# RESEARCH

# **BMC** Anesthesiology



# Effect of epidural dexmedetomidine in singledose combined with ropivacaine for cesarean section

Minghao Liu<sup>1</sup>, Xuezi Chen<sup>2</sup> and Dan Guo<sup>1,3\*</sup>

# Abstract

**Background** Dexmedetomidine has arousal sedation and analgesic effects. We hypothesize that epidural dexmedetomidine in single-dose combined with ropivacaine improves the experience of parturient undergoing cesarean section under epidural anesthesia. This study is to investigate the effect of 0.5 µg/kg epidural dexmedetomidine combined with epidural anesthesia (EA) in parturients undergoing cesarean section.

**Methods** A total of 92 parturients were randomly divided into Group R (receiveing epidural ropivacaine alone) Group RD (receiveing epidural ropivacaine with 0.5 µg/kg dexmedetomidine). The primary outcome and second outcome will be intraoperative NRS pain scores and Ramsay Sedation Scale.

**Results** All 92 parturients were included in the analysis. The NRS were significantly lower in Group RD compared to Group R at all observation timepoint (P > 0.05). Higher Ramsay Sedation Scale was found in Group RD compared to Group R (P < 0.001). No parturient has experienced sedation score of 4 and above. No significant difference regarding the incidence of hypotension, bradycardia and nausea or vomiting, Apgar scores and the overall satisfaction with anesthesia was found between Group R and Group RD (P > 0.05).

**Conclusion** Epidural dexmedetomidine of 0.5 µg/kg added slightly extra analgesic effect to ropivacaine in EA for cesarean section. The sedation of 0.5 µg/kg epidural dexmedetomidine did not cause mother-baby bonding deficit. Satisfaction with anesthesia wasn't significantly improved by epidural dexmedetomidine of 0.5 µg/kg. No additional side effect allows larger dose of epidural dexmedetomidine attempt.

Trial registration This study was registered at www.chictr.org.cn (ChiCTR2000038853).

Keywords Cesarean section, Dexmedetomidine, Epidural anesthesia, Pain, Sedation

\*Correspondence: Dan Guo 924251258@qq.com

<sup>1</sup>Department of Anesthesiology, Chengdu Fifth People's Hospital (The Second Clinical Medical College, Geriatric Diseases Institute of Chengdu/ Cancer Prevention and Treatment Institute of Chengdu, Affiliated Fifth People's Hospital of Chengdu University of Traditional Chinese Medicine), Chengdu, China



 $^{\rm 2}{\rm Department}$  of Anesthesiology, the First Affiliated Hospital of Chongqing Medical University, Chongqing, China

<sup>3</sup>Department of Ultrasound Imaging, Chengdu Fifth People's Hospital (The Second Clinical Medical College, Geriatric Diseases Institute of Chengdu/Cancer Prevention and Treatment Institute of Chengdu, Affiliated Fifth People's Hospital of Chengdu University of Traditional Chinese Medicine), Chengdu 611137, China

© The Author(s) 2024. **Open Access** This article is licensed under a Creative Commons Attribution 4.0 International License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons licence, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons licence, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons licence and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this licence, visit http://creativecommons.org/licenses/by/4.0/. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated in a credit line to the data.

# Background

Cesarean section is mostly done under general anesthesia (GA) or neuraxial anesthesia. Epidural anesthesia (EA) is one of the preferred neuraxial anesthetic technique for cesarean section, which avoids the risks related to GA (especially failed intubation and aspiration), allows the parturient to maintain favorable early motherchild bonding and has less influence on hemodynamics compared to spinal anesthesia [1-4]. Nevertheless, the main shortcomings of EA resides in inadequate for visceral pain relief during surgery [5] and slow onset of action. The combination of adjuvant (such as sufentanil) and local anesthetics has nowadays became a common method to improve epidural anesthesia [6]. However, there are several side-effects related to neuraxial opioids such as pruritus, nausea and vomiting and utmost vigilance needy respiratory depression which can be lifethreatening [7, 8].

Sedation can decrease the need of opioids during regional anesthesia, thus reduce the rate of postoperative nausea and vomiting [9]. Besides, Sedation contributes to patients' higher satisfaction and increase patients' acceptance of regional anesthesia [10, 11]. In an obstetrical setting, early skin-to-skin contact between mother and newborn benefits a lot, such as reducing postpartum bleeding rates [12], promoting the release of oxytocin and endorphins [13, 14], thus improve mother's mood tone [14], while inappropriate sedation might affect skinto-skin contact [15].

