



# Evaluation of Maternal and Fetal Hemodynamic Alterations in Delivery in Epidural and Combined Spinal-Epidural Analgesia: A Randomized Clinical Trial

Hojjat Pourfathi<sup>1</sup>, Haleh Farzin<sup>2</sup>, Hanie Sakha<sup>3</sup>, Mohamad Mahdi al Miski<sup>4</sup> and Nabiha Aldarir<sup>4,\*</sup>

<sup>1</sup>Teghani Hospital, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>2</sup>Alzahra Hospital, Faculty of Medicine, Tabriz University of Medical Sciences, Tabriz, Iran

<sup>3</sup>Tehran North University, Tehran, Iran

<sup>4</sup>Tabriz University of Medical Sciences, Tabriz, Iran

\*Corresponding author: General Practitioner, Tabriz University of Medical Sciences, Tabriz, Iran. Email: dr.nabiha.aldarir@gmail.com

Received 2019 March 18; Revised 2019 June 08; Accepted 2019 July 20.

## Abstract

**Background:** The pain of vaginal delivery is considered as the worst experience in women life that negatively affects mother and fetus. The most important methods advised by anesthesiologists for pain reduction include epidural and combined spinal-epidural analgesia. The ideal method provides convenient pain relief and guarantees maternal and fetal safety, simultaneously. Fetal heart rate (FHR), fetal movement (FM), and maternal hemodynamics (i.e. blood pressure (BP), heart rate (HR), and SpO<sub>2</sub>) monitoring are the most available ways for controlling the fetus and mother's conditions during the delivery process.

**Methods:** This randomized-blinded clinical trial was performed on 100 pregnant women (50 cases in each group) during labor under epidural or combined spinal-epidural analgesia using lidocaine, fentanyl, and bupivacaine. FHR, FM, BP, HR, and SpO<sub>2</sub> were monitored and recorded by blinded nurses. Data were analyzed by SPSS 22.

**Results:** There were no significant differences in FHR, FM, and Apgar scores between the two groups. No significant difference was found between the two groups in maternal hemodynamics. Generally, FHR, maternal BP, and HR were in the normal ranges. The C/S rate was lower in the epidural group but not statistically significantly.

**Conclusions:** In our survey, epidural and combined spinal-epidural analgesia were comparable in terms of FHR, FM, and maternal hemodynamics. Therefore, there is no priority in using each of the methods. The monitoring of FHR and maternal hemodynamics is essential during analgesia. It is suggested that further surveys evaluate the incidence and causes of C/S after analgesia.

**Keywords:** Epidural Analgesia, Combined Spinal-Epidural Analgesia, Fetal Heart Rate, Fetal Movement, Hemodynamic

## 1. Background

Throughout history, mothers have delivered with the severe pain experience of natural delivery (1-3). This event led anesthesiologists to advise pain relief methods (4-6). Various methods have been suggested in this regard, such as psychological procedures, systemic opioids, and inhaled/local anesthetics (4-7). Epidural anesthesia has been suggested as the method of choice in some hospitals (7-9) and it has been associated with better outcomes than systemic opioids (10-12). However, low maternal satisfaction and several side effects (12, 13) have resulted in attempts for modifying this method to have higher analgesia and lower complications in the last 20 years (14).

Combined spinal-epidural (CSE) anesthesia was developed in the early 1990s (14) and it has recently been more popular (9, 14, 15). In several studies, the CSE method has

shown superiority to the epidural method, due to the minimal motor block (16, 17), faster onset (14, 16, 18), better analgesia quality (17), faster cervical dilatation, shorter delivery time, and lower doses of anesthetics (16, 19). Although delivery outcomes were comparable in some surveys, the CSE method was associated with complications such as prolonged admission course, paresthesia, back pain, itching (17, 18), and fetal distress (20). Therefore, the CSE method remains controversial. The ideal analgesia provides convenient pain relief and guarantees maternal and fetal safety, simultaneously (17, 21). Fetal heart rate (FHR) and fetal movement (FM) are the important indicators of fetal health status (22) and maternal hemodynamics (BP, HR, and SpO<sub>2</sub>) monitoring is the best available way to control mother's condition during delivery and intervention (23, 24).

