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ORIGINAL RESEARCH

Sensory Block Height and Risk of Maternal Fever in Epidural Labour Analgesia: A Prospective Cohort Study

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Background: Epidural anaesthesia is commonly utilized for pain relief during labour. However, it has been observed that this method can lead to maternal fever (temperature≥38 °C). The mechanism of epidural-related maternal fever (ERMF) remains unclear. This study aims to explore the correlation between the level of sensory blockade and the occurrence of ERMF.

Methods: This cohort study included primigravid women who received patient-controlled epidural analgesia (PCEA). We employed a wireless continuous temperature-monitoring device to capture minute-by-minute fluctuations in maternal temperature. Additionally, various indicators pertaining to the mother, neonate, and anaesthesia were recorded throughout the labour process. Receiver operating characteristic curves were used to evaluate the predictive performances of the sensory block level and duration of block level for fever. Logistic regression was used for multifactorial analyses. Propensity score matching was employed to eliminate endogeneity and control confounding factors.

Results: The study included a sample of 953 primigravid women, among whom an average of 29.8% (284/953) experienced intrapartum fever. The highest level of sensory block was significantly higher in febrile women than in nonfebrile women. Women with labour analgesia may be more prone to fever when the duration of block level above innervation level of thoracic 8 was longer than 135 minutes. Factors influencing ERMF include the highest level of sensory blockade, duration of block level (above T8), and the meconium-stained amniotic fluid (MSAF).

Conclusion: During epidural labour analgesia, the highest level of sensory block was significantly higher in febrile women than in nonfebrile women. When the maternal sensory block plane surpasses the innervation level of thoracic 8 and persists for longer than 135 minutes, the likelihood of maternal fever increased. Therefore, maintaining the maternal sensory block plane below T8 may reduce fever.

Keywords: epidural-related maternal fever, patient-controlled epidural analgesia, sensory block level

Introduction

Epidural anaesthesia has been widely used for labour analgesia. While it provides effective pain relief during labour, it can also cause maternal fever (temperature ≥38 °C) with an incidence of up to 20%.[1,2] The mechanism of epidural-related maternal fever is not clear. Aseptic inflammation caused by local anaesthetics is also thought to be a possible cause of epidural-related maternal fever (ERMF).[1,3,4] Chorioamnionitis during labour may also result in elevated body temperature, but its incidence (3.9%) is significantly lower than that of ERMF.[5] Thus, clarifying the causes of maternal

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fever during epidural labour analgesia may reduce the risk of antibiotic overuse and other related risks. It has also been suggested that epidural analgesia leads to sympathetic blockade, but due to the unique dual sympathetic supply of the cutaneous circulation, the body temperature before neural blockade is therefore the factor that determines whether sympathetic blockade results in vasodilation or vasoconstriction. Maternal heat production increases during labour, and labour epidural anaesthesia blocks active cutaneous vasodilation, resulting in decreased cutaneous heat loss and skin blood flow. As a result, mean body temperature increases.[6,7]

Several studies have found lower rates of maternal fever with epidural use of relatively low concentrations of ropivacaine (0.068%, 0.075%) than with high concentrations of ropivacaine (0.1%).[8–10] Zhao's team concluded that there was a time- and dose-dependent relationship between patient-controlled epidural analgesia (PCEA) and maternal fever.[11] Our previous studies also found that parturient in the fever group who had longer duration of epidural analgesia and used more analgesic drugs.[12] In contrast, Arran Seiler et al found that while the route of administration and dose of bupivacaine differed between epidural and spinal labour analgesia, these two groups had no significant difference in the rate of maternal fever, and epidural-related maternal fever may be due to altered thermoregulation from central neuraxial block.[13] In the context of painless labour, the central nervous system was subjected to varying degrees of blockade among all women; however, only a subset of these individuals experienced fever. Currently, few studies have directly linked the height or duration of epidural sensory block to maternal fever, and we aim to identify the potential relationship between the level of nerve blockade and the occurrence of fever through our research.

