Randomized, Double Blind Study of Intrathecal Low Dose Dexmedetomidine plus Bupivacaine Versus Bupivacaine for surgical repair of hip fracture in Elderly Patients

Emaddeen S. Nasr 1, Adham A. Elgeidi 2
Lecturer of Anaesthesia and surgical intensive care / Faculty of Medicine / Mansoura University Hospitals / Egypt
Lecturer of Orthopedic Surgery / Faculty of Medicine / Mansoura University Hospitals / Egypt

Background:
In the elderly neuraxial anesthesia is associated with exaggerated responses to conventional doses of local anesthetics, thereby increasing the incidence of hemodynamic complications. This study was carried out to compare the efficacy and safety of dexmedetomidine as an small dose hyperbaric bupivacaine with the conventional dose of hyperbaric bupivacaine in patients undergoing hip fracture surgeries in terms of hemodynamic stability, efficacy of intraoperative and postoperative analgesia and avoidance of other complication of spinal anesthesia.

Patients & Methods:
Fifty patients were recruited in this Prospective, randomized double blind study to receive either intrathecal 1.5 ml (7.5 mg) bupivacaine with dexmedetomidine 3 μg (in normal saline 1 ml) as an adjuvant (Group BD), or 2.5 ml (12.5mg) of 0.5% hyperbaric bupivacaine alone (Group B). The onset and duration of sensory and motor block were assessed intraoperatively. The hemodynamic parameters, duration of complete and effective analgesia was recorded, pain score was assessed postoperatively. The incidence of side effects such as excessive sedation, nausea, vomiting and shivering were recorded.

Results:
The Demographic data were comparable in the two groups. There was a significantly more stable intraoperative blood pressure, prolonged duration of sensory block in the BD group. The duration of effective analgesia were also significantly prolonged in the postoperative period in BD group.

Conclusions:
Intrathecal reduced dose of dexmedetomidine (3 μg) as an adjuvant to small dose bupivacaine provide more hemodynamic stability with good intraoperative and postoperative analgesia and less side effects.

Keywords: Intrathecal dexmedetomidine, bupivacaine, hip fracture surgeries.

Introduction
Neuraxial anesthetic blockade is a popular anesthetic technique for orthopedic lower limb surgeries as it is simple and effective procedure of producing anaesthesia and good postoperative analgesia. It has a definite advantage in elderly patients over general anesthesia, because it reduces surgical stress by blocking nociceptive impulses from the operative site and a decreased sympathetic efferent nerve activity, so minimizing cardio-respiratory complications and overall morbidity and mortality (1,2). Most patients undergoing hip fractures are elderly and frequently has impaired cardiac, respiratory or other body organ function. Their spinal anesthesia are commonly managed by administration of small dose of local anesthetic to limit the block level so minimize the hemodynamic changes. However, sometimes it may not achieve the required level of sensory block. So, intrathecal additive is frequently administered with local anesthetic to compensate for the deficient analgesic effect and considered good if they conserving hemodynamic stability, respiratory efficiency and mental integrity. Dexmedetomidine is a new highly selective α2-agonist and it is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic parameters, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects (3,4).

Patients and Methods
We conducted a randomized, prospective, double-blind study which approved by the Ethics committee of Mansoura University and written informed consent was obtained from the patients. Fifty patients with class American Society of Anesthesiologist (ASA) I-III aged from 55 to 85 years, were scheduled for hip surgery (e.g. hemiarthroplasty, Dynamic Hip Screw “DHS”) under spinal anesthesia. By Using the sealed envelope method, the patients were randomly allocated into two equal groups (n=25).

Patients with uncontrolled or labile hypertension, dysrhythmia, bradycardia, or on therapy with adrenergic receptor antagonist, ACE inhibitor or calcium channel blocker were excluded from the study. Also allergy to the study drugs and any contraindication to spinal anesthesia such as hemorrhagic diathesis, spine deformity, increased intracranial pressure, neurological disorders, or infection at the puncture site were excluded.

