women undergoing epidural labor analgesia.

Methods

Study population

The study was approved by the Ethics Board of the International Peace Maternity and Child Health Hospital of Shanghai, and written informed consent was obtained from all participants. The trial was registered at www.chictr.org.cn (Registration number: ChiCTR1800017097). From August 2018 to July 2022, a total of 401 full-term primiparous parturients demanding labor analgesia were enrolled in this study. Inclusion criteria included American Society of Anesthesiologists (ASA) physical status grades II, age 21-35 years, weight 55-90 kg and gestational week ≥ 37 weeks. Exclusion criteria included temperature from the ear canal > 37°C, platelet count < 80×10^9/L, coagulation disorder, puncture point infection, serious cardiopulmonary disease, liver and renal function disorder. The parturients were randomly assigned into the S group (n=201) and the control group (n=200).

Randomization

Parturients were randomly assigned to either the S group or the control group using a computer-generated randomization table, with group allocation hidden in closed opaque covers. Study medications were prepared by a nurse blind to groups. Participants, anesthesiologists, midwives and investigators were blind to the group allocation.

Analgesia methods

Blood pressure, heart rate (HR) and pulse oxygen saturation (SpO_2) were monitored at 10-min intervals, and venous access was established in the delivery room. After infiltration with 1% lidocaine, the epidural technique was performed at a level of L2-3 in the left lateral position using the method of decreasing resistance to air when the cervical dilation was about 2 cm. An epidural catheter was advanced 4 cm into the epidural space. A test dose of 3 mL of 1.5% lidocaine was administered via the epidural catheter, followed by an initial loading dose of 10 mL of analgesic solution. The anesthetic solution consisted of 0.1% ropivacaine and sufentanil 0.5 μg/mL in the S group. While the anesthetic solution consisted of 0.1% ropivacaine alone in the control group. The epidural catheter was attached to an electronic infusion pump with a background dose of 8 ml/h, a bolus dose of 6 mL and an interval of 15 minutes. Parturients were instructed how to use the electronic infusion pump. If the visual analogue scale (VAS) value 30 minutes after analgesia was > 3, a bolus of medication was given. If the pain was not alleviated, epidural analgesia was considered invalid, and the patient was excluded. The number of boluses was recorded. Maternal temperature from the ear canal (T) was measured by thermometer (Kaz USA, Inc., PRO 4000, MA, USA) at 30-min intervals. The measurements were recorded 5 min before analgesia (T0), 30 min after analgesia (T1), 60 min after analgesia (T2), at 3 cm of cervical dilatation (T3), 5 cm of cervical dilatation (T4), 7 cm of cervical dilatation (T5), and 10 cm of cervical dilatation (T6). Hypotension was defined as systolic blood pressure below 80% of baseline, and treated with intravenous 40 μg phenylephrine. Supplemental oxygen was administered if maternal oxygen saturation (SpO_2) was below 94%. Pain intensity was assessed using visual analogue scale (VAS) (0, no pain; 10, worst pain unimaginable). Parturients were asked to evaluate their overall satisfaction with pain relief using a satisfaction score when leaving the delivery room, where 0 corresponded with highly dissatisfied and 10 with highly satisfied. Motor block was assessed using Bromage score (0= no motor loss, 1= inability to flex hip, 2= inability to flex hip and knee, 3= inability to flex hip, knee and ankle). Apgar scores were recorded at 1 and 5 minutes. The incidence of hypotension, shivering, respiratory depression, itching, nausea and vomiting were recorded. Hypotension was defined as systolic blood pressure < 80% of the baseline and was treated with ephedrine 6 mg by intravenous injection. HR below 60 beats/minute was treated with atropine 0.3 mg by intravenous injection. Respiratory depression was defined as respiratory rate < 10 breaths/min and SpO_2 < 91%. Intrapartum fever was defined as the maternal temperature from the ear canal of ≥ 38°C.

