

Original Article

Analgesic effects of continuous epidural anesthesia for painless labor in Chinese parturient women: a systematic review and meta-analysis

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Abstract: Objective: The aim of this study was to evaluate the analgesic effects of continuous epidural anesthesia for painless labor. Methods: PubMed, Wiley Online Library, Springer's database, Wanfang Data, CBM, CNKI, and other Chinese and English databases were searched. Quality of included RCTs was assessed according to criteria in the Cochrane Handbook for Systematic Review. Results were analyzed using Review Manager 5.1.0. Results: A total of eight RCTs were included in the analysis, involving a total of 1,133 patients. Continuous epidural anesthesia shortened the active period of the first stage of labor ($Z = 11.48, P < 0.00001$) during painless labor. It also shortened the second stage of labor ($Z = 12.5, P < 0.00001$). Compared with traditional spontaneous labor, painless labor, under continuous epidural anesthesia, reduced the rate of Cesarean section ($OR = 1.06, 95\% CI = 0.24-0.56, Z = 4.65, P < 0.00001$). It did not increase incidence of postpartum hemorrhage ($OR = 1.03, 95\% CI = 0.57-3.03, Z = 0.63, P = 0.53$), fetal distress ($OR = 1.03, 95\% CI = 0.49-1.68, Z = 0.63, P = 0.53$), or neonatal asphyxia ($OR = 1.03, 95\% CI = 0.5-1.76, Z = 0.19, P = 0.83$). Conclusion: The results show that continuous epidural anesthesia has good analgesic effects regarding labor. It shortened the active period of first and second stages of labor, reduced rate of Cesarean sections, and did not increase incidence of postpartum hemorrhage, fetal distress, neonatal asphyxia, or other complications.

Keywords: Analgesic, Chinese primipara, continuous epidural anesthesia, newborns, painless labor

Introduction

With continuous improvement in techniques for Cesarean section, many women have chosen to deliver via Cesarean section due to fear of labor pain. Therefore, the Cesarean section rate is as high as 60% in many Chinese hospitals, far exceeding the Cesarean section alert rate of 15% specified by the World Health Organization [1]. Although spontaneous labor is good for maternal postpartum recovery, severe pain caused by childbirth brings great fear to parturient women. Therefore, studies on painless labor have now become a common concern of gynecologists and anesthesiologists. In the USA, UK, and other countries, clinical coverage of painless labor technology during maternal delivery has been high [2]. In China, however, clinical promotion and application of painless labor are still under development, thus, promotion of labor anesthesia technology re-

mains highly imperative. During spontaneous labor, intense pain caused by uterine contractions and other factors may induce anxiety, nervousness, and fear in parturient women and increase the release of exogenous and endogenous stress hormones, such as adrenal cortex hormones and catecholamines, leading to vasoconstriction and impairing maternal and fetal health. Therefore, taking effective analgesic measures during the process of delivery can protect the health of pregnant women and fetuses and reduce the present high Cesarean section rate in China. After nearly 20 years of extensive study and exploration, the continuous epidural anesthesia delivery technique has become widely used in clinical settings due to its advantages of simple operation and ideal analgesic effects. However, the effects of continuous epidural anesthesia on analgesia, stages of labor, postpartum complications, and effects of narcotic drugs on fetuses have re-

mained controversial. In addition, due to the relatively small stature of Chinese parturient women, pelvic conditions of Chinese parturient women are inferior to those of European and American parturient women [3]. Studies on labor analgesic effects of continuous epidural anesthesia in Chinese primipara are currently insufficient. In this paper, RCTs related to the use of continuous epidural anesthesia for painless labor in Chinese primipara were summarized. The studies were screened in strict accordance with inclusion and exclusion criteria. A meta-analysis was performed on data obtained from the studies. The effects of continuous epidural anesthesia on Chinese primipara and fetuses were quantitatively compared. Analgesic effects of continuous epidural anesthesia and effects on primipara and fetuses were evaluated to provide scientific and reliable basis for clinical practice.

Methods

Inclusion criteria

Study type: RCTs with sufficient valid data for calculation of odds ratios (ORs) for 95% confidence intervals (CIs).

Subjects: Age: 24-36 years; Gestational week: 38-41; Singleton pregnancy; Normal fetal position; Primipara; No hypertension, diabetes, or any other comorbidity.

Intervention: The anesthetist performed an epidural puncture at the L3-L4 intervertebral space when parturients in the test group entered the active period of first stage of labor and when the uterine cervix dilated up to 2-3 cm. Epidural catheters were subsequently inserted at a depth of approximately 3 cm from the head end. First dose (consisting of a 3 mL mixture of 0.5% fentanyl and 0.2% ropivacaine) was administered during an interval of uterine contraction. Patients were observed for 20-30 minutes. If no adverse reactions were found, a 6-7 mL mixture of 0.5% fentanyl and 0.2% ropivacaine was injected. The mixture was administered every 60-90 minutes (at doses of 5-6 mL), depending on specific conditions of the women. Administration was stopped when the maternal cervix was fully dilated. If fetal distress or other conditions were observed during painless labor, it was terminated, immediately, and Cesarean section was performed.