Dexmedetomidine is a highly selective  $\alpha 2$  agonist which has arousal sedation effects, analgesic, and antisympathetic effects. Compared to intrathecal opioids, the intrathecal use of dexmedetomidine can reduce respiration depression, nausea, vomiting, shivering and other drawbacks associated with opioids [1, 16, 17]. Intrathecally used dexmedetomidine in combination with local anesthetics has been proved to enhance intraoperative anesthetic effects of neuraxial anesthesia and improved maternal satisfaction after cesarean section [18–20]. It's still not well-understood the effect of combining epidural dexmedetomidine with local anesthetic in cesarean section under epidural anesthesia.

This prospective, randomized, double-blind controlled study was to investigate the effectiveness of epidural dexmedetomidine in combination with ropivacaine on parturients undergoing cesarean section with epidural anesthesia.

#### Methods

# Ethics

This study was registered at www.chictr.org.cn (ChiCTR2000038853 07/10/2020) and its protocol was accredited by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University. Participants

were well-informed of the study protocol and written informed consent was taken from all the participants present in the study. This study was conducted at The First Affiliated Hospital of Chongqing Medical University, Chongqing, China, between December 2020 and July 2021. The trail was conducted as per the declaration of Helsinki and submitted in the format of CONSORT guidelines.

## Participant recruitment

Parturients who are scheduled for elective cesarean section under EA between December 2020 and July 2021 were eligible for this study. The inclusion criteria for the study were as follows: age between 18 and 39 years old; singleton pregnancy; American Society of Anesthesiologists (ASA) physical status II;  $\geq$  37 weeks's gestation. The exclusion criteria of the study were as follows: EA is contraindicated; organ dysfunction such as hypertension, cardiopulmonary disease, placenta previa, fetal distress in utero, and cardiac conduction or rhythm abnormalities; allergy or intolerance to one of the study medications, chronic analgetic use for longer than 3 months; any previous EA or abdominal surgery.

# Randomization and masking

Parturients who were eligible according to criteria were allocated, in a 1:1 ratio, to receive epidural 90 mg ropivacaine (group R) or 90 mg ropivacaine with 0.5  $\mu$ g/kg dexmedetomidine (group RD) (*n*=46 parturients per group), via a computer-generated randomization table. The protocol statistician created the randomization schedule. On the day of surgery, a research assistant provided the coinvestigator anesthesiologist with an opaque card containing the randomization details. The unblinded coinvestigator anesthesiologist prepared the solutions but was not involved in data collection. The blinded study anesthesiologist administered the aesthetic procedure and collected the data. Nulliparas remained unaware of their intervention assignment.

## Anesthesia procedure

All parturients were anesthetized with epidural anesthesia and routine epidural puncture was performed at 2 to 3 lumbar interspace with parturients in the right lateral decubitus position. An epidural catheter was inserted 4 cm cephalad into the epidural space. Then parturients were immediately positioned supine with a 15-degree left tilt and received a test dose of 3 mL of 1% lidocaine through the epidural catheter in order to avoid accidental intrathecal or intravascular misplacement. After that, parturients received epidural 90 mg ropivacaine or 90 mg ropivacaine with 0.5  $\mu$ g/kg dexmedetomidine according to the group allocation via epidural catheter. Effectiveness of EA was defined as bilateral T6-S5 or above sensory block to pinprick within 30 min after injection of study medications. If it was not achieved, additional ropivacaine was administered with the total amount not exceeding 200 mg. Otherwise, EA was turned into GA. An experienced anesthesiologist performed all anesthesia procedures. Surgery started after a T6 level of analgesia was reached and all surgical procedures were performed by the same group of surgeons.

# Monitoring and interventions

After arriving in the operating room, all parturients received standard monitoring including electrocardiography, respiratory rate, pulse oximetry, non-invasive blood pressure monitoring (NIBP), and temperature. A reservoir mask was placed on parturients and oxygen was given at a rate of 4 L/min to all parturients. 5 ml/kg of lactated Ringer's solution was administrated intravenously to all parturients before anesthesia.

Intraoperative pain severity assessment was done on 0 to 10 numerical rating scale (NRS) with 0 and 10 regarded as "no pain" and "worst imaginable pain" [21]. If parturients suffered from visceral pain of NRS>4, intravenous 5  $\mu$ g of sufentanil would be injected after cord clamping and cutting.

Intraoperative sedation was rated by using the Ramsay Sedation Scale [22]: 1, patient anxious and agitated or restless or both; 2, patient co-operative, orientated, and tranquil; 3, drowsiness but can respond to instructions; 4, brisk response; 5, a sluggish response; and 6, no response.

Satisfaction with anesthesia was assessed by using a five-point Likert scale: 1, very dissatisfied; 2, dissatisfied; 3, averagely satisfied; 4, satisfied; and 5, very satisfied. Hypotension, defined as mean arterial pressure (MAP)<60mmHg or >20% decline from the baseline BP, was treated with intravenous 50  $\mu$ g phenylephrine, repeated if needed. Bradycardia was defined as a heart rate (HR)<60 beats/min and was treated by intravenous atropine 0.25 mg if no hypotension was present, and if hypotension was present with bradycardia, then ephedrine 6 mg was given. Intraoperative respiratory depression was defined as respiratory rate less than or equal to 8 breaths/min or SpO2<95% and treated with assisted ventilation.