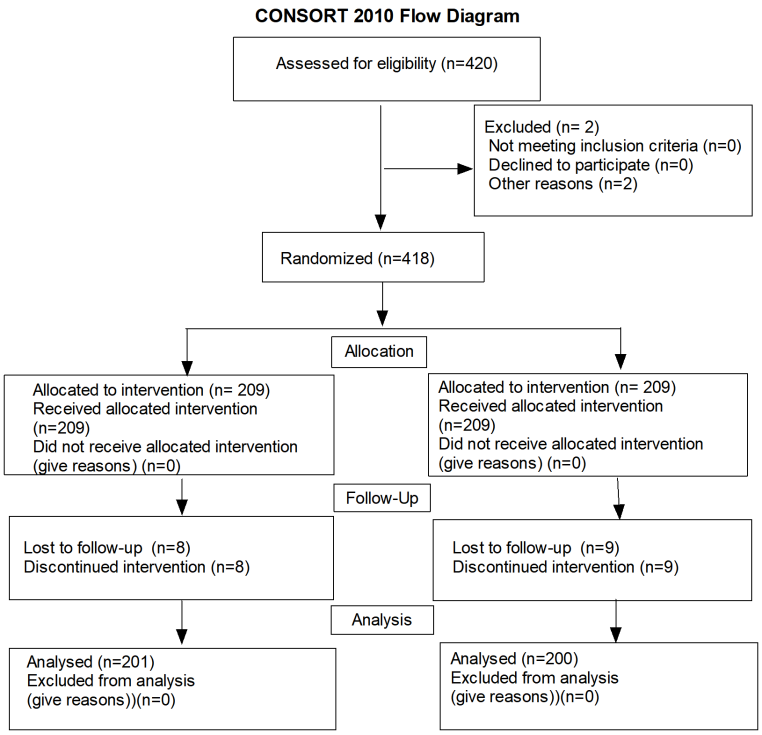

Figure 1. Flow diagram of study.

Sample size

The primary outcome was the incidence of intrapartum fever, and the secondary outcome was the analgesic effect. The sample size was calculated with the probability of an alpha level of 0.05, a beta level of 0.20 and a power of 0.80, and each group needed 200 subjects according to our pilot study (the incidence of intrapartum fever from 8% to 2%). A total of 420 parturients were enrolled to allow for dropouts in this study.

Statistical analysis

Statistical analysis was performed using SPSS 22.0 (IBM, NY, USA) software package. Numerical variables with normal distribution were presented as mean and standard deviation (SD) and analyzed by *t* test, and numerical variables with nonnormal distribution were analyzed by Mann-Whitney U test. Categorical data were presented as numbers and analyzed using Fisher's exact test or Chi-square test. The significance level was set at a $P < 0.05$.

Results

Initially, 420 women were enrolled in this study, then 418 women were randomly allocated. Finally, 401 women were analyzed (**Figure 1**). A total of 13 women did not receive allocated intervention because of in-labor cesarean section, and two women did not continue the trial due to the VAS score > 5 for more than 30 min after analgesia. Two patients did not follow up because the duration of the first stage of labor was less than 2 h. In the end, 401 women finished this study.

The data of the women are shown in **Table 1**. There were no significant differences in terms of maternal age, height, weight, gestational weeks, duration of labor stages, oxytocin use and anesthetic dosage between the two groups. The total anesthetic doses and PCA numbers were lower in the S group than the control group. The degree of satisfaction was higher in the S group compared with the control group ($P < 0.05$).

The incidence of intrapartum fever decreased in the S group (2.5% vs. 7.0%, P=0.033). Five women experienced intrapartum fever in the S group, while 14 women experienced intrapartum fever in the control group. The incidence of hypotension, itching, shivering, motor block, fetal distress, nausea and vomiting was similar in both groups. There were no significant differences in side effects between the 2 groups (in **Table 2**).

Blood pressure and HR of women are shown in **Figure 2**. Blood pressure and HR at T1 was lower in group S than in the control group, there were significant differences between the two groups (*$P < 0.05$). There were no significantly different in blood pressures and HR at other time points between the two groups.

