The efficacy and safety of intrathecal dexmedetomidine for parturients undergoing cesarean section: a double-blind randomized controlled trial

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Abstract

Background

The efficacy and safety of spinal anesthesia by intrathecal dexmedetomidine (DEX) for parturients undergoing cesarean section are still lack of evidence. This aim of our study was to evaluate the efficacy and safety of intrathecal DEX for parturients undergoing cesarean section to provide more data evidence for intrathecal applications.

Methods

300 parturients undergoing cesarean section under spinal anesthesia from two centers were randomly assigned into 3 groups : group B: 9.0 mg (1.2 ml) of bupivacaine 0.75% with saline (1 ml) ; group FB: 9.0 mg (1.2 ml) of bupivacaine 0.75% with 20 μg of fentanyl (1 ml) ; group DB : 9.0 mg (1.2 ml) of bupivacaine 0.75% with 5 μg of DEX (1 ml). Intraoperative block characteristics, parturients' postoperative quality of recovery, maternal and neonatal outcomes and the plasma concentration of DEX were measured. All parturients were followed up for 30 days to determine whether nerve injury occurred.

Results

Compared with group B, the duration of sensory block in group FB and group DB were significantly prolonged (108.4 min [95% Confidence Interval (CI) = 104.6-112.3] in group B, and 122.0 min [95% CI = 116.8-127.3] in group FB, 148.2 min [95% CI = 145.3-151.1] in group DB). The overall score of quality recovery in group DB (71.6 [95% CI = 71.0-72.2]) was significantly higher than that in group FB (61.5 [95% CI = 60.8–62.2]) and group B (61.7 [95% CI = 61.0-62.4]). There were no statistically significant among the 3 groups for PH, PaO2, and PaCO2 in the umbilical artery and umbilical vein blood of newborn. The concentration of DEX in umbilical artery and umbilical vein was too low to be detected. The 30-days follow-up of parturients did not show any new onset of back, buttock or leg pain or paresthesia.

Conclusion

DEX is a potential local anesthetics adjuvant and the combination of 5 μg of DEX can exhibit a facilitatory effect when administered intrathecally as part of spinal anesthesia. However, large sample clinical studies to support the safety of intrathecal DEX use in the clinical setting are still needed.

Trial registration :

Chinese Clinical Trail Registry (Registration number # ChiCTR1900022019; Date of Registration on March 20th, 2019).

Background

Spinal anesthesia, with the advantage of easy-operating and avoiding the risk of general anesthesia, including tracheal intubation failure, aspiration and lung infection, has been recommended as the preferred anesthesia for cesarean section [1–3]. However, some disadvantages caused by single spinal anesthesia such us the limited duration of action and insufficient postoperative analgesia, which will lower the maternal postoperative recovery quality, and increasing local anesthetics doses is prone to cause maternal and neonatal adverse events [4, 5]. Therefore, several adjuvants [6, 7] in combination with local anesthetics have gradually been applicated to further improve spinal anesthesia, of which dexmedetomidine (DEX) is a good choice.

DEX, a highly selective α-2 adrenergic receptor agonist, provides sedative, analgesic, anti-sympathetic effects and has no significant effect on respiration [8]. Many clinical trials [9–12] have shown that DEX can be applicated as an auxiliary for spinal anesthesia through enhancing the anesthetic effects, preventing and reducing adverse reactions caused by local anesthetics. However, the existing studies were mostly small sample size, and whether the parturients recovery quality will be improved and whether DEX will adversely affect the fetus are still lack of concentration evidence. Therefore, this study was to evaluate the efficacy and safety of intrathecal DEX for parturients undergoing cesarean section to provide more data evidence for intrachecal applications.

Methods

Study participants

This trial was registered at the China Clinical Trial Registration Center (ChiCTR1900022019) in March 2019 and approved by the Pei County People's Hospital ethics committee (FRY2018-KY6325-01). Written informed consent was obtained from all enrolled participants. This manuscript adheres to the applicable CONSORT guidelines. This study is a two-centers, prospective, double-blind, randomized controlled trial, and the two centers are the Affiliated Hospital of Xuzhou Medical University and Pei County People's Hospital of Jiangsu Province. Patient recruitment and data collection were started in April 2019 and ended in July 2019. The inclusion criteria of our study were: (1) Full-term pregnant women undergoing elective cesarean section under spinal anesthesia; (2) Age: 20 ~ 35 years; (3) ASA physical status II ~ III; The exclusion criteria were: (1) Multiple pregnancies; (2) Cardiovascular disease (e.g., pre-eclampsia and hypertension); (3) Serious hepatic dysfunction (Child-Pugh class C); (4) serious renal dysfunction (undergoing dialysis before surgery); (4) History of alcohol or opioid addiction; (5) Contraindication to spinal anesthesia; (7) Refusing to sign informed consent.

Randomization, blinding and allocation concealment

According to the random number generated by computer, parturients were randomly allocated into 3 equal groups to receive either DEX, or normal saline or fentanyl in combination with bupivacaine. The results of randomization were placed in serially numbered opaque envelopes. Before the start of spinal

anesthesia, an anesthesiologist prepared relevant drugs according to the randomization sequence and the anesthesiologist would not participate in the follow-up, data collection, and analysis.

