A Study to Evaluate the Effect of Low Dose Intrathecal Dexmedetomidine as an Adjuvant to Low Dose Hyperbaric Bupivacaine in Spinal Anaesthesia in elderly Patients

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ABSTRACT

BACKGROUND

In developed and developing countries, the elderly patients, because of associated co-morbidities, due to physiological changes of aging, are at risk of hemodynamic changes after spinal anaesthesia with conventional dose of local anaesthetics. Therefore, lower doses of local anaesthetics along with an adjuvant are preferred for spinal anaesthesia in elderly patients. Intrathecal a2- adrenoceptor agonists as adjuvant drugs have been shown to decrease the required doses of local anaesthetics and are devoid of major side effects.

METHODS

A prospective, interventional study was done after obtaining ethical committee clearance and written informed consent. Patients undergoing Infraumbilical surgeries under spinal anaesthesia were selected and divided into 2 groups of 60 patients. Group BN received bupivacaine 2 mL with Normal saline 0.1 mL and Group BD, bupivacaine 2 mL with dexmedetomidine 0.1 mL. Hemodynamic parameters, sensory and motor blocks were assessed periodically.

RESULTS

There were no clinically and statistically significant changes in heart rate and blood pressure. We found statistically significant decrease in the time to onset of sensory and motor block (min) in Group BD (1.68 ± 0.96 and 2.42 ± 1.12) compared to Group BN (2.24 ± 0.81 and 3.33 ± 1.06). Duration (min) of analgesia and the time for first rescue analgesia were prolonged in Group BD (457.23 ± 77.31 and 520.85 ± 87.93) in comparison to Group BN (323.61 ± 59.87 and 377.6 ± 56.37) respectively. There were no side effects except for mild sedation in Group BD.

CONCLUSIONS

Addition of dexmedetomidine 5 mcg to intrathecal bupivacaine in elderly patients causes minimum haemodynamic changes, prolongs sensory and motor block and delays the time for the first rescue analgesia. In the said dose, it is safe without severe adverse effects.

KEYWORDS

Anaesthesia, Dexmedetomidine, Sensory Block, Haemodynamic Changes

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BACKGROUND

Aging is an irreversible and progressive physiological phenomenon characterized by degenerative changes in the structure and functional reserve of organs and tissue.[1] In almost every country, the proportion of people aged over 65 years is growing faster than any other age Group, as a result of both longer life expectancy and declining fertility rates. By the year 2040, persons aged 65 years or older are expected to comprise 24% of the population and account for 50% of health care expenditures. With the rising longevity and 1/3 of the surgical patients being elderly, geriatric anaesthesia has come into prominence.

Elderly patients pose a serious challenge to anaesthesia not only due to associated co-morbidities but also due to natural changes during aging. Both the peripheral and central nervous system degenerate with advancing age. A reduction in the number of neurons within the spinal cord, deterioration of myelin sheaths and connective tissue barriers and slowing of the conduction velocity in peripheral nerves, especially the motor nerves, all these changes contribute to altered nerve block characteristics (dose-response relationship). Thus reduction in the intrathecal dose (fixed volume and concentration) of local anaesthetic may prevent major changes in the vital parameters and further modification of the given dose by use of spinal adjuvants like dexmedetomidine may be rewarding in terms of prolonged analgesia and motor block. Dexmedetomidine by acting on the alpha-2 adrenoreceptors located on the primary afferent terminals of neurons in spinal cord, brain stem and peripheral tissue, will exhibit synergistic effects with Local anaesthetics and will also produce analgesic effects.