In some clinical studies of maternal fever, the interval between temperature measurements is too long or the method of temperature measurement is not clearly described.[13–15] During labour, it is possible for a woman to experience fluctuations in body temperature, such as fever or a return to normal levels, which may not be readily observed by the doctors and nurses. In this study, we searched for the change rule of maternal temperature by using a wireless continuous temperature-monitoring device to record minute-by-minute changes in maternal temperature.

This study examined whether higher or prolonged sensory block levels during epidural labour analgesia increase the risk of maternal fever. Also to find the level of sensory blockade that is most likely to cause maternal fever.

Methods

Study Population

This prospective study was approved by the Ethics Committee of Sichuan Provincial People's Hospital (approval no. 2020356) and the Ethics Committee of Chengdu Jinjiang District Women & Children Health Hospital (approval no. 202114). It was registered at the Chinese Clinical Trials Registry (Registration number ChiCTR 2000037802). Parturient who received PCEA in Sichuan Provincial People's Hospital from September 2020 to June 2021 and those who received PCEA in Chengdu Jinjiang District Women & Children Health Hospital from January to August 2021 were enrolled in the study. Our research was in line with the Declaration of Helsinki. All participants in the trial signed a written informed consent form.

Inclusion criteria: 1. Primigravids who requested and had no contraindications to receive epidural analgesia were eligible. 2. Parturient who were ≥ 18 years were able to understand and sign the informed consent form. 3. Parturient with singleton cephalic gestation at term. 4. Normal maternal coagulation function and platelets. 5. Normal maternal temperature before epidural analgesia.

Exclusion criteria: 1. Autoimmune diseases. 2. Sepsis, pneumonia, and various types of infections. 3. Continuous temperature data interruption of ≥30 min for any reason. 4. Parturient who had dislodged their epidural catheters. 5. Parturient who voluntarily withdrew from the study.

Definition of Maternal Fever and Body Temperature Measurement Method

Maternal fever was defined as a maternal temperature ≥38 °C during labour. After the labouring woman entered the delivery room, she was infused with compound sodium chloride solution at 2~4 mL kg^{-1} $hour^{-1}$. The temperature of the delivery room was maintained at 22~26 °C. We fixed the wireless thermometer (iThermonitor, Rui Ren Medical, China) with waterproof adhesive tape in the axilla of the maternal upper limb that was not infused with fluids and asked the

woman to adduct the ipsilateral arm for 8 minutes and to move freely only after the temperature display stabilized. The thermometer recorded the axillary temperature every 4 seconds, calculated the average temperature per minute through a signal processor and transmitted it to the monitor. This wireless thermometer can well represent core temperature in adults with a proprietary algorithm.[16] When the maternal body temperature was higher than 38 degrees, the monitor sounded to alert nurses and doctors. The wireless thermometer was worn until 2 hours postpartum.

Patient-Controlled Epidural Labour Analgesia

When the maternal contractions were regular and the cervical opening was dilated to 2 cm, epidural analgesia was performed. An epidural catheter was placed at the lumbar 3–4 or lumbar 2–3 interspace, and 3 mL of 1.5% lidocaine was given through the catheter as a trial dose. After 5 minutes, 10 mL of 0.1% ropivacaine hydrochloride (AstraZeneca, USA) with 0.5 μg mL^{-1} sufentanil (Yichang Renfo Pharmaceuticals, China) was added, and then an epidural pulse pump was connected (TuoRen, China). The epidural pulse pump was a combination of a programmed intermittent epidural bolus and PCEA. Parameter settings: ropivacaine 0.1%; sufentanil 0.5 μg mL^{-1}; programmed intermittent epidural bolus 10 mL; programmed intermittent epidural bolus interval 60 min; PCEA bolus 5 mL; lock time 20 min; and maximum hourly 25 mL. The women could press the analgesic pump button to add more drugs according to their own needs for analgesic drugs.

Sensory Block Level Measurement and Visual Analogue Scale Analgesic Score

Twenty minutes after completion of the first epidural administration, cold sensory block assessment was performed on the patient using an ice pack. Starting from the blocked area at the L1 (first lumbar vertebra) anesthetic level, bilateral segmental examinations were conducted upward toward the thoracic vertebrae block level. The sensory block level was determined when the parturient perceived the cold sensation from the ice pack as identical to that in the control area, which is the C3-C5 (third to fifth cervical vertebrae) innervated area above the clavicle. Sensory level measurements were performed every 1 hour thereafter. The last determination was made when the analgesic pump was turned off. The level of sensory blockage experienced by the woman during labour was recorded.

