ORIGINAL ARTICLE

Programmed Intermittent Epidural Bolus at Different Intervals Combined with Patient-controlled Epidural Analgesia on Body Temperature during Labour Analgesia

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ABSTRACT

Objective: To explore the effects of programmed intermittent epidural bolus (PIEB) combined with patient-controlled epidural analgesia (PCEA) at different intervals on body temperature and serum CRP, TNF-α, IL-6 levels in parturient women receiving analgesia.

Study Design: Descriptive study.

Place and Duration of Study: The First Affiliated Hospital of Shaoyang University, China, from September 2018 to February 2020.

Methodology: One hundred and seventy primiparous women, who had vaginal delivery and required labour analgesia, were randomly divided into Groups A and B (n=85 for each group). In both groups, PIEB plus PCEA mode was applied when cervical dilatation reached 2-3 cm. The interval was 30 minutes with a pulse dose of 5 mL in Group A; and 60 minutes with a pulse dose of 10 mL in Group B. Indicators related to body temperature and serum markers were compared in both the groups.

Result: Maternal temperature in Group A was higher than that in Group B at the time of cervix being completely dilated, and 2 hours after delivery (both p <0.001). incidence of intrapartum fever in Group A was higher than that in Group B (p = 0.036). Epidural analgesic dosage, VAS score, serum CRP, TNF-α, and IL-6 levels in Group A were higher than those in Group B at two hours after delivery (all p <0.001).

Conclusions: PIEB plus PCEA mode at regular intervals of 60 minutes can reduce epidural analgesic dosage and incidence of intrapartum fever during delivery, thus exerting better analgesic effects.

Key Words: *Programmed intermittent epidural bolus (PIEB), Patient-controlled epidural analgesia (PCEA), Delivery, Analgesia, Parturient, Body temperature.*

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INTRODUCTION

Epidural labour analgesia is a catheter-based technique to provide continuous analgesia during labour. The technique involves insertion of a specialised catheter between vertebral spinous processes in the back, into the epidural space and repeated or continuous injections of analgesic drugs to paralyse the area dominated by the corresponding spinal nerve roots.[1,2] Epidural labour analgesia enables flexible adjustment of drug types and concentrations to meet the requirements of labour analgesia.

Patient-controlled epidural analgesia (PCEA) is a self-steering analgesia using a PCA pump.[3] Programmed intermittent epidural bolus (PIEB), an improved method based on PCEA, can significantly improve poor effect on severe pain, high consumption of analgesics, and other drawbacks in PCEA.[4] However, there is no consistent conclusion for recommended method regarding the interval of PIEB administration.

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Fusi *et al.* found that the body temperature of parturient women receiving epidural analgesia may slightly increase without obvious fever (body temperature exceeding 38°C.[5] Parturient women who received epidural analgesia had a significantly higher probability of elevated body temperature or fever during delivery than those who did not.[6] Intrapartum fever may be related to labour progression and epidural analgesia.[7]

Maternal fever after epidural analgesia is idiopathic, and the specific mechanism is not yet clear. At present, the most likely suggestion is that after the parturient women receive epidural analgesia, a high inflammatory state is activated, the endocrine immune balance is disturbed, and the sterile inflammatory response is amplified in the body, producing a large number of endogenous heating media like CRP, TNF-α and IL-6, and leading to body temperature rise and even fever.[8,9] At present, there are few reports on the effects of PIEB with different intervals combined with PCEA on body temperature changes at different time points during latent labor analgesia.

The aim of this study was to explore the effects of PIEB combined with PCEA at different intervals on the body temperature and serum CRP, TNF-α, and IL-6 levels in parturient women receiving analgesia.