Control group: Women in the control group underwent spontaneous labor without analgesic measures. If fetal distress or prolonged labor was observed, Cesarean section was performed.

Outcome measures: Active period of first stage of labor, duration of second stage of labor, number of women with VAS score = 0, number of women that underwent Cesarean section, postpartum hemorrhage in parturient women, number of fetuses with asphyxia, and number of newborns with respiratory distress.

Literature search

Databases: PubMed, Wiley Online Library, Springer's database, Wanfang Data, CBM, CNKI, and other Chinese and foreign databases. Search terms: continuous epidural anesthesia, painless labor, epidural anesthesia, primipara, China. Search time: Until October 2017. All retrieval strategies were determined after several pre-retrievals to prove feasibility. Language restriction was not applied for retrieval. In addition, references, meeting minutes, and other data of certain articles were retrieved. A total of 48 articles were obtained using retrieval strategies. Further review of study titles excluded studies relating to painless labor analgesia combined with various analgesic methods and studies involving multipara. Finally, eight articles were included for analysis.

Literature screening and data extraction

Preliminarily screened articles were analyzed by two independent investigators, in strict accordance with inclusion and exclusion criteria. Obviously non-compliant articles were excluded. Full texts of included articles were read carefully and results of included studies were cross-checked. Discrepancies were resolved by a third investigator. General data of included studies were recorded using a uniform table that contained the following: (1) General information, containing study title, primary author, and time of publication; (2) Subjects, including study sample size; and (3) Outcome measures, including evaluation of related conditions of parturient women and newborns.

Quality evaluation

Cochrane Handbook for Systematic Reviews 5.1.0 was used to evaluate the risk of bias and

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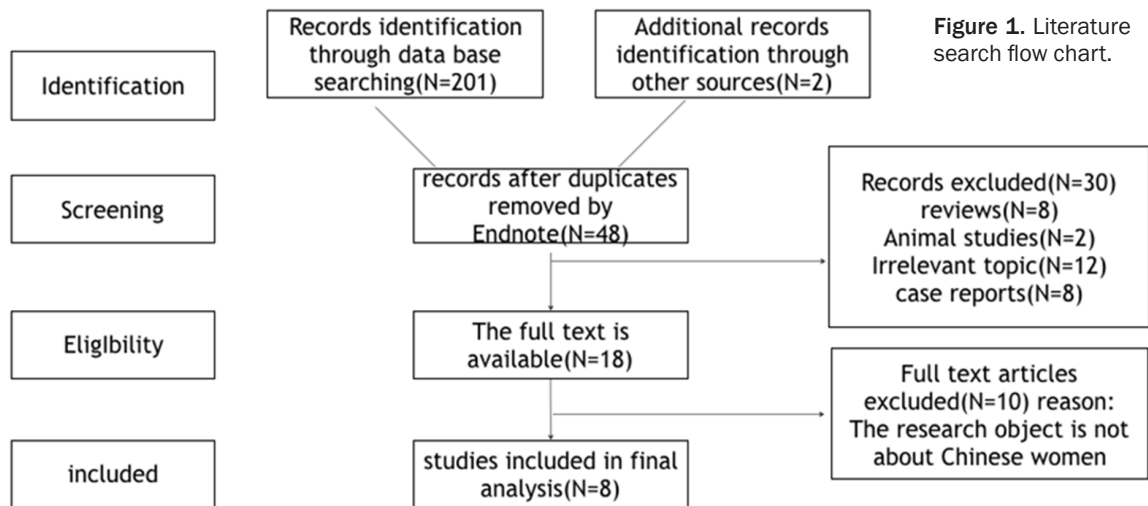
Table 1. Summary of characteristics of eight studies and evaluations

Study		Yang J 2017	Guo X 2015	Ping J 2009	Qing Zh 2017	Li W 2017	Mei L 2015	Huang L 2013	Wei X 2015	
Study period		2015-2016	2012-2014	2006-2009	2015-2016	2012-2015	2012-2014	2011-2013	2014-2015	
Case		64	75	160	50	57	40	100	80	
Control		61	75	160	50	57	40	100	78	
The first stage of labor	Active period	Case	114.6±37	109.8±94.2	109.2±99	114.84±67.96	-	115.63±58.45	115.6±68.4	158±18
		Control	230.16±95.71	159.6±87	160.2±81.6	225.14±103.52	-	178.21±60.21	224.6±102.2	214±12
	VAS = 0	Case	-	71	154	49	43	-	-	-
		Control	-	0	0	0	0	-	-	-
The second stage of labor	Duration	Case	44.16±20.07	44.4±28.8	45±31.8	44.89±20.89	-	62.35±10.68	45±30.2	48±12
		Control	60.12	55.8±34.2	55.2±37.2	57.16±25.13	-	57.78±7.34	56.8±24.6	96±18
	VAS = 0	Case	-	60	130	41	36	-	-	-
		Control	-	0	0	0	0	-	-	-
Cesarean section	Case	6	13	28	1	9	0	3	6	
	Control	18	21	45	2	17	5	25	13	
Postpartum bleeding	Case	-	2	3	3	1	-	4	-	
	Control	-	2	2	2	1	-	13	-	
Fetal distress	Case	-	3	6	4	1	-	6	-	
	Control	-	4	7	3	1	-	7	-	
Neonatal asphyxia	Case	1	2	5	3	1	-	7	-	
	Control	1	3	6	4	2	-	6	-	