Study interventions

All parturients included in the study routinely fasted for 6–8 hours before surgery, and none of them received pre-medication. When parturients arrived to the operating room, continuous monitoring for pulse oxygen saturation (SpO2), Heart Rate (HR), Electrocardiogram (ECG), and noninvasive blood pressure (NIBP) was carried out. All parturients were given a supplementation of 3L/min O_2 through the nasal catheter. Then an intravenous 18 G cannula was inserted and patients were preloaded with ringer lactate 10 ml/kg 15–20 min before anesthesia.

Parturients were in the left lateral position when performing the spinal anesthesia. Spinal blocks were performed at the L3-L4 interspace with a 25 G spinal Quincke-tip needle and study drugs were injected slowly within 15 s after the cerebrospinal fluid flowing out. The 3 groups were scheduled to receive drugs as follows: Bupivacaine Group (Group B): 9 mg (1.2 ml) of bupivacaine 0.75%, with 1.0 ml of normal saline. Bupivacaine + fentanyl group: (Group FB): 9 mg (1.2 ml) of bupivacaine 0.75%, with 20 μg of fentanyl in 1.0 ml of normal saline. Bupivacaine + DEX group (Group DB): 9 mg (1.2 ml) of bupivacaine 0.75%, with 5 μg of DEX in 1.0 ml of normal saline. After blockade, patients were turned to supine position immediately. If hypotension (systolic blood pressure (SBP) < 90 mmHg or descending baseline values by 30%) persisted, intravenous 6 mg of ephedrine was administered; If bradycardia (HR < 50 bpm) occurs, intravenous 0.5 mg of atropine was administered. Repeat if necessary. Intraoperative ephedrine and atropine consumption were recorded. Before the end of surgery, all patients underwent PCIA with sufentanil 2 μg/kg + tropisetron 10 mg.

Outcomes

The primary outcome of our study was the duration of sensory block, which was defined as time taken from intrathecal injection to sensory regression to S1 dermatome. The sensory level was tested by pinprick method using a blunt 25 G needle every minute for the first 10 min, then at 5 min until regression to S1 dermatome.

The secondary outcomes of our study were as follows: the onset time of sensory block, which was defined as time taken from intrathecal injection to sensory blockade to T10 dermatome; the onset time of motor block, which was defined as time taken from intrathecal injection to modified Bromage scale (MBS, 0 = no paralysis,1 = inability to raise the leg, 2 = inability to flex the knee, and 3 = inability to flex the ankle) [13] > 1; the duration of motor block, which was defined as time taken from intrathecal injection to MBS = 0; the peak sensory level; the blood gas analysis for PH, PaO2, and PaCO2 of the umbilical artery and umbilical vein blood samples of the newborn, which was performed immediately after collection; the plasma concentration of DEX, which was determined by High-Performance Liquid Chromatography Tandem Mass Spectrometry methods [14]; Apgar scores, which were assessed at 1st and 5th minutes by a pediatrician who was blinded to the study; the hemodynamic parameters of parturient including BP, HR,

which were evaluated at: baseline values (T0), immediately after blockcade (T1), 5 min (T2), 10 min (T3), 15 min (T4) and 20 min (T5) after blockcade. BP and HR at T0 were defined as the average values measured for 3 consecutive times at rest after entering the operating room; the recovery quality of parturients within 24 h after surgery, which was assessed by obstetric quality of recovery-11 score [15] (ObsQoR-11, score from 0–10 in each term, where 0 = strongly agree and 10 = strongly disagree, the higher of the score, the higher of recovery quality), which is designed for parturients and presented by Ciechanowicz S; intraoperative and postoperative adverse reactions including nausea, vomiting and shivering, time to the first analgesic request; total sufentanil comsumption at 24 h after surgery. Parturients were contacted by telephone for a post-operative 30 days following discharge to determine whether nerve injury occurred, including new neurological impairment of lower limbs and buttocks. All of these measurements were done by an anesthesiologist who was not involved in any other aspect of the study.

Statistical analysis

The sample size was calculated using PASS 15.0 software. Based on our pre-test results, the average duration of sensory block was 107.7 ± 27.4 min for group B, 120.3 ± 31.5 min for group FB, 131.30 ± 29.71 min for group DB. With significance set at 0.05 and power set at 80%, the sample size required to detect differences was 42 patients in each group. Considering a loss-to-follow-up rate of about 15%, 48 patients are required for each group.

Statistical analysis was performed using IBM SPSS 22.0 software. Numeric variables were analysed for normality by the Kolmogorov-Smirnov test. Normally distributed continuous variables are expressed as mean with a standard deviation and compared using ANOVA with post hoc analysis using Bonferroni test. The categorical variables were presented as number (%) and compared using Chi-square test and Fischer exact test. The time to first analgesic request results were calculated with the Kaplan-Meier analysis, with differences between groups compared by the log-rank test. Results of hemodynamic characteristics were compared by repetitive measurement deviation analysis. $P < 0.05$ was considered statistically significant.