METHODS

This study was conducted in the Department of Anaesthesiology, Yenepoya Medical College, and Mangalore. After ethics committee approval and written informed consent, patients belonging to American society of Anaesthesiology (ASA) grade 1, 2 and 3, aged more than 60 years, scheduled for surgery which require spinal anaesthesia were selected. Haemodynamically unstable patients, patients having impaired coagulation profile, local sepsis at lumbar spine were excluded. Thorough pre-anaesthetic evaluation and routine investigations was carried out before taking up the patient for surgery. Sample size Based on the study by Seop Chang Y et al (2015) and considering the mean difference 6.1 mmHg and SD 11.7 in mean blood pressure between study and control Group, with 95% CI and 80% power, sample size will be 43 in each Group,[2] Considering the nonresponsive rate of 20% We have included 60 patients in each Group. Patients posted for infraumbilical surgeries were chosen. 120 patients were randomized using closed sealed envelopes, selected by chit method, into 2 Groups (60 each): -Group BN (bupivacaine 2 mL + Normal saline 0.1 mL) and Group BD (bupivacaine 2 mL+ dexmedetomidine 0.1 mL). Under aseptic conditions lumbar puncture is performed in sitting position at L3-4 / L4-5 interspace and 2.1 mL of study agents is administered. Group BN will receive 10 mg of 0.5% hyperbaric bupivacaine with 0.1 mL normal saline and Group BD will receive 10 mg of 0.5% hyperbaric bupivacaine and 5 mcg of dexmedetomidine. The Drug was injected over 6 seconds with no barbotage followed by immediate placing the patient in supine position with the operating table in neutral position. In all cases monitoring of Blood pressure, ECG, Oxygen Saturation and Respiratory rate was done at regular intervals intra-operatively. Sensory block and motor blocks were assessed periodically.

Intraoperative fluid requirement was managed taking into account the cardiopulmonary status of the patients. Hypotension was defined as a decrease in Systolic blood pressure (SBP) of >20% of the Basal SBP and was initially treated with crystalloids and if necessary, vasopressors. Bradycardia defined as a decrease in heart rate of >20% of the Basal value and was treated with intravenous atropine (0.6 mg). At 10 minutes after spinal injection, the inability to reach a sensory block at T12 and a Modified Bromage Score of 0 was considered as a block failure and was excluded from further study. In case of intra-operative discomfort or pain patients were administered appropriate anaesthesia based on the patient's physical status and was excluded from the study. At the end of surgery patients were shifted to post-anaesthesia care unit. The duration of analgesia was considered as the period from the injection of the study drug to patient perceiving sensation and time for first rescue analgesia was considered as period from the injection of the study drug to the first request made by the patient for analgesics. For rescue analgesia intravenous infusion of preservative free Diclofenac 75 mg was given, which was repeated after 12 hours, if needed.

Statistical Analysis

Data was entered in MS Excel and analysed in SPSS v20. Continuous variables were summarized as mean or median with standard deviation (SD) or interquartile range (IQR). Categorical variables were expressed as percentages with 95% confidence interval (95% CI). T test was used to test the statistical significance of difference between the groups in continuous variables like age, body mass index (BMI), Total duration of sensory block, motor block, duration of analgesia. Two way ANOVA was used to test the statistical significance of difference in variation of heart rate, systolic, diastolic, and mean arterial blood pressure. Chi square test was used test the statistical significance of deference in distribution of categorical variables like gender, and side effects of drugs between the groups. P value less than 0.05 was considered as statistically significance.

RESULTS

The demographic variables are outlined in Table 1. As evident from the table 1, all the demographic variables were

comparable between the groups ('p' value >0.05). The heart rate was recorded as basal value and then periodically in all the patients (Figure 1). In Group BN the mean basal HR was 79.43 ± 8.74 bpm and at 90th minute was 71.58 ± 7.20 bpm with a difference of 7.85. In Group BD the mean basal HR was 78.75 ± 11.15 bpm and at 90th minute was 70.38 ± 7.75 bpm with mean difference of 8.37. The mean of maximum fall in HR (bpm) Group BN was 12.68 ± 4.75 and in Group BD was 13.03 ± 8.27 the mean difference in the HR between Group BN and Group BD was statistically insignificant with 'p' value of 0.067. The MAP was recorded as basal value and then periodically in all the patients (Figure 1). In Group BN the mean basal MAP was 99.51 ± 8.28 mm/hg and at 90th minute was 90.8 ± 5.29 with a difference of 7.85. In Group BD the mean basal MAP was 102.02 ± 9.87 mmHg and at 90th minute was 89.76 ± 6.83.

