Original Research Article

Comparison of Efficacy and Safety of Combine Spinal Epidural (CSE) And Epidural for Labor Analgesia, A Single center Retrospective Observational Study

Prathibha S[1*], Amera S[2]

[1,2]Department of Anesthesia, NMC Royal women's Hospital, Abu Dhabi, UAE.
Email: dr.prathibha@yahoo.com

Abstract

Background: Epidural analgesia is the most commonly used technique for labor analgesia. It has a drawback of prolonged labor and delayed onset. In comparison, CSE technique, combination of both spinal and epidural analgesia is reported to have less adverse effects. This study aimed to compare the efficacy of analgesia between combined spinal- epidural and epidural analgesia during child birth. **Methods:** A retrospective study was performed. Data of 100 women (50 in each group) were collected. The CSE group (Group 1) received 2mg bupivacaine + 25mcg Fentanyl into the subarachnoid space, followed by 0.08% bupivacaine + fentanyl 2mcg/ml at rate of 8-10ml/hour epidural infusion and epidural group (Group 2) received 0.08% bupivacaine + fentanyl 2mcg/ml at rate of 8-10ml/hour. Vital signs of both mother and the foetus, verbal numeric pain score, onset time and duration of analgesia, need of analgesia and other obstetric and neonatal outcomes were recorded. **Results:** Rapid onset of analgesia in Group 1 (CSE) compared to Group 2 (Epidural) (3.7 ± 1.15 vs 12.36 ± 3.44, P=<0.001*) and patient reported reduction in pain score at 15mins after injection in CSE group (3.74 ± 0.6 vs 4.5 ± 1.05, P=<0.001*). Most of the patient in CSE group required an additional dose (44% vs 24%, P=0.035) and duration of second stage of labor is prolonged in CSE group (74.6 ± 26.36 vs) compared to epidural group (54.7 ± 25.74), (P=<0.001). **Conclusion:** As compared to epidural technique, CSE technique offer rapid onset of analgesia and prolonged second stage labor. Mode of delivery was comparable between both groups. Requirement of rescue analgesia was more in CSE group, as compared to Epidural group. Thus, CSE can be used as an alternative to epidural analgesia in terms of efficacy and pain management.

Keywords: combined spinal epidural, epidural analgesia, pain assessment, obstetric.

[*]**Address for Correspondence:**
Dr Prathibha Santosh, MBBS, DNB, Department of Anesthesia, NMC Royal women's Hospital, Abu Dhabi, UAE.
Email: dr.prathibha@yahoo.com

Received Date: 07/06/2023 Revised Date: 19/07/2023 Accepted Date: 03/08/2023

Access this article online

Quick Response Code:

Website: www.medpulse.in

Published Date: 10 August 2023

INTRODUCTION

Labor pain has been reported to be one of the most severe pains ever evaluated.[1] It can have detrimental effects on the respiratory, cardiovascular, neuroendocrine systems of the foetus predisposing to foetal hypoxia.[2,3] Pain may also contribute to maternal exhaustion.[3] Therefore, providing effective pain relief throughout labor is essential to minimize perinatal complications and preventing unnecessary caesarean sections performed due to maternal anxiety.[1]

Several techniques have been developed to alleviate this pain while minimizing effects on the mother, foetus, and the progression of labor.[4] Regional analgesia had been proven to be most effective method of labor analgesia. It can be administered through epidural, spinal or a combination of both.[5]

In epidural analgesia, local anaesthetic is directly injected into epidural space surrounding the spinal column through

How to site this article: Prathibha S, Amera S. Comparison of Efficacy and Safety of Combine Spinal Epidural (CSE) And Epidural for Labor Analgesia, A Single center Retrospective Observational Study. *MedPulse International Journal of Anesthesiology.* August 2023; 27(2): 16-22. http://medpulse.in/Anesthsiology/index.php

a catheter positioned in the epidural space.[3,5] When compared to non-epidural methods, epidural analgesia is regarded as the more efficient and safe way to provide labor pain relief.[6] Epidural solutions are administered either by bolus or infusion which permits analgesia to sustain throughout labor.[7]

Also, there are concerns regarding use of high concentrations of local anaesthetic drugs in epidural analgesia. It may cause leg weakness, decrease maternal satisfaction, poor mobility and difficulty in giving birth. This may be the reason for higher risk of instrumental births with associated risk of Lacerations, pain and incontinence.[2,5] Combination of low-dose local anaesthetic drugs combined with opioids has been proposed as a superior alternative.[5] This seems to result in excellent labor analgesia without compromising the motor function[8] which helps the parturient to actively participate in labor process without instrumental assistance.