VAS scores after analgesia were significantly lower in both groups compared with those at T0 (in **Figure 3**) (*$P < 0.01$). The VAS score was lower in the S group at T4, T5 and T6 compared with the control group (3.6±0.81 vs. 3.9±0.78, 3.8±0.86 vs. 4.3±0.98, 3.5±0.85 vs. 3.8±0.71,

Table 1. Data of women in both groups

Variables	Group S (n=201)	Control group (n=200)	*P value*
Age (yr)	28.7±2.8	29.8±2.97	0.921
Height (cm)	163.6±4.7	161.8±4.8	0.141
Weight (kg)	69.5±7.9	69.9±7.8	0.801
Gestational weeks (week)	38.9±1.2	39.4±1.1	0.059
Onset time of analgesia (min)	18.3±6.7	18.6±5.5	0.515
First stage of labor (min)	366.5±81.4	393.9±78.4	0.136
Second stage of labor (min)	64.2±20.3	57.4±16.8	0.646
Total stage of labor (min)	457.7±91.4	479.5±75.5	0.852
Degree of satisfaction	9.6±0.6	9.1±1.3	0.035*
Total anesthetic dosage (ml)	59.4±7.2	65.8±8.7	0.002*
PCA numbers	2 [1-4]	3 [1-6]	0.042*
Use of oxytocin	55	49	0.444
Apgar scores ≤ 7	0	0	/

Data were presented as mean ± SD or numbers, *$P < 0.05$.

Table 2. Adverse events of women and infants

Index	Group S (n=201)	Control group (n=200)	*P*-Value
Intrapartum fever	5	14	0.033*
vomiting and nausea	7	6	0.785
Hypotension	8	5	0.403
Itching	2	0	0.499
Bromage score > 0	0	0	/
Shivering	2	4	0.449
Fetal destress	1	2	0.623

Data are shown as number, *$P < 0.05$.

respectively, $P < 0.05$). There were no significant differences in VAS scores at other time points between the two groups.

Maternal temperature is shown in **Figure 4**. The body temperature of parturents gradually rose and reached the peak value at 5 cm of cervical dilatation following epidural analgesia. Temperature value at T4 was lower in the S group than in the control group (36.73±0.25 vs. 36.84±0.37°C, P=0.01). Temperatures at other time points were similar in both groups, there were not significantly different between the 2 groups ($P > 0.05$).

Discussion

The present study showed that epidural sufentanil can reduce the incidence of intrapartum fever and improve analgesic effect during labor analgesia without increasing the adverse events of the mothers and neonates.

Five women experienced intrapartum fever in group S, while 14 women experienced intrapartum fever in the control group. The body temperature of parturents gradually rose and reached the peak value at 5 cm of cervical dilatation following epidural analgesia. The etiology of intrapartum fever is not well understood. It is noninfectious inflammation. Epidural-related maternal fever contributes to the development of intrapartum fever [3]. The association between epidural analgesia and maternal fever is complex and controversial [12]. At present, the mechanism of intrapartum fever is unknown, it may be relevant to an unbalance of heat and cold after labor analgesia. At first, heat loss increases due to vasodilation during epidural block and compensatory contraction of the blood vessels after epidural analgesia. Secondly, sufentanil inhibits the maternal temperature regulation center resulting in lower heat production. Finally, the analgesic effect reduces the anxiety of patients and energy consumption. Alternatively, insufficient analgesia contributes to the development of intrapartum fever. Recent document reports indicate that lower concentrations of ropivacaine could reduce the intrapartum febrile rate during labor analgesia [6]. The main reason is that intrapartum febrile is defined as body temperature > 37.5°C, although intrapartum fever is defined