Timepoint was defined as: T0, before EA; T1, 15 min after EA; T2, fetal delivery; T3, uterus suture; T4, peritoneal closure.

#### Data collection

Data collection included parturients demographics (age, weight, height, and gestational age) and intraoperative measures. NRS pain scores was assessed at T2, T3 and T4. Ramsay Sedation Scale, NIBP and HR were collected at T0, T1, T2, T3 and T4. Any episode of side effects such as hypotension, bradycardia, nausea and vomiting were

recorded. Neonatal Apgar scores were measured at 1 min and 5 min after fetal delivery. Satisfaction with anesthesia was collected at 3 months after hospital discharge via a telephone follow-up. The primary outcomes were NRS, Ramsay Sedation Scale and satisfaction with anesthesia. The secondary outcomes were vital signs, incidence of adverse reactions, and Neonatal Apgar scores.

## Statistical analysis

SPSS 23.0 was used for data statistics in the current study. Side effects were expressed as number (%), and comparisons was expressed by  $\chi^2$  test. Baseline characteristics, vital signs and operative characteristics were expressed as mean±standard deviation (x±SD) and analyzed using independent sample t test. The remaining measures were expressed as x±SD and analyzed using Mann-Whitney U test. *P*<0.05 was considered statistically significant.

# Results

Ninety-two parturients who were scheduled for elective caesarean section under EA were randomized to receive either epidural 90 mg ropivacaine with 0.5  $\mu$ g/kg dexmedetomidine or 90 mg ropivacaine alone, and all parturients successfully completed the study (Fig. 1). Demographics of parturients and intraoperative characteristics are outlined in Table 1. The demographic data, initial vital signs, intraoperative measures were similar between two groups. The NRS were significantly lower in Group RD compared to the Group R at T2, T3, and T4 (Table 1).

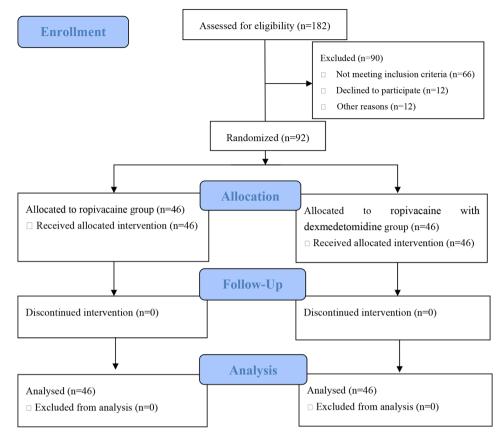
Sedation score between Group R and Group RD was similar at T0 (P>0.05) while it was significantly higher in Group RD than that in Group R at T1, T2, T3 and T4 (P<0.001). No parturient has experienced sedation score of 4 and above (Table 2).

There was no significant difference between Group R and Group RD regarding any intraoperative side effect and Apgar scores at 1-5 min after fetal delivery. The overall satisfaction with anesthesia was comparable between two groups (Table 3).

There was no significant difference in SBP, DBP, and MAP between the two groups at the observed timepoint. HR of the two groups was comparable except at T4 (6.5 [95% CI, 0.7 to 12.3]; P<0.001). (Fig. 2)

# Discussion

In this prospective, randomized, double-blind, placebocontrolled study, we observed that adding 0.5  $\mu$ g/kg dexmedetomidine to ropivacaine for epidural anesthesia in parturients improved intraoperative analgesia significantly. Additionally, it enhanced the sedation level of parturients without inducing excessive sedation or other side effects. However, despite these benefits of epidural



# Fig. 1 Flow diagram of study

Table 1 Baseline characteristic	s and intraoperative characteristics
---------------------------------	--------------------------------------

