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RESEARCH ARTICLE

Hemodynamic and analgesic effect of intrathecal dexmedetomidine with low dose hyperbaric bupivacaine in spinal anaesthesia, caesarean section: a randomized controlled trial

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ABSTRACT

Objectives: Hypotension is the major side effect of spinal anaesthesia during caesarean section. Since the adverse effects are dosage-dependent, various methods have been tried to prevent spinal anaesthesia induced complications, such as lowering the local anaesthetic dose and combining it with additives like neuraxial opioids, alpha-2 agonist e.g. dexmedetomidine. Here we are investigating the efficacy dexmedetomidine with hyperbaric bupivacaine for improved postoperative analgesia and more stable hemodynamic during caesarean section. **Methodology:** An institutional-based RCT was conducted on 60 patients randomly allocated in two groups. Low dose hyperbaric bupivacaine L-DG group (n=30) received 7.5 mg hyperbaric bupivacaine with 5µgm dexmedetomidine and control group S-CG (n=30) received standard dose of hyperbaric bupivacaine of 12.5mg. The hemodynamic parameters, postoperative analgesia, other adverse effects and neonatal outcomes were monitored. **Result:** The L-DG group had significantly more rapid and persistent sensory block ($p < 0.05$), stable maternal hemodynamic which was maintained by fewer IV fluids ($p < 0.01$), lower vasopressor dosages ($p < 0.01$), no evidence of foetal distress, and a lower incidence of postoperative maternal shivering. Post operative duration of analgesia in L-DG group was more significant ($p < 0.001$). **Conclusion:** L-DG group shows stable maternal hemodynamic with fewer demands for vasopressors and fluids, effective sensory blockade and excellent postoperative analgesia.

Keywords: Dexmedetomidine, bupivacaine, caesarean section, hypotension, spinal aesthesia.

Spinal anaesthesia has become the anaesthetic technique of choice for caesarean section and has led to a reduction in maternal mortality [1, 2]. Women who receive spinal anaesthesia during caesarean delivery often experience post-spinal hypotension with an incidence of up to 58.4% [3]. Spinal hypotension is often associated with maternal nausea and vomiting, decreases uteroplacental blood flow, which can lead to foetal acidosis, especially in situations where the foetus is already at risk, and it can be an important factor in maternal death associated with regional anaesthesia [4]. Neuraxial administration of adjuvants together with local anaesthetics improves the quality of intraoperative analgesia and provides longer-lasting postoperative pain relief than local anaesthetics alone [5, 6].

In obstetric anaesthesia, there has been growing interest in the use of low-dose (LD) intrathecal hyperbaric bupivacaine "LD regimen" (< 8 mg) compared with the conventional dose (≥ 8 mg) [7]. Both doses were comparable to values studied using dose-response curve modelling by logistic regression at an effective dose in 50 per cent of the population (ED50) or an effective dose in 95 per cent of the population (ED95) [8, 9]. Alpha-2 agonists such as clonidine and dexmedetomidine are non-opioid adjuvants that play a significant role in prolonging the analgesic duration of

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subarachnoid block [10-12].

We hypothesised that intrathecal dexmedetomidine might decrease the ED95 (95% effective dose) value of spinal hyperbaric bupivacaine. In this study, it was suggested that the use of LD - hyperbaric bupivacaine and dexmedetomidine as an adjuvant would provide optimal intraoperative conditions, potent postoperative analgesia, more stable haemodynamic without any adverse foetal outcome.

Therefore, we designed the study to compare the low dose hyperbaric bupivacaine 7.5 mg and 5µgm dexmedetomidine with the standard dose of hyperbaric bupivacaine of 12.5mg intrathecally in spinal anaesthesia for caesarean section.

Aims and objectives of the study were -

- to compare the characteristics of spinal block.
- duration of sensory block and postoperative analgesia.
- compare the hemodynamic changes if any.
- presence of any untoward effects and adverse foetal outcome.

Materials and method

An institutional randomised control trial was conducted from 1 April 2021 to 31 March 2022 in a tertiary care hospital, one of the government medical colleges and hospitals in northeast India. Ethical clearance was obtained from the institutional ethics committee with IEC number 030/2021/TMCH before commencement of the study. Both verbal and written informed consent was obtained from each participant. Pregnant women aged 18to 35 years with a singleton pregnancy and American Society of Anaesthesiologists (ASA) physical status classes I and II were enrolled in the study, excluding high-risk pregnancies, patients with comorbidities and height greater than 170 cm in this study.

On arrival of the patients in the operating theatre and after applying the routine monitoring protocol of the hospital, HR, non-invasive blood pressure and SPO2 were recorded before induction of spinal anaesthesia. Subsequently, all patients receiving spinal anaesthesia received either 7.5 mg hyperbaric bupivacaine and 5µg dexmedetomidine (L- DG) or 12.5 mg hyperbaric bupivacaine (control group) in the sitting position at the vertebral level of L2-L3. All doses were diluted with normal saline to a total volume of 3.0 ml in an unlabelled syringe. The study medication was prepared by a 2nd anaesthetist who was not further involved in perioperative care, data collection or data analysis.