In spinal analgesia, medications are injected directly into the spinal column, resulting in comparatively quicker onset of analgesia. However, because of shorter duration of analgesia, they are not commonly used for labor analgesia. Additionally, higher probability of nerve injury is another concern with use of very fine catheters in the spinal region.[5]

Hence, single spinal injection in combination with epidural catheter for ongoing pain relief was developed. Combined spinal-epidural analgesia (CSE) involves injection of a small dose of local anaesthetic and/or opioid into the subarachnoid space in order to initiate analgesia, followed by bolus or continuous injection via the epidural catheter.[5] Combination of both epidural and spinal techniques, has a advantage of quicker onset, reliable analgesia with minimal motor blockade and mobilisation,[9] lower maternal and cord blood concentration of medication,[10] and improved maternal satisfaction.[11] CSE can also provide better overall pain relief with faster cervical dilation rate, as compared to epidural alone.[12-14] But there are few complications, which are common to both Epidural and CSE like maternal hypotension, post-dural puncture headache (PDPH), urinary retention, pruritis, itching and transient backache.[15]

The ideal combination of drugs to be used for labor analgesia should result in long duration pain relief with minimal motor blockade and minimal placental transfer. They should not have any significant adverse impact on the mother and foetus.[1] For this purpose, Bupivacaine is most commonly used for labor epidural analgesia. Compared with older local labors, bupivacaine provides better analgesia and also with less tachyphylaxis with long-term administration.[16] Cardiac and central nervous system toxicity with accidental IV injection may occur with the use of higher concentration.[17]

Opioids like fentanyl in addition to local bupivacaine is preferrable due to their dose minimizing and adverse-effect-reducing properties.[11] It reduces the local anaesthetic requirement by approximately 25%. Fentanyl was chosen rather than other opioids, considering high lipid solubility and higher affinity for the μ-opioid receptor.[18] The synergistic effect of opioids with local anaesthetic agents improves analgesia and reduce the side-effect of motor block especially in the lower limbs.[10]

Therefore, the purpose of this study is to compare the effectiveness of CSE analgesia with epidural analgesia for painless labor. Primary outcome studied was the efficacy of analgesia and pain assessment. Obstetric and neonatal outcomes between CSE technique and epidural technique were considered.

MATERIALS AND METHODS

This Retrospective case study was conducted from tertiary care hospital, for a period of six months in Abu Dhabi, UAE**.** Data of One hundred healthy pregnant women (50 in each group) aged between 20-40 years who requested epidural analgesia in active labor with cervical dilatation 3-4 cm, experiencing uterine contractions, uncomplicated term labor between 37-41 weeks of gestational age were collected from record. Exclusion criteria where complicated pregnancies, placenta previa, pregnancy-induced hypertension, contraindication for regional analgesia and pre-eclampsia. The study population is considered into 2 groups, viz. Group-1 received combined spinal epidural analgesia (CSE) and group 2 received only epidural analgesia. All regional blocks were performed in the flexed sitting position at the L2-L3or L3-L4 intervertebral space following a routine fluid preload of 500–1000ml Hartmann's solution under aseptic condition. All patient blood investigations checked and written consent taken after explaining the risks and benefits of the procedure. In Group1 (CSE): CSE technique was performed using the single interspace needle-through-needle technique (Pajunk). The epidural space was identified using loss of resistance to saline with a18-G Tuohy needle then intrathecal injection was performed using 27G sprotte needle, 2mg of Bupivacaine+25mcg of Fentanyl given. 20G multiport epidural catheter was inserted 4–5cm into the epidural space. After Negative aspiration (no blood or CSF) test dose of 3ml of 0.25% Bupivacaine given and then infusion started at 0.08% Bupivacine+2mcg/ml fentanyl at 8-10ml/hr.