The level of maternal pain was assessed using the visual analogue scale. The score ranges from 0, no pain, to 10, worst. The first assessment was conducted prior to the administration of epidural anaesthesia. Following this, visual analogue scale pain assessment was repeated 20 minutes after the initial administration of anaesthetic drugs.

Data Collection

Data were collected on various maternal, neonatal and labour-related factors, including age, body mass index, gestational age, number of uterine examinations, number of inductions of labour, number of people using antibiotics, visual analogue scale at different times, number of people who had meconium-stained amniotic fluid (MSAF), number of people who had preterm rupture of membranes(PROM), whether the mode of delivery was changed from vaginal to caesarean section, the first stage of labour duration, neonatal pneumonia, 1-minute Apgar score, 5-minute Apgar score,[17] white blood cell count before labour, total duration of analgesia, total amount of analgesic drugs, number of PCEA boluses, assisted delivery, episiotomy, perineal tear, blood loss during labour, duration of maternal fever, duration of hospitalization (from the beginning of the first stage of labour to hospital discharge), the highest level of sensory blockade during labour, and the duration of block level for fever.

Statistical Analysis

Normally distributed continuous variables were analysed using the independent *t* test and are expressed as the mean ± standard deviation. Continuous variables that did not fit a normal distribution were assessed for significance of differences between groups using the Wilcoxon rank sum test and are statistically described by the median. The chi-square test was used for categorical variables, which are statistically described by frequencies and percentages. Receiver operating characteristic curves were used to evaluate the predictive performances of the sensory block level and duration of block level for fever. Logistic regression was used for multifactorial analyses. Propensity score matching was employed to eliminate endogeneity and control confounding factors. In this study, the nearest neighbour matching

method with a 1:1 no-return match and a calliper value set at 0.02 was used to match febrile and nonfebrile maternity. The balance of control variables before and after matching was tested. The data management and statistical analysis were performed using R4.2.2 software R (https://www.r-project.org/). A two-sided *P* value of < 0.05 was considered significant.

Result

A total of 953 primigravid women were included in this study. The number of women with fever during labour was 284 (29.8%). Among them, 368 were included in Sichuan Provincial People's Hospital, with 86 (23.4%) having fever during labour; 585 were included in Chengdu Jinjiang District Women & Children Health Hospital, 198 (33.8%) of whom had fever during labour (Figure 1).

Comparison of Febrile and Nonfebrile Maternity

In the analysis of baseline conditions among labouring women, it was observed that febrile labouring women received a greater amount of antibiotics compared to nonfebrile labouring women ($P<0.05$). Following propensity score matching, no significant disparities in baseline variables were found between the two groups (Table 1). Examination of neonatal and maternal outcomes revealed a higher incidence of haemorrhage during labour and two hours postpartum, a higher level of the highest sensory blockade, greater analgesic pump consumption, and a higher incidence of MSAF in febrile mothers ($P<0.05$) (Table 2).

Association Between the Sensory Blockade Level and Maternal Fever

We drew receiver operating characteristic curves to evaluate the predictive performance of the sensory block level for fever. When the cut-off was 8.5, the sensitivity was 57.7%, the specificity was 67.9%, and the area under the curve was 0.638 (95% CI 0.59–0.68). The implication is that women undergoing labour analgesia may be more likely to develop fever when the highest sensory block level is higher than innervation level of thoracic 8 (Figure 2A). Subsequently, the duration of all maternal sensory block levels above T8 was collected, followed by the calculation of their mean values and the construction of receiver operating characteristic graphs. The average duration of sensory block level above T8 was found to be 129 ± 219 minutes. When the cut-off was 135, the sensitivity was 81.0%, the specificity was 54.8%, and