METHODOLOGY

This descriptive study was conducted at the First Affiliated Hospital of Shaoyang University, China, from September 2018 to February 2020. The study was approved by the Ethics Committee of the Hospital. A total of 170 primiparous women who had vaginal delivery and required labour analgesia were selected as the research subjects. Inclusion criteria were primiparous women with singleton pregnancy, cephalic presentation, term pregnancy, and required labour analgesia; American Society of Anesthesiologists (ASA) assessment grades I - Ⅱ; without any obstetric complications; and body temperature 36-37.5℃ before delivery. Exclusion criteria were contraindications for epidural block; obstetric complications such as placenta previa, placental abruption, gestational diabetes, gestational hypertension and preeclampsia; thyroid disease; diagnosed infection anywhere in the body, those who received antibiotics with ruptured membrane for over 12 hours or during delivery; who were using steroids; those who received analgesia not at the beginning of but during delivery; with a history of mental illness.

One hundred and seventy primiparous women were divided into Group A and Group B according to the random number table, with 85 cases in each group.

All women entered the delivery room when cervical dilatation reached 2-3 cm. The vein passage was opened in the upper limb, and compound sodium lactate was infused at 5 mL/kg/hour. The maternal blood pressure, heart rate, breathing and blood oxygen saturation were routinely monitored. The fetus ECG monitors were connected for continued fetal heart rate monitoring. Maternal pain scores were recorded using VAS score by an experienced anesthesiologist. After successful puncture, an epidural catheter was inserted 3 to 4 cm. A test dose with 3 mL 1.5% lidocaine (containing 1:200,000 U epinephrine) was administered, and observed for 5 min. After right position of the catheter was confirmed, 0.075% ropivacaine and 8 mL of sufentanil citrate solution 0.5 μg · mL^{-1} (first dose) was injected through an epidural catheter. The analgesia pump was connected from the epidural catheter when the level of epidural block reached T_{10}, and VAS score <4. In Group A, PIEB was applied 30 min after the first dose, with an interval of 30 min, and the pulse dose was 5 mL; and in Group B, PIEB was applied 60 min after the first dose, with an interval of 60 min, and the pulse dose was 10 mL. PCEA doses were set to 5 mL and the lock time was 30 minutes in both groups. If VAS score was still >3 during labour analgesia, the mother was instructed to press the analgesia pump by herself. The mothers in both groups stopped administration when cervical dilation reached 10 cm.

The tympanic membrane (ear) temperature was recorded in both groups at different time points (entry into the delivery room, cervical dilation reached 4 cm, cervix completely dilated, 2 hours and 24 hours after delivery). An ear thermometer (TH839S) was used, and the maternal ear temperature >38°C was regarded as fever. Duration of the first, second, and third stages of labour, epidural drug dosage, bleeding volume, and VAS scores (entry into the delivery room and at 2 hours after delivery) in the mother, as well as birth temperature, and 1-minute and 5-minute Apgar scores in the fetus were observed. Peripheral venous blood was collected from all mothers at entry into the delivery room, 2 hours and 24 hours after delivery, and CRP, TNF-α, and IL-6 levels were detected by ELISA.

Table I: Comparison of body temperature at different time points and intrapartum fever between two groups.

Parameter	Group A (n=85)	Group B (n=85)	p-value
Body temperature at entry into the delivery room (℃)	36.75 ±0.14	36.76 ±0.17	0.616
Body temperature at cervical dilatation reached 4 cm (℃)	37.26 (37.11– 37.35)	37.23 (37.15-37.33)	0.608
Body temperature at cervix completely dilated (℃)	37.79 ±0.19	37.47 ±0.15	<0.001
Body temperature at 2 hours after delivery (℃)	37.98 ±0.21	37.73 ±0.24	<0.001
Body temperature at 24 hours after delivery (℃)	36.65 (36.54 – 36.81)	36.57 (36.46 – 36.77)	0.142
Incidence of intrapartum fever [n (%)]	15 (17.65)	6 (7.06)	0.036

Table II: Comparison of maternal and neonatal indicators between the two groups.