Group-2 (epidural): In epidural group, the epidural space was identified using loss of resistance to saline with a18-G Tuohy needle. As, mentioned in above technique, after a negative aspiration, 3 ml 0.25% bupivacaine was administered as a test dose, and then 0.08% bupivacaine

with fentanyl 2mcg/ml was continuously infused at a rate of 8-10 ml/hr.

Data was collected from the time of procedure to till the time of delivery by midwife , remaining data was collected from MRD. Intravenous fluid was started and routine monitoring including the verbal NRS (numeric pain score (0-10) was assessed in all parturients (0=no pain, 1-3 mild pain, 4-6 moderate pain, 7-10 severe pain). Vital parameters of the mother such as heart rate, blood pressure, respiratory rate, foetal heart rate before analgesia, 15mins after injection, 30 mins after injection and maternal satisfaction were recorded. Adverse effects such as PDH, nausea, vomiting were recorded. The duration of the first and second stages of labor, need for additional dose, maternal satisfaction and mode of delivery were also recorded. Neonatal welfare was assessed using Apgar scores at 1 and 5 minutes. The similar investigations repeated and the details of the investigations along with demographic details were collected and recorded using pre-designed structured data collection sheet/ proforma. All the collected details were further utilised for statistical analysis.

Statistical analysis

Data were analysed using coGuide REAP software version 1.03.[19] Mean ± standard deviation of normally distributed numeric variables were compared between two groups using unpaired t-test. Median (IDR) of non-normally distributed numeric variables were compared using Mann Whitney u test. Categorical variables were compared using Chi square test/Fisher's exact test. P value of <0.05 was considered significant.

RESULTS

Data of 50 women in each group i.e, Group1 (CSE) (n=50) and Group 2(Epidural) (n=50) was extracted. Demographic characters were similar between two groups **(Table 1).**

Table 1: Comparison of Demographic characteristics between study group(N=100)

Parameter	Study Group	
	Combined Spinal epidural Analgesia (N=50)	Only Epidural Analgesia (N=50)
Age (in Years) (mean ± SD)	29.62 ± 4.62	29.9 ± 5.01
Height (in cm) (mean ± SD)	167.18 ± 3.77	166.32 ± 3.98
Weight (in kg) (mean ± SD)	81.32 ± 5.54	86.52 ± 6.78
BMI (mean ± SD)	29.1 ± 1.8	31.32 ± 2.71
Gravida n (%)		
Primi Gravida	9 (18%)	5 (10%)
Multi Gravida	41 (82%)	45 (90%)
Parity n (%)		
Nulli para	9 (18%)	7 (14%)
Primi Para	12 (24%)	15 (30%)
Multi para	29 (58%)	28 (56%)
ASA Group n (%)		
1	25 (50%)	25 (50%)
2	25 (50%)	25 (50%)

There was a significance difference in maternal heart rate at 30 mins after injection (Group 1: 96.02 ± 8, Group 2: 89.62 ± 5.69). No significance difference in terms of maternal respiratory rate, Blood pressure and foetal heart rate (before analgesia, 15 mins after injection and 30 mins after injection) in both groups. **(Table 2).** Line diagram of vital signs are presented in **fig1** and **fig2**