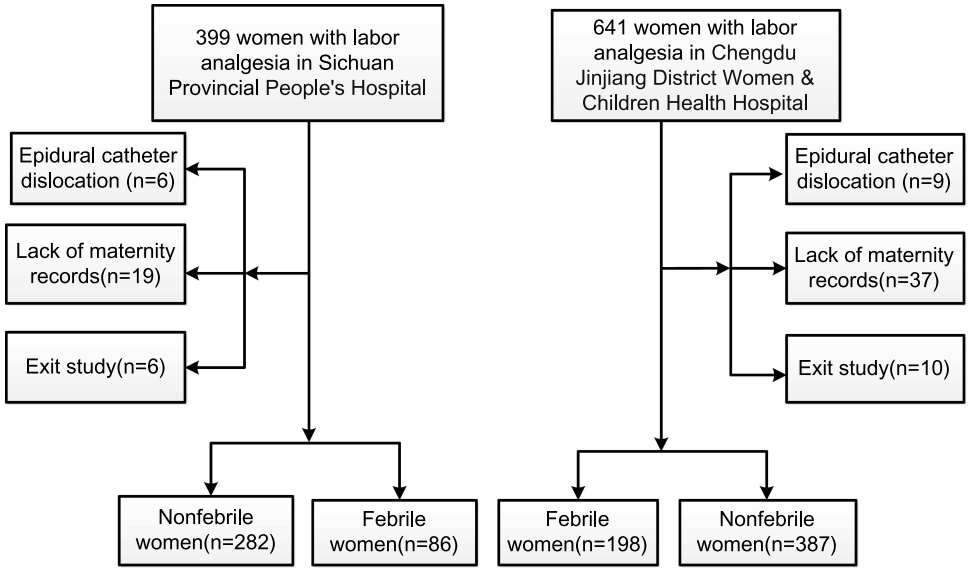

Figure 1 The flow chart for the study.

Table 1 Comparison of Baseline Variables

Variable	Before PSM		*P*	After PSM		*P*
	Maternal Fever			Maternal Fever		
	Yes (n=284)	No (n=669)		Yes (n=260)	No (n=260)	
Age (yr)	28.3(24.8–31.8)	28.2(25.2–31.2)	0.677	28.3(24.8–31.8)	28.3(25.3–31.3)	0.834
BMI (kg/m^2)	26.0(23.1–28.9)	25.9(23.1–28.7)	0.665	26.0(23.1–28.9)	26.0(23.2–28.8)	0.684
Gestational age (week)	38.8(37.6–40.0)	38.9(37.7–40.1)	0.325	38.8(37.6–40.0)	38.9(37.7–40.1)	0.635
Uterine examination (n)	5(3.0–7.0)	5(2.0–8.0)	0.486	5(3.0–7.0)	5(3.0–7.0)	0.834
Induction of labour (n)	2(1.0–3.0)	2(1.0–3.0)	0.174	2(1.0–3.0)	2(1.0–3.0)	0.426
PROM, n (%)	95(38.3%)	219(32.7%)	0.830	95(36.5%)	95(36.5%)	1.000
Antibiotic, n (%)	204(71.8%)	408(61.0%)	**0.001**	193(74.2%)	192(73.8%)	0.920
VAS (before epidural anaesthesia)	7.7(5.9–9.5)	7.9(6.3–9.5)	0.362	7.7(5.9–9.5)	7.7(6.0–9.4)	0.845
VAS (20 min after injection)	1.3(0.2–2.4)	1.3(0.1–2.5)	0.651	1.3(0.2–2.4)	1.3(0.1–2.5)	0.766
WBC count before labour (10^9/L)	9.2(6.9–11.5)	9.0(6.2–11.8)	0.289	9.2(6.9–11.5)	9.1(6.7–11.5)	0.628

Notes: Values are presented as medians and percentages. Propensity score matching was employed to eliminate endogeneity and control confounding factors. A two-sided *P*-value of < 0.05 was considered significant. Bold text indicates that the corresponding value is less than 0.05.
Abbreviations: BMI, body mass index; PROM, preterm rupture of membranes; PSM, propensity score matching; VAS, visual analogue scale; WBC, white blood cell.

