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Association of epidural labor analgesia with maternal and neonatal outcomes in women with preeclampsia: a propensity score-matched single-center retrospective cohort study

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Abstract

Background Epidural labor analgesia (ELA) is widely and safely used for labor pain relief. However, it remains unclear whether ELA affects maternal and neonatal outcomes in women suffering from preeclampsia.

Methods This study reviewed the medical records of women with preeclampsia at ≥ 28 weeks of gestation between January 2015 and December 2020. The medical records of women were divided into ELA and no analgesia (NA) groups. The primary endpoint was the cesarean section (CS) rate. Secondary endpoints included hypotension, operative vaginal delivery, fetal distress, neonatal intensive care unit admission, and complications. Using multivariate logistic regression analysis and propensity score matching (PSM), the association between ELA and maternal and neonatal outcomes was examined.

Results A total of medical records of 686 women were enrolled, with 242 (35.3%) receiving ELA. Of these, 126 (18.4%) had a higher incidence of CS in the ELA group than in the NA group (22.7% vs. 16.0%, P = 0.020). Multivariable analysis indicated greater risks of CS [adjusted Odds Ratio (aOR) = 1.71; 95% CI, 1.07–2.74; P = 0.025] and operative vaginal delivery (aOR = 2.810; 95% CI, 1.379–5.725; P = 0.004) in the ELA group than that of NA group. In the PSM, ELA did not increase the risk of CS (aOR = 1.56; 95% CI, 0.97–2.52; P = 0.067) and OVD (aOR = 2.048; 95% CI, 0.936–4.484; P = 0.073). The secondary endpoints showed no significant differences between the two groups.

Conclusion The study indicates an association between ELA and maternal and neonatal outcomes, supporting the safety of ELA in this population.

Keywords Epidural labor analgesia, Programmed intermittent epidural bolus, preeclampsia, propensity score-matched analysis

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Introduction

Preeclampsia manifests in 2%–8% of pregnancies worldwide [1–3], which is characterized by decline in uteroplacental blood flow and fetal growth restriction [1, 4]. Epidural labor analgesia (ELA) is considered as a safe and effective method for intrapartum pain relief [5]. However, ELA used in intrapartum women with preeclampsia is controversial. ELA may induce hypotension through maternal sympathetic blockade, thereby diminishing uteroplacental perfusion and potentially impeding fetal heart rate [6, 7]. On the contrary, epidural analgesia was shown to decrease maternal plasma concentrations of catecholamines, consequently enhancing uterine intervillous blood flow. A study with a small sample size reported that ELA contributed to elevate uteroplacental blood flow in women with preeclampsia, but not in those with normal gestation [8]. Little is known about whether ELA is safe and effectively used in women with preeclampsia.

In the past 20 years, a trend toward the ELA regimen was a low dose of local anesthetics combined with opioids, with a low risk of an insufficient uterine artery blood supply [9, 10]. The programmed intermittent epidural bolus (PIEB) technique is superior to patient-controlled epidural analgesia (PCEA) and continuous epidural infusion (CEI) for labor pain relief, reducing motor block, exhibiting less frequent breakthrough pain, improving patient satisfaction [11, 12]. However, women with preeclampsia are intolerant to a prolonged labor, particularly during the second stage of virginal delivery [13, 14]. A fundamental question arises regarding association of ELA using PIEB under a low concentration of local anesthetics with maternal and neonatal outcomes in women with preeclampsia.

One major obstacle to using PIEB in women with preeclampsia is hypotension. In contrast to CEI and PCEA, PIEB has a faster transfusion rate and a higher administration pressure with a wider dissemination of local anesthetics. A lower transfusion rate has a smaller incidence of hypotension in intrapartum women without preeclampsia, comparing 125 $mL{\cdot}hr^{-1}$ to 250 $mL{\cdot}hr^{-1}$ [15]. Given that hypotension is largely determined by transfusion rate during PIEB, the concentrate of local anesthetics should be reduced. There is no change in maternal mean arterial pressure and systolic arterial pressure, using 0.25% bupivacaine, 10 mg bolus and 5 mg each hour on CEI for six hours [8]. Actually, either bupivacaine or ropivacaine is used in epidural labor analgesia far lower than 0.25%. Current ELA protocols typically employ far lower concentrations of bupivacaine or ropivacaine, further minimizing this risk. Despite these adjustments, evidence remains limited regarding PIEB's impact on maternal and neonatal outcomes in women with preeclampsia.