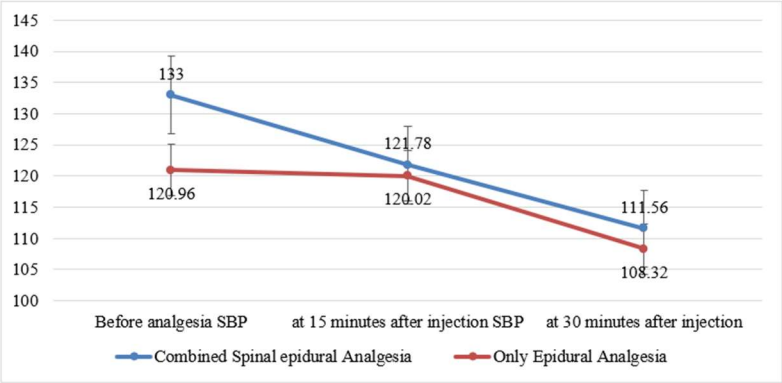

Figure 1: Line diagram of comparison of maternal SBP between the group

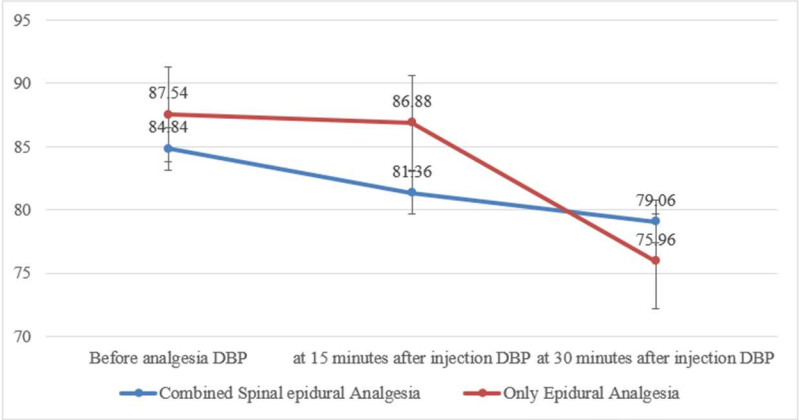

Figure 2: Line diagram of comparison of maternal DBP between the group

Table 2: Comparison of maternal and fetal hemodynamic parameters

Parameter	Study Group (Mean± SD)		P value
	Combined Spinal epidural Analgesia (N=50)	Only Epidural Analgesia (N=50)	
Maternal Heart rate			
Before analgesia	102.82 ± 8.74	99.3 ± 6.39	0.024
at 15 minutes after injection	99.6 ± 8.5	98.48 ± 6.85	0.470
at 30 minutes after injection	96.02 ± 8	89.62 ± 5.69	<0.001*
Maternal Respiratory rate			
Before analgesia	17.28 ± 1.26	17.24 ± 1.27	0.875
at 15 minutes after injection	16.26 ± 0.92	16.22 ± 0.93	0.830
at 30 minutes after injection	16.26 ± 0.92	16.22 ± 0.93	0.830
Maternal Systolic BP			
Before analgesia	133 ± 7.59	120.96 ± 9.79	<0.001
at 15 minutes after injection	121.78 ± 8.73	120.02 ± 10.07	0.353
at 30 minutes after injection	111.56 ± 10.96	108.32 ± 10.22	0.130
Maternal Diastolic BP			
Before analgesia	84.84 ± 6.45	87.54 ± 5.32	0.025
at 15 minutes after injection	81.36 ± 6.33	86.88 ± 5.31	<0.001*
at 30 minutes after injection	79.06 ± 6.67	75.96 ± 4.66	0.008
Fetal heart rate			
Before analgesia	150.06 ± 6.1	149.62 ± 6.01	0.717
at 15 minutes after injection	149.6 ± 6.02	149 ± 5.8	0.613
at 30 minutes after injection	149.06 ± 5.99	148.18 ± 5.74	0.455

There was a delay in onset of analgesia in Group 2 (Epidural): (12.36 ± 3.44 min) when compared to Group 1 (CSE): (3.7 ± 1.15 min) and duration of analgesia was not significantly different. Two groups were similar in pain score before

injection. However, at 15 mins after injection, pain score decreased in Group1(3.74 ± 0.6) compared to Group 2 (4.5 ± 1.05). Most of the patients in the CSE group required an additional dose medication to relieve their pain (44% in the CSE group vs. 24% in the epidural group, p = 0.035) Maternal satisfaction was mostly defined as good in both groups. (**Table 3)**

Table 3: Comparison of effectiveness of analgesics and pain assessment in both groups

Parameter	Study Group (Mean± SD)		P value
	Combined Spinal epidural Analgesia (N=50)	Only Epidural Analgesia (N=50)	
The onset time of analgesia (minute)	3.7 ± 1.15	12.36 ± 3.44	<0.001*
The duration of analgesia (In minutes)	518.2 ± 182.23	484.3 ± 171.67	0.341
Initial pain score before injection	8.4 ± 0.64	8.4 ± 0.64	1.000
Mild pain	0	0	
Moderate Pain (4 To 6)	2 (4%)	2 (4%)	
Severe Pain (7 To 10)	48 (96%)	48 (96%)	
15 minutes after injection	3.74 ± 0.6	4.5 ± 1.05	<0.001*
Mild Pain (1 To 3)	17 (34%)	8 (16%)	
Moderate Pain (4 To 6)	33 (66%)	40 (80%)	
Severe Pain (7 To 10)	0 (0%)	2 (4%)	
Number needed additional analgesic	22 (44%)	12 (24%)	0.035
Dose of additional analgesic (mg)	0.13 ± 0.06	0.17 ± 0.06	0.120