All patients were then placed in the supine position and the extent of sensory and motor blockade and haemodynamic parameters were assessed. Hypotension, defined as a drop in systolic blood pressure of more than 30% from baseline or a drop below 90 mmHg, was treated with a bolus of 100µgm intravenous phenylephrine repeatedly, if required, and additional IV fluid. Bradycardia, defined as heart rate < 60 beats per minute (bpm), was treated with IV atropine 0.5 mg.

The primary outcome was haemodynamic stability and total dose of IV fluids and vasopressors, density of motor block and need for postoperative analgesia. Sensory testing was assessed by loss of pinprick sensation at each dermatomal level at the level of the midclavicular line every 2 minutes until stabilisation of the highest level for four consecutive tests, every 10 minutes until regression of block in two segments and every 20 minutes until recovery of the S1 dermatome. Motor block was also assessed using the modified Bromage scale [13]. Pain score was initially recorded every 1 hour for 2 hours, then every 2 hours for the next 8 hours, and then every 4 hours until 24 hours. If the VAS score was above 3, IM tramadol 2mg/kg was given as a rescue analgesic. Haemodynamic parameters [NIBP and heart rate (HR)] were recorded every three minutes throughout the surgery. The total dose of fluids and vasopressors was recorded at the end of surgery. The degree of sedation was assessed intra- and postoperatively using the modified Ramsay Sedation Score [14]. The occurrence of other adverse effects such as nausea, vomiting, tremor, pruritus and respiratory depression was recorded. The neonatal Apgar score was obtained 1 and 5 minutes after birth. All data were recorded blindly by the assistant nurses.

Based on the results of Kanazi et al [15], we calculated that 21 patients per group would provide a power of 80% to detect differences in time to two-segment regression with a type I level of 5%. However, to compensate for possible drop-outs, a further 40% was added, so that the final sample size was 30 patients in each group. Patients were randomly assigned to either the low dose dexmedetomidine group (L-DG) or the standard dose control group (S-CG), with randomisation performed electronically.

All durations were calculated considering the time of spinal injection as time zero. Descriptive statistics were performed for all variables. Continuous, normally distributed data were reported as mean and standard deviation (SD). Ordinal data and continuous data that did not fit the normal distribution curve were presented as medians (range), while categorical data were presented as a percentage of the total.

As for the autonomic variables (SBP, DBP, HR), the 2 groups were compared in terms of their baseline data to ensure that there was no difference between the compared groups before our clinical trials. We then performed a stratified analysis to compare the mean change in these variables every 3 minutes to 60 minutes using a two-tailed t-test (Welch t-test). P-value < 0.05 was considered statistically significant.

Result

Patients in the two groups did not differ statistically in their baseline characteristics (p -value > 0.05). The mean height and weight of the L-DG group were 165.2 (3.9) cm and 72 (2.1) kg respectively, compared with 163.4 (3.1) cm and 71 (3.1) kg for the S-CG group. The patients' preoperative vital signs were also comparable without being statistically significant. Mean HR was 103(13.9) bpm versus 101 (17.6) bpm in the L-DG group and S-CG, respectively, while mean arterial pressure (MAP) was 90.1 (11.2) mmHg and 88.2 (12.5) mmHg in both groups. However, the mean duration of surgery was shorter in the L-DG group than in the control group 56.4(13.8) min and 62.2(8.6) min, respectively, p-value = 0.20 (table 1).

Table 1: Demographic data and Hemodynamic parameters

Parameters	L-DG	S-CG	P−Value
N (mean±SD)	30	30	
Age(years)	25.2(1.9)	25.7(1.9)	0.31
Height(cm)	165.2(3.9)	163.4(3.1)	0.526
Weight(Kg)	72(2.1)	71(3.1)	0.1481
Gestational age (weeks)	39(0.9)	39(1)	0.99
Duration of surgery (Min)	56.4(13.8)	62.2(8.6)	0.2056
HR(bpm)	103(13.9)	101(17.6)	0.6271
SBP(mmHg)	124.5(16.1)	122(12.1)	0.499
DBP(mmHg)	80.6(12.8)	75(12.3)	0.089
MAP(mmHg)	90.1(11.2)	88.2(12.5)	0.53
SP02	98.2(1.3)	98.5(1.4)	0.393