Patients were assured to be fasting 6 hours at least before surgery and preloaded with 10 ml Kg-1 of hydroxyethyl starch solution (6% HES 200/0.5 Braun Melsungen AG, Germany) through an 18-G peripheral IV cannula over 20:30 min in the preanesthetic area during which they were monitored with an ECG, automated noninvasive arterial
blood pressure, and pulse oximetry. An average of two readings of the mean arterial blood pressure (MABP) and heart rate (HR) taken 5 minutes apart was considered the basal readings. These monitoring were extended also after the patients were shifted to the operating room (OR). In the operating theatre, spinal anaesthesia was performed in the sitting position under complete aseptic technique and skin infiltration with 0.5ml of 1% lidocaine at site (L3-4 or L4-5) then a spinal needles 25-G pencil point type were used.

Patients were randomly divided into two equal groups (n = 25):

Group B: received intrathecal 2.5 mL (12.5 mg) of 0.5% hyperbaric bupivacaine hydrochloride (Astra Zeneca, Sweden) = (2.5) total volume.

Group BD: received intrathecal 1.5 mL (7.5 mg) of 0.5% hyperbaric bupivacaine and 3 µg dexametomidine in 1 mL of normal saline = (2.5) total volume.

Dexametomidine = Precedex 100µg/ml; Abbott Laboratories was diluted with preservative-free normal saline to 10µg/ml then 3 µg in 1 ml.

Intrathecal injection was given over approximately 10–15 s. Patients were made to lie supine immediately after completion of the injection. Oxygen (4L/min) was administered via a mask during surgery. Hypotension, defined as a decrease of systolic blood pressure by more than 25% from baseline or a fall of systolic pressure below 90 mmHg, was treated with incremental doses of IV ephedrine hydrochloride 5 mg and increase rate of IV fluids and blood replacement was assured if indicated. Bradycardia, defined as heart rate < 50 bpm, was treated with IV atropine 0.2–0.6 mg.

The incidence of hypotensive episodes, bradycardia and other adverse effects, such as nausea, vomiting, shivering and heavy sedation were recorded till the end of surgery. Non-invasive blood pressure, heart rate, respiratory rate and oxygen saturation were recorded every 2 min during 1st 20 min after injection of the spinal anesthetic drugs and then every 5 min till the end of surgery.

Sensory block level was assessed by loss of pinprick sensation on each side of the midsagittal line, every 2 min until the maximum level has established by 3 consecutive tests then surgery was allowed. Testing was then performed every 15 min and the point of two segment regression of the block and that of recovery of S2 dermatome was observed and all were recorded.

Sedation was assessed by a modified Ramsay sedation scale (5)(RSS; 1 = anxious and agitated, 2 =co-operative and tranquil, 3 =drowsy but responsive to command, 4 =asleep but responsive to glabellar tap, 5 =asleep with a sluggish response to tactile stimulation, 6 =asleep and no response) (5).

was used to measure sedation level every 20 min after spinal anesthesia. Motor block of the lower limb was assessed according to the Bromage scale every 2 min till the score of 3 or up to a maximum of 15 min, which of them was earlier, then every 15 min during operation till the end of surgery.

0- able to flex the whole lower limb at the hip
1- able to flex the knee but unable to raise the leg at the hip
2- able to planter flex the ankle but unable to flex the knee
3- no movement of lower limb

Intraoperative analgesia was supplemented by 20 mg fentanyl increments with a maximum of 100 µg and recorded. Patients received 100 mg fentanyl and those required supplementation of general anesthesia were excluded from the study.

In the PACU assessment of the level of sensory blockade continued every 15 min until the time of recovery of S2 dermatome.

Motor block was evaluated at the end of surgery and then at every 15 min interval, until full motor function recovery (score = 0).

Post-operative pain was assessed using a 0-10 linear VAS every 15 min until the first request of supplement analgesia. Rescue doses of analgesics consisted of intravenous paracetamol or ketoprofen were given if (VAS > 3/10) and recorded.