To explore these associations, this study employs rigorous statistical approaches, including multivariate regression and propensity score matching, to account for a wide range of potential confounders. Variables considered in these analyses include sociodemographic factors (e.g., maternal education level), obstetric characteristics (e.g., umbilical cord length), and clinical parameters. While some variables, such as education level and umbilical cord length, remain contentious due to inconsistent evidence of their relevance to maternal and neonatal outcomes, their inclusion ensures a comprehensive adjustment for potential confounding factors. The rationale for selecting these variables and their implications for interpreting the results will be discussed in detail later in this manuscript. This investigation aims to provide robust evidence on the association between PIEB and maternal and neonatal outcomes in preeclamptic women, contributing to the optimization of pain management strategies in this high-risk population.

Material and methods

Study approval and eligibility criteria

This retrospective cohort study was approved by the Research and Ethics Committee of Fujian Provincial Maternity and Children's Hospital (approval no:2021KLRD09022; Sep 24, 2021) and adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for cohort studies [16]. The requirement for informed consent was waived by our Institution Review Board. We retrospectively reviewed all the medical records of women diagnosed with pre-eclampsia who delivered at the hospital between January, 2015 and December, 2020. We included live births to women aged $\geq$18 years with pre-eclampsia, had a singleton pregnancy, presented with vertex position, and had a gestational age of $\geq$28 weeks. We excluded medical records of women with missing PIEB-related data, a history of previous cesarean section, major fetal anomalies, fetal chromosomal abnormalities, or fetal distress before the onset of labor. Additionally, those admitted to the labor ward within one hour of delivery because of insufficient time for fetal heart monitoring and PIEB implementation and those who planned for elective cesarean section or emergency cesarean section delivery before the onset of labor were also excluded.

Patient classification and diagnostic criteria

The patients were classified based on the discharge diagnosis summaries, utilizing International Classification of Diseases 10th Revision (ICD-10) codes for pre-eclampsia identification. The data were coded by

trained personnel with formal education and experience in medical coding and data abstraction. They strictly adhered to standardized protocols, focusing solely on physician-documented diagnoses without interpreting symptoms or test results. The codes used were as follows: O13 for mild pre-eclampsia, O14 for pre-eclampsia with severe features or unspecified pre-eclampsia, and O11 for chronic hypertension superimposed pre-eclampsia. This study enrolled patients who met the diagnostic standards outlined by the Hypertensive Disorders in Pregnancy Subgroup Chinese Society of Obstetrics and Gynecology Chinese Medical Association, which closely aligns with the American College of Obstetrics and Gynecology criteria for pre-eclampsia [16, 17]. Pre-eclampsia was defined as the new onset of hypertension (systolic blood pressure (SBP) > 140 mmHg or diastolic blood pressure (SBP) > 90 mmHg) and proteinuria (protein excretion ≥ 300 mg in a 24-h urine collection, a protein/creatinine ratio > 0.3, or a positive dipstick test at > 20 weeks of gestation. In the absence of proteinuria, signs or symptoms of end-organ or systemic damage that qualified as pre-eclampsia included: renal insufficiency, impaired liver function, cerebral or visual complications, thrombocytopenia, and uteroplacental dysfunction. Severe pre-eclampsia was defined as: (1) SBP ≥ 160 mmHg or DBP ≥ 110 mmHg on two occasions at least 4 h apart, (2) persistent headache, visual disturbances, or other central nervous system abnormalities, (3) persistent upper abdominal pain with subcapsular hematoma or symptoms of liver rupture, (4)impaired liver function indicated by liver enzyme elevation to twice of baseline levels, (5) progressive renal insufficiency (urine protein > 2.0 g/24 h, oliguria, or serum creatinine > 106 μmol/L), (6) hypoalbuminemia with ascites or pleural or pericardial effusion, (7) thrombocytopenia ($< 100{,}000 \times 10^9$/L) ormicro vascular hemolysis (anemia, jaundice, or increased blood lactate dehydrogenase levels), (8) heart failure, (9) pulmonary edema, and (10) fetal growth restriction, oligohydramnios, fetal mortality, and early placenta abruption.

