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ORIGINAL ARTICLE

EVALUATING THE EFFICACY OF LOW DOSE DEXMEDETOMIDINE WITH LOW DOSE BUPIVACAINE AS AN ADJUVANT FOR LOWER LIMB SURGERY IN ELDERLY AND HIGH RISK PATIENTS

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ABSTRACT: BACKGROUND: Various adjuvants are being used with local anesthetics for prolongation of intraoperative and postoperative analgesia and to decrease the dose of local anesthetics. Dexmedetomidine the highly selective α-2 adrenergic agonist is a new neuraxial adjuvant is gaining popularity**. AIMS:** We studied the effect of intrathecal low dose dexmedetomidine on the pattern of sensory and motor block postoperative analgesic requirement and its adverse effects in elderly patients. **MATERIAL AND METHODS:** A prospective double blind randomized study was conducted on 60 patients of ASA I, II and III status of both sexes in the age group of above 60 years undergoing lower limb surgeries. Patients were randomly allocated to two groups: Group D received 3μg dexmedetomidine with 7.5mg of 0.5% hyperbaric bupivacaine (1.5ml) to a total volume of 2.5ml; Group B received 12.5mg of 0.5% bupivacaine (2.5ml). The pattern of sensory and motor block postoperative analgesic requirement and its adverse effects in elderly patients were recorded. Observed parameters were statistically analyzed $p<0.05$ was considered statistically significant. **RESULTS:** Addition of dexmedetomidine as adjuvant to bupivacaine had significantly shortened the onset of sensory blockade prolonged the duration of motor and sensory block ($p<0.0001$ $p<0.0001$ respectively) and has postponed the time for first analgesic request 295.83±44.3minutes versus 183.0±31.0minutes (P value of 0.0001). Dexmedetomidine showed significantly less and delayed requirement of rescue analgesia. **CONCLUSION:** Low dose intrathecal dexmedetomidine is associated with better haemodynamic stability shortened onset of sensory and motor block prolonged sensory and motor block and reduced demand of rescue analgesia as compared to relatively high dose of bupivacaine alone.

KEYWORDS: α-2 adrenergic agonist dexmedetomidine bupivacaine spinal anaesthesia elderly.

INTRODUCTION: Surgery in old age poses an ongoing challenge to the anaesthetist. Elderly surgical patients undergo approximately 20% or more of all surgical procedures in acute care across the country. Older patients have age related systemic change and multiple comorbid conditions which limits their functional capacity and recovery and increase the risk of perioperative morbidity and mortality. It is agreed universally that regional anaesthetic technique which is most common choice for lower limb surgeries is subarachnoid blockade. Regional anaesthesia is generally well tolerated by elderly patients producing less postoperative confusion and delirium than general anaesthesia. It is also associated with lesser evidence of postoperative thromboembolism. Studies have shown that spinal anaesthesia for surgical repair of lower limb fracture in the elderly is associated with high incidence of hypotension.

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Peri-operative hypotension has been shown to increase risk of ischemia secondary to hypotension in coronary disease in elderly.[1] Various measures to overcome hypotension have been used like vasopressors and I/V fluids to prevent or treat hypotension of spinal anaesthesia. But none have been proven to be without potential adverse effects. Another approach has been to manage hypotension by using small or low dose local anaesthetic which might limit hypotension but may not provide acceptable anaesthesia for sufficient duration[2]. Various adjuncts are being used with local anaesthetics for prolongation of intraoperative and postoperative analgesia and to minimize Haemodynamic effects of bupivacaine.

Many clinical studies have been done on intrathecal α-2 adrenergic agonists are related to clonidine.[3] Dexmedetomidine a highly selective α-2 adrenoreceptor agonist has gained popularity and is being used in various procedures in the perioperative and critical care settings.[4] Intrathecal 3mg-15mg dose of dexmedetomidine have been studied.[5]

In view of few evidences[6,7,8,9] of dexmedetomidine efficacy as an adjuvant in elderly patients as to hyperbaric bupivacaine in spinal anaesthesia made us to study low dose dexmedetomidine with low dose bupivacaine as an effective alternative to conventional dose of bupivacaine in patients with comorbidities.

MATERIAL AND METHODS: This randomized double blinded prospective study was done in department of anesthesia and critical care Govt. medical college Srinagar on patients who were posted for lower limb surgeries under subarachnoid block.