So far, there have been few studies to compare the epidural and CSE methods in terms of abnormal changes in FHR and maternal hemodynamics. In general, it has been shown that neuraxial analgesia can lead to reduced secretion of catecholamines, placental-uterine blood flow complications, and thus undesirable effects on FHR (25). Hattler et al. in a meta-analysis of four studies reported a significant abnormal decrease in FHR in 64 out of 610 cases (10.4%) in the CSE analgesia group and 32 out of 606 cases (5.2%) in the epidural analgesia group (20). In the study by Palmer et al. Apgar scores and the incidence of cesarean deliveries were comparable, but abnormal FHR changes were 6% and 12% in epidural and CSE groups, respectively (26). Patel et al. reported no differences in fetal outcomes and Apgar scores (27). Several studies comparing epidural and CSE methods have not reported any significant differences in the mode of delivery, 1-minute and 5-minutes Apgar scores, and the incidence of maternal hypotension (16, 17).

## 2. Objectives

The aim of this clinical trial was to investigate the changes in FHR and maternal hemodynamics during labor with epidural analgesia and CSE analgesia in Taleghani teaching Hospital.

## 3. Methods

This clinical trial was conducted in 2018 - 2019 after being approved by the Research Council and Ethics Committee of Tabriz University of Medical Sciences (IR.TBZMED.REC.1397.240) and upon registration at the Iranian Registry of Clinical Trials (IRCT20180626040241N1). The study enrolled 100 healthy, full-term, singleton pregnant women in the active phase of delivery using simple consecutive sampling. Following the gynecologist's confirmation of the possibility of normal vaginal delivery, informed consent to performing both analgesia methods was obtained from all patients without determining the type of the analgesia method to keep the research blind. The parturients were randomly classified into two groups of 50 including epidural and CSE analgesia groups using online randomization software (Rand List). The inclusion criteria included the probability of normal vaginal delivery, the active phase of delivery, and the request of neuraxial labor analgesia by the patient. The exclusion criteria were the patients' unwillingness, restlessness during intervention, contraindications of local anesthesia (i.e. increased intracranial pressure, history of sensitivity to anesthetics, coagulation disorder, hemodynamic

disorders, and cardiovascular diseases), fetal distress, gestational age < 37 weeks, malpresentation, previous C/S history, uterine surgery scar, and BMI > 40 Kg/m<sup>2</sup>.

After the gynecologist's confirmation of the active phase of delivery (characterized by regular painful uterine contractions, a substantial degree of cervical effacement, and increased cervical dilatation from 5 cm until full dilatation), 500 ml of intravenous fluid (lactated Ringer's solution) was infused within half an hour. Neuraxial block was performed after topical skin anesthesia by lidocaine 2% and aseptic precautions at intervertebral space L3-4 or L4-5 using a packed set containing an 18-gauge epidural needle, 20-gauge epidural catheter, and 25-gauge spinal needle (B Braun), by the loss-of-resistance technique (2 mL normal saline and 0.25 mL air bubble) in the sitting position. Then, a 3-mL epidural test dose of lidocaine 2% was given through the epidural catheter for the confirmation of epidural catheter location. In the epidural group, the 6 mL-bolus doses of fentanyl 50 µg (Abouryhan, Iran) with bupivacaine 2.5 mg (AstraZeneca, UK) was administered and after that, 6 mL/h was infused by the epidural catheter. The CSE group underwent spinal block performed with 1.5 mL of the same solution (fentanyl 50 µg with bupivacaine 2.5 mg) via the spinal needle, followed by the epidural block based on the same protocol as the epidural group (6 mL/h infusion by the epidural catheter). After injections, parturients were positioned supine with left uterine displacement to continue the delivery process. If necessary, the vaginal examination and determination of cervical dilatation were performed by the gynecologist in the lithotomy position.