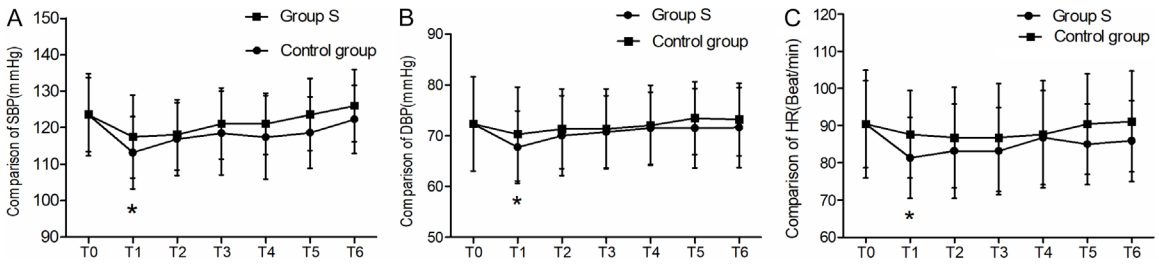

Figure 2. Comparison of blood pressure and HR in both groups. Blood pressure and HR at T1 were lower in group S compared with the control group (*$P < 0.05$). While there were no significant differences in blood pressure and HR at other time points between the two groups ($P > 0.05$). SBP: systolic blood pressure, DBP: diastolic blood pressure, HR: heart rate. T0: 5 min before analgesia, T1: 30 min after analgesia, T2: 60 min after analgesia, T3: 3 cm of cervical dilatation, T4: 5 cm of cervical dilatation, T5: 7 cm of cervical dilatation, and T6: 10 cm of cervical dilatation.

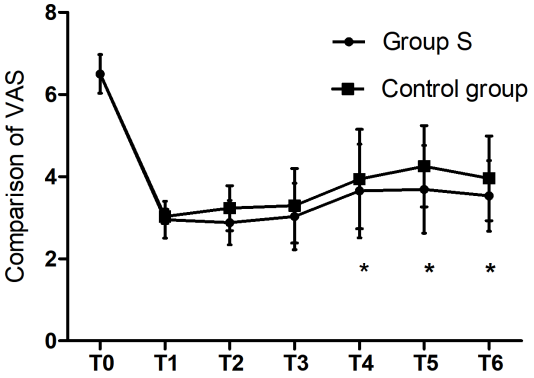

Figure 3. VAS at different time points in both groups. VAS scores after analgesia were obviously lower than those before analgesia in both groups ($P < 0.01$). The VAS score was lower in group S at T4, T5 and T6 compared with the control group ($P < 0.05$). T0: 5 min before analgesia, T1: 30 min after analgesia, T2: 60 min after analgesia, T3: 3 cm of cervical dilatation, T4: 5 cm of cervical dilatation, T5: 7 cm of cervical dilatation, and T6: 10 cm of cervical dilatation.

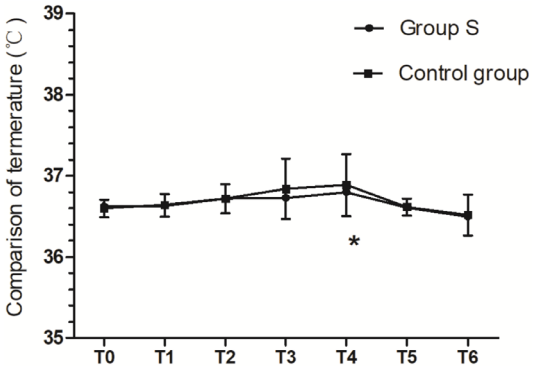

Figure 4. Maternal temperature at different time points in both groups. The temperature value was significantly lower at T4 in group S compared with the control group ($P < 0.05$). There were no significant differences in maternal temperature at other time points between the two groups. T0: 5 min before analgesia, T1: 30 min after analgesia, T2: 60 min after analgesia, T3: 3 cm of cervical dilatation, T4: 5 cm of cervical dilatation, T5: 7 cm of cervical dilatation, and T6: 10 cm of cervical dilatation.

as the body temperature > 38.0°C in our study. Their study indicated that intrapartum fever occurred at 5 cm of cervical dilatation, which is similar to our results. Li and his collegues reported that dexmedetomidine decreased the incidence of intrapartum maternal fever during labor [10]. Dexmedetomidine, an α_2-adrenoceptor agonist, inhibits the thermoregulation center to reduce heat production by activation of the central α_2-adrenoceptor and suppression of c-Jun N-terminal kinases [13]. Camann and colleagues [14] found that maternal temperatures were not increased when opioids were parenterally administered for analgesia. This indicates that opioids decrease the incidence of intrapartum fever.