Results

Between April 1st and July 30th in 2019, 342 pregnant women at two centers were screened for study participation. Of these, 18 women did not meet the inclusion criteria, 20 women refused to participate, and 4 women were excluded for other reasons (Fig. 1). Finally, 300 patients were randomly 1:1:1 divided into group B (n = 100), group FB (n = 100) and group DB (n = 100). During the study period, all patients completed the assessment and received postoperative follow-up for 30 days.

The 3 groups were comparable with regard to baseline variables include age, height, weight, BMI, ASA physical status, gestational age. There were also no significant differences in perioperative variables include spinal-to-delivery time, peak sensory level, duration of surgery, intraoperative fluid volume and blood loss (Table 1).

Table 1
Baseline and perioperative characteristics of parturients.

Characteristic	Group B (n = 100)	Group FB (n = 100)	Group DB (n = 100)	*P*-Value
Age (y)	27 (26–29)	27 (25–30)	27 (25–29)	0.244
Height (cm)	161.5 (159.0-164.0)	162.0 (159.0-165.0)	160 (159.0-164.0)	0.284
Weight (kg)	72.3±6.2	72.8±5.3	72.6±5.3	0.771
BMI (kg/m^2)	27.6±2.5	27.6±2.2	27.8±2.3	0.865
ASA				0.394
II	78 (78)	74 (74)	82 (82)	
III	22 (22)	26 (26)	18 (18)	
Gestational week (Wk.)	39 (38–39)	39 (38–39)	39 (38–39)	0.379
Spinal-to-delivery time (min)	4.0 (4.0–5.0)	4.0 (4.0–5.0)	4.0 (4.0–5.0)	0.969
Peak sensory level				0.846
T2	2 (2)	1 (1)	1 (1)	
T4	37 (37)	36 (36)	42 (42)	
T6	61 (61)	63 (63)	57 (57)	
Surgery duration (min)	41.0 (38.0–44.0)	41.0 (39.0–44.0)	41.0 (39.0–44.0)	0.746
Intraoperative fluid volume (ml)	1351.1 ± 115.4	1361.6 ± 97.8	1356.5 ± 98.7	0.775
Intraoperative blood loss (ml)	421.2 ± 36.0	424.5 ± 30.5	423.1 ± 30.7	0.773

Notes: Data are presented as n (%) or mean±SD or median (range); There were no significant differences among the three groups (P>0.05). Group B = bupivacaine group; Group FB = bupivacaine and fentanyl group; Group DB = bupivacaine and dexmedetomidine group.

Abbreviations: ASA= American Society of Anesthesiologists; BMI= Body Mass Index.

Compared with group B, the duration of sensory block in group FB and group DB were prolonged (108.4 min [95% Confidence Interval (CI) = 104.6-112.3] in group B, and 122.0 min [95% CI = 116.8-127.3] in group FB, 148.2 min [95% CI = 145.3-151.1] in group DB) with statistical significance ($P < 0.001$) (Fig. 2a). The duration of sensory block was significantly longer in group DB as compared with group FB ($P < 0.001$). Compared with group B, the onset time of sensory block (Fig. 2b) in group DB was significantly shorter (12.2 s [95% CI = 12.0-12.4]) in group DB, 14.5 s [95% CI = 14.0-15.1] in group B, $P < 0.001$). Besides, compared with group B and group FB (Fig. 2c), the onset time of motor block in group DB

was statistically shorter (2.9 min [95% CI = 2.7-3.0] in group DB, 3.1 min [95% CI = 3.0-3.3] in group FB, 3.4 min [95% CI = 3.2–3.6], in group B, $P < 0.001$). However, compared with group B (147.5 min [95% CI = 143.7-151.3]), the duration of motor block (Fig. 2d) in group DB (190.3 min [95% CI = 186.9-193.8]) was prolonged by 43 min ($P < 0.001$), while that in group FB (154.9 min [95% CI = 150.0-160.0]) was prolonged by 7 min($P = 0.038$).

There were 11 items in ObsQoR-11 score Table (Table 2) to evaluate the quality of postoperative recovery. The overall score of group DB (71.6 [95% CI = 71.0-72.2]) was higher than that of group FB (61.5 [95% CI = 60.8–62.2], $P < 0.001$) and group B (61.7 [95% CI = 61.0-62.4], $P < 0.001$). All items showed recovery quality of group DB was significantly better than that of group B, except in terms of feeling dizzy ($P > 0.05$). Moreover, the ObsQoR-11 score results showed no statistical difference between group B and group FB.

Table 2
ObsQoR-11 of parturients.