Parameter	Group A (n=85)	Group B (n=85)	p-value
Duration of the first stage of labour (min)	421.17 ±44.21	423.68 ±58.93	0.754
Duration of the second stage of labour (min)	50.21 ±5.27	51.38 ±8.24	0.270
Duration of the third stage of labor (min)	9.54 ±1.00	9.32 ±1.51	0.255
Epidural drug dosage (mL)	62.90 ±2.74	59.24 ±4.15	□0.001
Bleeding volume (mL)	197.51 ±8.60	194.40 ±13.43	0.074
VAS score at entry into delivery room□score□	8.77 ±0.05	8.76 ±0.04	0.312
VAS score at 2 hours after delivery □score□	0.94 ±0.10	0.24 ±0.07	<0.001
Neonatal birth temperature (℃)	36.61 ±0.33	36.59 ±0.34	0.716
Neonatal birth 1-minute Apgar score (score)	9.29 ±0.05	9.28 ±0.04	0.643
Neonatal birth 5-minute Apgar score (score)	9.78 ±0.11	9.79 ±0.13	0.516

SPSS 25.0 statistical software was used for analysis. Enumeration data was expressed in n (%), and Chi-square test was used for comparison between groups. Kolmogorov-Smirnov test was used for evaluation of the normality of quantitative data. Measurement data with normal distribution were expressed by Mean ± S-D and independent sample t-test was conducted. Variables with non-normal distribution were expressed as Median (IQR) and analysed by using Mann-Whitney U-test. P <0.05 was statistically significant.

RESULTS

One hundred and seventy parturient women were included, aged 21-30 (26.28 ±2.31) years, with gestational age of 37-41 (39.4 ±0.5) weeks; and there were 150 cases (88.24%) of ASA grade I and 20 cases (11.76%) of ASA grade Ⅱ.

There were no significant differences in the body temperature between the two groups of women at entry into the delivery room, cervical dilatation reached 4 cm, and 24 hours after delivery (p = 0.616, 0.608 and 0.142, respectively, Table I). Maternal temperature in Group A was significantly higher than that in Group B at cervix completely dilated and 2 hours after delivery (both p <0.001, Table I); and the incidence of intrapartum fever in Group A was higher than that in Group B (p = 0.036,Table I).

There were no significant differences in duration of the first, second, and third stages of labour, bleeding volume, VAS score at entry into delivery room, neonatal birth temperature, and 1-minute and 5-minute Apgar scores between the two groups (p = 0.754, 0.270, 0.255, 0.074, 0.312, 0.716, 0.643 and 0.516, respectively, Table II); and the epidural drug dosage and VAS score at 2 hours after delivery in Group A were higher than those in Group B (p <0.001, Table II).

There were no significant differences in serum CRP, TNF-α, and IL-6 levels between the two groups at entry into the delivery room and 24 hours after delivery (p = 0.617, 0.840, 0.480, 0.738 0.864 and 0.420, respectively, Table III); and the serum CRP, TNF-α, and IL-6 levels in Group A were higher than those in Group B at 2 hours after delivery (all p <0.001, Table III).

Table III: Comparison of serum inflammatory factor levels between the two groups.

Parameter	Group A (n=85)	Group B (n=85)	p-value
Serum CRP at entry into the delivery room (mg/L)	6.57 ±0.04	6.56 ±0.03	0.617
Serum CRP at 2 hours after delivery (mg/L)	53.49 ±5.06	48.42 ±4.91	<0.001
Serum CRP at 24 hours after delivery (mg/L)	8.07 ±0.78	8.10 ±0.79	0.840
Serum TNF-α at entry into the delivery room (ng/mL)	1.48 ±0.16	1.52 ±0.43	0.480
Serum TNF-αat 2 hours after delivery (ng/mL)	2.30 ±0.24	2.04 ±0.58	<0.001
Serum TNF-αat 24 hours after delivery (ng/mL)	1.64 ±0.17	1.63 ±0.45	0.738
Serum IL-6 at entry into the delivery room (pg/mL)	9.13 ±0.95	9.16 ±0.93	0.864
Serum IL-6 at 2 hours after delivery (pg/mL)	67.79 ±6.85	62.04 ±6.49	<0.001
Serum IL-6 at 24 hours after delivery (pg/mL)	15.31 ±4.32	14.80 ±3.86	0.420

DISCUSSION

In recent years, PIEB combined with PCEA in labour analgesia has become the main technique for some institutions. However, further research still needs to be conducted on the administration intervals of PIEB.[10] In this study, the VAS score in Group A was higher than that in Group B at 2 hours after delivery, suggesting that the analgesic effect of administration mode at an interval of 60 min was better in PIEB plus PCEA mode.