Variables	Group BN	Group BD	p
Age (years) (mean ± SD)	68.08 ± 4.91	69.3 ± 5.75	0.40
Male to female ratio	28: 32	31: 29	0.148
Height (cms) (mean ± SD)	166.58 ± 5.15	160.95 ± 8.30	0.10
Weight (Kgs) (mean ± SD)	64.26 ± 5.10	61.50 ± 7.31	0.30
BMI (Kg/m^2) (mean ± SD)	23.16 ± 23.78	23.78 ± 2.88	0.9

Table 1. Demographic Variables

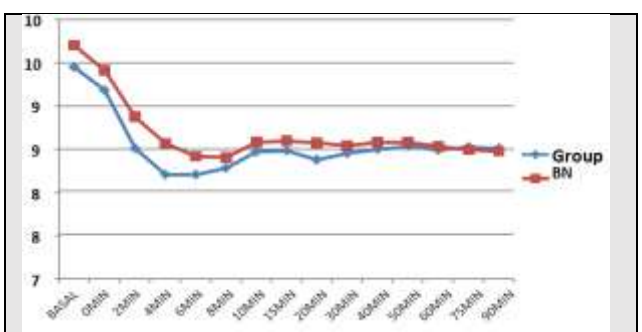

Figure 1. Graph Showing Comparison of Mean Heart Rate between the Groups at Various Time Intervals

	Total No.	Group BN		Group BD		p
		Mean	± S.D.	Mean	± S.D.	
TOSB	60	2.24	0.81	1.68	0.96	<0.0001
TOMB	60	3.33	1.06	2.42	1.12	<0.0001
TDMB	60	299.56	59.66	416.30	79.61	<0.0001
TDA	60	323.61	59.87	457.23	77.31	<0.0001
TRA	60	377.60	56.37	520.85	87.93	<0.0001

Table 2. Characteristics of Sensory and Motor Block of the Studied Groups (Minutes)

TOSB: Time of onset of sensory block, TOMB: Time of onset of motor block, TDMB: Total duration of motor block, TDA: Total duration of analgesia, TRA: time of rescue analgesia)

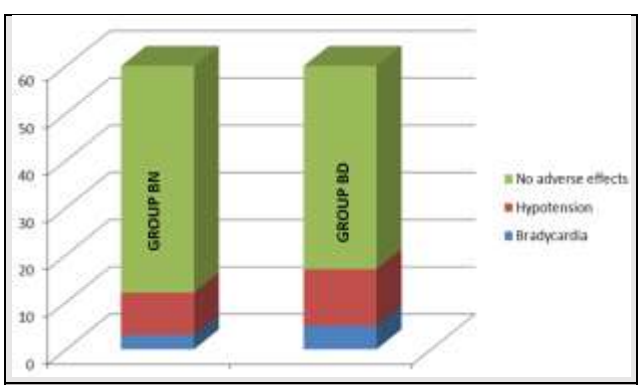

Figure 2. Graph Comparing the Incidence of Bradycardia, Hypotension and Other Adverse Effects between the Groups

Even though there was a statistically significant fall in MAP from the baseline value to the 90th minute in both the Groups, the mean difference in the fall of MAP from the basal to the 90th minute between the two Groups was statistically insignificant with a P value of 0.30. The sensory and motor characteristics are outlined in (Table 2). As evident from the table 2, all the sensory and motor characteristics were comparable between the groups ('p' value <0.001). In Group BN the mean TOSB (Time of Onset of Sensory Block), TOMB (Time of Onset of Motor Block), TDMB (Total Duration of Motor Block), TDA (Total Duration of Analgesia), TRA (Time to Rescue Analgesia) was 2.24, 3.33, 299.56, 323.6, 377.60. In Group BD, the mean TOSB, TOMB, TDMB, TDA, TRA was 1.68, 2.42, 416.20, 457.27, 520.85. The mean TOSB, TOMB, TDMB, TDA, TRA between Group BN and Group BD was statistically significant with 'p' value of 0.001, indicating that adding adjuvant produces significant changes in spinal anaesthesia.