Characteristic	Group B (n = 100)	Group FB (n = 100)	Group DB (n = 100)	*P*-Value
Moderate pain	3.6 ± 1.1	5.6 ± 0.9*	7.3 ± 1.2*#	< 0.001
Severe pain	4.4 ± 1.2	5.0 ± 2.1*	7.5 ± 1.6*#	< 0.001
Nausea or vomiting	5.2 ± 1.0	6.0 ± 0.9*	7.3 ± 1.2*#	< 0.001
Feeling dizzy	6.3 ± 1.2	5.0 ± 0.8*	6.3 ± 1.1#	< 0.001
Shivering	3.7 ± 0.8	5.3 ± 0.7*	7.2 ± 1.0*#	< 0.001
Have been comfortable	6.4 ± 1.0	6.4 ± 0.6	7.4 ± 1.8*#	< 0.001
Able to mobilize independently	6.0 ± 1.9	6.9 ± 1.5*	6.9 ± 1.1*	< 0.001
Can hold baby without assistance	6.9 ± 0.8	8.2 ± 0.7*	8.1 ± 0.8*	< 0.001
Can feed/nurse baby without assistance	6.6 ± 0.7	7.0 ± 1.0*	7.1 ± 0.7*	< 0.001
Can look after personal hygiene/toilet	5.6 ± 0.9	6.3 ± 0.6*	6.5 ± 0.9*	< 0.001
Feeling in control	7.0 ± 0.8	7.3 ± 1.0*	8.0 ± 0.8*#	< 0.001
Total	61.7 ± 3.3	61.5 ± 3.6	71.6 ± 3.1*#	< 0.001

Notes: Data are presented as mean±SD; Group B = bupivacaine group; Group FB = bupivacaine and fentanyl group; Group DB = bupivacaine and dexmedetomidine group; 0-10 in each term, where 0 = strongly agree and 10 = strongly disagree.

* *P*<0.017 Group DB or Group FB vs Group B; # *P*<0.017 Group DB vs Group FB.

Kaplan-Meier curve (Fig. 3) showed that time to first analgesic request in group DB was longer than that in group FB and group B. The log-rank tests demonstrated that time to first analgesic request in group DB was longer ($P < 0.017$) compared with group FB and in group FB compared with group B ($P < 0.017$). However, the sufentanil dosage within postoperative 24 h was not statistically different among 3 groups ($P = 0.681$).

The maternal hemodynamic characteristics including HR and mean arterial pressure (MAP) were found significantly higher in group DB than that in group B (Fig. 4). The incidence of shivering (Table 3) was

statistically lowered in group DB (3%) compared with group FB (18%) and group B (35%). The incidence of hypotension in group DB (33%) was higher than that in group FB (25%) and group B (28%) but with no statistical difference. There was no statistical difference for the dosage of ephedrine and atropine, intra-operative or post-operative nausea and vomiting among 3 groups.

Table 3
Maternal outcomes

Characteristic	Group B (n = 100)	Group FB (n = 100)	Group DB (n = 100)	*P*-Value
Shivering (%)	35 (35)	18 (82) *	3 (97) *#	< 0.001
Hypotension (%)	28 (28)	25 (25)	33 (33)	0.450
Dose of ephedrine (mg)	2.8±3.9	2.1±3.6	1.5±3.0	0.029
Nausea and/or vomiting (%)	11 (11)	17 (17)	14 (14)	0.474
SufentanII consumption (μg)	106.0±9.2	105.5±7.7	105.0±7.8	0.681

Notes: Data are presented as n (%) or mean±SD; Group B = bupivacaine group; Group FB = bupivacaine and fentanyl group; Group DB = bupivacaine and dexmedetomidine group.

* *P*<0.017 Group DB or Group FB vs Group B; # *P*<0.017 Group DB vs Group FB.

For PH, PaO2, and PaCO2 in the umbilical artery and umbilical vein blood of newborn (Table 4), there were no statistically significant among the 3 groups. The concentration of DEX in umbilical artery and umbilical vein was too low to be detected by High-Performance Liquid Chromatography Tandem Mass Spectrometry. The mean values of Apgar scores at 1 and 5 min were all beyond 8, which also showed no statistical significance. Moreover, the 30-days follow-up did not show any new onset of back, buttock or leg pain or paresthesia.

Table 4
Neonatal outcomes.

Characteristic	Group B (n = 100)	Group FB (n = 100)	Group DB (n = 100)	*P*-Value
Umbilical artery				
pH	7.3 ± 0.3	7.3 ± 0.2	7.3 ± 0.4	0.581
PaO2 (mmHg)	15.6 ± 2.0	15.0 ± 2.3	15.4 ± 2.4	0.217
PaCO2 (mmHg)	49.9 ± 3.4	49.8 ± 4.0	50.4 ± 4.6	0.545
Umbilical vein				
pH	7.4 ± 0.2	7.4 ± 0.1	7.4 ± 0.5	0.711
PaO2 (mmHg)	30.0 ± 3.4	30.7 ± 4.4	30.80 ± 3.5	0.277
PaCO2 (mmHg)	42.6 ± 3.2	41.6 ± 3.8	42.0 ± 3.2	0.111
Neonatal Apgar score				
1 min	8.7 ± 0.5	8.7 ± 0.5	8.7 ± 0.5	0.752
5 min	9.7 ± 0.5	9.7 ± 0.4	9.7 ± 0.5	0.809

Notes: Data are presented as mean±SD; Group B = bupivacaine group; Group FB = bupivacaine and fentanyl group; Group DB = bupivacaine and dexmedetomidine group.

* *P*<0.017 Group DB or Group FB vs Group B; # *P*<0.017 Group DB vs Group FB.

Discussion

Our results showed that compared with 9 mg of bupivacaine alone, the combination of 9 mg of intrathecal bupivacaine with 5 μg of DEX for the cesarean section significantly prolonged the duration of sensory block and the time to first analgesic request, shortened the onset time of sensory and motor block, reduced the incidence of maternal shivering, improved recovery quality of paturients, and caused no adverse effects on newborns or no neurological impairment on parturients in the short term.

