



## RESEARCH ARTICLE

### INTRATHECAL DEXMEDETOMIDINE VERSUS DEXAMETHASONE FOR PREVENTION OF SHIVERING DURING CAESAREAN SECTION: A RANDOMISED CONTROLLED TRIAL

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#### ARTICLE INFO

##### Article History:

Received 15<sup>th</sup> October, 2021

Received in revised form

14<sup>th</sup> November, 2021

Accepted 19<sup>th</sup> December, 2021

Published online 30<sup>th</sup> January, 2022

##### Keywords:

Dexmedetomidine, Dexamethasone, Shivering, Comparative study, Cesarean sections.

#### ABSTRACT

**Background:** Perioperative shivering is one of the most common problems in parturients receiving regional anesthesia during cesarean section. Although shivering is a protective reflex to increase the core temperature by involuntary contraction of muscles, it also leads to adverse effects like increasing oxygen consumption and affecting wound healing. The aim of this work is to compare the efficacy of dexamethasone and dexmedetomidine in prevention of perioperative shivering when added to hyperbaric bupivacaine intrathecally in cesarean sections (CS) and their effect on the intraoperative hemodynamics, intensity of the block, sedation, and postoperative analgesic requirement. **Results:** Study included 60 obstetric patients who were randomized into 2 equal groups, each consisting of 30 patients, namely group A (dexmedetomidine group) and B (dexamethasone group). Group A patients received 5 µg dexmedetomidine with 12.5 mg hyperbaric bupivacaine 0.5% intrathecally. Group B patients received 8 mg dexamethasone then 12.5 mg hyperbaric bupivacaine 0.5% intrathecally. The comparison included assessment of intra- and postoperative hemodynamics, duration of surgery, assessment of sensory and motor block, assessment for shivering and sedation, and assessment of adverse events. This study showed that there were a small number of patients complaining of shivering (five patients in group A and seven patients in group B) with no statistical difference between both groups in the incidence and intensity of shivering. Time to two segment regression (minutes) was longer in group B compared to group A, and also, time to first analgesic rescue was longer in group B compared to group A. For sedation intensity, there was statistical difference between both groups as all patients in group A were sedated compared to six patients only in group B. There was no statistical difference between both groups as regards incidence of adverse effects. **Conclusion:** We concluded that both drugs can be added safely to bupivacaine, and both decreased the incidence and the intensity of shivering. Dexamethasone was found to prolong the duration of sensory block and delay opioid requirements post-operatively, while dexmedetomidine is more effective in sedating the patients intra- and postoperatively.

#### INTRODUCTION

Shivering is one of the common troublesome complications in parturients receiving regional anesthesia, and causes discomfort and dissatisfaction in parturients. It usually interferes with the readings of SpO<sub>2</sub> and ECG. It can likewise expand the need for oxygen and increase production of carbon dioxide about four folds; it also increases the intensity of the pain arising from the wound; it can delay the healing of the wound and can also increase the length of stay in the post anesthesia care unit (PACU) (Nasseri *et al.*, 2017). The thermoregulatory system is usually disrupted by spinal anesthesia (SA) through inhibiting of vasoconstriction which has an important role in the regulation of the temperature. The spinal anesthesia also redistributes the central core heat to the tissues in the periphery. Those two effects lead to hypothermia and shivering (Yanshuai & Shuang, 2017). Dexmedetomidine is a highly selective  $\alpha_2$ -adrenoreceptor agonist that binds to a transmembrane G protein-binding receptor.

The studies done showed that it can be added to local anesthetics in the spinal anesthesia to decrease time needed for the start of the block, decrease the pain severity postoperatively, increase the time of the block, and decrease the analgesic use postoperatively. It decreases the incidence of shivering through increasing vasodilatation and inhibition of central thermoregulation (Zhang *et al.*, 2017). Dexamethasone is known to modify the inflammatory reaction of the body and reduce the gradient between central and peripheral tissue temperatures that is why it has been used as an intravenous medication to decrease shivering. It has also been used to be injected in the cerebrospinal fluid safely and can be given as an adjuvant to local anesthetics to enhance the efficacy of regional anesthesia, so we considered that dexamethasone can be used as an adjuvant to local anesthetics intrathecally to decrease the intensity of shivering (Solphour *et al.*, 2016). The aim of this work is to compare the efficacy of dexamethasone and dexmedetomidine in prevention of perioperative shivering when added to hyperbaric bupivacaine intrathecally in cesarean sections (CS) and their effect on the intraoperative

hemodynamics, intensity of the block, sedation, and postoperative analgesic requirement.