ELA administration protocol

Participants were divided into ELA group and NA group. The ELA protocol was implemented under the informed discretion of parturient women, in conjunction with the supervision of seasoned obstetricians and anesthesiologists. Prior to commencing ELA, 18-gauge peripheral venous access was meticulously secured to facilitate prompt medication administration as warranted during the labor process. Continuous surveillance incorporated electrocardiographic (ECG) monitoring for cardiac rhythm assessment, noninvasive blood pressure (BP) measurement for hemodynamic evaluation, heart rate (HR) observation to gauge autonomic function, and oxygen saturation (SpO2) tracking for respiratory status assessment. All PIEB was administered utilizing an 18-gauge needle, targeting the L3–L4 or L4–L5 vertebral interspace, with the patient positioned laterally. A meticulous approach was employed to insert a 19-gauge catheter into the epidural space at a depth of approximately 4 cm. After ensuring the absence of blood or cerebrospinal fluid (CSF) through gentle aspiration, a test dose consisting of 3 mL of lidocaine 1.5% was administered through the 19G catheter. Following a meticulous 5-min observation period, during which no aberrant indications were detected, a solution composed of approximately 10 mL of ropivacaine 0.08% combined with sufentanil 0.4 μg/mL was methodically administered over a duration of 2 min to instigate PIEB therapy. Following, female participants underwent PIEB combined with PCEA, delivering a solution containing 0.08% ropivacaine alongside sufentanil at a concentration of 0.4 μg/mL. A median PIEB volume was 8 (7–12) mL, with an interval duration ranged from 45 to 60 min. Median PCEA volume was 5 (3–10) mL, with a PCEA lockout time of 15 (9–21) min. Visual analog scale (VAS) pain scores and complications associated with epidural labor analgesia were evaluated at 5-min intervals initially, followed by assessments every 30 min until fetal delivery. VAS pain scores were consistently maintained below three points.

Outcome measures

The primary outcome was the incidence of intrapartum cesarean section. Secondary outcomes included VAS, the occurrence of operative vaginal delivery, fetal distress, neonatal intensive care unit (NICU) admission for a minimum of 24 h, and complications associated with ELA. Operative vaginal delivery was performed using an outlet forceps. Fetal distress was defined as Category II or III fetal heart rate (FHR) tracings, which included either absent baseline FHR variability and any of the following: recurrent late decelerations, recurrent variable decelerations, bradycardia, or sinusoidal patterns [18]. Admission to the NICU < 28 days post-birth was determined subjectively by a neonatologist and recorded as a "yes" or "no". Neonatal outcomes were extracted from birth hospitalization data, obtained from linked birth and hospitalization records. A standardized labor management protocol at our hospital was implemented for specific sequential interventions when inadequate labor progress was suspected. Continuous fetal electronic monitoring was systematically conducted throughout labor to identify complications, including uterine tachysystole and non-reassuring/pathological fetal heart rate patterns.

Data retrieved

All clinical data were retrieved from our hospital's Anesthesia Information System (AIMs), Version 5.0. This system ensures accurate and standardized documentation of patient information, including demographic details, clinical history, and procedure-related data. For this study, we employed a structured data abstraction approach. Specifically, trained researchers used predefined data extraction templates to retrieve relevant information directly from the AIMs. To minimize errors and ensure consistency, two independent reviewers cross-checked the extracted data. Discrepancies were resolved through consensus or consultation with a third senior researcher. Extracted data were securely stored in an encrypted database managed using Microsoft Access, Version 16.7 with restricted access to authorized personnel only, ensuring compliance with institutional and regulatory data protection standards.

Statistical analysis

Pearson's chi-squared test, Fisher's exact test, t-test, and Wilcoxon Rank-Sum test were employed to compare covariates, as deemed appropriate. The association between ELA and maternal intrapartum cesarean delivery was explored using univariate and multivariate logistic regression analyses. The confounding factors included in the multivariable analysis were as follows: age, parity, body mass index (BMI), highest completed education level, anemia, prenatal care initiation, nuchal cord, labor induction or augmentation time (LAT), gestational age, basic SBP, basic DBP, infant weight, diagnostic SBP, diagnostic DBP, and umbilical cord length. The selection of these confounding factors was informed by a comprehensive review of pertinent literature detailing the association between PIEB and perinatal outcomes, coupled with considerations of data accessibility within medical records [19–21]. We also included potential confounders, such as blood pressure prior to pregnancy (basic SBP and DBP) and at diagnosis of pre-eclampsia (diagnostic SBP and DBP), as characteristics of pre-eclampsia.

In light of the substantial potential for selection bias, propensity score matching (PSM) was utilized to rigorously examine the correlation between PIEB and the incidence of intrapartum cesarean delivery. By balancing covariates between the PIEB group and no analgesia group based on their propensity scores, PSM facilitates a more robust evaluation of the association of interest. BMI data were missing in 66 patients (9.62%) and represented the covariate with the largest amount of missing information (Table 1). Missing values were imputed using a nonparametric missing-value imputation procedures (miss Forest) before PSM [22]. The propensity score represented the probability of receiving PIEB based on specific maternal characteristics. We performed one-by-one nearest-neighbor matching on the average propensity score without replacement. Covariate imbalances post-matching were assessed using a propensity score distribution and standardized mean differences. The same analysis strategy was used to explore the association between ELA and operative vaginal delivery, fetal distress, and NICU admission. Associations were quantified as odds ratios (ORs) with 95% confidence intervals (CIs). A subgroup analysis was conducted in order to examine the association between ELA and the outcomes of women with severe preeclampsia and women with late-onset preeclampsia (Fig. 1).