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Table 2. Quality evaluation of eight studies and evaluations

Study	Random sequence generation	Distribution of hidden	Blinded for the object of study or intervention	Blinded for the outcome measure	Incomplete data report	Select the report	Other sources of bias	The quality of evidence
Yang J 2017	High	High	High	Low	Low	Low	Low	B
Guo X 2015	Low	Low	High	Low	Low	Low	Low	B
Ping J 2009	High	High	High	Low	Low	Low	Low	B
Li W 2017	Low	Low	Low	Low	Low	Low	Low	A
Mei L 2015	High	High	High	Low	Low	Low	Low	B
Huang L 2013	High	High	High	Low	Low	Low	Low	B
Wei X 2015	High	High	High	Low	Low	Low	Low	B



quality of RCTs included in this analysis. The following seven evaluation criteria were included: (1) Generation of the random sequence; (2) Allocation concealment; (3) Double-blinding of investigators and subjects; (4) Blinding of outcome assessment; (5) Integrity of outcome data; (6) Selective reporting; and (7) Other sources of bias. Each item was evaluated by “low risk of bias”, “unclear”, and “high risk of bias”. Grade A: Original study satisfied the above criteria completely, indicating that occurrence of various biases was the smallest. Grade B: Partially met the above quality standards, indicating that possibility of bias was moderate. Grade C: Original study completely failed to meet the above quality standards, indicating that possibility of bias was high (Table 2).

Statistical analyses

All data were analyzed using Review Manager 5.1.0 (The Cochrane Collaboration, Software Update, Oxford). $P < 0.05$ indicated statistical significance. When the analytical indicator was

a continuous outcome (also known as a numerical variable), weighted mean difference (WMD) was selected as the combined statistic. WMD is the difference between two means. It eliminates the influence of absolute value between multiple studies. When analysis index was a binary variable outcome, odds ratio (OR) was selected as the combined statistic. Relative risk ratio (RR) is incidence of an event in the test group in a prospective study (eg, RCT) and an event in the control group. Incidence ratio P was used to describe how many times the incidence rate of a trial group is compared with the control group. To simplify the calculation process, OR was used to estimate RR and the confidence interval of OR was used to estimate the confidence interval of RR. When there was no obvious heterogeneity, the random effects model and fixed effects model had the same effect. When there was heterogeneity, the random effects model was more accurate. I^2 was used for heterogeneity test. If $I^2 > 50\%$, there was statistical heterogeneity and heterogeneity was analyzed.

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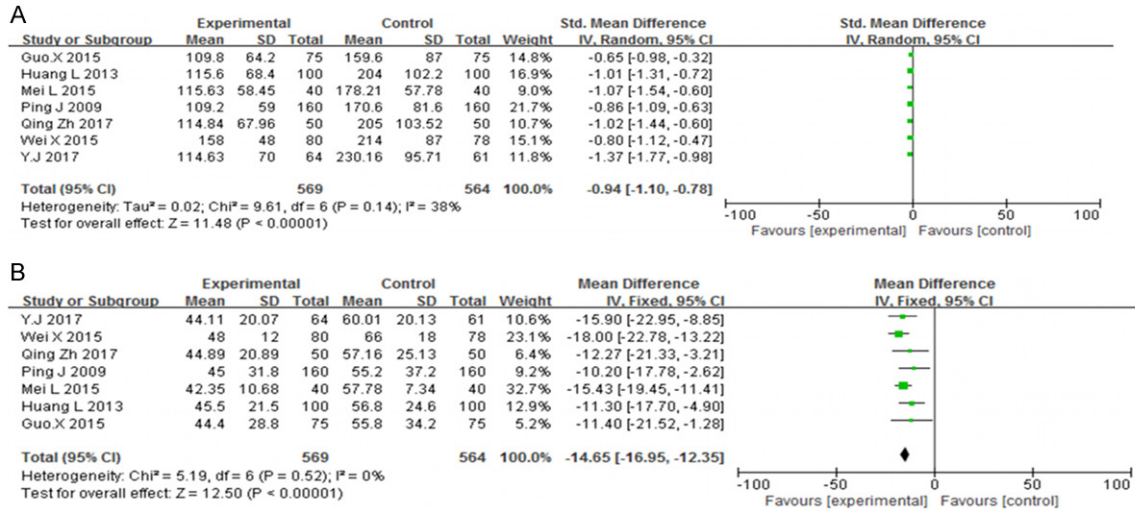


Figure 2. Comparison of labor times. A. Comparison of the first stage of active labor time. B. Comparison of the second stage of labor time.

Results

After a comprehensive database search, a total of 201 articles were selected. Title assessment excluded 30 articles. Finally, only eight articles were retained after assessing full texts [4-12]. The literature search flow chart is shown in **Figure 1**. **Table 1** summarizes the characteristics of these eight studies and evaluations.