After inducing analgesia, the anesthesia assistant left the room and trained anesthesia nurses and midwives who were blinded to the analgesia type, monitored the FHR and FM by a cardiotocograph and maternal hemodynamics 5 min before analgesia administration, and then at intervals of 5, 10, 20, 40, and 60 minutes, and every 30 minutes until the end of delivery. The data were recorded in questionnaires.

The sample size was calculated based on 2 proportional formula (28) with assuring a 25% incidence of hypotension after neuraxial blocks (maximum error type 1 of 0.05 and power of 80%). Therefore, 50 cases in each group were selected and blinded to the type of analgesia (29).

Statistical analysis was performed by SPSS version 22 software (IBM SPSS Inc.) using the chi-square test for nominal variables. We used the independent *t*-test for continuous variables with normal distribution and Mann Whitney U test for non-normally distributed variables. We assessed normal distribution by the Kolmogorov-Smirnov test and the equality of variances by the Leven test. A P value of 0.05 was considered statistically significant.

#### 4. Results

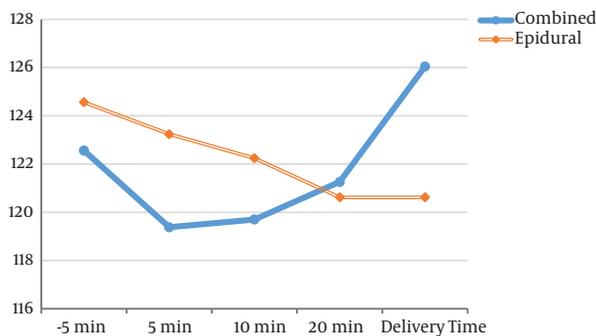
In this study, 100 women were enrolled in two groups (50 in the EA group and 50 in the CSE group). Table 1 shows the age, 1-minutes and 5-minutes Apgar scores, and the type of delivery in both groups.

The delivery type was not significantly different between the groups, as shown in Table 1. The percentages of mothers who underwent C/S were 4% and 14% in the EA and CSE groups, respectively ( $P = 0.08$ ). The indications of cesarean section were as follows: prolonged labor phase (4 cases), bradycardia and fetal distress (3 cases), and meconium-stained amniotic fluid (2 cases).

Table 1 summarizes the mean FHR at the pre-definite intervals. There was no significant difference in the mean FHR between the groups ( $P > 0.05$ ).

Table 2 also shows FM in both groups, with no significant difference between the groups ( $P > 0.05$ ). We observed one undesirable FM in the EA group and two cases in the CSE group. The mothers underwent C/S in all of these cases.

Maternal hemodynamic variables were monitored pre and post-block until delivery. SBP, DBP, HR, and SpO<sub>2</sub> showed no significant differences between the two groups (Table 1). As depicted in Figure 1, SBP decreased initially after block in both groups and reached the lowest values at the time of delivery in the EA group. DBP and HR showed almost the same changes during delivery in both groups, as indicated in Figures 2 and 3.

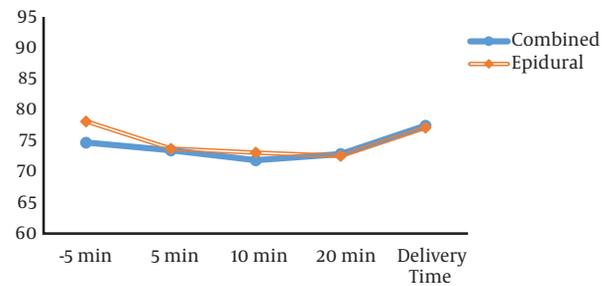


-5 min: 5 minutes before anesthesia. 5 min: 5 minutes after anesthesia.

**Figure 1.** Systolic BP alteration trend in two groups. -5 min: 5 minutes before anesthesia, 5 min: 5 minutes after anesthesia.