Regular monitoring of vital signs was performed. Side-effects such as hypotension, bradycardia, nausea, vomiting, respiratory difficulty or oxygen desaturation (SpO2<90%) or any other complication were managed and recorded.

Patients were discharged from the PACU after sensory regression to the S1 segment, Bromage 0 and an Aldrete score of 9 were achieved (6).

The anesthesiologists performing the block recorded the intra-operative data and the nurse followed the patients post-operatively until discharged from the post-anesthesia care unit (PACU), both were blind to the group to which the patient was allocated. Follow-up was carried out 5 days postoperatively for any side-effects

As shown in (Table 1), All patients ages were above 61 years and the mean age in group B was 71.23±4.35 as compared to 70.03±3.45 in group BD. A majority of patients in both groups were male, being 60% in group B and 64% in group D. Female patients formed 40% in group B and 36% in group D. The mean weight in group B was 69.04±3.23, its range was 65-76 kg, whereas the corresponding values in group D showed a mean weight of 71.68 ± 6.35, its range was 58–82 kg. Mean height of the patients in group B was 168.18±2.25 cm, with a range of 154-171cm, which was comparable with height of group II population, with a mean of 165.11±3.29 and a range of 158-171cm. Similarly, mean values for duration of surgery were

Statistical analysis:

At the end of the study, SPSS for Windows version 16 was used for the statistical analysis and the tabulated data was analyzed using the analysis of variance and Chi-square test with a P-value of <0.05 as significant.

Results

The present study was conducted to assess the effect of low-dose hyperbaric bupivacaine and dexametomididine intrathecally in causing minimal hypotension after spinal anesthesia in elderly patients undergoing hip fracture surgeries.
identical in both groups. On statistical analysis, the demographic profile in both groups was comparable and non-significant on statistical analysis (P > 0.05).

Table 1: Demographic profile of patients in studied groups B and BD

<table>
<thead>
<tr>
<th>Demographic data</th>
<th>GROUP B (n=25)</th>
<th>GROUP BD (n=25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age Range Mean±SD</td>
<td>62-82 71.23±4.35</td>
<td>64-85 70.03±3.45</td>
<td>0.09</td>
</tr>
<tr>
<td>Sex Male No. (%)</td>
<td>18(60%) 7(40%)</td>
<td>16(64) 9(36)</td>
<td>0.10</td>
</tr>
<tr>
<td>Weight(kg) Range Mean±SD</td>
<td>65-76 69.04±3.23</td>
<td>58.82 71.23±2.19</td>
<td>0.09</td>
</tr>
<tr>
<td>Height(cm) Range Mean±SD</td>
<td>154-171 168.18±2.25</td>
<td>158-171 165.11±3.29</td>
<td>0.07</td>
</tr>
<tr>
<td>Duration of surgery(min)</td>
<td>45-88 72.45±3.36</td>
<td>41.00-78.00 67.35±2.48</td>
<td>0.08</td>
</tr>
</tbody>
</table>

* = Significant difference between GB and GBD (P < 0.05).

In group B, the mean SBP at 5 min of spinal block (100.44±13.37) and at 10 min (104.11±11.13) showed highly significant lower values from corresponding values at 5 min (126.44±17.90) and 10 min (128.51±14.46) in group D (P < 0.001). By the arrival to 15 min post block, this highly statistically significant variation between the two groups still detected but with lesser extent. On the other hand, mean SBP in both groups remained stable and no statistical significant difference was observed between both groups (P > 0.05) throughout the remaining time of operation.