Figure 2 shows the incidence of adverse effects**,** three patients in Group BN and Five patients in Group BD had bradycardia which required treatment with atropine 0.6mg iv. And 9 patients in Group BN and 12 in Group BD had hypotension and required injection mephentermine in addition to iv fluids.

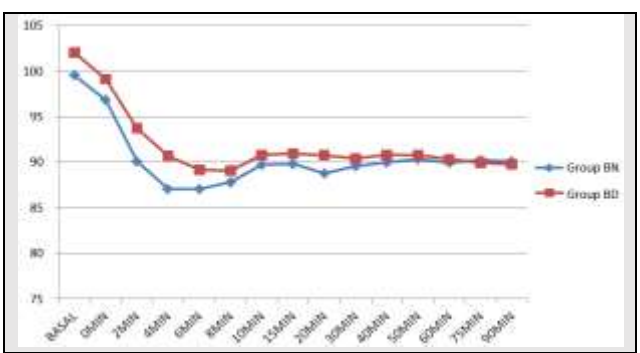

Figure 3. Graph Comparing Mean Blood Pressure (MAP) between the Groups at Various Time Intervals

Figure 3 shows variations in the MAP (mean arterial pressure) between the two groups. In Group BN the mean basal MAP was 99.51 ± 8.28 mmHg and at 90th minute was 90.08 ± 5.29. In Group BD the mean basal MAP was 102.02 ± 9.87 mmHg and at 90th minute was 89.76 ± 6.83. Even though there was a statistically significant fall in MAP from the baseline value to the 90th minute in both the Groups, the mean difference in the fall of MAP from the basal to the 90th minute between the two Groups was statistically insignificant with a p-value of 0.30.

Parameters	Group BN	Group BD
Gender	M- 28, F- 32	M-31, F-29
Age (Yrs.)	68.08 ± 4.91	69.3 ± 5.75
BMI (Kg/m^2)	23.16 ± 1.69	23.78 ± 2.88
Mean maximum fall in HR (bpm)	12.68 ± 4.75	13.03 ± 8.27
Mean maximum fall in SBP (mmHg)	25.41 ± 12.41	25.06 ± 14.33
Mean maximum fall in DBP (mmHg)	14.81 ± 5.50	16.88 ± 8.66
Mean maximum fall in MAP (mmHg)	17.38 ± 6.19	18.81 ± 9.83
TOSB (min.)	2.24 ± 0.81	1.68 ± 0.96
TOMB (min.)	3.33 ± 1.06	2.42 ± 1.12
TDMB (min.)	299.56 ± 59.66	416.3 ± 79.61
TDA (min.)	323.61 ± 59.87	457.23 ± 77.31
TRA (min.)	377.6 ± 56.37	520.85 ± 87.93
VAS 4th Hour	3.26 ± 2.34	2.01 ± 1.34
VAS 8th Hour	5.98 ± 2.16	2.56 ± 1.82
Bradycardia	3(5%)	5(8.3%)
Hypotension	9(15%)	12(20%)

Table 3. Summary of Results between Group BN and BD

Table 3 illustrates the various parameters being compared between the two groups. VAS (Visual Analog Scale) score at 4th and 8th hours was compared, it was significant at 8th hour where in still having low values in group BD.

DISCUSSION

Reduction in the intrathecal dose (fixed volume and concentration) of local anaesthetic may prevent major changes in the vital parameters. Low-dose local anaesthetics can limit the block level and induce rapid recovery from anaesthesia, but sometimes these low-dose local anaesthetics may not provide an adequate anaesthetic level for surgery. Hence lower doses of local anaesthetics along with an adjuvant are preferred for spinal anaesthesia in elderly patients and many studies are done to find out minimal safety dose with maximal outcome.