All analyses were conducted using R software version 4.2.2, with the "net", "stats", and "match it" packages for propensity score analysis. The "ggplot2" package was also used to create standardized mean difference graphs of the covariates in the PSM analysis.

Results

Of the initial cohort comprising 2,310 records of women reviewed retrospectively in this study, 1,610 were excluded after closer evaluation for not meeting the predefined inclusion criteria. Additionally, record dada of 14 individuals were excluded due to factors such as breech delivery, multiple gestations, fetal anomalies, or incomplete data records. The final analytical cohort comprised a total of 686 women. (Fig. 1).

Based on record data, the baseline characteristics of the 686 women included in the study are presented in Table 1. Among the data analyzed, 504 women (73.5%) were nulliparous. Preterm delivery occurred in 66 cases (9.6%), with 16 women (2.3%) delivering before 34 weeks of gestation. Notably, chronic hypertension was observed in 4.4% (30/686) of cases. Overall, there were 242 women (35.3%) in the ELA group, with a median time of 7.9 h (interquartile range, 4.5–12.0 h). The ELA cohort exhibited a higher prevalence of certain demographic and obstetric characteristics compared to other groups. Specifically, a greater proportion of women in this cohort were under the age of 35 ($P=0.011$), were nulliparous ($P<0.001$), attained a university education or higher ($P=0.001$), and commenced prenatal care during the first trimester ($P<0.001$). Additionally, individuals in this cohort experienced extended latent phase durations ($P<0.001$), longer umbilical cord lengths measured postnatally by trained clinicians ($P=0.038$), and lower baseline systolic and diastolic blood pressure ($P=0.042$; $P=0.042$, respectively), along with decreased diagnostic systolic blood pressure ($P=0.028$). (Table 1).

The overall incidence of intrapartum cesarean section was 18.4% (126/686). The rate of intrapartum cesarean section in the ELA group was significantly greater than

Table 1 Characteristics of participants in the unmatched and matched cohorts

Variables	Full Set				Matched Set			
	No analgesia group (n = 444)	PIEB group (n = 242)	*P*-value	SMD	No analgesia group (n = 187)	PIEB group (n = 187)	*P*-value	SMD
Age (years)			0.011*	0.222			0.196	0.153
< 35	371 (83.6)	220 (90.9)			175 (93.6)	167 (89.3)		
≥ 35	73 (16.4)	22 (9.1)			12 (6.4)	20 (10.7)		
BMI (kg/m^2)			0.610	0.047			0.917	0.022
< 28	252 (56.8)	143 (59.1)			106 (56.7)	108 (57.8)		
≥ 28	192 (43.2)	99 (40.9)			81 (43.3)	79 (42.2)		
Parity			< 0.001#	0.606			0.879	0.031
0	288 (64.9)	216 (89.3)			163 (87.2)	161 (86.1)		
1	156 (35.1)	26 (10.7)			24 (12.8)	26 (13.9)		
Degree			0.001#	0.290			0.562	0.072
≥ bachelor	283 (63.7)	186 (76.9)			133 (71.1)	139 (74.3)		
< bachelor	161 (36.3)	56 (23.1)			54 (28.9)	48 (25.7)		
Prenatal Care Initiated			< 0.001#	0.519			1.000	0.011
0	122 (27.5)	126 (52.1)			73 (39.0)	72 (38.5)		
1	322 (72.5)	116 (47.9)			114 (61.0)	115 (61.5)		
Nuchal Cord			0.756	0.032			0.539	0.076
Yes	107 (24.1)	55 (22.7)			46 (24.6)	40 (21.4)		
No	337 (75.9)	187 (77.3)			141 (75.4)	147 (78.6)		
LAT			< 0.001#	0.353			0.795	0.070
No	250 (56.3)	96 (39.7)			80 (42.8)	85 (45.5)		
8–15 h	116 (26.1)	88 (36.4)			64 (34.2)	58 (31.0)		
≥ 16 h	78 (17.6)	58 (24.0)			43 (23.0)	44 (23.5)		
Anemia			0.440	0.069			1.000	0.011
Yes	165 (37.2)	82 (33.9)			72 (38.5)	71 (38.0)		
No	279 (62.8)	160 (66.1)			115 (58.6)	116 (63.4)		
Infant Weight (g)			0.015*	0.204			0.232	0.135
< 3000	177 (39.9)	73 (30.2)			71 (38.0)	59 (31.6)		
≥ 3000	267 (60.1)	169 (69.8)			116 (62.0)	128 (68.4)		
GA (week)			0.035*	0.187			0.341	0.118
< 38	51 (11.5)	15 (6.2)			18 (9.6)	12 (6.4)		
≥ 38	393 (88.5)	227 (93.8)			169 (90.4)	175 (93.6)		
Basic SBP (mmHg)	123.15 ± 13.42	121.02 ± 12.44	0.042*	0.165	121.54 ± 12.47	121.87 ± 12.35	0.798	0.027
Basic DBP (mmHg)	75.28 ± 10.37	73.70 ± 8.43	0.042*	0.168	74.02 ± 9.62	73.88 ± 8.00	0.874	0.016
Diagnostic SBP (mmHg)	145.31 ± 11.27	143.35 ± 10.99	0.028*	0.177	143.76 ± 10.32	143.66 ± 10.84	0.926	0.010
Diagnostic DBP (mmHg)	92.33 ± 8.89	93.31 ± 9.18	0.175	0.108	93.26 ± 8.33	92.42 ± 9.15	0.357	0.095
Length of Umbilical Cord (cm)	58.49 ± 11.45	60.43 ± 12.02	0.038*	0.165	59.65 ± 12.86	59.60 ± 11.86	0.973	0.003