Duration of 1st stage of labor did not differ between groups. But in case of duration of second stage, which lasted longer in Group 1 (74.6 ± 26.36 min) compared to Group 2 (54.7 ± 25.74). 54% in Group 1 and 50% in Group 2 are in need of oxytocin augmentation. The mode of delivery was similar between two groups with normal vaginal delivery rate in Group 1(CSE) was 90% and group 2 (epidural) was 84%. Apgar scores did not differ much in two groups (P=1.000). **(Table 4)**

Table 4: Obstetric characteristics and data of obstetric and neonatal outcomes

Parameter	Study Group		P value
	Combined Spinal epidural Analgesia (N=50)	Only Epidural Analgesia (N=50)	
Gestational weeks (Days)	38.11 ± 1.03	38.32 ± 0.93	0.298
Initial cervical dilatation (cm)	4 ± 0.9	4.06 ± 0.77	0.721
Initial cervical effacement (%)	65.8 ± 10.32	67.8 ± 12.34	0.381
Duration of first stage (minute)	443.2 ± 160.97	429.6 ± 154.43	0.667
Duration of second stage (minute)	74.6 ± 26.36	54.7 ± 25.74	<0.001*
Need For Oxytocin Augmentation (%)	27 (54%)	25 (50%)	0.689
Mode Of Delivery n (%)			
Instrumental delivery	5 (10%)	8 (16%)	0.372
NVD (normal vaginal delivery)	45 (90%)	42 (84%)	
Need for Episiotomy (n) (%)	11 (22%)	13 (27%)	0.640
Apgar score at 1 minute	7.38 ± 1.05	7.38 ± 1.05	1.000
Apgar score at 5 minutes	8.64 ± 0.53	8.64 ± 0.53	1.000

DISCUSSION

Epidural technique is considered as a gold standard procedure for more than 40 years. CSE technique has become popular because it provides more rapid onset pain relief with minimal motor weakness.[20,21] This retrospective study was conducted to compare combined spinal epidural analgesia versus epidural analgesic technique in labor. As per the current study, CSE resulted in rapid onset of analgesia with 3.7 minutes faster onset than epidural alone. Cascio M *et al.*[22] suggests that use of CSE technique, leads to rapid onset of analgesia. Similar findings were reported by many previous studies.[23,24] A study by Ngamprasertwong P *et al.*[4] had shown 7.8 minutes faster onset of anaesthesia in CSE as compared to epidural alone. The time difference in onset of anaesthesia varied between 8 minutes to 3 minutes as per various studies. The variation in the time differences can be attributed to the composition and dosage of anaesthetic substances used. 2mg of Bupivacaine+ 25mcg of Fentanyl, 0.08% Bupivacine+2mcg/ml fentanyl at 8-10ml/hr in CSE group and dose of 0.08% bupivacaine with fentanyl 2mcg/ml was continuously infused at a rate of 8-10 ml/hr in epidural group.

As per the current study duration of analgesia was not statistically significant (P=0.341) as studied by Ngamprasertwong P *et al.*[4] (P=0.542).Verbal NRS (numeric pain score (0-10) was assessed in all parturient (0=no pain, 1-3 mild pain, 4-6 moderate pain, 7-10 severe pain). There was a reduction in Pain score at 15 mins after injection in CSE group compared to epidural technique and more number of patients suffered moderate pain (4-6) in both the groups.