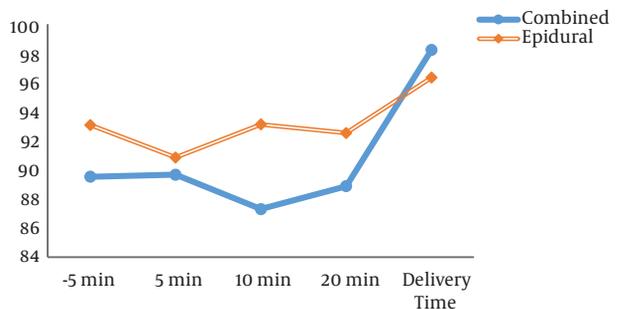
#### 5. Discussion

The present study demonstrated no significant differences between EA and CSE analgesia groups in terms of



-5 min: 5 minutes before anesthesia. 5 min: 5 minutes after anesthesia.

**Figure 2.** Diastolic BP alteration trend in two groups. -5 min: 5 minutes before anesthesia, 5 min: 5 minutes after anesthesia.



**Figure 3.** Heart rate alteration trend in two groups

FHR, FM, and 1-minutes and 5-minutes Apgar scores. Maternal hemodynamic variables (SBP, DBP, HR, and SpO<sub>2</sub>) were comparable in both groups. However, the failed vaginal delivery rate was lower in the EA group than in the CSE group. There was no statistically significant difference in the incidence of C/S between the groups. Therefore, the two methods had no priority to each other. FHR, FM, BP, and HR are essential parameters to measure during neuraxial analgesia.

Evidence suggests that the CSE technique is associated with more rapid analgesia onset, more efficacy in the first stage of labor (14, 17, 18) and lower rescue analgesia than the epidural technique (16). However, CSE analgesia is associated with more abnormal FHR changes, as reported in some studies. Valensise et al. demonstrated from among 86 parturients who received CSE analgesia, 14 cases showed abnormal FHR changes after neuraxial injection (30). In a meta-analysis conducted by Hattler et al. comparing CSE and epidural analgesia, the CSE method was associated with a more significant decrease in FHR (10.4%) than the epidural technique (5.2%) (20). It has been suggested that epidural analgesia is safer for the fetus than the systemic methods. Reynolds et al. compared fetal outcomes and

**Table 1.** The Comparison of the Groups in Age, Apgar Score, Delivery Type, and FHR at Definite Intervals<sup>a</sup>

Variable	Epidural	CSE	P Value
<b>Age</b>	27.80 ± 4.59	27.62 ± 4.49	0.84
<b>1-min Apgar score</b>	8.82 ± 0.59	8.84 ± 0.42	0.84
<b>5-min Apgar scores</b>	9.46 ± 0.54	9.58 ± 0.49	0.25
<b>NVD, No. (%)</b>	48 (96)	43 (86)	0.08
<b>C/S, No. (%)</b>	2 (4)	7 (14)	
<b>FHR, min</b>			
-5	140.9 ± 11.4	138.9 ± 11.6	0.39
5	138.6 ± 12.7	139.5 ± 12.8	0.70
10	139.8 ± 17.1	139.0 ± 19.1	0.81
20	140.5 ± 10.3	142.8 ± 11.4	0.31
delivery time	140.9 ± 13.0	138.9 ± 13.7	0.45
<b>SBP, min</b>			
-5	124.5 ± 11.8	122.5 ± 14.4	0.39
5	123.2 ± 14.5	119.3 ± 13.3	0.70
10	122.2 ± 16.8	119.7 ± 14.5	0.81
20	120.6 ± 13.5	121.2 ± 16.0	0.31
delivery time	128.6 ± 12.6	126.0 ± 12.1	0.45
<b>DBP, min</b>			
-5	78.1 ± 9.6	74.6 ± 10.8	0.10
5	73.7 ± 12.4	73.4 ± 11.4	0.90
10	73.0 ± 11.3	71.8 ± 12.1	0.60
20	72.5 ± 12.1	72.8 ± 13.0	0.90
delivery time	77.1 ± 10.4	77.4 ± 10.7	0.88
<b>HR, min</b>			
-5	93.2 ± 13.5	89.6 ± 13.3	0.18
5	90.9 ± 13.8	89.7 ± 11.6	0.64
10	93.2 ± 14.8	87.3 ± 12.0	0.32
20	92.6 ± 15.6	88.9 ± 12.8	0.19
delivery time	96.5 ± 15.1	98.4 ± 16.4	0.54
<b>Sat, min</b>			
-5	97.3 ± 1.2	97.6 ± 0.9	0.28
5	97.5 ± 1.1	97.5 ± 1.2	0.93
10	97.7 ± 1.0	97.7 ± 1.4	1.00
20	97.7 ± 1.0	97.5 ± 1.4	0.59
delivery time	97.5 ± 15.1	97.8 ± 16.4	0.19