Quantitative variables are expressed as mean ± SD or median (IQR). Categorical variables are expressed in number and percentage n (%)

Abbreviations: BMI Body mass index, *GA* Gestational age, *DBP* Diastolic blood pressure, *LAT* Labor augmentation or induction time, *SBP* systolic blood pressure, *SMD* standardized mean difference

*: $P < 0.05$

#: $P < 0.01$

that of no analgesia group (22.7% (55/242) vs. 16.0% (71/444); $P = 0.020$). Intrapartum cesarean sections were performed most frequently for arrest of dilation or fetal head descent (37.3%, 47/126), followed by pre-eclampsia (29.4%, 37/126), fetal distress (23.8%, 30/126), intrauterine infection (6.3%, 8/126), and others (3.3%, 4/126).

In the propensity score analysis, 187 (77.2%) of women in the ELA group were matched with 187 (42.1%) of women in the no analgesia group (Table 2).

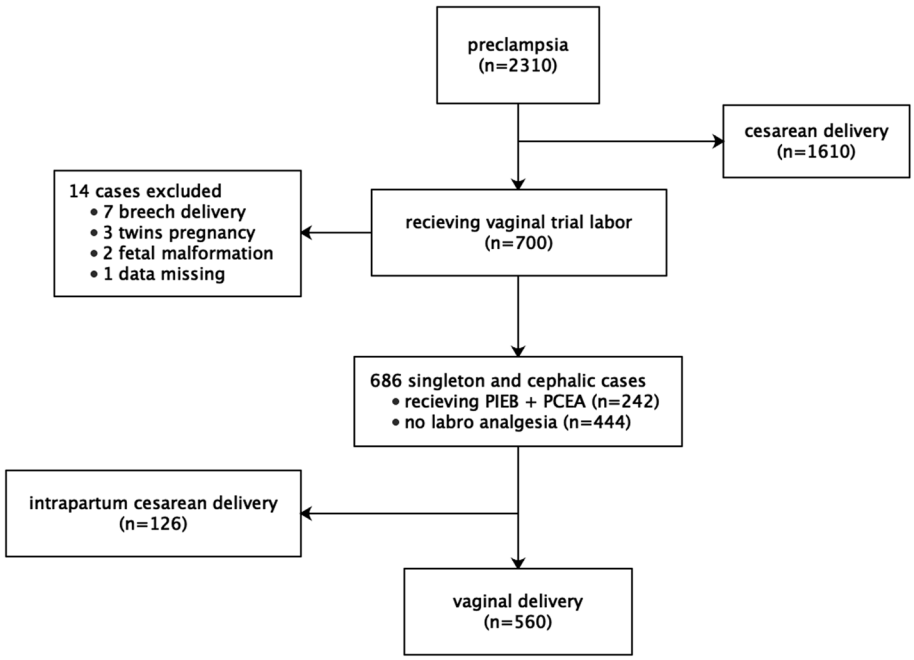

Fig. 1 Flow chart of the study population

Table 2 Association between PIEB and perinatal outcomes analyzed using logistic regression and propensity score-matching

