Comparison of Dexmedetomidine Versus Dexamethasone as Adjuvants to Intrathecal Bupivacaine in Emergency Orthopedic Lower Limb Operations

Mohamed E. Elshahawy, Hani I. Taman, Mostafa S. Elawady, Ahmed M. Farid*
Anaesthesia and Surgical Intensive Care Department, Faculty of Medicine, Mansoura University, Egypt
*Corresponding author: Ahmed M. Farid, Mobile: (+20)1002356222, E-Mail: ahmfarid15@hotmail.com

ABSTRACT
Background: Various adjuvants were added to intrathecal anesthetics to improve quality of the block and postoperative analgesia.

Objective: The aim of the current work was to compare the efficacy of adding dexmedetomidine versus dexamethasone as adjuvants to intrathecal bupivacaine in emergency orthopedic lower limb surgery.

Patients and Methods: This prospective comparative double blinded study included a total of 90 patients with lower limb trauma requiring surgery, attending at Mansoura University emergency Hospital. Cases were randomly divided into three groups; each consisted of 30 cases. Group A received dexmedetomidine as an adjuvant to bupivacaine, Group B received dexamethasone as an adjuvant, and Group C received spinal bupivacaine plus 1 cm of normal saline. Sensory and motor blocks as well as post-operative VAS score in addition to need for analgesics were assessed.

Results: Demographic data did not differ between the three study groups (p > 0.05). Group A showed a significantly earlier onset of sensory block (p = 0.005), motor block (p = 0.009), as well as late regression to L1 sensory level (p < 0.001). Additionally, longer analgesia (p < 0.05) and longer time before the first call for analgesics (p = 0.005) was associated with group A. However, complications encountered did not differ between the three study groups (p > 0.05).

Conclusion: It could be concluded that intrathecal dexmedetomidine is superior to both dexamethasone and bupivacaine alone regarding duration of analgesia and pain severity. Moreover, it has more rapid onset and longer duration of sensory blockade. No significant side effects were noted when compared to the remaining groups.

Keywords: Adjuvants, Intrathecal, Emergency, Orthopedic, Analgesia.

INTRODUCTION
Although lower limb procedures can be conducted under local or general anesthesia, neuraxial blocking is the preferable approach. Spinal blockade is distinguished by its cost-effectiveness, fast start, and ability to achieve deep block with a lesser risk of infection. Nonetheless, because the medications used for this sort of block have a short duration of effect, the patient’s experience with post-operative pain is critical. As a result, pain management requires the use of postoperative analgesics (1,2).

Multiple adjuvants have been proposed to extend the duration of action and lessen the negative effects of local anesthetic medicines (3). Opioids, alpha 2 agonists, steroids, neostigmine, and vasoconstrictors are examples of adjuvants (2, 4).

Clonidine and dexmedetomidine are two 2 agonists that impact 2 receptors pre- and postsynaptically (5). Dexmedetomidine is a 7-fold more selective alpha2 receptor agonist than clonidine and works in a similar way to block hyperpolarization activated cation channels. Dexmedetomidine has a long history of usage as an analgesic and anesthetic. It is known for its analgesic, anti-anxiety, neuroprotective, and anesthetic sparing properties (6). Additionally, it was utilized to prolong analgesia in epidural, subarachnoid, and caudal blocks (7,8). Intrathecal dexmedetomidine has been demonstrated to have a longer duration of block. It also enhances postoperative analgesia without causing any major side effects, especially when given at dosages of less than 5g (9).

Dexamethasone is a strong anti-inflammatory drug that has been studied for its function as an adjuvant to local anesthetics in neuraxial and peripheral nerve blocks throughout the last decade (10).

Steroids’ methods for potentiating analgesic effects appear to be distinct from its inherent anti-inflammatory activity (11,12). There’s additional evidence that dexamethasone’s analgesic actions are amplified by both local and systemic effects on nerve fibers (13).

Research compared the effects of 8 mg (preservative-free) intrathecal dexamethasone with conventional dosages of 0.5 percent hyperbaric bupivacaine in orthopedic procedures. It has been proven to extend the duration of sensory block in spinal anesthesia without causing any notable side effects (14).

This study was aimed to compare the efficacy of adding dexmedetomidine compared with dexamethasone to intrathecal bupivacaine regarding duration of anesthesia and post-operative analgesia for emergency lower limb orthopedic operations.

PATIENTS AND METHODS
This prospective comparative double blinded study included a total of 90 patients with lower limb trauma requiring surgery, attending at Mansoura University emergency Hospital. Cases were randomly divided into three groups; each consisted of 30 cases.