Table 2 Comparison of Neonatal and Maternal Outcome Variables

Variable	Maternal Fever		*P*
	Yes (n=284)	No (n=669)	
Uterine atony, n (%)	23(8.1%)	38(5.7%)	0.163
Caesarean delivery, n (%)	63(22.2%)	131(19.6%)	0.362
Assisted delivery, n (%)	4(1.4%)	24(3.6%)	0.068
Episiotomy, n (%)	65(22.9%)	137(20.5%)	0.264
Perineal tears, n (%)	162(57.0%)	371(55.5%)	0.726
Highest level of sensory blockade	7.3(5.4–9.2)	8.6(6.4–10.8)	**0.001**
Total PCEA duration (h)	9.6(5.0–14.2)	7.2(2.3–13.1)	**0.038**
Total PCEA amount (mL)	87.2(44.1–130.3)	75.4(13.2–137.6)	**0.002**
Bolus (n)	1.7(0.8–2.6)	1.5(0.7–2.3)	**0.003**
MSAF (n)	55(19.4%)	86(12.9%)	**0.001**
Blood loss during labour (mL)	278.2(147.2–409.2)	260.5(137–384.0)	**0.047**
First stage of labour duration (h)	11.6(7.0–16.2)	11.7(6.5–16.9)	0.779
Blood loss two hours after delivery (mL)	87.3(51.1–123.5)	73.8(46.1–101.5)	**<0.001**
Duration of hospitalization (day)	2.9(1.8–4.0)	2.5(1.7–3.3)	0.054
1-min Apgar score	9.3(8.6–10.0)	9.4(8.6–10.2)	0.068
5-min Apgar score	9.9(9.7–10.1)	9.9(9.2–10.6)	0.636
Neonatal pneumonia, n (%)	38(13.4%)	66(9.9%)	0.111

Notes: Values are presented as medians and percentages. A *P*-value of < 0.05 was considered significant. Bold text indicates that the corresponding value is less than 0.05.
Abbreviations: PCEA, patient-controlled epidural analgesia; MSAF, meconium-stained amniotic fluid.

the area under the curve was 0.688 (95% CI 0.64–0.73). Women with labour analgesia may be more prone to fever when the duration of block level above innervation level of thoracic 8 was longer than 135 minutes (Figure 2B).

Comparison of Variables Affecting Maternal Fever

We conducted univariate and multivariate analyses of six variables that differed between febrile and nonfebrile women in comparison, including the highest level of sensory blockade, duration of block level above innervation level of thoracic