Outcome	Model	OR (95% CI)	*P* value
CS			
	Confounder adjusted[a]	1.779 (1.127, 2.806)	0.013
	Propensity matching[b]	1.672 (0.989, 2.826)	0.055
OVD			
	Confounder adjusted[a]	2.717 (1.356, 5.444)	0.005
	Propensity matching[b]	2.288 (0.993, 5.273)	0.052
Fetal Distress			
	Confounder adjusted[a]	1.560 (0.735, 3.257)	0.238
	Propensity matching[b]	1.411 (0.605, 3.405)	0.429
NICU Admission			
	Confounder adjusted[a]	1.282 (0.796, 2.060)	0.305
	Propensity matching[b]	1.322 (0.710, 2.492)	0.381

Abbreviations: *CS* cesarean section, *OVD* operative vaginal delivery, *NICU* neonatal intensive care unit admission, *OR* odds ratio, *CI* confidence interval

[a] Logistic regression model with no imputation and adjustment for GA, parity, education, anemia, prenatal care initiated, nuchal cord, LAT, age, BMI, basic SBP, basic DBP, infant weight, diagnostic SBP, diagnostic DBP, and umbilical cord length ($N=686$)

[b] Logistic regression model with multiple imputations and adjustment for the same variables ($N=374$)

A good post-matching balance was achieved between both groups, with a similar distribution of propensity scores and covariates. (Fig. 2).

In the entire cohort, after adjusting for multiple variables, our analysis demonstrated that the incidence of maternal intrapartum cesarean section was notably elevated in ELA group compared to the absence of analgesia (adjusted odds ratio [OR] = 1.71; 95% confidence interval [CI] (1.07–2.74); $P=0.025$). However, in the matched sample, ELA administration was not associated with maternal intrapartum cesarean section (adjusted OR = 1.56; 95% CI, 0.97–2.52; $P=0.067$) (Table 2). Similarly, operative vaginal delivery initially showed a higher risk in the ELA group in the multivariate analysis (adjusted OR = 2.810; 95% CI, 1.379–5.725; $P=0.004$) but was not significant in the propensity score analysis (adjusted OR = 2.048; 95% CI 0.936–4.484; $P=0.073$) (Table 2). No elevated risk of fetal distress rate or NICU admission was observed in the ELA group in either the multivariable analysis [OR = 1.57; 95% CI (0.71–3.43); $P=0.260$; OR = 1.28; 95% CI (0.70–1.81); $P=0.617$] or propensity score analysis [OR = 1.60; 95% CI (0.68–3.93); $P=0.285$; OR = 1.32; 95% CI (0.64–2.00); $P=0.666$] (Table 3). Subgroup analysis revealed that ELA was associated with a reduced risk of CS in women with severe preeclampsia (OR 0.578, 95% CI 0.365–0.917). However, no significant association was observed between ELA and CS risk in women with late-onset preeclampsia (OR 1.079, 95% CI 0.996–1.117).