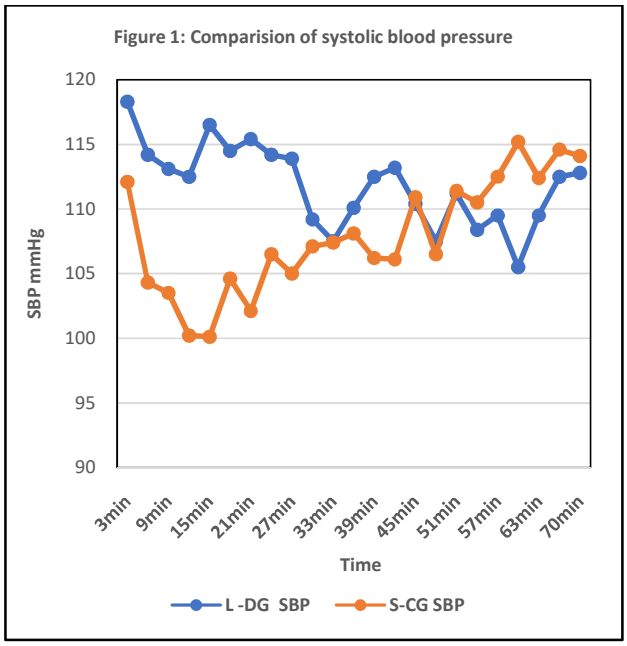
L-DG = Low dose dexmedetomidine group, S-CG = Standard control group, SD = Standard deviation, HR = Heart rate, SBP = Systolic blood pressure, DBP = Diastolic blood pressure, MAP = Mean arterial pressure.

The S - CG group had a shorter time to peak sensory blockade - rapid onset - and a shorter duration of S1 dermatome pain sensation, as well as a lower postoperative analgesic effect, with a cut-off pain value of about 3 hours, where VAS score > 3(p < 0.05) in all. Whereas post-operative duration of analgesia in L-DG group was 6.1 (1.9) hrs (p ≤ 0.001) except regression to S1 dermatome which was statistically insignificant (p = 0.135) (table 2).

Regarding motor block, the S-CG group showed a denser block, 26 patients (86.6%) achieved a grade 1 block, while only 4 patients (13.4%) were left with a grade 2 block, in contrast to all participants in the L- DG group 30 patients (100%) who were left with a grade 2 block, resulting in early ambulation with L-DG group after about 200(58.3) min (p < 0.001) (table 2).

Table 2: Regional block characteristics and analgesia

Parameters	L-DG	S-CG	P−Value
N (% or mean ± SD)	30	30	
Sensory block and analgesia			
Duration to highest level (Min)	14(5.9)	10.2(3.5)	0.0011
Sensory regression to S1(Min)	460.1(170.2)	400 (123.3)	0.135
Post operative analgesia (VAS ≥3)	6.1 (1.9)	3(1.7)	<0.001
Motor block			
Motor block grade=2	30(100)	4(14.3)	<0.01
Duration till ambulation (Min)	200(58.3)	418.2(120.2)	<0.001
Vasopressors and fluids			
Vasopressors (µg)	200(18.6)	300(16.1)	<0.001
Fluids (ml)	1800(320.5)	2402(295.2)	<0.001



There was no significant difference between the two groups in sequential tracking of autonomic parameters at the sixty-minute measurements. However, patients in the L-DG group showed a significant increase in SBP at 15 minutes (p = 0.025) (figure1), a significant increase in DBP at 12 and 21 minutes (p = 0.035, p = 0.015) (figure 2) and a significant decrease in HR at 12 and 54 minutes (p = 0.036, p = 0.006) (figure 3). In the S-CG group, higher doses of phenylephrine 300 (16.1) µgm and IV fluids 2402.1(295.2) ml whereas in L-DG group phenylephrine 200 (18.6) µgm and IV fluids 1800(320.5) ml (p < 0.001) (table 2).

S-CG group showed higher incidence of shivering (p < 0.05) than the L-DG group, while nausea and vomiting were equally common in both groups. Traction pain, especially during uterine externalisation, was higher in the L-DG

group, but not statistically significant (p - value = 0.13). All patients showed a sedation score < 2 at every time point with no need for oxygen supplementation all over the operation. In both groups, the new-borns showed no signs of foetal distress, as evidenced by the Apgar score at 1 minute and 5 minutes (p > 0.05) (table 3).