Meanwhile, whether there was a difference in the effect of PIEB administration at different intervals on body temperature during labour analgesia was also observed. The results showed that PIEB plus PCEA mode at intervals of 30 and 60 minutes for labour analgesia would lead to an increase in body temperature during delivery, which would return to normal after 24 hours. But PIEB plus PCEA mode at regular intervals of 60 minutes could reduce the incidence of intrapartum fever during delivery. The reason may be that epidural drug dosage in PIEB plus PCEA mode is less at an interval of 60 minutes, which can avoid the central temperature disorder caused by epidural labour analgesia.[11] Meanwhile, the extension of the interval allows the cooling function to recover and reduces heat retention caused by sympathetic nerve blocks.[12]

Mantha *et al.* found that compared with continuous epidural labour analgesia, the intermittent administration of epidural labour analgesia could significantly reduce the rate of intrapartum fever during delivery, which is inferred to be related to the partial recovery of the body's heat dissipation function at the interval of administration.[13]

CRP can stimulate monocytes to release inflammatory mediators such as TNF-α and IL-6.[14,15] Among them, IL-6 is a key pro-inflammatory cytokine and one of the vital signs of early inflammatory response with strong inflammatory activity.[16,17] Neal *et al*. found that compared with those who have not started labour, the serum concentrations of neutrophils, IL-6, and IL-10 in women with cervical dilation <6 cm increased significantly.[18]

Roberts *et al*. confirmed that intrapartum fever was associated with epidural analgesia and histological chorioamnionitis. But it was histologically confirmed that chorioamnionitis was a non-infectious inflammation.[19] Other study found that even the prophylactic use of antibiotics could not reduce the intrapartum fever rate during delivery of analgesic women undergoing intravertebral block.[20]

In this study that there were no significant differences in serum CRP, TNF-α, and IL-6 levels between the two groups at entry into the delivery room and 24 hours after delivery; and the serum CRP, TNF-α, and IL-6 levels in Group A were higher than those in Group B at 2 hours after delivery; it followed that PIEB plus PCEA administration mode at a regular interval of 60 minutes could reduce the duration of inflammatory stimuli related to epidural labour. Thus reducing the incidence of intrapartum fever. Riley *et al*. confirmed that IL-6 levels in febrile women who received epidural anesthesia during delivery are higher than those who did not.[21]

Intrapartum fever can lead to adverse birth outcomes such as chorioamnionitis, umbilicalitis, neonatal encephalopathy, fetal distress, and even intrauterine death.[22] However, no adverse effects of PIEB plus PCEA mode at regular intervals of 30 minutes and 60 minutes were found on newborns in this study. Alexander also noted that maternal fever was unlikely to adversely affect the fetus.[23]

Despite earnest research by the authors, there are some limitations to be noted. First, sweating plays a key role in the fever, but the amount of sweating is not measured in this study. Second, although the maternal temperature from entry into the delivery room to 24 hours after delivery is recorded, the change of body temperature is not recorded thereafter. These limitations need to be addressed in further research in the future.

CONCLUSION

PIEB plus PCEA mode at regular intervals of 30 and 60 minutes

respectively, for labour analgesia led to an increase in body temperature during delivery, which returned to normal after 24 hours. The increase in body temperature may be related to epidural labour associated inflammation. PIEB plus PCEA mode at regular intervals of 60 minutes can reduce epidural analgesic dosage and the incidence of intrapartum fever during delivery, thus exerting better analgesic effects.

ETHICAL APPROVAL:
This study was conducted with the approval from the Ethics Committee of the First Affiliated Hospital of Shaoyang University, China.

PATIENTS' CONSENT:
All patients signed a document of informed consent.

CONFLICT OF INTEREST:
Authors declared no conflict of interest.

AUTHORS' CONTRIBUTION:
BL: Acquired data; drafted the manuscript; contributed substantially to its revision.
SY, AC, DM: Acquired data; drafted the manuscript.
WF: Drafted the manuscript; read and approved the final manuscript.

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