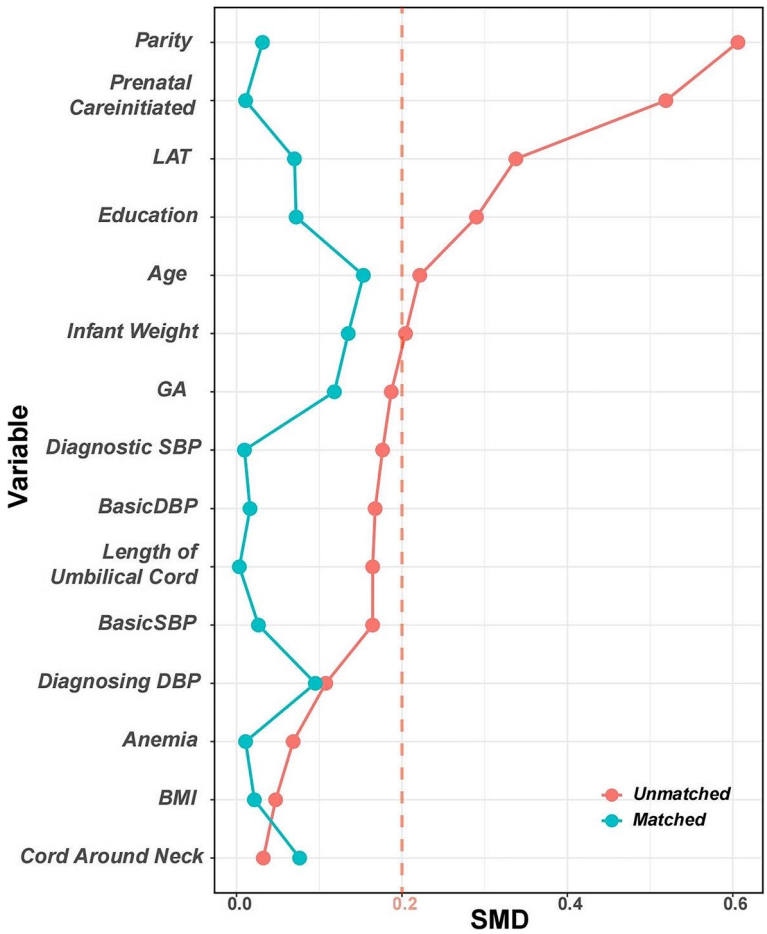

Fig. 2 Comparison of covariate equilibrium between the PIEB + PCEA group and no analgesia group. BMI, body mass index; DBP, diastolic blood pressure; GA, gestational age; LAT, labor induction or augmentation time; SBP, systolic blood pressure; SMD, standardized mean difference

Discussion

This study suggests that ELA is not associated with an increased likelihood of cesarean section in women with preeclampsia. Additionally, ELA was not found to be associated with a higher incidence of adverse perinatal outcomes, including maternal hypotension, operative vaginal delivery, fetal distress, NICU admission, or complications related to ELA. These findings support the potential efficacy and safety of ELA for labor pain relief in women with preeclampsia. However, further studies with larger sample sizes are needed to confirm these results.

A large multicenter cross-sectional survey revealed that labor neuraxial analgesia reduced the risk of cesarean delivery in intrapartum those with hypertensive disoder [20]. In a cohort study of 106,845 women who underwent operative vaginal delivery, 92,518 (86.6%) received neuraxial analgesia. Compared to no neuraxial analgesia, the study identified links between receiving neuraxial analgesia and having higher education levels, gestational hypertension or preeclampsia, late admission to labor and delivery, and initiation of prenatal care in the first trimester, compared to those without neuraxial analgesia [21]. In our study, the overwhelming majority (90.4%) of enrolled women underwent full-term deliveries, with a smaller fraction (2.3%) delivering at < 34 weeks of gestation, consistent with previous findings [23]. The majority of the study participants experienced late-onset preeclampsia characterized by a distinct pathogenesis and more favorable neonatal outcomes, unlike whose with early-onset preeclampsia, consistent with previous study finding [24]. Early-onset preeclampsia induces a low cardiac output and a high vascular resistance, while late-onset preeclampsia exhibits high cardiac output, normal or low vascular resistance, and intravascular fluid overload [25]. ELA might decrease peripheral vascular resistance through sympathectomy and increase cardiac output in women with early-onset pre-eclampsia. Intravascular fluid overload in women with late-onset preeclampsia contributes to decline in the risk of hypotension

Table 3 Logistic regression analysis of perinatal outcomes

Outcome	Variable	OR (95% CI)	*P* value
CS	PIEB + PCEA (Yes *VS* No)	1.779 (1.127, 2.806)	0.013
	Parity (≥ 2vs.1)	0.112 (0.048, 0.262)	< 0.001#
	Prenatal Care Initiated (Yes *VS* No)	4.740 (2.729, 8.233)	< 0.001#
	Nuchal Cord (Yes *VS* No)	0.290 (0.151, 0.556)	< 0.001#
	Age (≥ 35 *VS* < 35 years)	2.200 (1.014, 4.773)	0.046*
	BMI (≥ 28 *VS* < 28)	1.113 (0.722, 1.715)	0.629
	Infant Weight (≥ 3 kg *VS* < 3 kg)	1.788 (1.115, 2.866)	0.016*
	Anemia (Yes *VS* No)	1.284 (0.827, 1.994)	0.265
OVD	ELA (Yes *VS* No)	2.717 (1.356, 5.444)	0.005#
	Parity (≥ 2 *VS* 1)	0.177 (0.052, 0.608)	0.006#
	Prenatal Care Initiated (Yes *VS* No)	1.456 (0.725, 2.925)	0.291
	Nuchal Cord (Yes *VS* No)	1.397 (0.696, 2.804)	0.347
	Age (≥ 35 *VS* < 35)	2.564 (0.865, 7.603)	0.090
	BMI (≥ 28 *VS* < 28)	0.393 (0.186, 0.831)	0.014
	Infant Weight (≥ 3 kg *VS* < 3 kg)	1.881 (0.915, 3.869)	0.086
	Anemia (Yes *VS* No)	2.200 (1.156, 4.189)	0.016*
Fetal Distress	Nuchal Cord (Yes *VS* No)	0.420 (0.122,1.097)	0.111
	LAT (8–15 h *VS* No)	0.346 (0.113,0.871)	0.037*
	LAT (≥ 16 h *VS* No)	0.667 (0.239,1.605)	0.397
	Diagnostic SBP	0.964 (0.928,0.999)	0.051
NICU Admission	Parity (≥ 2 *VS* 1)	0.533 (0.307, 0.895)	0.021*
	Degree (≥ bachelor *VS* < bachelor)	1.647 (1.043, 2.587)	0.031*
	Prenatal care Initiated (Yes *VS* No)	0.676 (0.438, 1.048)	0.077
	Infant Weight (≥ 3 kg *VS* < 3 kg)	0.552 (0.352, 0.869)	0.010*
	GA (≥ 38w *VS* < 38w)	0.164 (0.088, 0.300)	< 0.001#