Quantitative data integration and analysis

Quality evaluation: All eight studies were RCTs regarding Chinese parturient women. A total of 1,133 parturient women were included in these studies. All parturient women met the strict inclusion and exclusion criteria.

Included studies consisted of 3 randomized controlled trials and 5 clinical control studies. Three studies reported random specific methods (37%) and eight described the loss of cases. Only one article was "A" but the results of the study included better homogeneity between the groups in meta-analysis. Seven studies reported the age of the patients and results showed that baseline data differences between the experimental group and control group were not statistically significant and comparable (**Table 2**).

Effects of continuous epidural anesthesia on stage of labor in Chinese primipara

Results of heterogeneity testing were as follows: Chi-square = 9.61, P = 0.14, I² = 38%.

Fixed effects model was used for combined effect amount of WMD. The combined effect amount (total) of WMD was 0.94, 95% CI (-1.10, -0.78), (test for overall effect, Z = 11.48, P < 0.00001) (**Figure 2A**). Based on results of this analysis, it can be concluded that continuous hard epidural anesthesia, compared with routine delivery, has a statistically significant difference in WMD during the first stage of labor. The 95% CI line of WMD falling to the left of the invalid vertical line indicates that continuous epidural anesthesia can shorten the active period of first stage of labor. Continuous epidural anesthesia also shortened the second stage of labor in parturient women. Heterogeneity test results were as follows: Chi-square = 5.19, P = 0.93 and I² = 0%. Subsequently, a fixed effects model was used to calculate WMD and 95% CI. Results showed that painless labor under continuous epidural anesthesia also shortened the second stage of labor in Chinese primipara (Z = 12.5, P < 0.00001) (**Figure 2B**).

In four studies [9, 13-15], intensity of pain during labor was assessed. Among 684 parturient women that underwent continuous epidural anesthesia in the active period of the first stage of labor, 310 had a pain visual analogue scale (VAS) score of 0 and effective rate of analgesia was 90.64%. All parturient women in the spontaneous labor group had severe pain. Heterogeneity test results were as follows: Chi-square = 0.45, P = 0.93 and I² = 0% (**Figure 3A**). Subsequently, a fixed effects model was used

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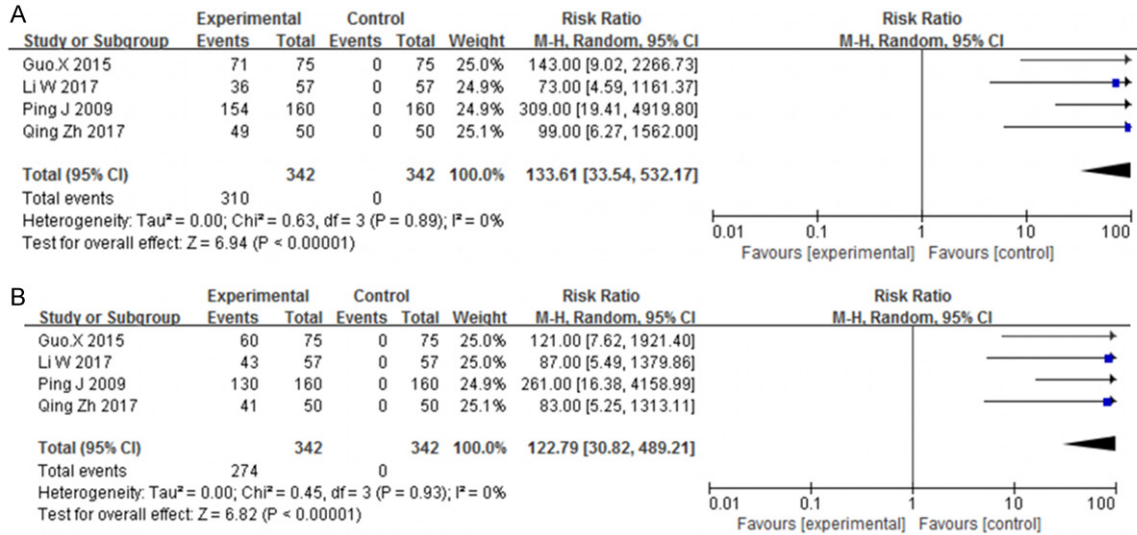


Figure 3. Comparison of number of people. A. Comparison of the first stage of labor VAS = 0. B. Comparison of the second stage of labor VAS = 0.