Group A received dexmedetomidine as an adjuvant to bupivacaine, Group B received dexamethasone as an adjuvant, and Group C received spinal bupivacaine plus 1 cm of normal saline.

Ethical Consideration:
An approval from Institutional Review Board (IRB-MFM) of Mansoura University, Faculty of...
Medicine with code number (R/16.12.32, March 2017) was obtained. Every patient signed an informed written consent for acceptance of participation in the study. Ethics guidelines for human experimentation were adhered to in line with the Helsinki Declaration of the World Medical Association.

Inclusion criteria: Age range between 20 and 60 years, scheduled for orthopedic lower limb surgery with ASA scores 1 and 11.

Exclusion criteria: Patients outside the previously mentioned range, presence of any contraindication for regional anesthesia, history of allergy to one of the study medications, and cases with severe cardiac, renal, or hepatic illness.

Patient preparation:
Before surgery, the patients were transferred to the operation theater, and they were connected to all noninvasive monitors. Pulse, non-invasive arterial blood pressure (BP) as well as oxygen saturation were noted for every patient. Moreover, electrocardiography monitoring was enabled. All cases were preloaded with 10 ml/kg Ringer's lactate.

Procedure:
Under strict aseptic precaution, 25-gauge spinal needle was inserted in L3-L4 interspinal space with patient in sitting position using a midline approach. After confirmation with free flow of cerebrospinal fluid, patients allocated to Group A were injected by bupivacaine 0.5% heavy × 3.0 ml + 1 ml of preservative free normal saline containing 5 μg dexmedetomidine. Patients allocated to Group B received injection bupivacaine 0.5% heavy × 3.0 ml + 1 ml fentanyl equivalent to 4 mg. In addition, Patients in group C received bupivacaine 0.5% heavy × 3.0 ml + 1 ml of normal saline.

Intraoperative complaints were managed by increments of fentanyl 25 μg, midazolam 1–2 mg, and propofol 50 mg in consequence as required. General anesthesia was applied using a laryngeal mask and sevoflurane inhalation if the patient still cannot tolerate pain, and these patients excluded from the study.

Outcome measures:
VAS score was the primary outcome and it was measured at different time points (2h, 4h, 6h, 8h, 10h, 12h, and 24 hours postoperatively). The secondary outcome included the effect of these adjuvants on sensory and motor blockade. If the postoperative VAS was higher than 3, it was treated by analgesics according to the WHO analgesic ladder.

Bromage scale (0–3)15; 0: The patient is able to move the hip, knee and ankle. 1: The patient is unable to move the hip, but can move knee and ankle. 2: The patient is unable to move the hip and knee but can move the ankle. 3: The patient cannot move the hip, knee and ankle.

Complications:
Hypotension was defined as a mean arterial blood pressure (MAP) < 60 mmHg, and it was managed by bolus doses of ephedrine 5 mg, fluids and blood transfusion as indicated. Bradycardia was defined as heart rate (HR) < 60 b/min, and it was managed by atropine 0.5 mg increments. Desaturation was defined as SaO2 < 90% and managed by an oxygen face mask. Vomiting was treated with metoclopramide 10 mg or granisetron 1 mg if persistent.

Statistical analysis
Data were analyzed by SPSS software version 24. Qualitative data were expressed as number and percentage within group. Quantitively data were tested for normality using Kolmogorov Smirnov test and they were expressed as mean±standard deviation or median and range. Comparison between the quantitative data of three study groups was carried out by one-way ANOVA test. Qualitative data were compared between the three groups using Chi square test. P value < 0.05 was considered significant in all used tests.

RESULTS
Regarding demographics, there were no significant differences between the three study groups when it comes to age, sex, or BMI (p > 0.05) (Table 1).

<table>
<thead>
<tr>
<th>Table (1): Baseline findings.</th>
<th>Group A (n = 30)</th>
<th>Group B (n = 30)</th>
<th>Group C (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>34.86 ± 11.68</td>
<td>36.27 ± 14.59</td>
<td>41.00 ± 12.82</td>
<td>0.170</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-Male</td>
<td>21 (70%)</td>
<td>19 (63.33%)</td>
<td>18 (60%)</td>
<td></td>
</tr>
<tr>
<td>-Female</td>
<td>9 (30%)</td>
<td>11 (36.67%)</td>
<td>12 (40%)</td>
<td>0.274</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.23 ± 3.32</td>
<td>25.22 ± 3.45</td>
<td>25.74 ± 7.59</td>
<td>0.248</td>
</tr>
</tbody>
</table>

When compared to groups B and C, group A reported a faster start of sensory blocking at the T 10 level (p = 0.005) and a shorter duration to reach maximal sensory intensity. In addition, Group B had a faster start of sensory block and a shorter time to reach maximal block than Group C. Despite this, there was no significant difference in the highest sensory level attained across the three groups. When compared to the other groups, Group A had a considerably longer duration for sensory block regression down to the L1 dermatome (p 0.001), and the same when comparing Group B to Group C. (Table 2).
When compared to the other groups, group A had a significantly earlier start of motor block (p = 0.003). The three research groups had the same maximum Bromage score. When compared to the other two groups, group A had a substantially longer total time of motor blockage (p 0.001) (Table 3).