## MATERIALS AND METHODS

Randomized prospective double blinded comparative study was carried out in our hospital after obtaining approval from ethical committee and written informed consent from all participants was obtained. Inclusion criteria ASA II female patients, gestational age > 37 weeks and age from 20 to 40 years who are scheduled for cesarean section under spinal anesthesia

**Exclusion criteria:** Patient refusal, age < 20 or > 40, known allergy to the study medication, patients with coagulopathies or on anticoagulant medications, cerebrovascular insufficiency, neuromuscular diseases, severe preeclampsia, cardiopulmonary disease, hyperthyroidism, diabetic neuropathy, peripheral vascular diseases, renal and hepatic disorders, and patients with psychiatric disorders were excluded from the study. The study included 60 obstetric patients who fulfill all the points in the inclusion and exclusion criteria and were randomized into 2 equal groups, each consisting of 30 patients, namely group A (dexmedetomidine group) and B (dexamethasone group). Group A patients received 5 µg dexmedetomidine with 12.5 mg hyperbaric bupivacaine 0.5% intrathecally. Group B patients received 8 mg dexamethasone with 12.5 mg hyperbaric bupivacaine 0.5% intrathecally. Routine preoperative assessment was done for each patient including routine history taking, clinical examination and routine laboratory investigations. Patients did not receive any premedication. All the patients were preloaded with 10 ml/kg of lactated Ringer's solution through 18 gauge intravenous cannula and monitored with five leads electrocardiography, pulse oximetry and non-invasive blood pressure (NIBP) (which records systolic, diastolic, and mean blood pressure every 5 min intraoperatively and every 15 min in the recovery room, heart rate was recorded at the same intervals). Under complete aseptic technique, local anesthetic in the form of 3 ml of lidocaine 2% was given at the site of spinal injection. Subarachnoid block was administered in the sitting position midline approach with 27 gauge (Quincke needle) at L3–L4/L4–L5 space. For group A, the preservative-free dexmedetomidine 100 µg/ml was loaded into a 100 unit insulin syringe (1 µg/unit) and 5 units was given, after that patients received 2.5 ml (12.5mg) of 0.5% hyperbaric bupivacaine. For group B, dexamethasone 8 mg/2 ml was given intrathecally, after that 2.5 ml (12.5 mg) of 0.5% hyperbaric bupivacaine was given separately. Patients were immediately placed in the supine position after completing the spinal block. The assessment of sensory blockade was performed by pin prick method using a 25 gauge needle at every 2 min until the highest level was achieved, and then every 15 min interval until two segment regression of the block occurs. Motor blockade was assessed at the same time intervals using a modified Bromage scale (Moeen & Moeen, 2017) (0 = no paralysis, 1 = unable to raise extended legs, 2 = unable to flex knee, 3 = unable to flex ankle). Peak sensory level and time to reach this level, time to two segment regression, duration of sensory block, motor block onset (time to reach Bromage 4), duration of motor blockade, and time to first analgesic rescue were recorded. Shivering intensity was assessed with a five-point scale validated by Crossley and Mahajan, where 0 = no shivering, 1 = piloerection or peripheral vasoconstriction but no visible shivering, 2 = muscular activity in only one muscle

group, 3 = muscular activity in more than one muscle group, and 4 = whole body shivering (Nasseri *et al.*, 2017). Shivering incidence and intensity was registered every 15 min during surgery and in the recovery room. Sedation was checked every 15 min during surgery and in the recovery room and quantified as 0 = fully awake; 1 = somnolent; 2 = closed eyes, opens to call; 3 = closed eyes, opens to physical stimuli; and 4 = closed eyes, nonresponsive to painful stimuli (Nasseri *et al.*, 2017). Hypotension is defined as fall in blood pressure of more than 30% of baseline value and was treated with incremental doses of 6 mg IV injection of mephentermine and IV infusion of 250 ml lactated Ringer. Bradycardia is defined as heart rate less than 60 beats per minute and treated with injection of bolus of 0.01–0.02 mg/kg of atropine; duration of surgery was noted; nausea/vomiting was treated with injection ondansetron 4 mg IV.

**Statistical analysis:** The collected data was revised, coded, tabulated, and introduced to a PC using Statistical Package for Social Sciences (SPSS 15.0.1 for windows; SPSS Inc, Chicago, IL, 2001). Data was presented as mean and standard deviation ( $\pm$  SD) for quantitative parametric data and median and interquartile range for quantitative nonparametric data. Frequency and percentage was used for presenting qualitative data. Suitable analysis was done according to the type of data obtained. Student's t test was used to analyze quantitative data while Chi square test and Fisher exact test was used to analyze qualitative data. P value <0.05 was considered statistically significant.