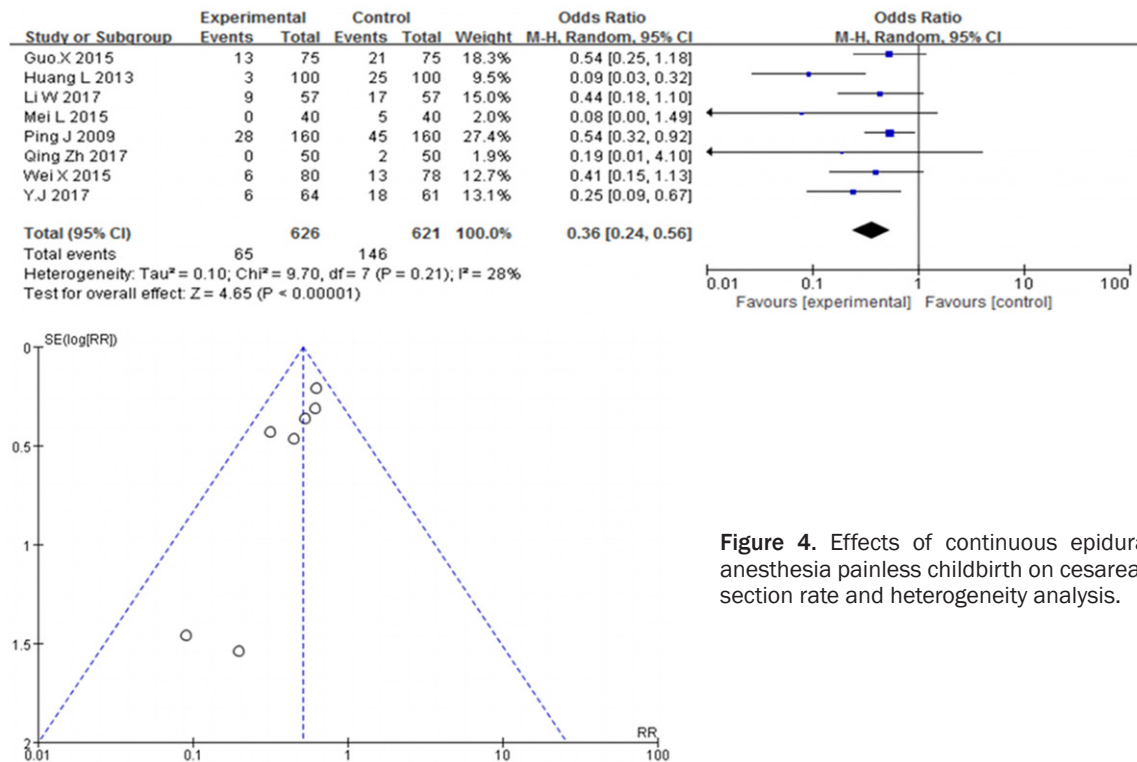


Figure 4. Effects of continuous epidural anesthesia painless childbirth on cesarean section rate and heterogeneity analysis.

to calculate OR and 95% CI. In the second stage of labor, 274 parturient women had a pain VAS scores of 0 and the effective rate of analgesia was 80.12%. All parturient women in the spontaneous labor group had severe pain. Heterogeneity test results were as follows: Chi-square = 0.63, P = 0.89 and I² = 0% (**Figure**

3B). Therefore, a fixed effects model was used to calculate pooled or 95% CI. Results showed that continuous epidural anesthesia could achieve good labor analgesia. After the active period of the first stage of labor had ended and parturient women entered the second stage of labor, continuous epidural anesthesia still sh-

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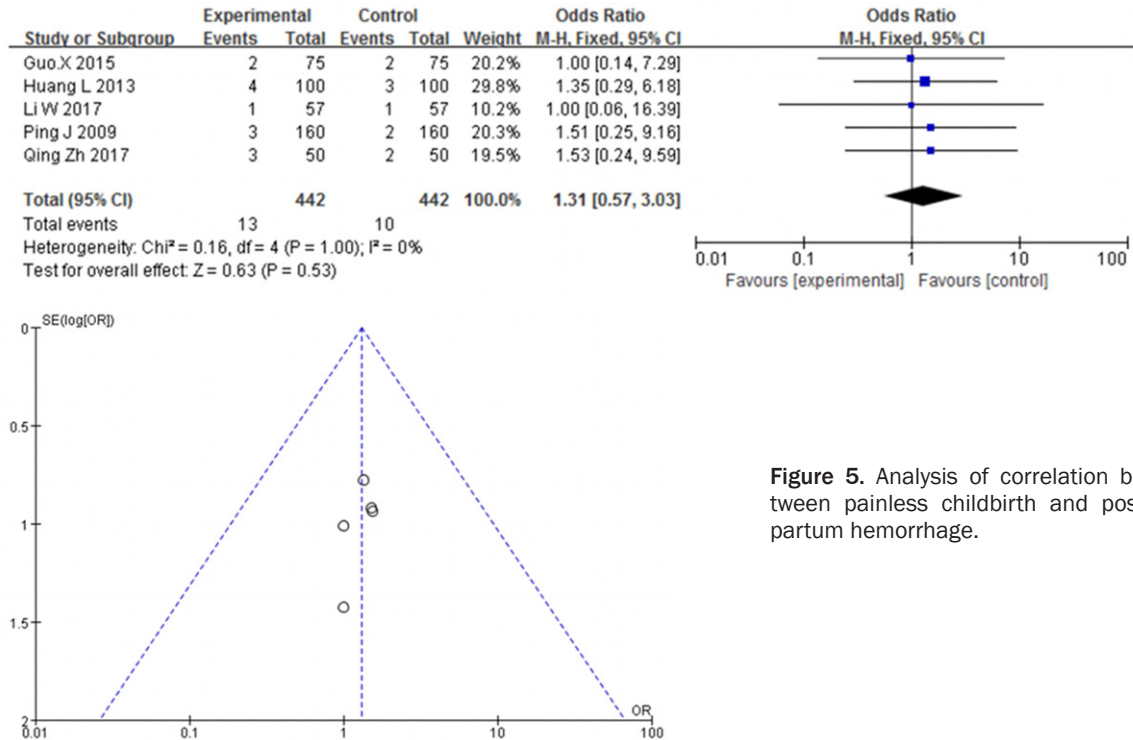


Figure 5. Analysis of correlation between painless childbirth and postpartum hemorrhage.

owed good labor analgesia although injection of narcotic drugs was stopped.