	Group R ( <i>n</i> = 46)	Group RD (n=46)	F/Z	<i>p</i> -value
			F	
Average age (years)	$30.5 \pm 3.7$	29.8±3.3	0.338	0.563
Weight (kg)	67.6±8.4	69.2±9.4	0.188	0.665
Height (cm)	159.4±5.8	$158.4 \pm 5.0$	1.659	0.201
Gestation(weeks)	38.6±1.0	$39.0 \pm 1.1$	0.003	0.956
Initial vital signs				
Systolic BP (mmHg)	115.7±10.3	$117.6 \pm 10.0$	0.360	0.550
Diastolic BP (mmHg)	72.7±9.4	72.6±7.8	2.694	0.104
Heart rate (beats/min)	$84.5 \pm 13.4$	85.8±13.1	0.005	0.941
Intraoperative measures				
Length of surgery (min)	$37.5 \pm 6.3$	39.3±6.8	0.216	0.643
Blood loss (ml)	$251.0 \pm 61.5$	$281.5 \pm 62.7$	0.124	0.725
Urine volume (ml)	81.3±51.5	$104.1 \pm 78.5$	3.115	0.081
			Z	
Intraoperative pain (NRS)				
T2	$1.96 \pm 1.69$	$0.96 \pm 1.40$	-3.017	0.003
Т3	$1.20 \pm 1.39$	$0.20 \pm 0.62$	-4.559	< 0.001
T4	$1.43 \pm 1.47$	$0.43 \pm 1.00$	-3.973	< 0.001
Sufentanil consumption (µg)	$0.43 \pm 1.42$	0.11 ± 0.737	-1.372	0.170

Data are expressed as mean  $\pm$  SD; statistical analysis was conducted using independent-samples t test or Mann-Whitney U test; Group R, ropivacaine group; Group RD, ropivacaine with dexmedetomidine group; BP, blood pressure; T2, fetal delivery; T3, uterus suture; T4, peritoneal closure; p<0.05 was considered statistically significant

 Table 2
 Comparison of intraoperative Ramsay Sedation Scale

 between the two groups
 Figure 1

	Group R ( <i>n</i> = 46)	Group RD ( <i>n</i> = 46)	Z	<i>p</i> -value
TO	$2.00 \pm 0.00$	$2.02 \pm 0.15$	-1.000	0.317
T1	$2.09 \pm 0.29$	$2.78 \pm 0.51$	-6.309	< 0.001
T2	$1.93 \pm 0.25$	$2.26 \pm 0.54$	-3.590	< 0.001
Т3	$1.98 \pm 0.15$	$2.57 \pm 0.24$	-5.839	< 0.001
T4	$1.96 \pm 0.21$	$2.65 \pm 0.57$	-6.309	< 0.001

Data are expressed as mean±SD; statistical analysis was conducted using Mann-Whitney U test; Group R, ropivacaine group; Group RD, ropivacaine with dexmedetomidine group; TO, before anesthesia; T1, 15 min after EA; T2, fetal delivery; T3, uterus suture; T4, peritoneal closure. Ramsay Sedation Scale: 1, patient anxious and agitated or restless or both; 2, patient co-operative, orientated, and tranquil; 3, drowsiness but can respond to instructions; 4, brisk response; 5, a sluggish response; and 6, no response. p < 0.05 was considered statistically significant

dexmedetomidine, overall satisfaction with anesthesia did not show a significant improvement.

Anesthesia plays an important role in surgery. Good anesthetic practice is composed of adequate analgesia, appropriate sedation, satisfying surgical requirements and rare side effect, thus contributes to good patient satisfaction. Nowadays, most cesarean sections are conducted under neuraxial anesthesia of which EA is one of the most popular anesthesia techniques, due to it's simple, well controllable and cost effective [23]. However, many parturients (around 45-90%) didn't get completely analgesia and high comfort during surgery as a possible consequence of incomplete blockade of large nerve roots such as L5, S1 and S2 [5], which may result in serious visceral pain when surgeon's handling intraperitoneal organs or uterine contraction [6]. Besides, unlike other surgeries, there exists contradiction between sedation and good mother-baby contact in obstetric settings [15], thus parturient requires more suitable sedation level.

Previous studies have investigated the effect of applying a low dose of opioids (such as fentanyl) added to local anesthetics for neuraxial anesthesia, to enhance the neural block [24, 25]. Although anesthetic effect was improved, neuraxial opioids can also lead to serious side effects [7, 8], and parturients still didn't benefit from appropriate sedation. Neuraxial dexmedetomidine mediates sedative, anxiolytic, analgesic and sympatholytic effect via central and peripheral  $\alpha$ 2-adrenergic receptor

Table 3 Comparison of side effects, Apgar scores, and satisfaction with anesthesia between the two groups

	Group R	Group RD	χ <sup>2</sup> /Ζ	<i>p</i> -value
	( <i>n</i> = 46)	( <i>n</i> = 46)		
Hypotension, n (%)	15(32.6)	19(41.3)	0.756	0.388
Bradycardia, n (%)	7(15.2)	6(13.0)	0.090	0.765
nausea or vomiting, n (%)	14(30.4)	9(19.6)	1.449	0.229
1 min Apgar scores, mean $\pm$ SD	9.78±0.417	$9.70 \pm 0.511$	-0.769	0.442
5 min Apgar scores, mean $\pm$ SD	$10.00 \pm 0.000$	$10.00 \pm 0.000$	0.000	1.000
Satisfaction, mean $\pm$ SD	4.68±0.702	4.82±0.476	-0.628	0.530