## RESULTS

Sixty obstetric patients who fulfilled all the inclusion criteria were randomized into two equal groups, each consists of 30 patients namely group A (dexmedetomidine group) and group B (dexamethasone group). Demographic data Age, weight, height, and gestational age were recorded for each patient at the beginning of the study and were compared statistically as shown in Table 1.

**Table 1 Demographic data**

	Group A (n=30)	Group B (n=30)	P value
Age (years)	29.2 $\pm$ 2	28.7 $\pm$ 2.7	0.399
Weight (kg)	78.2 $\pm$ 4.7	76.8 $\pm$ 2.4	0.159
Gestational age(weeks)	38.44 $\pm$ 0.45	38.3 $\pm$ 2	0.624
Height	164.38 $\pm$ 4.76	163 $\pm$ 4.43	0.249

Data are presented as mean  $\pm$  SD, ratio of patients p value > 0.05 is considered statistically non-significant. There was no statistical difference between both groups as regards demographic data. Assessment for shivering and sedation. There were a small number of patients complaining of shivering (five patients in group A and seven patients in group B) with no statistical difference between both groups in the incidence and intensity of shivering as shown in Table 2.

**Table 2. Incidence and grade of shivering, grade of sedation**

	Group A	Group B	P value
Incidence of shivering (no. Of patients)	5/30	7/30	0.119
Grade of shivering (0/1/2/3/4) no. of patients	25/2/3/0/0	23/2/3/2/0	0.119
Sedation grade (0/1/2/3/4) no. of patients	0/15/13/2/0	24/6/0/0/0	<0.001

For sedation intensity, there was statistical difference between both groups as all patients in group A were sedated while six patients only in group B as shown in Table 3.

**Table 3. Grade of sedation**

	Group A (n=30)	Group B (n=30)	P Value
0	0	24	<0.001
1	15	6	
2	13	0	
3	12	0	
4	0	0	

Assessment of intra- and postoperative hemodynamics Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), and heart rate (HR) were recorded intraoperatively every 5 min and postoperatively every 15 min, and there was no statistical difference between both groups. Duration of surgery and assessment of sensory and motor block As shown in Table 4, there was no statistical difference between both groups as regards duration of surgery. For peak sensory level and the time to reach this level and also for motor blockade onset and motor block duration, there was no statistical difference between the two groups as shown in Table 4. As regards time to two segment regression (minutes), there was statistical significance as it was longer time in group B ( $96.32 \pm 9.8$ ) compared to ( $76.24 \pm 8.34$ ) group A as shown in Table 4; also, duration of sensory block was longer in group B ( $161.83 \pm 7.00$ ) compared to ( $124.50 \pm 6.72$ ) group A. Also time to first analgesic rescue was statistically significant as it was longer time in group B ( $198.21 \pm 21.22$ ) compared to ( $174.44 \pm 16.3$ ) as shown in Table 4.

**Table 4.**

	Group A (n=30)	Group B (n=30)	P value
Surgery duration ( in min)	41.26±3.57	40.59±3.72	0.016
Peak sensory level	T4(T4-T5)	T4(T4-T5)	0.277
Time to reach peak sensory level (min)	6.5±0.61	6.93±0.32	0.67
Time to two segment regression	76.68±4.62	96.71±3.77	0.001
Duration of sensory block	124.50±6.72	161.83±7.00	0.001
Onset of motor block (time to reach bromage score 4)	6.44±1	6.56±0.38	0.526
Duration of motor block	182.27±10.1	178.89±4.5	0.1
Time to 1st rescue analgesia	174.26±12.1	196.69±5.4	0.001

Assessment of adverse events Most of the patients in both groups complaining of hypotension (blood pressure < 30% of the pre induction value) especially at the first 15 min after spinal anesthesia were treated with incremental doses of 6 mg mephentermine with no statistical difference between both groups. The same for bradycardia, three cases in group A and two cases in group B were treated with atropine sulphate 0.01–0.02 mg/kg with no statistical difference as shown in Table 5. Only two cases complaining of nausea and vomiting in group A and three cases in group B were treated with ondansetron 4 mg IV with no statistical difference.

## DISCUSSION

Perioperative shivering is a frequent complication during caesarean sections under neuraxial anaesthesia which causes increased needs for oxygen and increased release of carbon dioxide and metabolic rate. Shivering causes disruption of the reading of the electrocardiogram, blood pressure, and oximetry.