Table 2: Systolic blood pressure during surgery in both groups

<table>
<thead>
<tr>
<th>Time Interval(min)</th>
<th>GROUP B (n=25)</th>
<th>GROUP BD (n=25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Basal</td>
<td>112-155</td>
<td>128.12±17.13</td>
<td>116-156</td>
</tr>
<tr>
<td>5</td>
<td>80-125</td>
<td>100.44±13.37</td>
<td>90-145</td>
</tr>
<tr>
<td>10</td>
<td>83-120</td>
<td>104.11±11.13</td>
<td>90-147</td>
</tr>
<tr>
<td>15</td>
<td>85-129</td>
<td>106.80±11.65</td>
<td>95-141</td>
</tr>
<tr>
<td>20</td>
<td>90-134</td>
<td>105.01±14.32</td>
<td>93-131</td>
</tr>
<tr>
<td>25</td>
<td>84-137</td>
<td>111.80±15.28</td>
<td>88-135</td>
</tr>
<tr>
<td>30</td>
<td>88-127</td>
<td>107.42±11.34</td>
<td>80-120</td>
</tr>
<tr>
<td>40</td>
<td>93-132</td>
<td>111.06±14.42</td>
<td>97-138</td>
</tr>
<tr>
<td>50</td>
<td>88-136</td>
<td>107.60±11.80</td>
<td>85-140</td>
</tr>
<tr>
<td>60</td>
<td>90-128</td>
<td>109.00±6.60</td>
<td>94-130</td>
</tr>
<tr>
<td>70</td>
<td>92-133</td>
<td>101.53±10.54</td>
<td>87-128</td>
</tr>
<tr>
<td>80</td>
<td>103-127</td>
<td>113.83±8.08</td>
<td>100-127</td>
</tr>
</tbody>
</table>

Table 3: Diastolic blood pressure during surgery in both groups
The mean time to reach the onset of an adequate level of sensory analgesia at T10 in group B was 5.88±1.42, with a range of 3-9 min when compared to a mean time of 6.23±1.54 with a range of 4-9 min in group BD it revealed no significant difference (P > 0.05).

The mean time to reach a peak level of sensory block in group B (8.97±1.23) was achieved more lately than that of group BD (6.24±1.18), and it was significant (P < 0.05) on comparison. Mean time to reach S2 segment regression in group B (133.77±4.77) it was significantly higher than that of group BD (145.54±5.34) on statistical analysis (P > 0.05).

However, the duration of complete recovery of motor power in the group D (138.50±5.30) as compared to group DB (136.71±4.43) revealed no significant statistical difference (Table 4).

Table 4: Characteristics of the blockade in studied groups

<table>
<thead>
<tr>
<th>Characteristic of blockade</th>
<th>GROUP B (n=25)</th>
<th>GROUP BD (n=25)</th>
<th>value</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of sensory analgesia at T10(min)</td>
<td>3-9 5.88±1.42</td>
<td>4-9 6.23±1.54</td>
<td>0.07</td>
<td></td>
</tr>
<tr>
<td>Range and Mean±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time to peak sensory level (min)</td>
<td>6-12 8.97±1.23</td>
<td>4-8 6.24±1.18</td>
<td>0.03*</td>
<td></td>
</tr>
<tr>
<td>Range and Mean±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Segmental regression to S2(min)</td>
<td>130-140 133.77±4.77</td>
<td>135-152 145.54±5.34</td>
<td>0.05*</td>
<td></td>
</tr>
<tr>
<td>Range and Mean±SD</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of motor block(min)</td>
<td>137-144 138.50±5.30</td>
<td>135-145 136.71±4.43</td>
<td>0.06</td>
<td></td>
</tr>
</tbody>
</table>

* = Significant difference between GB and GBD (P < 0.05).

The incidence of hypotension was much higher in group B (44%) as compared to group BD (8%), which was statistically significant (P < 0.05). As a result the consumption of vasopressors was significantly higher (P < 0.05) in group B as compared to group BD. Bradycardia (HR<50/min) occurred in one patient in group BD and it was managed with 0.4 mg atropine given once.

Postoperatively, consumption of analgesic doses (given when VAS > 30%) was significantly higher (P < 0.05) in the group B (Table 5).

Shivering was observed in eight cases in group B as compared to five in group BD, which showed a significant value on statistical comparison (P < 0.05). No patients in either group experienced nausea, vomiting or respiratory depression. Sedation scores level were in the range 0:1 with a median of zero in both groups.