Spinal anesthesia, which is block-well, easy to operate, not as complicated as epidural anesthesia [16], and avoiding the risk of general anesthesia, has become the preferred anesthesia type for cesarean section. However, in clinical practice, single spinal anesthesia is often not sufficient to inhibit visceral pain and causes maternal discomfort during the surgery and insufficient postoperative analgesia, which affect parturients' postoperative recovery quality [5]. Increasing the doses of local anesthetics to prolong the analgesic time can cause adverse effects such as central nervous system problems and cardiotoxicity. In our study, compared with intrathecal 9 mg of bupivacaine alone, the onset time of sensory and motor block of parturients in combination of 9 mg of intrathecal bupivacaine with 5 μg of DEX was significantly shortened, and the duration of sensory block was significantly prolonged by 40 minutes, which is consistent with the research results of Suthar's [17] and Sushruta's [18]. The mechanism may be as follows:

in the spinal cord, DEX can activate α-2 adrenergic receptor in the dorsal horn neurons, activate the spinal cord intermediate neurons by reducing the neurotransmitter released by the primary afferent end and G-protein-mediated potassium channel, and make the spinal cord intermediate neurons hyperpolarized, thus reducing the pain transmission. In addition, DEX can also block the internal flow of Na + and enhance the blocking effect of local anesthetics on the sodium channel of the cell membrane [19, 20]. However, consisted with the results of a meta-analysis [21] that included 9 RCTs, our study found that motor block duration of paturients in combination of 9 mg of intrathecal bupivacaine with 5 μg of DEX was significantly prolonged, which may suggest that combination with DEX may increase the risk of falls and cause the delay of parturients' early rehabilitation.

Currently, the commonly used postoperative recovery quality scales were QoR-40 [22] and QoR-15 [23]. However, both of them are developed and verified in non-obstetric patients and day surgery population [24], so there are many items unrelated to cesarean section, and lack of critical elements to evaluate postoperative recovery after delivery, such as the ability to care for newborns [15]. The ObsQoR-11 table proposed by Ciechanowicz S. proved to be reliable, clinically acceptable, and feasible, is effective in patients undergoing elective and emergency cesarean section [15, 25]. In this study, all questionnaire feedback had been received and the results showed that scores in group DB was higher than in both group FB and group B ($P < 0.017$), suggesting that parturients in combination with 5 ug of DEX have a better recovery quality.

The incidence of shivering was statistically lowered in group DB, which is consistent with Miao's [11] study results. According to the results of meta-analysis by Miao, DEX can significantly reduce the incidence of shivering in parturients (relative risk (RR) = 0.40; 95% CI = 0.26–0.62; $P < 0.001$) among 360 women underwent cesarean section with spinal anesthesia. The mechanism of anti-shivering effect of DEX can be inferred that DEX can reduce central thermos-sensitivity by weakening the electrical conductivity of neurons through mediating the α-2 adrenergic receptors in the brain and spinal cord [26, 27]. Hypotension is the common side effect of DEX, but the results of our study found that there were only 33 parturients suffered hypotension in the group DB, although more than patients in group B, the difference was not statistically significant. This may be due to the low dose of intrathecal DEX use.

Compared with group FB, both the onset time of sensory and motor block in group DB were shorter, the duration of sensory and motor block was prolonged, and ObsQoR-11 score was higher, suggesting that the intrathecal 5 μg of DEX was more effective than 20 μg of fentanyl, which may have a better clinical application prospect.

As DEX is applied intrathecally during cesarean section, what we are worried about were the neurological complications and whether DEX affects the fetus. In our study, 300 patients were followed up for 30 days postoperatively, and none of them showed neurological complications of lower limbs and buttocks, proving that intrathecal DEX would not lead to nerve injury in the short term. Ozdamar [28] injected 10 rats with DEX 10 μg through the subarachnoid path and extracted spinal medulla for histological and electron microscopy examination after 7 days, and the results showed that compared with saline group, no signs

of neuronal or axonal injury, gliosis, or myelin sheath damage was found. PH, PaO2, and PaCO2 values of umbilical artery and umbilical vein of newborns in 3 groups were within the normal range and showed no statistical difference. Neonates' Apgar scores at 1 min and 5 min were all beyond 8, and comparisons between groups were not statistically different, and concentration of DEX in umbilical artery and umbilical vein in neonates was too low to be detected, which all suggested that intrathecal 5 μg of DEX could not cause damage on neonates. Li et al. [29] showed similar results, which further confirmed our conclusion.

However, our study also has some limitations. Firstly, the inclusion criteria exclude the parturients over 35 years old, so the external authenticity of the conclusion in our research needs to be further proved. Secondly, we did not investigate the dose-response reaction of DEX via the intrathecal path, and the optimal clinical dose was not determined. Furthermore, the postoperative follow-up period in this study was only 30 days, so it is unknown whether patients had delayed adverse neuron reactions.

Conclusion

DEX is a potential local anesthetics adjuvant and the combination of 5 μg of DEX can exhibit a facilitatory effect when administered intrathecally as part of spinal anaesthesia. However, large sample clinical studies to support the safety of intrathecal DEX use in the clinical setting are still needed.