Moreover, it is an unpleasant experience for the pregnant woman (Varshney *et al.*, 2019). A lot of attempts have been tried to prevent shivering whether pharmacological or non-pharmacological, but a gold standard method has not yet been determined. Dexmedetomidine is highly specific alpha 2 adrenergic receptor agonist, affecting mainly the central nervous system without respiratory depression. Dexmedetomidine was proved to decrease post anesthetic shivering when given intravenously in a dose 0.5 to 1 µg/kg. In contrast to intravenous dexmedetomidine, the effect of intrathecal dexmedetomidine on shivering is not well-known (Rai & Bhutia, 2017); this study hypothesized that intrathecal dexmedetomidine could decrease the incidence and intensity of shivering. Dexamethasone also was used to reduce postoperative shivering and known to be effective; there was no significant difference between the three groups of dexamethasone, pethidine, and normal saline receivers regarding the reduction of shivering in the study done to compare the dexamethasone with pethidine in the control of perioperative shivering during transurethral prostatectomy (Moeen & Moeen, 2017). The aim of this study is to evaluate the efficacy of both dexamethasone and dexmedetomidine in prevention of perioperative shivering when added to hyperbaric bupivacaine intrathecally in cesarean sections and their effect on the intraoperative hemodynamics, intensity of the block, sedation, postoperative pain, and analgesic requirement. Randomized prospective comparative study was carried out at a gynecology and obstetrics hospital after obtaining approval from ethical committee. The study population comprised of 60 patients with ASA physical status II, scheduled for elective caesarean section. As regards results from the current study, hemodynamic data including systolic blood pressure (SBP), diastolic blood pressure (DBP), mean blood pressure (MBP), and heart rate (HR) were statistically insignificant between both groups. As regards the duration of surgery, peak sensory level, time to reach peak sensory level, motor blockade onset, and motor blockade duration, there was no statistical significance between the 2 groups. But as regards the time of 2 segment regression (minutes), it was longer in dexamethasone group ( $96.71 \pm 3.77$ ) compared to ( $76.68 \pm 4.62$ ) in dexmedetomidine group.

This results agreed well with the study which revealed that the addition of intrathecal dexamethasone to bupivacaine for spinal anesthesia in orthopedic surgeries significantly prolong the duration of sensory block and decrease opioid requirements in post-operative management (Bani-Hashem *et al.*, 2011). Another study which studied the effect of lignocaine plus dexamethasone 4 mg compared to lignocaine plus 100 µg epinephrine intrathecally in patients undergoing cesarean sections and revealed that intrathecal dexamethasone increased the sensory block duration and prolonged the duration of analgesia more than epinephrine (Naziri *et al.*, 2010). The same results agreed with the results of the study in which they added dexamethasone (4 mg) to levobupivacaine in parturients receiving combined spinal epidural analgesia for vaginal delivery and concluded that it prolonged the duration of analgesia (Wahdan *et al.*, 2017). Also, this study results agreed with the results of the study in which dexamethasone 5 mg was added to 0.5% hyperbaric bupivacaine in spinal anesthesia for patients undergoing lower abdominal urological and lower limb orthopedic surgeries and revealed that the addition of dexamethasone to bupivacaine in spinal anesthesia significantly improve the duration of sensory block/surgical analgesia as well as postoperative analgesia/pain-free period

without any complications (Haque *et al.*, 2018). It was reported that there is a lower incidence of shivering (2 in 31) following Spinal anaesthesia by heavy bupivacaine 0.5% plus 5 µg intrathecal dexmedetomidine for lower abdominal surgeries compared with (12 of 31) in the control group (Abdelhamid & El-Lakany, 2013). Eighty patients selected for transurethral resection of prostate under spinal anesthesia were divided into 2 groups; one received 12.5mg hyperbaric bupivacaine plus 0.5ml isotonic saline; the other group received 12.5 mg hyperbaric bupivacaine plus 10 µg dexmedetomidine in 0.5ml isotonic saline. The incidence of shivering was significantly lower (15%) in the dexmedetomidine group than the saline group (57%). They concluded that adding 10 µg dexmedetomidine to hyperbaric bupivacaine in the transurethral resection of the prostate procedure could reduce the incidence of shivering; this result agreed with the current study in spite of using higher dose of dexmedetomidine 10 µg (Moawad & Elawdy, 2015). Another study compared the effects of 5 µg intrathecal dexmedetomidine with 100 µg morphine as supplements to 10mg bupivacaine in 120 parturients undergoing elective CS under SA. Only 7.7% of patients in the dexmedetomidine group had shivering, while 30% and 35.9% of patients in the morphine and the bupivacaine groups experienced shivering, respectively. This result is in agreement with our current study (Qi *et al.*, 2016b).