Table (3): Motor block characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 30)</th>
<th>Group B (n = 30)</th>
<th>Group C (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean onset time of motor block (min)</td>
<td>9.33±0.61</td>
<td>12.09±2.03*</td>
<td>13.36±3.16†</td>
<td>0.003</td>
</tr>
<tr>
<td>Maximum Bromage scale</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Total duration of motor block (min)</td>
<td>229.2±35.4</td>
<td>181.3±22.5*</td>
<td>167.89±29.05†</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*P<0.05 when group B compared to group A. †P=0.05 when group C compared to group A. ‡P<0.05 when group C compared to group B.

Although postoperative pain scores did not differ between the three study groups during the early 8 hours after operation (p > 0.05). However, 10-, 12-, and 24-hour VAS scores were significantly lower for group A when compared to group B and C (Table 4).

Table (4): Post-operative VAS scores.

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 30)</th>
<th>Group B (n = 30)</th>
<th>Group C (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>2h</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>2 (1–3)</td>
<td>1</td>
</tr>
<tr>
<td>4h</td>
<td>2 (1–3)</td>
<td>2 (1–4)</td>
<td>2 (2–4)</td>
<td>0.245</td>
</tr>
<tr>
<td>6h</td>
<td>3 (2–4)</td>
<td>3 (3–4)</td>
<td>3 (3–4)</td>
<td>0.226</td>
</tr>
<tr>
<td>8h</td>
<td>3 (3–4)</td>
<td>4 (3–4)</td>
<td>4 (3–4)</td>
<td>0.156</td>
</tr>
<tr>
<td>10h</td>
<td>3 (3–4)</td>
<td>4 (3–5)*</td>
<td>5 (4–6)†</td>
<td>0.039</td>
</tr>
<tr>
<td>12h</td>
<td>3 (3–4)</td>
<td>4 (4–5)*</td>
<td>5 (4–6)†</td>
<td>0.018</td>
</tr>
<tr>
<td>24h</td>
<td>4 (3–4)</td>
<td>5 (4–6)*</td>
<td>6 (4–7)†</td>
<td>0.008</td>
</tr>
</tbody>
</table>

*P<0.05 when group B compared to group A. †P<0.05 when group C compared to group A. ‡P<0.05 when group C compared to group B.

Adverse effects including bradycardia, hypotension, as well as nausea and vomiting did not differ between the three study groups (Table 5).

Table (5): Adverse effects.

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 30)</th>
<th>Group B (n = 30)</th>
<th>Group C (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradycardia</td>
<td>3 (10%)</td>
<td>2 (6.67%)</td>
<td>3 (10%)</td>
<td>0.756</td>
</tr>
<tr>
<td>Hypotension</td>
<td>2 (6.67%)</td>
<td>3 (10%)</td>
<td>3 (10%)</td>
<td>0.698</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>2 (6.67%)</td>
<td>2 (6.67%)</td>
<td>2 (6.67%)</td>
<td>1</td>
</tr>
</tbody>
</table>

*P<0.05 when group B compared to group A. †P=0.05 when group C compared to group A. ‡P<0.05 when group C compared to group B.

Post-operative call for analgesics took longer time for group A compared to other study groups (p = 0.005) and in group B when compared to C group (Table 6).
Table (6): post-operative call for analgesics.

<table>
<thead>
<tr>
<th></th>
<th>Group A (n = 30)</th>
<th>Group B (n = 30)</th>
<th>Group C (n = 30)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to firstcall for</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>analgesics (hours)</td>
<td>4.93 ± 1.86</td>
<td>2.86 ± 0.79*</td>
<td>2.41 ± 0.78††</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Surgery is frequently associated with a high rate of pain. Previous research found that in industrialized nations, 41-61% of patients have moderate or severe postoperative pain (16).

Adjuvant to local anesthetics is a rapidly changing and interesting field of anesthesia, with new technologies promising to increase patient pleasure and safety. While opioids are still the most widely used local anesthetic adjuvants in clinical practice, alpha2 receptor antagonists, particularly dexametomidine, have been found to augment the efficacy of local anesthetics while maintaining a safe profile (10).