Data are expressed as a number (%) or mean  $\pm$  SD; statistical analysis was conducted using  $\chi$ 2 Test or Mann-Whitney U test; Satisfaction with anesthesia was assessed by using a five-point Likert scale: 1, very dissatisfied; 2, dissatisfied; 3, averagely satisfied; 4, satisfied; and 5, very satisfied; p<0.05 was considered statistically significant

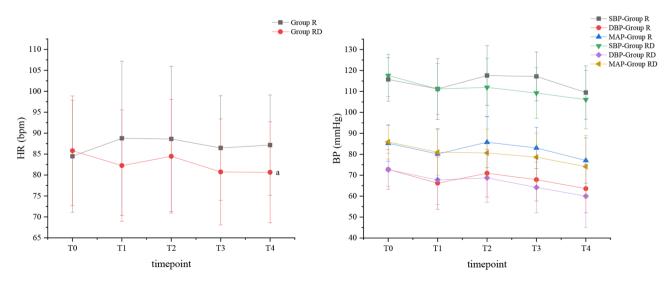


Fig. 2 BP and HR between the two groups over study timepoints; Data are expressed as mean  $\pm$  SD; BP, blood pressure; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; a p < 0.05 compared with Group R

[18, 26], which may fits well the good anesthetic practice requirements as adjuvant drug to local anesthetic in cesarean section under EA.

The NRS is a common tool for the evaluation of the patient's subjective feeling of the present pain intensity [21]. Dexmedetomidine epidural anesthesia could regulate the synthesis and release of catecholamines, reduce oxidative stress and attenuate inflammation which could alleviate pain [18, 27-30]. Yang et al. [31] investigated the effectiveness and safety of epidural injection of 0.75% ropivacaine (12 ml) and morphine (2 mg) combined with dexmedetomidine (0.5  $\mu$ g/kg) for cesarean surgery. They found that NRS scores of visceral pain during operation were lower in group with dexmedetomidine than that without it. In our study, epidural ropivacaine with dexmedetomidine was more effective against intraoperative pain than ropivacaine alone (P < 0.05), which may be attributable to the aforementioned mechanism. Although the result was statistically significant, as small as a 1.0 difference in NRS pain score may not indicate a clinically meaningful difference [32]. In addition, supplemental analgesia of sufentanil was comparable between two groups at the present study, which was different from the report of Salem, and Moustafa et al. [33] who investigated the analgesic effect of epidural dexmedetomidine by adding 0.5 µg/kg dexmedetomidine to epidural bupivacaine and fentanyl in parturients undergoing elective cesarean section using combined spinal-epidural anesthesia for less additional intraoperative fentanyl consumption was found in the group of dexmedetomidine. This discrepancy could be due to fentanyl administered together with dexmedetomidine, for they can act synergistically to analgesic effect [33]. It is still not clear the analgesic effect, regarding pain NRS and requirement for supplemental analgesia, of a higher dose of epidural dexmedetomidine on parturients undergoing cesarean section.

When parturients undergo cesarean section under EA, they can stay awake, achieve early family contact and early food intake, which maintain the popularity of this anesthesia techniques [10]. However, the benefits mentioned above do come at a cost. The surgery procedure could easily result in parturients psychological stress which can further progress to anxiety and hyperalgesic responses [10, 34]. Patient satisfaction with sedation has been investigated widely and is generally very high [35, 36]. Therefore, it is very important to offer sedation in obstetric anesthesia. However, of equal importance is the maternal-neonatal contact immediately after birth, which can be affected by deep sedation. Thus, moderate or conscious sedation is more appropriate, let alone it's much more cost efficient and safer than deep sedation. Dexmedetomidine acts through eliminating the inhibitory effect of the locus coeruleus on basal forebrain y -amino butyric acid to produce sedative and hypnotic effects,

from which patients are easily aroused [37]. At present study, the sedation level of parturients with dexmedetomidine was significantly higher than those without it. Gratifyingly, no parturient was experiencing sedation level of score  $\geq 4$  at the time of fetus delivery due to conscious sedation of dexmedetomidine which guaranteed the mother-baby bonding.

Satisfaction is a multidimensional concept, with influencing factors spanning physiological, psychological, and social aspects. Maternal satisfaction is associated with factors such as pain, sedation, and occurrence of adverse reactions [38, 39]. In our study, although dexmedetomidine significantly reduced maternal pain scores, as previously mentioned, a 1.0 difference in NRS pain score may not necessarily hold clinical significance, thus the alleviation of pain may have limited impact on satisfaction. Furthermore, dexmedetomidine improved maternal sedation levels, yet none of the parturients experienced excessive sedation in this study; therefore, the dexmedetomidine used did not adversely affect maternal-infant contact, making the sedative effect negligible in influencing satisfaction. Additionally, the occurrence rates of adverse reactions were similar between the two groups of parturients. These factors may explain the close similarity in satisfaction between the two groups of parturients.