Exclusion Criteria for these Patients were:

- Patients with contraindication to regional anaesthesia.
- History of severe cardiac or respiratory disease.
- Impaired renal function.
- Rheumatoid arthritis and severe liver disease.
- Known allergy to study drugs.
- Patients on α-2 adrenergic agonists or antagonists.
- Patients with AV block.

After obtaining approval from the hospital ethical committee along with written informed consent from the patients participating in the study sixty patients in the age group of above 55 years were randomly allocated in the two groups

All patients were examined and investigated a day prior to surgery and were familiarized with visual analogue scale (VAS)[10] and its use for measuring postoperative pain. They were advised fasting for 6-8 hours.

Patients received no premedication before arrival in the operating theatre. Psychological preparation was done and procedure explained to all the patients in advance. On arrival in the operation theatre electrocardiogram (ECG), pulse oximetery and non-invasive blood pressure were attached and baseline parameters were recorded and monitoring was initiated.

Intravenous (IV) access was secured and all patients were preloaded with ringer lactate 10ml/kg. These patients were randomly assigned into two groups in double blinded manner.

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The Two Groups were as:

Group D: Received Intrathecal bupivacaine 7.5mg (1.5ml)±3mg of dexmedetomidine (1ml) 2.5ml (Total volume).

Group B: Received Intrathecal bupivacaine 12.5mg (2.5ml).

The study solutions were prepared in a 5ml syringe by an anaesthesiologist and who then handed them in a coded form to the attending anaesthesiologist blinded to nature of drug given to him/her.

Subarachnoid block was administered at L2-L3 or L3-L4 vertebral level using 26 gauge Quincke's spinal needle with patients in the sitting, under all aseptic precautions. Patients were made supine following the block. The anaesthesiologist performing the block recorded the intraoperative data. The onset and duration of sensory block highest dermatomal level of sensory block reached onset of motor block time to complete motor recovery. Duration of segment sensory regression and time of need of rescue analgesia were recorded. The onset of sensory block was defined as the time between injection of intrathecal anaesthetic and absence of pain at the T10 dermatome assessed by sterile pin prick every 2 minute till T10 dermatomal level was achieved. Highest level of sensory block was evaluated by pinprick at mid-clavicular line anteriorly every 5 min for 20 min after injection thereafter every 15 min. Duration of sensory block was defined as time of regression of dermatomal segments in the maximum block height evaluated by pinprick.

The motor level was assessed according to modified Bromage score.[11] Bromage 0 the patient is able to move the hip, knee and ankle Bromage 1 unable to move hip but is able to move the knee and ankle Bromage 2 the patient is unable to move the hip and knee but able to move the ankle and Bromage 3 the patient is unable to move the hip knee and ankle. Time for motor block onset was defined as modified Bromage score of 3. Complete motor recovery was assumed when modified Bromage score was 0.

The duration of spinal anaesthesia was defined as period from spinal injection to first occasion when the patient complained of pain in the postoperative period. All durations were calculated considering the time of spinal injection as time zero.

Surgery was allowed to commence on achieving adequate sensory block height vitals were recorded every 5 minutes before intrathecal injection 5 10 15 20 and 25 min after a subsequently every 15 minutes. I/V fluids were given to maintain the blood pressure. Oxygen supplementation was administered at the rate of 4Ltr/min via oxygen mask. Hypotension was defined as a decrease in systolic blood pressure (SBP) by 30% from baseline or less than 90mmHg or decrease of 30% from the baseline mean arterial pressure. Reaching either criterion was considered hypotension and was treated with intravenous bolus of mephentermine 6mg or crystalloid fluid. Heart rate (HR) <50 beats /min was corrected using 0.6mg of IV atropine sulfate. The incidence of nausea vomiting sedation bradycardia shivering respiratory depression and hypotension were recorded.

Dekock sedation scale[12]1 = patient somnolent but responding to verbal command 2 = patients somnolent but not responding to verbal command but responding to manual stimulation and 3= patient somnolent not responding to verbal command or manual stimulation. Postoperative → motor block recovery (modified Bromage recovery modified Bromage score of zero). Time of request for first rescue analgesia along with vital signs was recorded. VAS ≥3 was supplemented with dose of IV tramadol. The amount required by the patients in the next 24 hour was recorded in all the groups.