Abbreviations: C/S: cesarean section; DBP: diastolic BP; FHR: fetal heart rate; HR: heart rate; NVD: normal vaginal delivery; Sat: O<sub>2</sub> saturation; SBP: systolic BP.

<sup>a</sup>-5 min: 5 minutes before anesthesia. 5 min: 5 minutes after anesthesia.

Apgar scores between epidural analgesia and systematic opioids. They found that both variables had better conditions in the EA group (25). In a comparative study of NVD (normal vaginal delivery) with epidural analgesia and

CSE, Palmer et al. evaluated FHR, Apgar scores, and the incidence of C/S. The incidence of FHR abnormal trends in the epidural and CSE groups was 6% and 12%, respectively, while there was no significant difference in other variables

**Table 2.** Fetal Movement at Definite Intervals<sup>a</sup>

FM	Group	Good	Bad	P Value
FM -5 min	Epidural	50	0	-
	CSE	50	0	
FM 5 min	Epidural	50	0	-
	CSE	50	0	
FM 10 min	Epidural	50	0	-
	CSE	50	0	
FM 20 min	Epidural	50	0	-
	CSE	50	0	
FM delivery time	Epidural	49	1	0.55
	CSE	48	2	

Abbreviation: FM, fetal movement.

<sup>a</sup>-5 min: 5 minutes before anesthesia. 5 min: 5 minutes after anesthesia.

between the groups (26). However, many studies have found no significant differences between epidural and CSE techniques in terms of fetal safety and neonatal outcomes (31). Some studies have suggested that the incidence of C/S is similar in both methods and the analgesic technique was not considered a significant factor. A comparative study of normal delivery with epidural and CSE analgesia conducted by Simmons et al. suggested that the CSE method resulted in more rapid pain relief and that there were no significant differences between the two groups in terms of Apgar scores, the incidence of C/S, and hypotension (16). The comparison of the two anesthesia groups [CSE (n = 1964) and epidural (n = 4533)] in Maternal La Paz Hospital showed that the analgesic quality was better in the CSE than in the EA group, but there was no significant difference in obstetrical outcomes and maternal/fetal safety (17). Bhagwat et al. (19) studied the CSE method versus epidural analgesia among 60 pregnant women with normal vaginal delivery. The CSE group was associated with faster cervical dilation and shorter first labor phase. The C/S rate was not significantly different between the two groups (2 patients (6.6%) in the CSE group versus none in the epidural group). There was no significant difference between 1-minute and 5-minute Apgar scores (19). In the study by Patel et al., CSE (n = 62) and epidural (n = 53) anesthesia were administered for NVD, showing no significant difference in terms of FHR and Apgar score between the groups (27).

Several studies comparing epidural and CSE methods have shown no differences in maternal safety and hypotension incidence (16, 17). Similar results were obtained in the present study, as well. There were no significant differences between the two groups in terms of fetal safety (i.e. FHR and FM) and maternal safety (i.e. hemodynamic variables). Apgar scores were approximately equal at the first

and fifth minutes in both groups, and they did not show significant differences. Overall, this study supports other studies that both methods of analgesia are safe for mother and fetus, and they do not increase the rate of cesarean delivery.

In conclusion, the present study demonstrated no significant difference between the EA and CSE techniques in terms of fetal and maternal hemodynamic alterations, Apgar scores, and C/S incidence. More research is needed to investigate the incidence and causes of C/S after analgesia.

### Acknowledgments

The authors would like to thank all anesthesiologists, anesthesia nurses, and midwives at the labor room of Taleghani teaching hospital for their assistance in this study.