The study conducted by Collis RE *et al.*[23] anaesthetist chose to increase the dose of bupivacaine in the combined spinal-epidural group and to give 50-100 µg fentanyl as a bolus in the standard epidural group. The average number of additional epidural analgesic doses was significantly higher in the CSE group than in the epidural alone group (4.6 [SD 2.8] vs 3.5 [2.0], p=0.008). In this study, whomever required an additional dose were given to achieve satisfactory analgesia. The number of patients required additional dose were more in CSE group than epidural group with no statistical difference. Mean of required additional dose was ((0.13 ± 0.06) vs (0.17 ± 0.06), p =0.120) between two groups. Initial cervical dilation in Group 1(4 ± 0.9) and Group 2 (4.06 ± 0.77) has no significant difference, which was comparable to the study by Bhagwat AG *et al.*[25]

Many studies have shown a relationship between the use of epidural and prolonged second stage labor.[24,25,26] This study shows no differences between groups in duration of first stage of labor.[22] Duration of second stage of labor was prolonged in CSE group compared to epidural group.

Use of traditional, local anaesthetic-based epidural analgesia was reported be associated with more frequent use of oxytocin induction and higher risk of instrumental vaginal delivery.[24] In our study there was no statistical difference in case of need of oxytocin augmentation in both the groups with P=0.690 and higher percent of normal vaginal delivery in both the groups (90% and 84%) compared to instrumental delivery (10% and 16%) as same as the study conducted by Pascual-Ramirez J *et al.*,[28] which has higher NVD compared to instrumental delivery. All the neonates had Apgar score of 8 at 1 min and 5 min.

The study was a retrospective observational study, comparing the treatment efficacy and safety of two different modalities of labor analgesia. Key limitation of the study was we didn't do a priori sample size calculation. Post-hoc power analysis for the primary outcome showed, the study had adequate power, hence the role of chance is very minimal. Also, possibility of natural selection bias influencing the choice of modality and reporting bias, outcome ascertainment bias etc. due to lack of blinding can't be ruled out totally. But the study findings are more closer to real world scenario than a controlled clinical trial. There were very minimal differences in baseline characteristics of the population between both groups with minimal possibility of confounding effect. The role of unknown confounding effect by other parameters can't be ruled out completely as there was no randomization.

CONCLUSION

In conclusion, CSE technique provides more rapid onset analgesia and more second-stage analgesia compared regional epidural technique. there is a difference in initial pain score and 15 mins after injection in both the groups. Most of the patients in CSE group, required an additional dose. We found no differences between groups in terms of first-stage labor, FHR, maternal BP, need for oxytocin augmentation, need for episiotomy and mode of delivery. Obstetric and neonatal outcomes were similar between groups.

REFERENCES

1. Gündüz Ş, Eriş Yalçın S, Karakoç G, Akkurt MÖ, Yalçın Y, Yavuz A. Comparison of bupivacaine and ropivacaine in combination with fentanyl used for walking epidural anesthesia in labor. Turk J Obstet Gynecol. 2017 ;14(3):170-175.
2. Bolukbasi D, Sener EB, Sarihasan B, Kocamanoglu S, Tur A. Comparison of maternal and neonatal outcomes with epidural bupivacaine plus fentanyl and ropivacaine plus fentanyl for labor analgesia. Int J Obstet Anesth. 2005;14(4):288–93.
3. Anwar S, Anwar MW, Ahmad S. EFFECT OF EPIDURAL ANALGESIA ON LABOR AND ITS OUTCOMES. J Ayub Med Coll Abbottabad. 2015;27(1):146–50.
4. Ngamprasertwong P, Kumwilaisakmd K, Indrambarya T, Supbornsug K, Ngarmukos S. Combined spinal-epidural analgesia and epidural analgesia in labor: effect of intrathecal fentanyl vs. epidural bupivacaine as a bolus. J Med Assoc Thai. 2007;90(7):1368–74.
5. Simmons SW, Taghizadeh N, Dennis AT, Hughes D, Cyna AM. Combined spinal-epidural versus epidural analgesia in labour. Cochrane Database Syst Rev. 2012;10(10):CD003401.
6. Anim-Somuah M, Smyth RM, Cyna AM, Cuthbert A. Epidural versus non-epidural or no analgesia for pain management in labour. Cochrane Database Syst Rev. 2018;5(5):CD000331.
7. Hibbard BM. Report on confidential enquiries into maternal deaths in the United Kingdom 1991-1993. (No Title) [Internet]. [cited 2023 Jul 31]; Available from: https://cir.nii.ac.jp/crid/1130282269402137856
8. Akerman B, Arweström E, Post C. Local anesthetics potentiate spinal morphine antinociception. Anesth Analg. 1988;67(10):943–8.
9. Collis RE, Baxandall ML, Srikantharajah ID, Edge G, Kadim MY, Morgan BM. Combined spinal epidural analgesia with ability to walk throughout labour. Lancet. 1993;341(8847):767–8.