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STATISTICAL ANALYSIS: Data obtained were tabulated and analyzed using statistical package for social science (SPSS 15.0 evaluation version). To calculate the sample size a power analysis of $\alpha = 0.05$ and $\beta=1.00$ showed that 30 patients were needed per group were needed per study group to detect an increase of 30 min difference between the median duration of spinal sensory block between the groups was reported. Data were expressed as mean and standard deviation (SD) medians and ranges or numbers and percentages. For categorical co variates (Sex, ASA, class, nausea/vomiting use of additive analgesia hypotension and bradycardia) chi-square test or Fischer's exact test was used as appropriate with p value reported at the 95% confidence interval (CI). Continuous variegates (Age, duration of surgery) were compared using analysis of variance (ANOVA).

RESULTS: All patients (n=60) completed the study. There was no statistical difference in the socio-demographic profile of patients or duration of surgery.

Variable	Group D	Group B	P value
Age (Years)	73±15.6	70±14.8	0.56
Sex (M:F)	20 : 10	18 : 12	
Weight (Kg)	66.6±7.9	63.6±11.2	0.16
Duration of surgery	99.8±33.7	93.8±32.4	

Table 1: Patients demographics

Type of Lower Limb Surgeries Performed	Group D	Group B
Dynamic hip screw fixation	8	8
Tibia ORIF	8	10
Shaft of femur ORIF	8	5
Hip arthroplasty	6	7

Table 2: Type of Lower Limb Surgeries Performed

Table 2 shows the number of patients in each group undergoing different types of lower limb surgeries.

Average duration of surgery in both groups was 120 to 150 minutes. The study showed equal distribution of males and females in both groups sand majority of patients in both the groups were of ASA II. The time of onset of adequate level of sensory block (T10) was longer for group (B) than group (D).

When compared the time of onset of both sensory and motor block was statistically significant. T6 was the highest level of sensory block attained. Time of onset of sensory block in Group (B) was 7.8±1.8 whereas in group (D) was 5.3±2.4. Time of onset of motor block 9.2±2.9 (B) whereas in group D is 7.5±2.5.

Time to reach maximum sensory level was 10.1±3.5 minutes in B. Time to reach maximum sensory level was 10.2±3.3 minutes with p value 3.32.

The duration of spinal anaesthesia was shorter in Group B and significantly delayed requirement in Group D ($p < 0.001$).

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Duration of spinal anaesthesia was 183.0±31.0 min and in group D was 295.5±44.3 (p value 0.0001.)

Variable	Group (D)		Group (B)		P-value
	Mean	SD	Mean	SD	
Time of onset of sensory block	5.3	1.25	7.9	1.67	<0.001*
Time of onset of motor block	7.4	1.76	9.1	1.71	<0.001*
Time to reach highest sensory level	9.8	1.99	10.2	2.46	0.556
Duration of spinal anesthesia	301.4	22.87	185.4	19.72	<0.001*

Table 3

The mean value of heart rate mean and arterial pressure was comparable between the two groups throughout the intraoperative and postoperative period.

Heart rate values are mean ± standard deviation. No significant differences were noted between the groups.

Figure 1: Heart rate (HR) values are mean ± standard deviation. No significant differences were noted between the two groups:

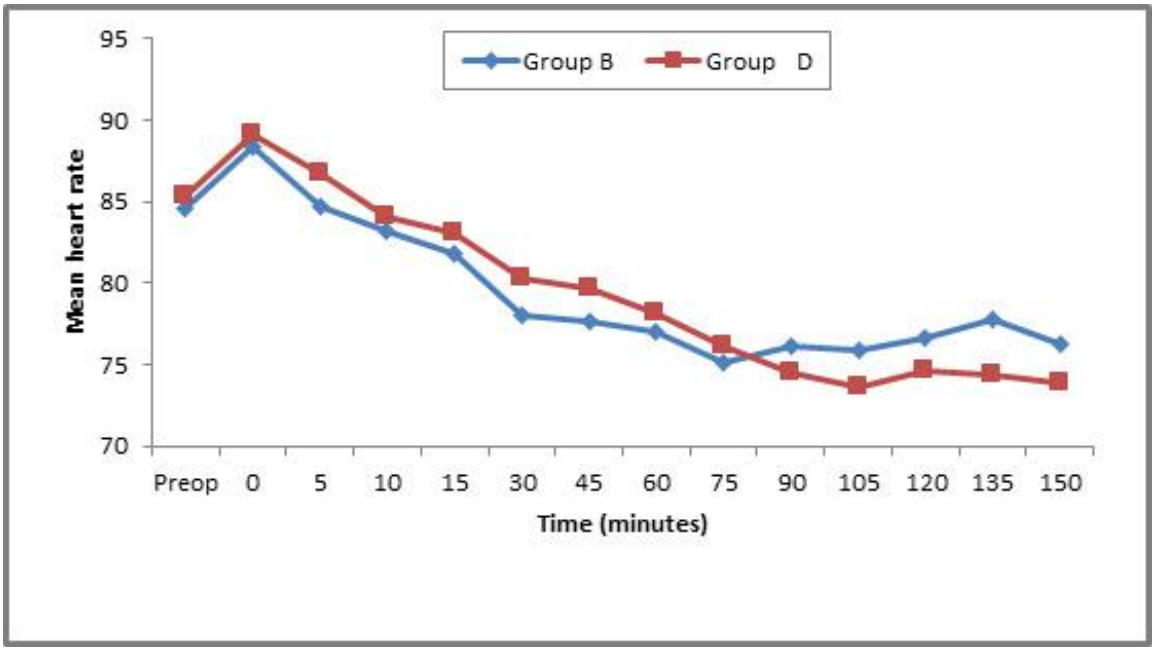

Fig. 1

Mean arterial pressure (MAP) values are mean ± SD. No significant difference noted between the groups.

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Figure 2: Mean arterial pressure (MAP) values are mean ± standard deviation. No significant differences were noted between the two groups:

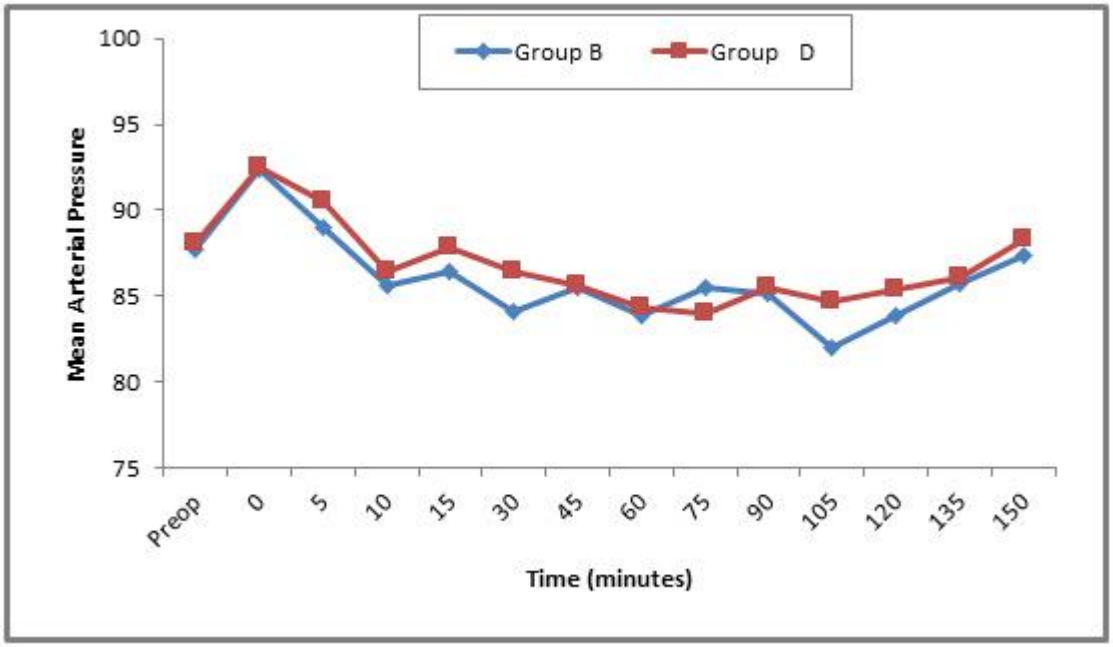

Fig. 2

None of the patients experienced respiratory distress at any point of time. All the patients had peripheral oxygen saturation greater than 95% at all times. No patients were sedated incidence of hypotension and shivering was high in group (B) as compared to (D) group. Three patients in group B (10%) and none in D group had shivering. Hypotension occurred in 12 patients in group B (40%) and 3 in group D (10%).The incidence of bradycardia was higher in group D 6.6% as compared to B 1 (3.3%). No patient suffered from nausea and vomiting in both the groups.