Kalso et al (1991) reported that dexmedetomidine affinity to α2- adrenoceptor agonists is 10 times as compared to clonidine.[3] As adjuvant, neuraxial administration is the appropriate route to dexmedetomidine, because the analgesic effect of α2-agonists mostly occurs at spinal level, and dexmedetomidine's high lipophilicity facilitates rapid absorption into the cerebrospinal fluid and binding to the spinal cord α2-adrenoreceptor.[4] dexmedetomidine has synergistic effect with local anaesthetic agents as suggested by Salgado et al (2008) and also produce analgesia by depressing release of C-fiber transmitters and by hyperpolarization of dorsal horn post synaptic neurons.[5] Kim JE[6] & colleagues in their study evaluated the effect of 3 µgm of dexmedetomidine to bupivacaine in TURP surgeries and found the similar results to our study. The time to request for rescue analgesia was 487 min while in our study it was 520 min, probably because we added more quantity of the drug. Basuni a & Ezz H[7] in their study compared fentanyl & dexmedetomidine as an adjuvant to levobupivacaine in knee arthroscopic surgeries, found out that adding the study drug fastens the onset of sensory block similar to our study. Duration of analgesia was not comparable as bupivacaine dose was higher in our study patients. Bhure AR et al (2016)[8] used Normal saline, 10 mcg and 15 mcg of dexmedetomidine as adjuvant to 3.4mL 0.5% bupivacaine (H) and showed that mean intraoperative heart rate was 72.23 ± 8.41 bpm, 70.23 ± 10.20 bpm and 69.28 ± 8.86 bpm respectively and the difference was found to be statistically insignificant among these Groups. Similar results were observed in our study. Group BN showed a mean fall of 7.85 bpm from basal heart rate during the study period compared to a value of 8.37 bpm in Group BD. The mean of maximum fall of HR in Group BN was 12.68 ± 4.75 and in Group BD was 13.03 ± 8.27 which was insignificant in between the Groups. The main adverse events were bradycardia (10%) and hypotension (16%), which was comparable to our study (8 & 20%), though dexmedetomidine dose is reduced the risk of bradycardia cannot be avoided. Hypotension may be effect of spinal anaesthesia per say. The dose at 5 µgms can be used safely for the infraumbilical surgeries. Mohamed T et al (2017)[9] conducted a study on fixed dose 5 mcg dexmedetomidine with different doses of bupivacaine and showed that group which received higher dose of bupivacaine 9 mg had 5.40 ± 0.675 hours of motor block when compared to Group which received 8 mg and 7 mg had 4.73 ± 0.711 hours and 4.67 ± 0.691 respectively. Similar results was observed in our study where patients in Group BD had mean duration of 416.30 ± 79.61 minutes for motor blockade. Duration of postoperative analgesia was 6.82 ± 1.5 hours which was similar to our study 457 ± 77 minutes. Songir S et al (2016)[10] observed that sedation score 0 in nine patients, sedation score 1 in sixteen patients and sedation score 2 in five patients who received dexmedetomidine 5 mcg as an adjuvant, while all patients from control Group showed sedation score 0. Similar results was observed in our study in which fifteen patients in Group BD had a Ramsay scale sedation score of 2 and the forty five patients had a score of 1 when compared to Group B where only three patients had a score of 2 and remaining fifty seven patients had a score of 1. Though patients from dexmedetomidine Group were found to be more sedated, respiratory depression was not observed. Respiratory rate and oxygen saturation (SpO2) were similar in both Groups. There was no need for oxygen supplementation to any of the Group. There was no statistically significant difference between the two Groups in the occurrence of other side effects like nausea, vomiting and urinary retention. Limitations of our study were that identical surgeries could not be studied, United State Food and Drug Administration has no approval for perineural application of dexmedetomidine, and lower dose of bupivacaine (H) and dexmedetomidine as adjuvant could have been studied.

CONCLUSIONS

Addition of dexmedetomidine 5 mcg as an adjuvant to intrathecal bupivacaine heavy, 10 mg in elderly patients causes similar hemodynamic changes which are minimal, as intrathecal bupivacaine heavy, 10 mg alone. However, as an adjuvant it prolongs sensory and motor block and delays the time for the first rescue analgesia. It produces good sedation without respiratory depression. In the said dose, it is safe without severe adverse effects.

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