Effects of painless labor under continuous epidural anesthesia on Cesarean section rate in parturient women

Incidence of Cesarean section due to difficult delivery was analyzed in the eight studies. Cesarean section rate in primipara was 10.38% (65/626) in the continuous epidural anesthesia group and 23.5% (145/621) in spontaneous labor group. No significant heterogeneity was found in this study (Chi-square = 9.7, P = 0.21, I² = 28%) and a fixed effects model was used to calculate OR and 95% CI. Results showed that painless labor under continuous epidural anesthesia reduced Cesarean section rates in Chinese primipara, compared to that during spontaneous labor (OR = 1.06, 95% CI = 0.24-0.56, Z = 4.65, P < 0.00001, **Figure 4**).

Analysis regarding relationship between painless labor under continuous epidural anesthesia and postpartum hemorrhage

Five articles [9, 13-16] included analysis on the relationship between painless labor under continuous epidural anesthesia and postpartum hemorrhage in parturient women. Incidence of postpartum hemorrhage in parturient women

was 2.94% (13/442) in the painless labor group and 2.26% (10/442) in spontaneous labor group. No significant heterogeneity was found (Chi-square = 0.16, P = 1.0, I² = 0%) and a fixed effects model was used to calculate WMD and 95% CI. Results showed that continuous epidural anesthesia did not increase incidence of postpartum hemorrhage in parturient women (OR = 1.03, 95% CI = 0.57-3.03, Z = 0.63, P = 0.53, **Figure 5**).

Analysis regarding relationship between painless labor and fetal distress

Five articles included analysis on the relationship between painless labor and fetal distress. Incidence of fetal distress was 4.52% (20/442) in the painless labor group and 5.01% (22/442) in spontaneous labor group. No significant heterogeneity was found (Chi-square = 0.36, P = 0.99, I² = 0%) and a fixed effects model was used to calculate OR and 95% CI. Results showed that continuous epidural anesthesia did not increase incidence of fetal distress (OR = 1.03, 95% CI = 0.49-1.68, Z = 0.63, P = 0.53, **Figure 6**).

Analysis regarding relationship between painless labor and neonatal asphyxia

Five articles [9, 13-16] included analysis on the relationship between painless labor and neo-

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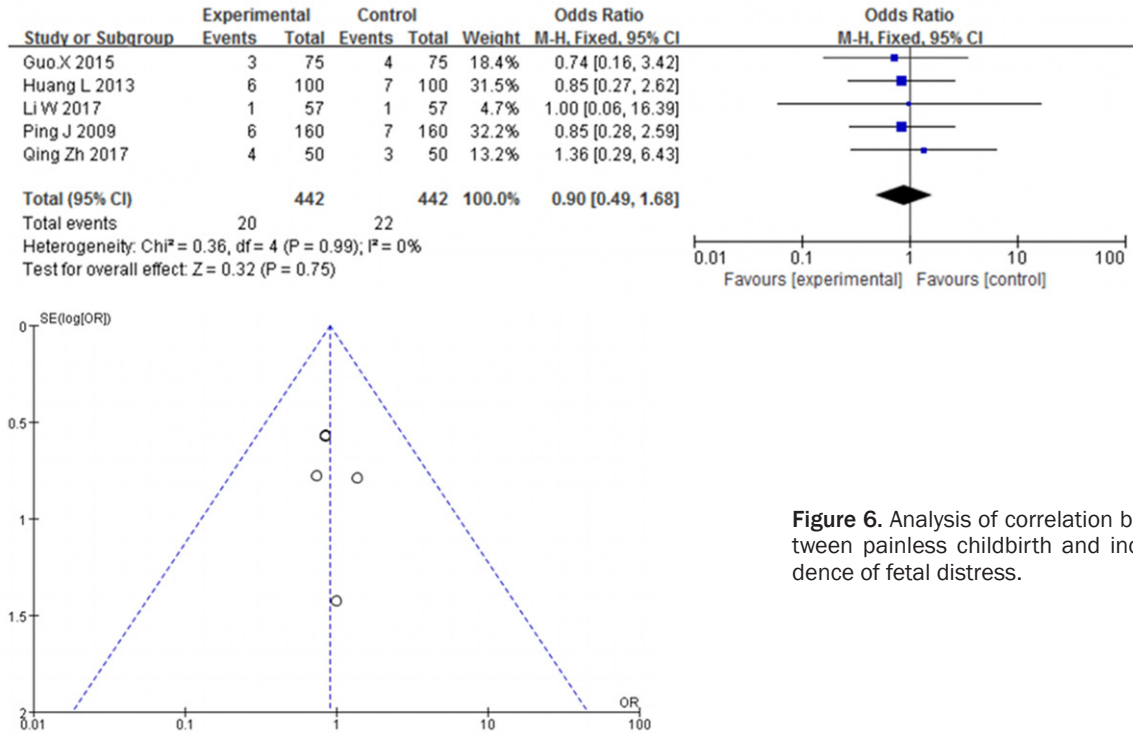