### Footnotes

**Conflict of Interests:** It is not declared by the authors.

**Funding/Support:** None declared by the author.

### References

1. Lowe NK. The nature of labor pain. *Am J Obstet Gynecol.* 2002;**186**(5 Suppl Nature):S16–24. doi: [10.1067/mob.2002.121427](https://doi.org/10.1067/mob.2002.121427). [PubMed: [12011870](https://pubmed.ncbi.nlm.nih.gov/12011870/)].
2. Butterworth JF, Mackey DC, Wasnick JD. *Obstetric anesthesia*. 6th ed. Morgan & Mikhail's Clinical anesthesiology; 2018. p. 890–921.
3. Rucklidge M. *Analgesia for Labour*. Consultant Anaesthetist Royal Devon and Exeter Hospital; 2003. 5 p.
4. Miller RD, Pardo M. *Basics of Anesthesia*. 7th ed. Elsevier Health Sciences; 2017. p. 36–42.
5. Rooks JP. Labor pain management other than neuraxial: What do we know and where do we go next? *Birth.* 2012;**39**(4):318–22. doi: [10.1111/birt.12009](https://doi.org/10.1111/birt.12009). [PubMed: [23281953](https://pubmed.ncbi.nlm.nih.gov/23281953/)].
6. Kozlov I, Ackert M. Introduction of a new concept of pain management during labor and a novel technique for pain free labor. *Open J Anaesthesiol.* 2012;**2**(3):79–83. doi: [10.4236/ojanes.2012.23019](https://doi.org/10.4236/ojanes.2012.23019).
7. Agrawal D, Makhija B, Arora M, Haritwal A, Gurha P. The effect of epidural analgesia on labour, mode of delivery and neonatal outcome in nullipara of India, 2011-2014. *J Clin Diagn Res.* 2014;**8**(10):OC03–6. doi: [10.7860/JCDR/2014/9974.4930](https://doi.org/10.7860/JCDR/2014/9974.4930). [PubMed: [25478409](https://pubmed.ncbi.nlm.nih.gov/25478409/)]. [PubMed Central: [PMC4253227](https://pubmed.ncbi.nlm.nih.gov/PMC4253227/)].
8. Leighton BL, Halpern SH. The effects of epidural analgesia on labor, maternal, and neonatal outcomes: A systematic review. *Am J Obstet Gynecol.* 2002;**186**(5 Suppl Nature):S69–77. doi: [10.1067/mob.2002.121813](https://doi.org/10.1067/mob.2002.121813). [PubMed: [12011873](https://pubmed.ncbi.nlm.nih.gov/12011873/)].
9. Singh SK, Yahya N, Misiran K, Masdar A, Nor NM, Yee LC. [Combined spinal-epidural analgesia in labour: Its effects on delivery outcome]. *Rev Bras Anestesiol.* 2016;**66**(3):259–64. Portuguese. doi: [10.1016/j.bjan.2014.09.009](https://doi.org/10.1016/j.bjan.2014.09.009). [PubMed: [26993410](https://pubmed.ncbi.nlm.nih.gov/26993410/)].
10. Halpern SH, Leighton BL, Ohlsson A, Barrett JF, Rice A. Effect of epidural vs parenteral opioid analgesia on the progress of labor: A meta-analysis. *JAMA.* 1998;**280**(24):2105–10. doi: [10.1001/jama.280.24.2105](https://doi.org/10.1001/jama.280.24.2105). [PubMed: [9875879](https://pubmed.ncbi.nlm.nih.gov/9875879/)].