It needs to be noted the potential hypotension and bradycardia associated with dexmedetomidine [33, 40]. In our study, although HR in Group RD was only significantly lower compared to Group R at T4, the incidence of hypotension and bradycardia was similar, which indicated the safety of the dexmedetomidine dosage used in our study, compared to a higher dose of dexmedetomidine 1.5 µg/kg that significantly decreased MAP and HR [41]. The relationship between pain and BP is poorly understood [42], While it is widely recognized that pain can raise BP through increasing sympathetic nerve activity. In our study, parturients in both groups experienced a slight decreasing trend of BP over the observational timepoints except for the timepoint of fetal delivery (T2) when the BP of parturients in Group R significantly increased compared to T1 (difference of MAP mean: 5.609 [95% CI, 0.755 to 10.462]; P=0.013). The BP of Group RD was relative stable between T1 and T2 which also demonstrated the analgesic effect of dexmedetomidine from this perspective. We found no differences in Apgar scores between the two groups. This similarity also reflected the safety of epidural dexmedetomidine because of hemodynamic stability on the one hand, and because of its lipophilicity thus it easily retained in the placental tissue and transferred little to the fetus on the other hand [33].

The current study has several limitations. Firstly, some of the data collected was observational rather than based on laboratory indicators, which may have introduced documentation bias. Secondly, we were unable to measure the blood concentration of dexmedetomidine in both maternal and infant subjects due to technological limitations.

# Conclusion

Epidural dexmedetomidine of 0.5  $\mu$ g/kg added slightly extra analgesic effect to ropivacaine in EA for cesarean section. The sedation of 0.5  $\mu$ g/kg epidural dexmedetomidine did not cause mother-baby bonding deficit. Satisfaction with anesthesia wasn't significantly improved by epidural dexmedetomidine of 0.5  $\mu$ g/kg. No additional side effect allows larger dose of epidural dexmedetomidine attempt.

#### Abbreviations

- EA epidural anesthesia GA general anesthesia ASA American Society of Anesthesiologists
- NIBP non-invasive blood pressure
- NRS numerical rating scale
- MAP mean arterial pressure
- HR heart rate

# **Supplementary Information**

The online version contains supplementary material available at https://doi.org/10.1186/s12871-024-02519-4.

Supplementary Material 1 Supplementary Material 2

#### Acknowledgements

Not applicable.

#### Author contributions

M.L. collected, analyzed and interpreted all data and was a major contributor in writing the manuscript. X.C. enrolled the patients and guided informed consent. D.G. conducted statistics and analysis of data, guided paper writing and provided financial and technical support.

#### Funding

This work was supported by Funding Chongqing Science and Technology Bureau (cstc2018jscx-msybx002) and Chongqing Health Bureau (2018GDRC009, 2018 jstg011, 2019jstg003, 2021jstg045).

#### Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

## Declarations

#### Ethics approval and consent to participate

This study was accredited by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University. Participants were well-informed of the study protocol and written informed consent was taken from all the participants present in the study.

#### Consent for publication

Not applicable.

#### **Competing interests**

The authors declare no competing interests.

Received: 22 December 2023 / Accepted: 31 March 2024 Published online: 08 April 2024