Figure 6. Analysis of correlation between painless childbirth and incidence of fetal distress.

natal asphyxia. Incidence of neonatal asphyxia was 4.23% (18/426) in the painless labor group and 5.01% (19/420) in spontaneous labor group. No significant heterogeneity was found (Chi-square = 0.86, $P = 0.97$, $I^2 = 0\%$) and a fixed effects model was used to calculate OR and 95% CI. Results showed that continuous epidural anesthesia did not increase incidence of neonatal asphyxia (OR = 1.03, 95% CI = 0.5-1.76, $Z = 0.19$, $P = 0.83$, **Figure 7**).

Publication bias

There was no publication bias in any of the randomized controlled studies and P -value was greater than 0.05. The funnel plot with standard error and accuracy was symmetrical.

Discussion

Delivery is the most important process of human reproduction. However, labor pain causes tremendous physical and psychological suffering for parturient women and may also have adverse effects on newborns [17]. Labor pain may increase parasympathetic excitability, accelerate respiratory rate, induce respiratory alkalosis, decrease release of oxygen from hemoglobin, or result in fetal distress [18]. Labor pain may cause anxiety, fear, nervousness, and other negative emotions in parturient women. These may induce production of many exoge-

nous and endogenous stress substances in the body, induce vasoconstriction, reduce uterine blood flow, induce uterine inertia, prolong stages of labor, and result in adverse consequences (such as fetal distress) [19]. In addition, many parturient women immediately choose Cesarean section due to fear of labor pain. Some parturient women cannot bear the pain of spontaneous labor and strongly require Cesarean section to accelerate delivery [20].

With the rapid development of China's medical and healthcare industry in recent years, painless labor techniques have gradually attracted the attention of gynecologists and anesthesiologists. Among these techniques, continuous epidural anesthesia has been widely used in clinical settings due to its relative simplicity and minor traumatic effects [21]. However, the effects of continuous epidural anesthesia on analgesia, stages of labor, and postpartum complications and the effects of narcotic drugs on fetuses have remained controversial. In addition, due to the relatively small stature of Chinese parturient women, their pelvic conditions are inferior to those of European and American parturient women [3]. Therefore, a meta-analysis on painless labor under continuous epidural anesthesia in Chinese primipara was performed.

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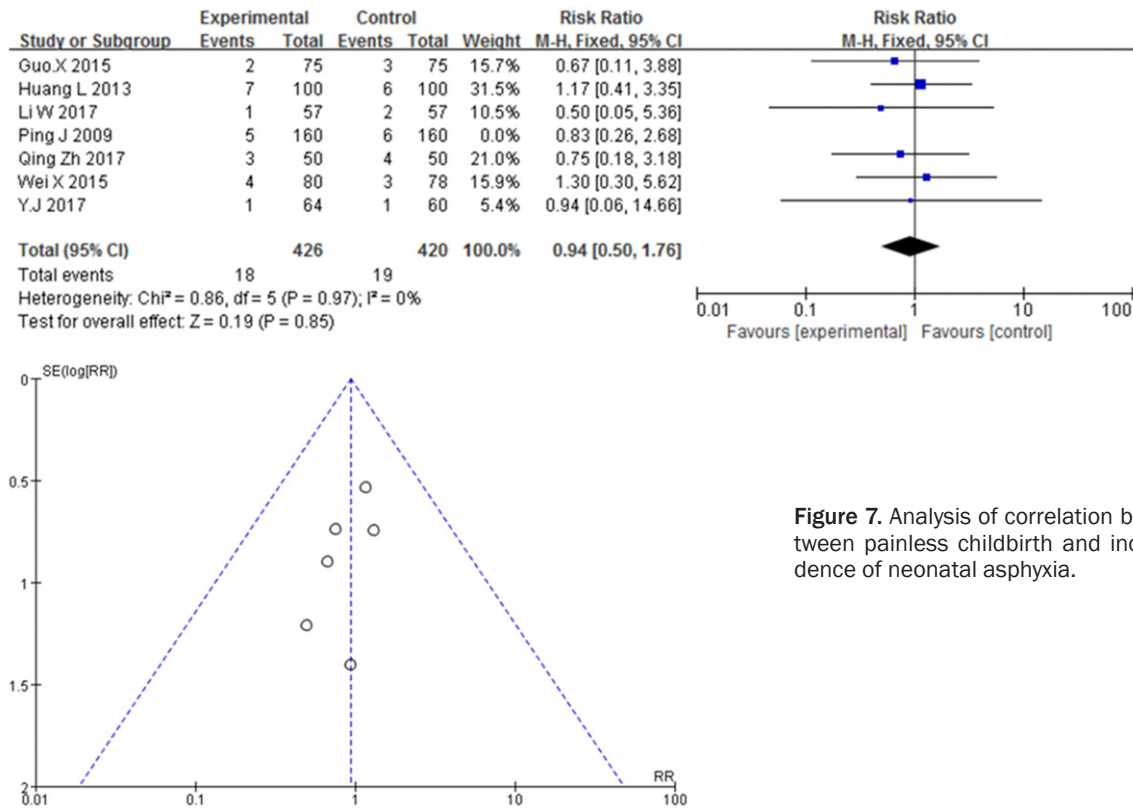


Figure 7. Analysis of correlation between painless childbirth and incidence of neonatal asphyxia.