11. Sharma SK, Alexander JM, Messick G, Bloom SL, McIntire DD, Wiley J, et al. Cesarean delivery: A randomized trial of epidural analgesia versus intravenous meperidine analgesia during labor in nulliparous women. *Anesthesiology*. 2002;**96**(3):546-51. doi: [10.1097/0000542-200203000-00007](https://doi.org/10.1097/0000542-200203000-00007). [PubMed: [11873026](https://pubmed.ncbi.nlm.nih.gov/11873026/)].
12. Howell CJ, Dean T, Lucking L, Dziedzic K, Jones PW, Johanson RB. Randomised study of long term outcome after epidural versus non-epidural analgesia during labour. *BMJ*. 2002;**325**(7360):357. doi: [10.1136/bmj.325.7360.357](https://doi.org/10.1136/bmj.325.7360.357). [PubMed: [12183305](https://pubmed.ncbi.nlm.nih.gov/12183305/)]. [PubMed Central: [PMC117883](https://pubmed.ncbi.nlm.nih.gov/PMC117883/)].
13. Mazul-Sunko B. Low-dose spinal versus epidural anaesthesia for delivery and expected caesarean section. *Period Biol*. 2011;**113**(2):275-7.
14. Gambling D, Berkowitz J, Farrell TR, Pue A, Shay D. A randomized controlled comparison of epidural analgesia and combined spinal-epidural analgesia in a private practice setting: Pain scores during first and second stages of labor and at delivery. *Anesth Analg*. 2013;**116**(3):636-43. doi: [10.1213/ANE.0b013e31827e4e29](https://doi.org/10.1213/ANE.0b013e31827e4e29). [PubMed: [23400985](https://pubmed.ncbi.nlm.nih.gov/23400985/)].
15. Van de Velde M, Mignolet K, Vandermeersch E, Van Assche A. Prospective, randomized comparison of epidural and combined spinal epidural analgesia during labor. *Acta Anaesthesiol Belg*. 1999;**50**(3):129-36. [PubMed: [10529851](https://pubmed.ncbi.nlm.nih.gov/10529851/)].
16. Simmons SW, Taghizadeh N, Dennis AT, Hughes D, Cyna AM. Combined spinal-epidural versus epidural analgesia in labour. *Cochrane Database Syst Rev*. 2012;**10**. CD003401. doi: [10.1002/14651858.CD003401.pub3](https://doi.org/10.1002/14651858.CD003401.pub3). [PubMed: [23076897](https://pubmed.ncbi.nlm.nih.gov/23076897/)].
17. Miro M, Guasch E, Gilsanz F. Comparison of epidural analgesia with combined spinal-epidural analgesia for labor: A retrospective study of 6497 cases. *Int J Obstet Anesth*. 2008;**17**(1):15-9. doi: [10.1016/j.ijoa.2007.07.003](https://doi.org/10.1016/j.ijoa.2007.07.003). [PubMed: [18162199](https://pubmed.ncbi.nlm.nih.gov/18162199/)].
18. Nakamura G, Ganem EM, Rugolo LM, Castiglia YM. Effects on mother and fetus of epidural and combined spinal-epidural techniques for labor analgesia. *Rev Assoc Med Bras (1992)*. 2009;**55**(4):405-9. doi: [10.1590/S0104-42302009000400014](https://doi.org/10.1590/S0104-42302009000400014). [PubMed: [19750306](https://pubmed.ncbi.nlm.nih.gov/19750306/)].
19. Bhagwat AG, Dua CK, Saxena KN, Srinivasan S, Dua K. Comparison of combined spinal epidural technique and low dose epidural technique in progress of labour. *Indian J Anaesth*. 2008;**52**(3):282-7.
20. Hattler J, Klimek M, Rossaint R, Heesen M. The effect of combined spinal-epidural versus epidural analgesia in laboring women on nonreassuring fetal heart rate tracings: Systematic review and meta-analysis. *Anesth Analg*. 2016;**123**(4):955-64. doi: [10.1213/ANE.0000000000001412](https://doi.org/10.1213/ANE.0000000000001412). [PubMed: [27509225](https://pubmed.ncbi.nlm.nih.gov/27509225/)].