#### References

- Siddik-Sayyid S, Zbeidy R. Practice guidelines for obstetric anesthesia. Middle East J Anesthesiol. 2008;19:1291–303.
- 2. Carrie LES. Extradural, spinal or combined block for obstetric surgical anaesthesia. Br J Anaesth. 1991;66(4):528.
- Zhou M, Liu W, Peng J, Wang Y. Impact of propofol epidural anesthesia on immune function and inflammatory factors in patients undergoing gastric cancer surgery. Am J Transl Res. 2021;13(4):3064–73.
- Xu W, Drzymalski DM, Ai L, Yao H, Liu L, Xiao F. The ED50 and ED95 of prophylactic norepinephrine for preventing Post-spinal Hypotension during Cesarean Delivery under Combined spinal-epidural anesthesia: a prospective dose-finding study. Front Pharmacol. 2021;12(July):1–7.
- Alahuhta S, Kangas-Saarela T, Hollmén AI, Edström HH. Visceral pain during caesarean section under spinal and epidural anaesthesia with bupivacaine. Acta Anaesthesiol Scand. 1990;34(2):95–8.
- Lu Q, Dong CS, Yu JM, Sun H, Sun P, Ma X, et al. The dose response of sufentanil as an adjuvant to ropivacaine in cesarean section for relief from somato-visceral pain under epidural anesthesia in parturients with scarred uterus. Med (United States). 2018;97(38):e12404. 2018/09/22.
- Armstrong S, Fernando R. Side effects and Efficacy of Neuraxial opioids in pregnant patients at delivery: a Comprehensive Review. Drug Saf 2016/02/03. 2016;39(5):381–99.
- Melo H, Basso L, Iftinca M, MacNaughton WK, Hollenberg MD, McKay DM et al. Itch induced by peripheral mu opioid receptors is dependent on TRPV1expressing neurons and alleviated by channel activation. Sci Rep [Internet]. 2018;8(1):1–9. https://doi.org/10.1038/s41598-018-33620-7.
- Avramov MN, White PF. Use of alfentanil and propofol for outpatient monitored anesthesia care: determining the optimal dosing regimen. Anesth Analg. 1997;85(3):566–72.
- 10. Höhener D, Blumenthal S, Borgeat A. Sedation and regional anaesthesia in the adult patient. 2007/12/12. Br J Anaesth. 2008;100:8–16.
- Li T, Ye Q, Wu D, Li J, Yu J. Dose-response studies of Ropivacaine in blood flow of upper extremity after supraclavicular block: a double-blind randomized controlled study. BMC Anesthesiol. 2017;17(1):1–7.
- Saxton A, Fahy K, Rolfe M, Skinner V, Hastie C. Does skin-to-skin contact and breast feeding at birth affect the rate of primary postpartum haemorrhage: Results of a cohort study. Midwifery [Internet]. 2015;31(11):1110–7. https:// www.sciencedirect.com/science/article/pii/S026661381500203X.
- Govoni L, Ricchi A, Molinazzi MT, Galli MC, Putignano A, Artioli G, et al. Breastfeeding pathologies: analysis of prevalence, risk and protective factors. Acta Biomed. 2019;90:56–62.
- Er M, Bergman N, Gc A, Medley N, Moore ER et al. Early skin-to-skin contact formothers and their healthy newborn infants. Cochrane Database of Systematic Reviews. 2016, Issue 11. Art. No.: CD003519. https://doi.org/10.1002/14651858.CD003519.pub4. Cochrane Database Syst Rev [Internet]. 2016;(11). https://www.cochranelibrary.com/cdsr/ doi/10.1002/14651858.CD003519.pub4/epdf/standard.
- Liu S, Peng P, Hu Y, Liu C, Cao X, Yang C, et al. The effectiveness and safety of intravenous dexmedetomidine of different concentrations combined with butorphanol for post-caesarean section analgesia: a randomized controlled trial. Drug Des Devel Ther. 2021;15:689–98.
- Conti G, Ranieri VM, Costa R, Garratt C, Wighton A, Spinazzola G et al. Effects of dexmedetomidine and propofol on patient-ventilator interaction in difficult-to-wean, mechanically ventilated patients: A prospective, open-label, randomised, multicentre study. Crit Care [Internet]. 2016;20(1):1–8. https:// doi.org/10.1186/s13054-016-1386-2.
- LA Via L, Santonocito C, Bartolotta N, Lanzafame B, Morgana A, Continella C, et al. α-2 agonists vs. fentanyl as adjuvants for spinal anesthesia in elective cesarean section: a meta-analysis. Minerva Anestesiol. 2023;89(5):445–54.
- Bi YH, Wu JM, Zhang YZ, Zhang RQ. Effect of different doses of Intrathecal Dexmedetomidine as an adjuvant combined with hyperbaric ropivacaine in patients undergoing Cesarean Section. Front Pharmacol. 2020;11:342.
- Bi YH, Cui XG, Zhang RQ, Song CY, Zhang YZ. Low dose of dexmedetomidine as an adjuvant to bupivacaine in cesarean surgery provides better intraoperative somato-visceral sensory block characteristcs and postoperative analgesia. Oncotarget. 2017;8(38):63587–95.