Results of analysis of the eight RCTs showed that continuous epidural anesthesia did not prolong stage of labor. On the contrary, it shortened the active period of first and second stages of labor in parturient women. Results were similar to those of a study by Salarian S [22]. Reasons for this are as follows: Continuous epidural anesthesia blocks nerves that control the lower uterine segment, cervical movement (sacrum 2-4), and vaginal and pelvic floor movement (L1-L4); Anesthesia also reduces resistance to a soft birth canal and facilitates opening of the uterine cervix and descent of the fetal head. Nerves that control uterine movement (T10 and above) are not blocked and no effect is produced on normal uterine contraction. In addition, effective relief of labor pain eases the nervous mood of parturient women, stabilizes breathing, reduces oxygen consumption, and further shortens the first stage of labor. It has been suggested, in a study by Ramin SM [23], that continuous epidural anesthesia might prolong the second stage of labor. In this meta-analysis, continuous epidural anesthesia shortened the second stage of labor. Reasons for this difference were analyzed. Narcotic drugs were continued in the second stage of labor in the study by Ramin SM. However, narcotic

drugs were discontinued in the second stage of labor in all other studies included in this meta-analysis. After parturient women enter the second stage of labor, delivery of the baby mainly depends on the contraction force of abdominal muscles and the diaphragm. Although administration of narcotic drugs in the second stage of labor blocks sensory nerves of the rectum and relieves pain, it may result in weakening of muscle strength required for delivery, prolonging the second stage.

Results of analysis of the eight RCTs showed that continuous epidural anesthesia did not increase the Cesarean section rate in parturient women. It was suggested, in studies by Ramin and Chestnut [23, 24], that continuous epidural anesthesia may increase Cesarean section rates and midwife-assisted vaginal delivery rates. One study by Fung BK [25] included 822 women that underwent painless labor under continuous epidural anesthesia. In this present study, results showed that continuous epidural anesthesia did not increase Cesarean section rates in parturient women. Cesarean section rate was 11.1% in the epidural anesthesia group and 16.2% in control group, with an odds ratio of 0.65 (95% CI: 0.37 to 1.08). No

significant differences were found between the two groups. Continuous epidural anesthesia did not increase Cesarean section rates in parturient women. In addition, continuous epidural anesthesia decreased Cesarean section rates in primipara. Results of this meta-analysis showed that continuous epidural anesthesia decreased Cesarean section rates in primipara, consistent with the findings of the study by Fung BK. Therefore, timely discontinuation of narcotic drugs at the end of the first stage of labor and active treatment of labor can reduce Cesarean section rates in Chinese primipara.

It was suggested, in one study by Impey I [26], that epidural anesthesia might increase incidence of postpartum hemorrhage. One study by Salim R [27] proposed that continuous epidural anesthesia does not inhibit uterine contraction in parturient women, having no effect on incidence of postpartum hemorrhage. Results of this meta-analysis showed that continuous epidural anesthesia did not increase postpartum hemorrhage in parturient women.

One study by Rizzo D [25] included 50 women that underwent continuous epidural anesthesia, with data on fetal distress and neonatal Apgar Scores. The study found that painless labor under continuous epidural anesthesia improved neonatal Apgar scores. A study by Palter [28] found that continuous epidural anesthesia altered fetal heart rate in rare cases but the changes spontaneously resolved after approximately 30 minutes. It was considered that changes were caused by blood pressure reduction in parturient women after continuous epidural anesthesia. Chatrath [29] proposed that the changes were related to intensity and frequency of uterine contraction in parturient women. Results of this meta-analysis showed that there were no statistically significant differences in incidence of fetal distress or neonatal asphyxia between painless labor under continuous epidural anesthesia and spontaneous labor, consistent with findings of the study by Fung BK.

There are several limitations to this study. Although this meta-analysis was performed in strict accordance with preferred reporting criteria for meta-analyses and studies included in the analysis had good homogeneity, the methodological quality of RCTs included in this analysis was poor. These RCTs may have had selection bias, measurement bias, and implementa-

tion bias. The main focus of this meta-analysis was Chinese primipara, therefore, only domestic articles were included in this analysis with the aim of reducing heterogeneity, although articles in Chinese and foreign languages were searched.

In summary, the results of this meta-analysis show that continuous epidural anesthesia has good labor analgesic effects in Chinese primipara. At present, prevalence of painless labor in China is low. Further prospective studies should be performed to reduce incidence of postpartum hemorrhage and fetal distress.

Disclosure of conflict of interest

None.

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