Abbreviations

DEX: Dexmedetomidine; CI: Confidence Interval; SpO2: Pulse Oxygen Saturation; HR: Heart Rate; ECG: Electrocardiogram; NIBP: Noninvasive Blood Pressure; SBP: Systolic Blood Pressure; MBS: Modified Bromage scale; ObsQoR-11: Obstetric Quality of Recovery-11 Score; MAP: Mean Arterial Pressure; RR: Relative Risk; ASA = American Society of Anesthesiologists; BMI = Body Mass Index.

Declarations

Acknowledgments

Not applicable.

Authors' contributions

LXX contributed to study design, interpretation of data, and drafted the manuscript. LS contributed to study design, and interpretation of the data, revised the manuscript, and approved the final version. LYM was primarily responsible for the processing and analysis of blood samples. LXL contributed to analysis, and approved the final version. WXH was responsible for the follow up. All authors have read and approved the final manuscript.

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Availability of data and materials

The datasets generated and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This two-centers, prospective, double-blind, randomized controlled trial was approved by the Pei County People’s Hospital ethics committee (FRY2018-KY6325-01). Written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The author reports no conflicts of interest in this work.

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Figures

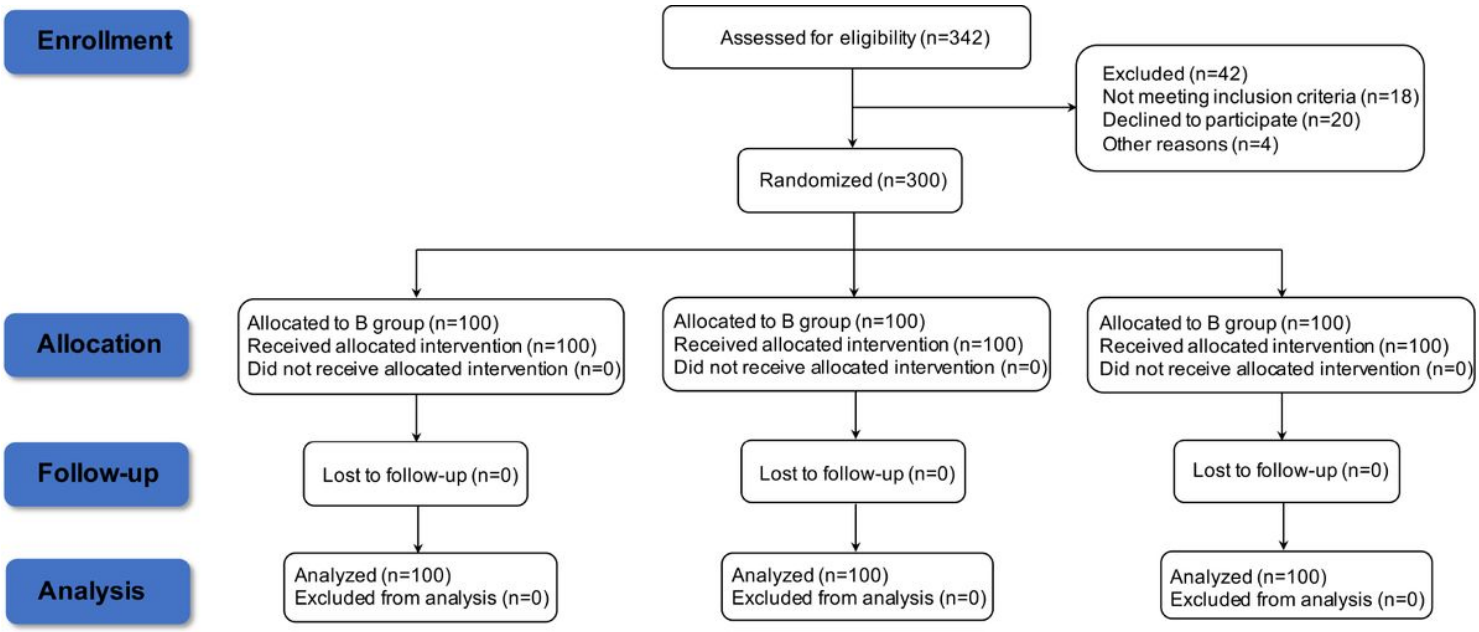

Figure 1

Study population flow diagram

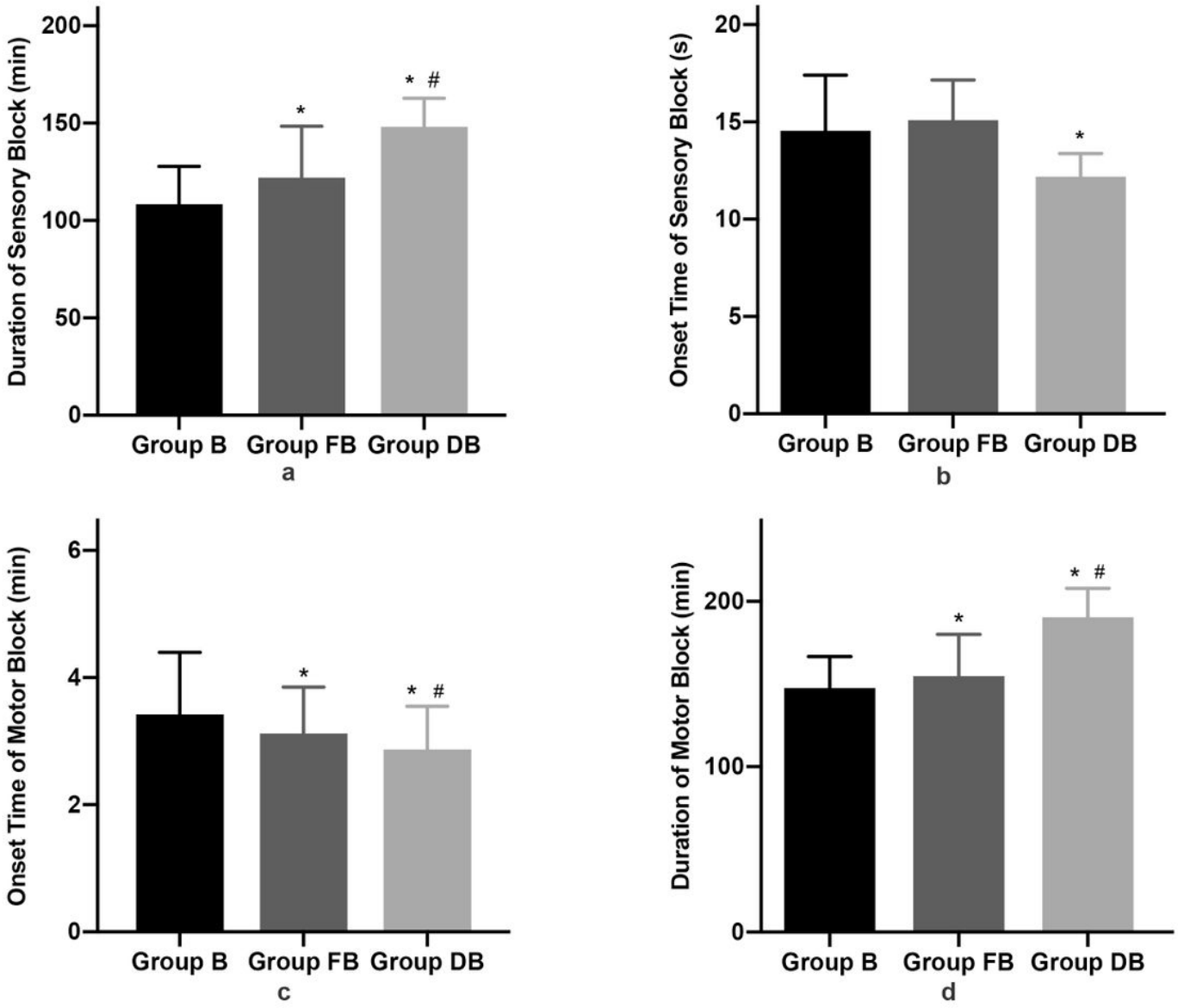

Figure 2

Block characteristics of parturients. Notes: Group B = bupivacaine group; Group FB = bupivacaine and fentanyl group; Group DB = bupivacaine and dexmedetomidine group. * P<0.017 Group DB or Group FB vs Group B; # P<0.017 Group DB vs Group FB