Side effects	Group D		Group B		P-value
	No.	% age	No.	%age	
Shivering	0	0	3	010	0.237
Hypotension	3	10	12	40	0.017*
Bradycardia	2	6.7	1	3.3	1.000

Table 4: Side Effects in Two Groups

Lower VAS values (<3) were observed in both the groups during the course of surgery and none of the patients required additional analgesic intraoperatively.

Postoperative VAS scores and total analgesic requirement in 24 hour were minimal in group D (p value <0.0001). Group B had statistically significant requirement of rescue analgesia as compared to group D.

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DISCUSSION: Our study has shown that the addition of low dose dexmedetomidine as adjuvant to low dose bupivacaine in spinal anaesthesia provides effective spinal anaesthesia and significantly shortened the onset of sensory block and motor block prolonged the duration of sensory and motor block and had increased the time of first analgesic requirement.

Various animal and human studies were conducted with intrathecal dexmedetomidine without any postoperative neurological deficits.[9,10]

In our study the results showed that the minimal dose of dexmedetomidine 3µg significantly prolonged both sensory and motor block[11] and provided effective spinal anaesthesia. Quality of analgesia significantly improved with use of dexmedetomidine as an adjuvant when compared to lone bupivacaine.

The mechanism of action responsible for prolongation of motor and sensory blockade with intrathecal dexmedetomidine is not well known. It was proposed that dexmedetomidine acts as an agonist on α-2 adrenoreceptor located in the presynaptic C-fibers and post synaptic dorsal horn neurons in the spinal cord. When it is given intrathecally it produces analgesia by depressing the release C-fiber excitatory nociceptive transmitters (Glutamate and substance P) and by hyperpolarization of post synaptic dorsal horn neurons.[13,14,15,16]

This may also be responsible for higher level of block[12] achieved with dexmedetomidine α-2 adrenoreceptor agonist by binding to α-2 receptor in motor neuron of dorsal horn of spinal cord inhibits the release of excitatory transmitter and prolongs the duration of motor blockade.[17]

Dexmedetomidine is eight times more specific and highly selective α-2 adrenoreceptor agonist as compared to clonidine thereby making it a useful and safe adjunct in diverse clinical application.

Gupta et al found the superiority of dexmedetomidine in sensory and motor block characteristics when added as adjuvant to ropivacaine intrathecally.[18] Kanazi et al found that 3µg of dexmedetomidine or 30µg clonidine added to 13mg spinal bupivacaine produced same duration of sensory and motor block with minimal side effects in urological surgical patients.

Time of onset of sensory block in our study in dexmedetomidine group was faster (5.3±1.25 min) than in control group significantly (7.9±1.67min).

Drug volume used in our study is 2.5ml which is comparable to Al-Ghanem et al study. We noted significantly delayed requirement of rescue analgesic and significantly reduced 24 hour rescue analgesic requirement with 3µg dexmedetomidine which supports the analgesic efficacy of dexmedetomidine as an intrathecal adjunct. A study done by Gupta et al also showed improved analgesic efficacy on comparison of dexmedetomidine and fentanyl as intrathecal adjuvant ($p < 0.001$).

In the present study side effects like bradycardia and hypotension sedation were not significant probably because of small dose of intrathecal dexmedetomidine. In our study the population involved includes elderly patients with cardiovascular comorbidities. In view of few evidences of efficacy low dose of dexmedetomidine as an adjuvant to low of hyperbaric bupivacaine in spinal anaesthesia we strived to explore usefulness and efficacy of low dose bupivacaine in elderly patients.

CONCLUSION: Spinal anaesthesia for elderly patients undergoing lower limb surgeries with 1.5 CC. of bupivacaine 0.5% and 3µg dexmedetomidine is safer with lower evidence of complications without compromising the surgical conditions. Intrathecal dexmedetomidine enhances analgesia from sub

therapeutic doses of local anaesthetics and hence make it possible to achieve successful spinal anaesthesia using otherwise inadequate doses of local anaesthesia.

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