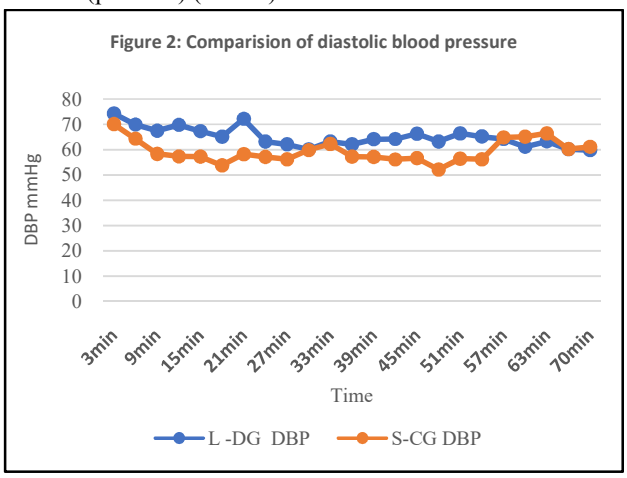
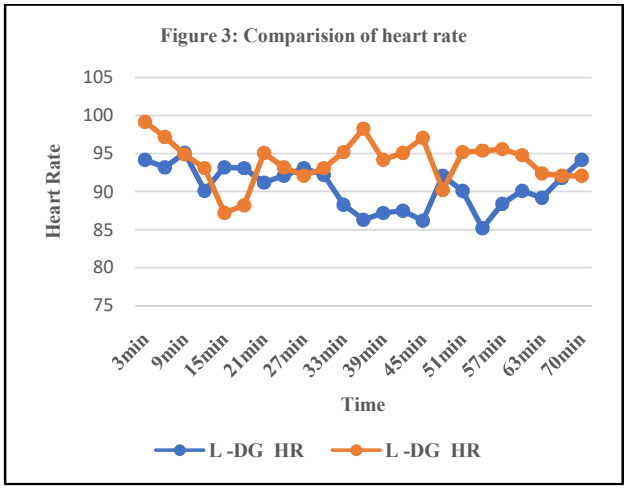


Table 3: Side effects and foetal outcomes in both groups

Parameters	L-DG	S-CG	P−Value
N (% or mean ± SD)	30	30	
Nausea	5 (19.0)	4(21.9)	0.85
Vomiting	2(4.9)	2(5.0)	0.99
Traction pain	8(30.0)	2(5.5)	0.28
Shivering	1(4.9)	8(5.1)	0.01
Apgar 1 min	8.8(0.5)	8.6(0.5)	0.12
Apgar 5 min	9.5(0.5)	9.3(0.5)	0.12



Discussion

In this prospective, randomised, double-blind, controlled trial, we observed that the addition of 5 µg of dexmedetomidine to low-dose hyperbaric bupivacaine resulted in stable maternal haemodynamic maintained by lower amounts of fluid and phenylephrine, better sensory blockade, longer postoperative analgesia, less dense motor blockade with earlier ambulation and less shivering without neonatal side effects. C Arzola et al compared the efficacy of spinal hyperbaric bupivacaine at low dose (LD ≤8 mg) with conventional dose (CD ≥8 mg) in elective caesarean deliveries [16]. Meanwhile, in our study, we used hyperbaric bupivacaine at a dose of 7.5 mg and 05 µgm dexmedetomidine as L- DG group versus 12.5 hyperbaric bupivacaine mg as S - CG control group. Low-dose bupivacaine resulted in a more stable maternal haemodynamic profile and lower IV fluid and phenylephrine requirements compared with the control group, consistent with studies by Al-Mustafa and colleagues [17] and El-lakany [18]. There was an initial increase in BP, which lasted for 12 minutes, followed by hypotensive episodes, which responded well to the administration of fluid IV. However, the biphasic response had no effect on mean blood pressure, which is also confirmed by Kanazi et al [19] considering different populations. Dexmedetomidine acts by binding to presynaptic C-fibres and postsynaptic dorsal horn neurons, resulting in decreased neurotransmitter release from C-fibres and hyperpolarisation of postsynaptic dorsal horn neurons [20, 21]. Our study shows that dexmedetomidine enhances the sensory blockade and postoperative analgesic effect of intrathecal hyperbaric bupivacaine (p < 0.05 in all except duration of S1 dermatome pain perception p=0.135), which is supported by other reports in the literature [22-24]. Regarding motor blockade, our results showed 2nd degree motor blockade according to the modified Bromage score [13] with low-dose hyperbaric bupivacaine. It aids in early locomotion and recovery of muscle strength during the postoperative period, reported to be 206 (60.9) minutes and parallel to 221.1 (1.37) minutes as reported by Fyneface-Ogan et al [24-26]. The L- DG group showed a lower shivering profile of 5%, which is significantly (p <0.05) and reported by Abdelhamid and El-lakany [18], Y Sun et al [27] and K Nasseri et al [28]. There is no difference in the frequency of nausea and vomiting and agrees well with Kang et al [29].

Conclusion

From our study we come to the conclusion that the L-DG regimen (7.5 mg hyperbaric bupivacaine + 5µgm dexmedetomidine) is a viable choice for intrathecal injection in patients planned for elective caesarean section as it provides more stable maternal hemodynamic with fewer demands for vasopressors and fluids, effective sensory

blockade, excellent postoperative analgesia, early ambulation, and shorter hospital stay.

Conflict of interest: None. **Disclaimer:** Nil.

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