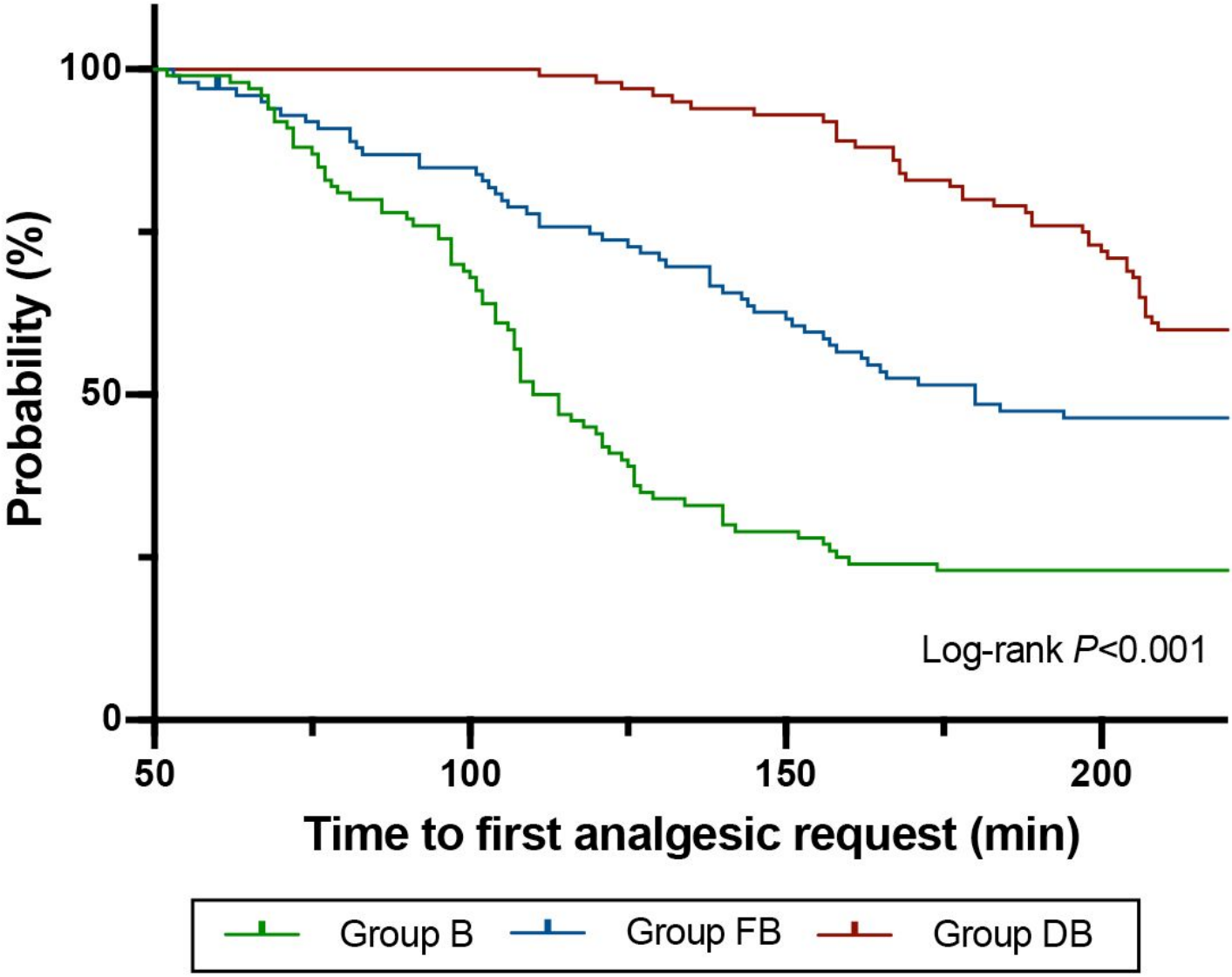

Figure 3

Kaplan-Meier curves for time to first analgesic request. Notes: Group B = bupivacaine group; Group FB = bupivacaine and fentanyl group; Group DB = bupivacaine and dexmedetomidine group

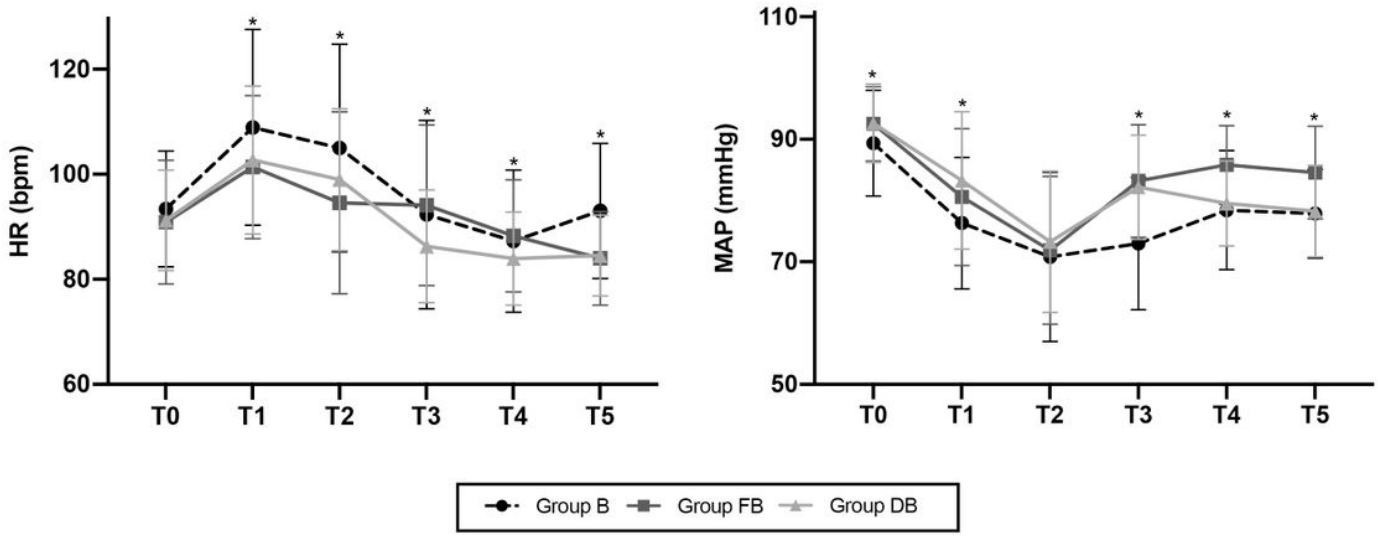

Figure 4

Hemodynamic indices. Notes: Group B = bupivacaine group; Group FB = bupivacaine and fentanyl group; Group DB = bupivacaine and dexmedetomidine group; T0=before spinal anesthesia, T1, T2, T3, T4, T5=0, 5, 10, 15, 20 min after spinal anesthesia. HR=Heart Rate; MAP=Mean Arterial Pressure; * There were significant differences among the three groups (P<0.05)