Also, the study compared intrathecal morphine and intrathecal dexmedetomidine in patient undergoing gynecological surgeries under SA, and has shown that dexmedetomidine may be safely used as an intrathecal supplement in cesarean delivery. Respiratory depression is a potential side effect of dexmedetomidine. But this side effect is just reported to occur by using high doses of dexmedetomidine. Intrathecal optimal dose 2.5 or 5 µg dexmedetomidine does not cause respiratory depression, and this dose agrees well with the dose used in our current study (Kurhekar *et al.*, 2016). Another study which used the same dose as our study, 5 µg intrathecal dexmedetomidine, as an adjuvant to hyperbaric bupivacaine in spinal anesthesia for patients undergoing CS concluded that the drug is safe and effective in decreasing the incidence and intensity of shivering using the dose of 5 µg, but 2.5 µg intrathecally did not alleviate shivering (He *et al.*, 2017). The same results agreed with the study which also used 5 µg intrathecal dexmedetomidine in spinal anesthesia in CS and concluded that it significantly reduced the incidence and intensity of shivering without major side effects (Nasseri *et al.*, 2017). Another study compared intrathecal dexmedetomidine and intrathecal magnesium sulfate for the prevention of post spinal anesthesia shivering in uroscopic surgeries, in which 5 µg of dexmedetomidine was used and concluded that both drugs were effective in reducing the incidence of post spinal shivering; 5 patients (14.3%) in dexmedetomidine group, 8 patients (22.8%) in magnesium sulfate group, and 21 patients (60%) in control group developed shivering, and the use of MgSO<sub>4</sub> was recommended as it is more physiologically, more readily available in most operating theater and much less expensive than dexmedetomidine (Omar *et al.*, 2019). The results of our current study showed that dexamethasone 8 mg used intrathecally combined with hyperbaric bupivacaine in cesarean sections was effective and safe in decreasing the incidence and intensity of post-spinal shivering. These results agree with study which investigated intrathecal dexamethasone versus meperidine for prevention of shivering during transurethral prostatectomy and concluded that intrathecal dexamethasone effectively prevented post-spinal shivering

with similar effects as intrathecal meperidine and with less side effects (Moeen & Moeen, 2017). As regards sedation score in the current study, there was high significance between both groups. As all the patient in dexmedetomidine group were sedated with different grades, 15 patients were mildly sedated (grade 1), 13 patients (grade 2), and only 2 patients were deeply sedated (grade 3) compared to only 6 patients in dexamethasone group who were mildly sedated (grade 1). These results agreed with the two studies in which all the patients of dexmedetomidine group were sedated with different grades of sedation (Fig. 2) (Nasseri *et al.*, 2017; Omar *et al.*, 2019). As regards side effects, most of the patients in both groups who complained of hypotension (blood pressure < 30% of the pre induction value) especially at the first 15 min after spinal anesthesia were treated with incremental doses of 6 mg of mephentermine with no statistical difference between both groups. The same for bradycardia, three cases in group A and two cases in group B were treated with atropine sulfate 0.01–0.02 mg/kg with no statistical difference. Only two cases complaining of nausea and vomiting in group A and three cases in group B were treated with ondansetron 4 mg IV with no statistical difference, and these results for both groups agreed with the results of the studies (Nasseri *et al.*, 2017; Moeen & Moeen, 2017; Miao *et al.*, 2018).

## Conclusion

This comparative study between dexmedetomidine and dexamethasone as an intrathecal adjuvant for prevention of perioperative shivering in cesarean sections showed that both drugs can be added safely to bupivacaine, and both dexmedetomidine and dexamethasone decreased the incidence and the intensity of shivering. Dexamethasone was found to significantly prolong the duration of sensory block and delay opioid requirements in postoperative management, while dexmedetomidine is more effective in sedating the patients during the intra and postoperative period.

## Abbreviations

CS: Cesarean section; SpO<sub>2</sub>: Oxygen plethysmography; ECG: Electrocardiogram; PACU: Post-anesthesia care unit; SA: Spinal anesthesia; ASA-PS: American Society of Anesthesiologists—physical status; SPSS: Statistical Package for Social Sciences; NIBP: Non-invasive blood pressure; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; MBP: Mean blood pressure; HR: Heart rate; NMDA: N-methyl D-aspartate

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