21. Correa Chacon OC, Fabregat Lopez J. Obstetric epidural analgesia and fetal heart rate: primum non nocere. *Minerva Anesthesiol*. 2010;**76**(5):314-5. [PubMed: [20395892](https://pubmed.ncbi.nlm.nih.gov/20395892/)].
22. Pildner von Steinburg S, Boulesteix AL, Lederer C, Grunow S, Schiermeier S, Hatzmann W, et al. What is the "normal" fetal heart rate? *PeerJ*. 2013;**1**. e82. doi: [10.7717/peerj.82](https://doi.org/10.7717/peerj.82). [PubMed: [23761161](https://pubmed.ncbi.nlm.nih.gov/23761161/)]. [PubMed Central: [PMC3678114](https://pubmed.ncbi.nlm.nih.gov/PMC3678114/)].
23. Gerhardt MA, Gunka VB, Miller RJ. Hemodynamic stability during labor and delivery with continuous epidural infusion. *J Am Osteopath Assoc*. 2006;**106**(12):692-8. [PubMed: [17242413](https://pubmed.ncbi.nlm.nih.gov/17242413/)].
24. Ankichetty SP, Chin KJ, Chan VW, Sahajanandan R, Tan H, Grewal A, et al. Regional anesthesia in patients with pregnancy induced hypertension. *J Anaesthesiol Clin Pharmacol*. 2013;**29**(4):435-44. doi: [10.4103/0970-9185.119108](https://doi.org/10.4103/0970-9185.119108). [PubMed: [24249977](https://pubmed.ncbi.nlm.nih.gov/24249977/)]. [PubMed Central: [PMC3819834](https://pubmed.ncbi.nlm.nih.gov/PMC3819834/)].
25. Reynolds F. The effects of maternal labour analgesia on the fetus. *Best Pract Res Clin Obstet Gynaecol*. 2010;**24**(3):289-302. doi: [10.1016/j.bpobgyn.2009.11.003](https://doi.org/10.1016/j.bpobgyn.2009.11.003). [PubMed: [20005180](https://pubmed.ncbi.nlm.nih.gov/20005180/)].
26. Palmer CM, Maciulla JE, Cork RC, Nogami WM, Gossler K, Alves D. The incidence of fetal heart rate changes after intrathecal fentanyl labor analgesia. *Anesth Analg*. 1999;**88**(3):577-81. doi: [10.1097/0000539-199903000-00021](https://doi.org/10.1097/0000539-199903000-00021). [PubMed: [10072009](https://pubmed.ncbi.nlm.nih.gov/10072009/)].
27. Patel NP, El-Wahab N, Fernando R, Wilson S, Robson SC, Columb MO, et al. Fetal effects of combined spinal-epidural vs epidural labour analgesia: A prospective, randomised double-blind study. *Anaesthesia*. 2014;**69**(5):458-67. doi: [10.1111/anae.12602](https://doi.org/10.1111/anae.12602). [PubMed: [24738803](https://pubmed.ncbi.nlm.nih.gov/24738803/)].
28. AbdElBarr T, Elshalakany NA, Shafik YM. Single dose spinal analgesia: Is it a good alternative to epidural analgesia in controlling labour pain? *Egypt J Anaesth*. 2019;**30**(3):241-6. doi: [10.1016/j.egja.2014.02.003](https://doi.org/10.1016/j.egja.2014.02.003).
29. Birnbach DJ, Browne IM. Anesthesia for obstetrics. In: Miller RD, editor. *Miller's anesthesia*. 10th ed. Ken Livingstone: Churchill Livingstone; 2010. p. 2203-40. doi: [10.1016/b978-0-443-06959-8.00069-8](https://doi.org/10.1016/b978-0-443-06959-8.00069-8).
30. Valensise H, Lo Presti D, Tiralongo GM, Pisani I, Gagliardi G, Vasapollo B, et al. Foetal heart rate deceleration with combined spinal-epidural analgesia during labour: A maternal haemodynamic cardiac study. *J Matern Fetal Neonatal Med*. 2016;**29**(12):1980-6. doi: [10.3109/14767058.2015.1072156](https://doi.org/10.3109/14767058.2015.1072156). [PubMed: [26333691](https://pubmed.ncbi.nlm.nih.gov/26333691/)].
31. Mattingly JE, D'Alessio J, Ramanathan J. Effects of obstetric analgesics and anesthetics on the neonate : A review. *Paediatr Drugs*. 2003;**5**(9):615-27. doi: [10.2165/00148581-200305090-00004](https://doi.org/10.2165/00148581-200305090-00004). [PubMed: [12956618](https://pubmed.ncbi.nlm.nih.gov/12956618/)].