Notes: Logistic regression model with no imputation and adjustment for GA, parity, education, anemia, prenatal care initiated, nuchal cord, LAT, age, BMI, basic SBP, basic DBP, infant weight, diagnostic SBP, diagnostic DBP, and umbilical cord length (N = 686)

Abbreviations: GA gestational age, *ELA* epidural labor analgesia, *GA* gestational age, *OVD* operative vaginal delivery, *CS* cesarean section, *LAT* labor augmentation time, *NICU* neonatal intensive care unit

*: $P < 0.05$

#: $P < 0.01$

induced by excessive peripheral circulation resistance reduction, following epidural labor analgesia [25, 26].

Neuraxial analgesia is not associated with an increased incidence of cesarean section as compared to parenteral opioids [27]. The multivariable analysis in this study showed that cesarean section rates among those with preeclampsia who received ELA was higher in the ELA with PIEB group compared to that in the NA group. Previous studies have demonstrated that ELA increases the incidence of operative vaginal delivery [27]. In line with this finding, the rate of operative vaginal delivery is also higher in women with preeclampsia under ELA. However, the propensity score analysis revealed that the association between ELA and CS or operative vaginal delivery is not significant. The difference might be attributed to such confusing factors as parity, prenatal care initiated, and education. Importantly, ELA was not associated with fetal distress and NICU admission based on the multivariate logistic regression and propensity score-matched analyses in this study. In contrast, a recent study involving 23,272 low-risk parturient women revealed correlation of intrapartum epidural analgesia is correlated with low Apgar scores and NICU admission in infants. Notably, mediation analysis suggests that the influence of ELA on adverse neonatal outcomes is primarily mediated by obstetric complications, such as maternal fever, labor augmentation, and fetal malpresentation, rather than directly by epidural labor analgesia itself [28]. Another retrospective study reported that preeclampsia or hypertension not labor epidural analgesia are triggers of newborn sepsis work-up [29]. Overall, ELA is not associated with increased incidence of CS, operative vaginal delivery, and NICU admission.

This study has several limitations. First, the sample size was insufficient for further subgroup and sensitivity analyses. Hence, we plan to conduct further research

to address this issue. Secondly, all participants included in this analysis were Asian. Thus, the homogeneity of the study population may impact the generalizability of these findings to other populations. Furthermore, the single-center design had potential unmeasured confounders despite propensity score matching. In the future, a randomized control trial should be conducted to assess the effect of ELA for labor pain relief in women with preeclampsia for labor pain relief. Thirdly, the most drawback was the inability to determine the relationship between ELA dose and CS incidence was not analyzed in this study, due to extensive missing data on ELA dose. Future studies will be designed to assess the dose-dependent effects of ELA on CS rates.

Conclusion

Our findings suggest that PIEB may be effective for labor pain relief in women with preeclampsia, though further studies are needed to confirm its safety and efficacy.

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Author's contribution
Study design: Guo-Lin Lu. Writing the first draft: Xi-Zhu Wu. Data interpretation, discussion, and final manuscript preparation: Xi-Zhu Wu, Tuan-Fang Fang, Yi-Han Zheng, Su-Jing Zhang, Yi Xie, Xiang Gao, and Guo-Lin Lu. All authors have read and approved the manuscript to be published.

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Data availability
Data is provided within the manuscript.

Declarations

Ethics approval and consent to participate
The need for informed consent to participate was waived by the Institutional Review Board (IRB) of the Research and Ethics Committee of Fujian Provincial Maternity and Children's Hospital. This waiver was granted because the study involved a retrospective review of existing medical records and did not require direct patient interaction or intervention. All procedures were conducted in accordance with the ethical standards of the IRB and the Declaration of Helsinki. The IRB reviewed and approved the study protocol under the reference number (Approval NO: 2021KLRD09022; Sep 24, 2021).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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