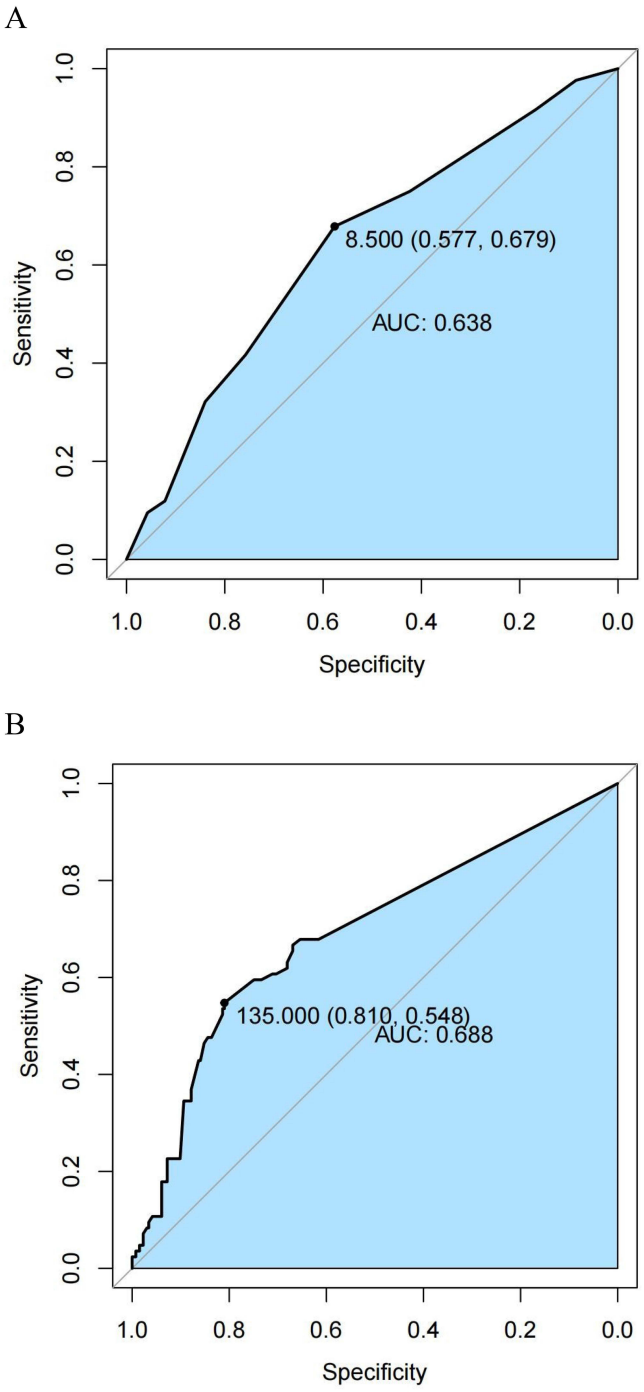

Figure 2 ROC curve for sensory block level (**A**) and duration of maternal sensory block level above T8 in the prediction of maternal fever (**B**).
Abbreviations: ROC, receiver operating characteristic; AUC, area under the curve.

8, total PCEA duration, total PCEA amount, bolus, and MSAF. The results revealed that three factors, specifically the highest level of sensory blockade, duration of block level above innervation level of thoracic 8, and MSAF, were statistically significant and had a significant impact on maternal fever (Table 3).

Table 3 Comparison of Variables Affecting Maternal Fever

Variable	Univariable Analyses				P	Multivariable Analyses				P
	Beta	S.E	Z	OR (95% CI)		Beta	S.E	Z	OR (95% CI)	
Highest level of sensory blockade	−0.24	0.04	−5.36	0.79(0.72–0.86)	**<0.001**	−0.12	0.06	−2.12	0.89(0.79–0.99)	**0.034**
Duration of block level (>T8)	0.00	0.00	6.04	1.01(1.01–1.01)	**<0.001**	0.00	0.00	3.60	1.01(1.01–1.01)	**<0.01**
Total PCEA duration(h)	0.03	002	2.00	1.03(1.01–1.06)	**0.045**					
Total PCEA amount(mL)	0.00	0.00	1.92	1.00(1.00–1.01)	0.055					
Bolus(n)	0.03	0.05	0.67	1.03(0.94–1.13)	0.506					
MSAF(n)	0.67	0.28	2.44	1.96(1.14–3.36)	**0.015**	0.71	0.30	2.39	2.04(1.14–3.66)	**0.017**

Notes: Logistic regression was used for multifactorial analyses. Bold text indicates that the corresponding value is less than 0.05.
Abbreviations: CI, confidence interval; PCEA, patient-controlled epidural analgesia; MSAF, meconium-stained amniotic fluid; S.E, standard error.

Discussion

Our study found that during epidural labour analgesia, the highest level of sensory block was significantly higher in febrile women than in nonfebrile women. When the maternal sensory block plane surpasses the innervation level of thoracic 8 and persists for longer than 135 minutes, there is an increased likelihood of the woman developing a fever. Therefore, proper control of the maternal sensory block plane during labour analgesia is crucial for reducing maternal fever.

Relationship Between Epidural-Related Maternal Fever and the Level of Anaesthetic Blockade

The study by Arran Seiler's team attributed maternal fever to altered thermoregulation due to blockade of the central nervous axis, but fever was not related to the dose of bupivacaine delivered to the epidural and subarachnoid spaces.[13] In contrast, Zhao et al found that there was a time- and dose-dependent relationship between PCEA and maternal fever, and a higher dose of medication resulted in a higher incidence of fever.[11] Whether epidural or spinal anaesthesia is used, a suitable level of sensory blockade needs to be achieved to reduce maternal pain during labour. With spinal analgesia, only a smaller amount of anaesthetic drug is needed to obtain the same sensory block level as that resulting from a larger dose of anaesthetic given in the epidural space. Past studies have found that higher doses of drugs given in the epidural cavity can lead to higher sensory blocked levels.[18–20] Consequently, we believed that an increased dosage of analgesia correlates with a heightened level of sensory blockade in the study conducted by Zhao et al, thereby increasing the likelihood of febrile episodes. The cause of fever may be related to the height of the sensory level of the nerve block. The higher the level of the nerve block and the longer the duration of a high-level block, the more likely it is to lead to the occurrence of maternal fever.