A local anesthetic in combination with adjuvants can improve analgesic effect while minimizing side effects [15-18]. In our study, the side effects such as hypotension, respiratory depression, itching, nausea and vomiting were similar between the 2 groups. The VAS values were significantly lower in group S at 5-10 cm of cervical dilatation than those in the control group. This indicates that sufentanil at 0.5 μg/mL increased the analgesic effect of ropivacaine during labor analgesia.

Motor block occurred frequently when higher concentrations of local anesthetics were used for epidural labor analgesia. Opioids were added to local anesthetics to lower their concentrations and reduce the side effects during labor analgesia [19-21]. The present study showed that no patients underwent motor block with 0.1% ropivacaine with or without suf-

entanil 0.5 ug/mL when we evaluated motor block using the modified Bromage scale, which was similar to previous findings [22].

No differences were observed in neonatal outcome in both groups. There were no significant differences in terms of hypotension, itching, motor block, shivering, nausea and vomiting, which was consistent with prior findings [23-25].

This study had several limitations. There was a bias in measuring the size of cervical dilation. Additionally, levels of magnesium might influence the occurrence of intrapartum fever.

Conclusion

Epidural sufentanil could reduce the incidence of intrapartum fever and improve analgesic effect during epidural analgesia without increasing the adverse events of the mothers and neonates.

Acknowledgements

The authors would like to thank the midwives of the delivery room. This work was supported by the Youth talent fund and Perinatal Potential Subject of International Peace Maternity and Child Health Hospital, Shanghai Jiao Tong University School of Medicine.

Disclosure of conflict of interest

None.

Address correspondence to: Dong Li, Department of Obstetrics, Women and Children's Hospital, Jiaxing University, Jiaxing 314000, Zhejiang, China. E-mail: anesthesia001@aliyun.com; Ying Zhang, Department of Emergency, Coast Guard General Hospital, Jiaxing 314000, Zhejiang, China. E-mail: zhang650679@sina.com

References

[1] Hawkins JL. Epidural analgesia for labor and delivery. N Engl J Med 2010; 362: 1503-10.
[2] Sharpe EE and Arendt KW. Epidural labor analgesia and maternal fever. Clin Obstet Gynecol 2017; 60: 365-374.
[3] Zhao W, Wang LZ, Chang XY, Zhang YF, Xiao F and Xia F. Maternal serum C-reactive protein and white blood cell count at hospital admission as predictors of intrapartum maternal fever: a retrospective case-control study in women having epidural labor analgesia. Int J Obstet Anesth 2022; 50: 103537.
[4] Leighton BL and Halpern SH. The effects of epidural analgesia on labor, maternal, and neonatal outcomes: a systematic review. Am J Obstet Gynecol 2002; 186: S69-77.
[5] Hlinecká Kristýna, Bartošová Tereza and Bláha Jan. Epidural fever. Ceska Gynekol 2021; 86: 355-361.
[6] Zhou X, Li J, Deng S, Xu Z and Liu Z. Ropivacaine at different concentrations on intrapartum fever, IL-6 and TNF-α in parturient with epidural labor analgesia. Exp Ther Med 2019; 17: 1631-1636.
[7] Sultan P, David AL, Fernando R and Ackland GL. Inflammation and epidural-related maternal fever: proposed mechanisms. Anesth Analg 2016; 122: 1546-53.
[8] Zhang T, Yu Y, Zhang W and Zhu J. Comparison of dexmedetomidine and sufentanil as adjuvants to local anesthetic for epidural labor analgesia: a randomized controlled trial. Drug Des Devel Ther 2019: 13: 1171-1175.
[9] Wang LZ, Hu XX, Liu X, Qian P, Ge JM and Tang BL. Influence of epidural dexamethasone on maternal temperature and serum cytokine concentration after labor epidural analgesia. Int J Gynaecol Obstet 2011; 113: 40-3.
[10] Li L, Yang Z and Zhang W. Epidural dexmedetomidine for prevention of intrapartum fever during labor analgesia: a randomized controlled trial. Pain Ther 2021; 10: 391-400.
[11] Lange EMS, Segal S, Pancaro C, Wong CA, Grobman WA, Russell GB and Toledo P. Association between Intrapartum Magnesium Administration and the Incidence of Maternal Fever: A Retrospective Cross-sectional Study. Anesthesiology 2017; 127: 942-952.
[12] Arendt KW and Segal BS. The association between epidural labor analgesia and maternal fever. Clin Perinatol 2013; 40: 385-98.
[13] Zhang X, Wang J, Qian W, Zhao J, Sun L, Qian Y and Xiao H. Dexmedetomidine inhibits tumor necrosis factor-alpha and interleukin 6 in lipopolysaccharide-stimulated astrocytes by suppression of c-Jun N-terminal kinases. Inflammation 2014; 37: 942-9.
[14] Camann WR, Hortvet LA, Hughes N, Bader AM and Datta S. Maternal temperature regulation during extradural analgesia for labour. Br J Anaesth 1991; 67: 565-568.
[15] Jin KX, Deng CM, Ding T, Qu Y and Wang DX. Impact of dexmedetomidine-ropivacaine versus sufentanil-ropivacaine combination for epidural labour analgesia on neonatal outcomes: a pilot randomised clinical trial. BMJ Open 2024; 14: e090208.