Table 5: Incidence of hypotension, use of vasopressors, and total local analgesic dose consumption postoperatively and other side effects

<table>
<thead>
<tr>
<th>Side effects</th>
<th>Group(n=25)</th>
<th>Group(n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NO %</td>
<td>NO %</td>
</tr>
<tr>
<td>Incidence of hypotension</td>
<td>12 (48%)</td>
<td>4 (16%)</td>
</tr>
</tbody>
</table>
As regard the post-operative periods, the mean values of MAP and HR were comparable in both groups throughout the intra- and post-operative periods. All patients in the PACU had a peripheral oxygen saturation higher than 94% all the time and did not require supplemental oxygen. Intra-

**Discussion**

The selection of this age group was deliberate so directed us to study the dose reduction of LA and addition of low-dose dexmedetomidine with the main aim of establishment of threatened hemodynamic stability in geriatric patients, as this category of population reveal exaggerated hemodynamic responses to different anesthetics. Although surgery of hip fracture repair with recent advances in orthopedic surgery it became of shorter duration but still with the potential of unexpected prolongation of time. Spinal anesthesia is a repeatedly used, simple and effective method of producing anaesthesia and early postoperative analgesia in patients undergoing lower limb orthopaedic surgeries. Various adjuvants have been used added to bupivacaine for prolonging the duration and improving the quality of analgesia. Intrathecal opioids provide pain relief for up to 24 hr but its use has been associated with delayed respiratory depression(7,8). This study was conducted to evaluate the effect of low-dose hyperbaric bupivacaine and dexmedetomidine intrathecally in causing minimal hypotension after spinal anesthesia in elderly patients undergoing hip fractures and proximal lower limb surgeries. Subarachnoid $\alpha_2$-adrenoceptor agonists prolong the motor and sensory block of local anesthetics with a not well-known mechanism. They may act by binding to presynaptic C-fibers and also postsynaptic dorsal horn neurons. Their analgesic action is due to depression of the release of C-fiber transmitters with hyperpolarisation of postsynaptic dorsal horn neurons (9). Al-Mustafa et al studied effect of dexmedetomidine 5 and 10 µg with bupivacaine in urological procedures and decided that dexmedetomidine prolongs the duration of spinal anesthesia in a dose-dependent manner (10).

Al-Ghanem et al (11) had studied the effect of addition of 5 µg dexmedetomidine or 25 µg fentanyl intrathecal to 10 mg isobaric bupivacaine in vaginal hysterectomy and found that 5 µg dexmedetomidine produces more prolonged motor and sensory block as compared with 25 µg fentanyl. Rajni Gupta et al (3) has demonstrated that the addition of 5 µg dexmedetomidine with hyperbaric bupivacaine significantly prolongs both sensory and motor block, also provided good quality intraoperative analgesia and operative or post-operative nausea or vomiting did not occur in any of the two groups of patients.

No delayed post operative onset of back, buttock or leg pain or paresthesia in the 1st two weeks

No hemodynamic stability and no patient perceived visceral pain during abdominal surgery under spinal anesthesia. Smaller dose of intrathecal dexmedetomidine (3µg) used in combination with bupivacaine in humans have been shown to shorten the onset of motor block and prolong the duration of motor and sensory block with hemodynamic stability and lack of sedation (4). These beneficial effects were also proved by the results of this study; however a lower dose of bupivacaine (7.5mg) was used. The less sedative adverse effect of dexmedetomidin observed in both studies may be attributed to the use of its small dose.

In this study there was a less incident hypotension present in the dexmedetomidine group than that in the bupivacaine group which was statistically significant and also required more number of ephedrine boluses. Also of The anti shivering property of $\alpha$-2 adrenergic drugs was significantly observed between the two groups of this study while Talke et al.(13) mentioned that no significance difference in the incidence of shivering in their study.

In conclusion: In elderly orthopedic surgical procedures, intrathecal low doses of both dexmedetomidine plus bupivacaine more superior than conventional bupivacaine dose as regard hemodynamic stability, intraoperative and postoperative analgesia with a minimal side effects.

**References**

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