- Shin DW, Kim Y, Hong B, Yoon SH, Lim CS, Youn S. Effect of fentanyl on nausea and vomiting in cesarean section under spinal anesthesia: a randomized controlled study. J Int Med Res. 2019;47(10):4798–807.
- 21. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Breivik Hals EK et al. Assessment of pain. Br J Anaesth [Internet]. 2008;101(1):17–24. https://doi.org/10.1093/bja/aen103.
- 22. Ramsay MAE, Savege TM, Simpson BRJ, Goodwin R. Controlled sedation with Alphaxalone-Alphadolone. Br Med J. 1974;2(5920):656–9.
- Yang Z, Liu L, Mu J, Guo W, Li S, Jing Y, et al. Local injection of dexamethasone helping to prevent lower back pain after epidural delivery analgesia. Exp Ther Med. 2018;16(4):3389–94.
- 24. Chen XR, Gao T, Zhang Y, Peng MQ. Addition of low-dose sufentanil to ropivacaine for reducing shivering and visceral traction pain during cesarean section. J Int Med Res. 2021/05/27. 2021;49(5):3000605211017000.
- Li G, Xiao Y, Qi X, Wang H, Wang X, Sun J et al. Combination of sufentanil, dexmedetomidine and ropivacaine to improve epidural labor analgesia effect: A randomized controlled trial. Exp Ther Med. 2020/06/17. 2020;20(1):454–60.
- 26. Ma P, Zeng H. Effects of epidural anesthesia combined with dexmedetomidine on blood pressure, sedation, analgesia and serum  $\beta$ -endorphin levels in patients with hip fractures. Am J Transl Res. 2021;13(6):6457–67.
- Zhang X, Wang D, Shi M, Luo Y. Efficacy and safety of Dexmedetomidine as an adjuvant in Epidural Analgesia and Anesthesia: a systematic review and Meta-analysis of Randomized controlled trials. Clin Drug Investig. 2017;(4):343–54.
- Capogna G, Celleno D, Zangrillo A, Costantino P, Foresta S. Addition of clonidine to epidural morphine enhances postoperative analgesia after cesarean delivery. Reg Anesth. 1995/01/01. 1995;20(1):57–61.
- Konakci S, Adanir T, Yilmaz G, Rezanko T. The efficacy and neurotoxicity of dexmedetomidine administered via the epidural route. Eur J Anaesthesiol. 2008;25(5):403–9.
- Schug SA, Saunders D, Kurowski I, Paech MJ. Neuraxial drug administration: A review of treatment options for anaesthesia and analgesia. 2006/10/19. Vol. 20, CNS Drugs. 2006. pp. 917–33.
- Yang Y, Song C, Song C, Li C. Addition of dexmedetomidine to epidural morphine to improve anesthesia and analgesia for cesarean section. Exp Ther Med. 2020;19(3).
- Haskins SC, Tseng A, Zhong H, Mamic M, Cheng SI, Nejim JA et al. Anterior Quadratus Lumborum Block does not provide Superior Pain Control after Hip Arthroscopy: a double-blinded Randomized Controlled Trial. Anesthesiology. 2021;(3):433–41.

- Yousef AA, Salem HA, Moustafa MZ. Effect of mini-dose epidural dexmedetomidine in elective cesarean section using combined spinal–epidural anesthesia: a randomized double-blinded controlled study. J Anesth. 2015/05/27. 2015;29(5):708–14.
- 34. Vambheim SM, Øien RA. Sex differences in fear of pain: item-level analysis of the fear of pain Questionnaire III. J Pain Res. 2017;10:825–31.
- 35. Wu CL, Naqibuddin M, Fleisher LA. Measurement of patient satisfaction as an outcome of regional anesthesia and analgesia: a systematic review. Reg Anesth Pain Med. 2001;26(3):196–208.
- Villeret I, Laffon M, Ferrandière M, Delerue D, Fusciardi J. [Which propofol target concentration for ASA III elderly patients for conscious sedation combined with regional anaesthesia?]. Ann Fr Anesth Reanim [Internet]. 2003;22(3):196–201. https://doi.org/10.1016/s0750-7658(02)00005-9.
- Ge C, Wu X, Gao Z, Xu Z, Hao D, Dong L. Comparison of different anesthesia modalities during percutaneous kyphoplasty of osteoporotic vertebral compression fractures. Sci Rep [Internet]. 2021;11(1):1–7. https://doi.org/10.1038/ s41598-021-90621-9.
- Morgan PJ, Halpern S, Lam-McCulloch J. Comparison of maternal satisfaction between epidural and spinal anesthesia for elective cesarean section. Can J Anesth. 2000;47(10):956–61.
- Botea MO, Lungeanu D, Petrica A, Sandor MI, Huniadi AC, Barsac C et al. Perioperative Analgesia and Patients' Satisfaction in Spinal Anesthesia for Cesarean Section: Fentanyl Versus Morphine. [Internet]. Vol. 12, Journal of Clinical Medicine. Department of Surgery, Faculty of Medicine and Pharmacy, University of Oradea, 410087 Oradea, Romania.; 2023. https://pubmed.ncbi. nlm.nih.gov/37834990.
- Yichen Y, Chengjun S, Chengwei S, Chengwen L. Addition of dexmedetomidine to epidural morphine to improve anesthesia and analgesia for cesarean section. Exp Ther Med. 2020;19(3).
- Singh Bajwa SJ, Bajwa SK, Kaur J, Singh G, Arora V, Gupta S et al. Dexmedetomidine and clonidine in epidural anaesthesia: a comparative evaluation. Indian J Anaesth. 2011;(2):116–21.
- Saccò M, Meschi M, Regolisti G, Detrenis S, Bianchi L, Bertorelli M, et al. The relationship between blood pressure and pain. J Clin Hypertens. 2013;15(8):600–5.

#### **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.