In our multifactorial analysis of variables affecting maternal fever, we also determined that the dosage of epidural anaesthesia drugs did not serve as the primary cause. The highest level of sensory blockade, duration of block level above innervation level of thoracic 8 and MSAF were the main factors affecting maternal fever. The longer duration of sensory level block above innervation level of thoracic 8 causes the sympathetic and sensory nerves to be blocked for a longer time. Skin blood flow is controlled by the sympathetic nervous system through noradrenergic vasoconstriction and cholinergic vasodilation. In normal and hypothermic conditions, noradrenergic vasoconstriction predominates, while in hyperthermic conditions, cholinergic vasodilation can increase skin blood flow by up to 80%.[6] Body temperature before neural blockade is therefore the factor that determines whether sympatholysis results in vasodilation or vasoconstriction. However, during labour, heat production increased. It was possible, therefore, that neuraxial blockade inhibited cutaneous vasodilation, resulting in limited heat loss and an increase in mean body temperature.[6,21] Epidural anaesthesia causes the level of sympathetic blockade in the skin to be higher than the level of sensory blockade. Thus, as the level of sensory blockade rises, the number of sympathetic nerves distributed across the skin that are blocked increases, further leading to decreased maternal heat dissipation and increased body temperature.

Maternal and Foetal Effects of Epidural-Related Maternal Fever

A comparison of deliveries and neonatal profiles of all febrile and nonfebrile women found no significant differences in caesarean section rates, neonatal Apgar scores and pneumonia rates, although women with fever had a higher proportion of MSAF. Whereas previous studies have found an increase in caesarean rates, some have found no difference.[22–26] In addition, we found that febrile women used more antibiotics. Nevertheless, we were unable to determine the relationship between antibiotics and maternal fever because we did not standardize the rules for antibiotic use but rather determined the use of antibiotics independently based on the clinical experience of obstetricians. Sharma et al found that fever and placental inflammation were not reduced with antibiotic prophylaxis before epidural anaesthesia.[27]

Limitations

There are some limitations to our study. First, due to the nature of our study being a cohort study, it was not feasible to allocate the mothers randomly into fever and no fever groups, thereby introducing potential bias. Second, we did not perform amniotic cell cultures or examine the placenta in all the labouring women and therefore did not include these data in the study. Third, since sensory block level, neonatal pneumonia, and neonatal Apgar score were subjectively determined by anaesthesiologists, obstetricians, and paediatricians, there is a possibility of bias.

Conclusions

In this study, the continuous monitoring of maternal temperature using a wireless thermometer and the comprehensive recording of maternal, labour, neonatal, and anaesthesia metrics during epidural labour analgesia were conducted. We found that the highest level of sensory block was significantly higher in febrile women than in nonfebrile women, and controlling the sensory block level below the 8th thoracic vertebra (T8) may reduce the incidence of fever.

Abbreviations

AUC, area under the curve; BMI, body mass index; CI, confidence interval; ERMF, mechanism of epidural-related maternal fever; MSAF, meconium-stained amniotic fluid; PCEA, patient-controlled epidural analgesia; ROC, receiver operating characteristic; PROM, preterm rupture of membranes; PSM, propensity score matching; S.E, standard error; VAS, visual analogue scale; WBC, white blood cell.

Data Sharing Statement

All data relevant to the study are included in the article. The data supporting the findings of this study are available from the corresponding author Min Xie.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Sichuan Provincial People's Hospital (approval no. 2020356) and the Ethics Committee of Chengdu Jinjiang District Women & Children Health Hospital (approval no. 202114). It was registered at the Chinese Clinical Trials Registry (Registration number ChiCTR 2000037802). Subjects who were enrolled provided informed written consent.

Consent for Publication

All participants signed consent to publish.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there are no conflicts of interest regarding the publication of this article.

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