[16] Xu L, Li S, Zhang C, Zhou Y and Chen X. Esketamine administered epidurally as an adjuvant to epidural ropivacaine for labour analgesia: a prospective, double-blind dose-response study. BMJ Open 2024; 14: e071818.
[17] R S R, Karigar SL, Kori S and S D P. A randomised clinical trial to compare the efficacy and safety of dexmedetomidine-ropivacaine versus fentanyl-ropivacaine for epidural labour analgesia. Cureus 2024; 16: e68076.
[18] Ni L, Yao S, Wu Y, Ni J, Wang Q, Mei Z and Yu J. Epidural dexmedetomidine or esketamine versus fentanyl to decrease ropivacaine use for labor analgesia: a randomized non-inferiority study. Heliyon 2024; 10: e30218.
[19] Zhang L, Hu Y, Wu X, J Paglia M and Zhang X. A systematic review and meta-analysis of randomized controlled trials of labor epidural analgesia using moderately high concentrations of plain local anesthetics versus low concentrations of local anesthetics with opioids. J Pain Res 2021; 14: 1303-1313.
[20] Jia C, Zou B, Sun YJ, Han B, Diao YG, Li YT and Cao HJ. The 90% effective concentration of alfentanil combined with 0.075% ropivacaine for epidural labor analgesia: a single-center, prospective, double-blind sequential allocation biased-coin design. J Anesth 2024; 38: 377-385.
[21] Ni F, Wu Z and Zhao P. Programmed intermittent epidural bolus in maintenance of epidural labor analgesia: a literature review. J Anesth 2023; 37: 945-960.
[22] Wang X, Xu S, Qin X, Li X, Feng SW, Liu Y, Wang W, Guo X, Shen R, Shen X and Wang F. Comparison between the use of ropivacaine alone and ropivacaine with sufentanil in epidural labor analgesia. Medicine (Baltimore) 2015; 94: e1882.
[23] Mazda Y. Labor neuraxial analgesia and clinical outcomes. J Anesth 2022; 36: 453-455.
[24] Li K, Chai Z, Deng C, Niu G, Geng X, Zhang Y, Wang Y and Wang T. Effects of epidural esketamine versus sufentanil on labor analgesia and postpartum depression: a retrospective cohort study. BMC Anesthesiol 2025; 25: 6.
[25] Wu XZ, Fang TF, Zheng YH, Zhang SJ, Xie Y, Gao X and Lu GL. Association of epidural labor analgesia with maternal and neonatal outcomes in women with preeclampsia: a propensity score-matched single-center retrospective cohort study. BMC Pregnancy Childbirth 2025; 25: 66.