10. Wong CA, Nathan N, Brown DL. Chapter 12 Spinal, Epidural, and Caudal Anesthesia: Anatomy, Physiology, and Technique. In: Chestnut's Obstetric Anesthesia: Principles and Practice. 2009. p. 223–45.
11. Lv BS, Wang W, Wang ZQ, Wang XW, Wang JH, Fang F, et al. Efficacy and safety of local anesthetics bupivacaine, ropivacaine and levobupivacaine in combination with sufentanil in epidural anesthesia for labor and delivery: a meta-analysis. Curr Med Res Opin. 2014;30(11):2279–89.
12. Dresner M, Bamber J, Calow C, Freeman J, Charlton P. Comparison of low-dose epidural with combined spinal-epidural analgesia for labour. Br J Anaesth. 1999;83(5):756–60.
13. Tsen LC, Thue B, Datta S, Segal S. Is combined spinal-epidural analgesia associated with more rapid cervical dilation in nulliparous patients when compared with conventional epidural analgesia? Anesthesiology. 1999;91(4):920–5.
14. Sia AT, Camann WR, Ocampo CE, Goy RW, Tan HM, Rajammal S. Neuraxial block for labour analgesia--is the combined spinal epidural (CSE) modality a good alternative to conventional epidural analgesia? Singapore Med J. 2003;44(9):464–70.
15. Chestnut's Obstetric Anesthesia: Principles and Practice - 5th Edition [Internet]. [cited 2023 Jul 31]. Available from: https://shop.elsevier.com/books/chestnuts-obstetric-anesthesia-principles-and-practice/chestnut/978-1-4557-4866-2
16. Beilin Y, Halpern S. Focused review: ropivacaine versus bupivacaine for epidural labor analgesia. Anesth Analg. 2010;111(2):482–7.
17. Polley LS, Columb MO. Ropivacaine and bupivacaine: concentrating on dosing! Anesth Analg. 2003;96(5):1251–3.
18. Meister GC, D'Angelo R, Owen M, Nelson KE, Gaver R. A comparison of epidural analgesia with 0.125% ropivacaine with fentanyl versus 0.125% bupivacaine with fentanyl during labor. Anesth Analg. 2000;90(3):632–7.
19. BDSS Corp. Released 2020. reap coGuide Statistics software, Version 1.0.3, India: BDSS corp. Available from: https://reap.coguide.in. [Last accessed on 2023 Jul 14.
20. Hughes D, Simmons SW, Brown J, Cyna AM. Combined spinal-epidural versus epidural analgesia in labour. Cochrane Database Syst Rev. 2003;(4):CD003401.
21. Hepner DL, Gaiser RR, Cheek TG, Gutsche BB. Comparison of combined spinal-epidural and low dose epidural for labour analgesia. Can J Anaesth. 2000;47(3):232–6.
22. Cascio M, Pygon B, Bernett C, Ramanathan S. Labour analgesia with intrathecal fentanyl decreases maternal stress. Can J Anaesth. 1997;44(6):605–9.
23. Collis RE, Davies DW, Aveling W. Randomised comparison of combined spinal-epidural and standard epidural analgesia in labour. Lancet. 1995;345(8962):1413–6.
24. Anim-Somuah M, Smyth R, Howell C. Epidural versus non-epidural or no analgesia in labour. Cochrane Database Syst Rev. 2005;(4):CD000331.
25. 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 Journal of Anaesthesia. 2008;52(3):282.
26. Liu EHC, Sia ATH. Rates of caesarean section and instrumental vaginal delivery in nulliparous women after low concentration epidural infusions or opioid analgesia: systematic review. BMJ. 2004;328(7453):1410.
27. 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.
28. Pascual-Ramirez J, Haya J, Pérez-López FR, Gil-Trujillo S, Garrido-Esteban RA, Bernal G. Effect of combined spinal-epidural analgesia versus epidural analgesia on labor and delivery duration. Int J Gynaecol Obstet. 2011;114(3):246–50.

Source of Support: None Declared
Conflict of Interest: None Declared