Our study included 90 cases who were divided into three groups each included 30 cases. The first group received dexametomidine as an adjuvant, the second one received dexamethasone as an adjuvant, and the last group received bupivacaine alone. Age and sex distribution did not differ significantly between the three study groups (p > 0.05).

Another study examined the effectiveness of adding dexametomidine to bupivacaine against dexamethasone to extend the duration of spinal anesthesia and analgesia during lower abdominal surgeries. A total of 60 cases were studied, with one group receiving dexametomidine as an adjuvant, another receiving dexamethasone as an adjuvant, and the third group receiving simply bupivacaine without any adjuvants. There was no significant difference between the three groups in terms of baseline variables (age and sex) (p > 0.05) in that research (17).

In our study, mean time of onset of sensory blockade in the dexametomidine group was 4.52 minutes and it was significantly shorter than the other two groups (p= 0.005). Moreover, time elapsed till reaching the maximum level of sensory blockade was 9.95 minutes (p = 0.001). In addition, mean time to regression to L1 dermatome was 302.44 minutes (p < 0.001).

Another study discovered that the time it took for sensory block to begin was 4.85 minutes, which was considerably less than the Mg sulphate group (p <0.001). The average time it took to attain the maximal sensory level was 10.03 minutes (p <0.001). Furthermore, the dexametomidine group's mean time for regression to the L1 dermatome was substantially longer (290.3 minutes – p< 0.001) (18).

Regarding motor block in our study, mean onset of block was achieved after 9.35 minutes in the dexametomidine group (p = 0.009). Furthermore, total duration of motor block was significantly longer for the same group (p < 0.001).

Makhni et al. (18) found that, the average onset of motor block was 9.02 minutes, which was substantially longer than the Mg sulphate group (p = 0.001). The average duration of the motor block was 224.2 minutes (P <0.05).

The current study found that dexametomidine was associated with faster onset of both sensory and motor blockade. Moreover, it was associated with prolonged post-operative analgesia compared to dexamethasone and bupivacaine alone. Addition of dexamethasone was better than bupivacaine alone regarding the same perspective. However, it was inferior to dexametomidine.

Because dexametomidine is a highly selective agonist of the 2-adrenergic receptor, it can extend sensory and motor blockage. Sedative, analgesic, perioperative sympatholytic, anesthetic-sparing, and hemodynamic-stabilizing characteristics are also present (19). It also has the benefit of not causing respiratory depression (20). It stimulates 2-adrenergic receptors in the superficial dorsal horn neurons in the spinal cord (21). It inhibits pain transmission directly by inhibiting the release of pronociceptive transmitters, substance P, and glutamate from primary afferent terminals, as well as hyperpolarizing spinal interneurons through G-protein-mediated potassium channel activation (22).

The possible explanation of the effect of adding dexametomidine to intrathecal bupivacaine lies in its synergistic effect being selective a2-adrenergic receptor agonist, which binds to the presynaptic C-fibers and postsynaptic dorsal horn neurons. Thus, it produces analgesia by depressing the release of C-fiber transmitters, hyperpolarization of postsynaptic dorsal horn neurons, whereas bupivacaine as a local anesthetic act by blocking sodium channels (23).

The study results went in line with the study conducted by Shukla et al. (24) who compared dexametomidine versus magnesium sulfate added to intrathecal bupivacaine and found that dexametomidine shortened the onset and prolonged the duration of spinal anesthesia. Also, Solanki et al. (25) study proved superiority of intrathecal dexametomidine in comparison with clonidine and fentanyl. It provided prolonged motor and sensory block and reduced demand of additional analgesics.

The current study results were in agreement with the two studies comparing clonidine and dexametomidine in different doses (5 and 3 μg,
respectively) as adjuncts to bupivacaine. Both found the duration of sensory and motor block to be prolonged with dexametomidine compared with clonidine. Postoperative analgesiawas comparable in these two groups and superior compared with bupivacaine alone (26, 27).

Makhni et al. (18) study found that dexametomidine was associated with faster sensory and motor blocks. In addition, the total duration of analgesia was significantly better when compared to Mg sulphate group.

Almost all of the previously mentioned studies as well as the current study confirmed safety and hemodynamic stability of dexametomidine, whether administered intravenously or intrathecally as an adjuvant to spinal bupivacaine anesthesia.

In our study, the detected complications (bradycardia, hypotension, as well as nausea and vomiting) did not differ significantly between the three groups. Moreover, they occurred with a low incidence as no one of such complications occurred in more than 10% of cases in each group. In addition, these complications were properly managed as discussed in patients and methods.

On the contrary, in this study, dexamethasone was found to prolong the sensory blockade and prolong the time to first call for analgesia when added to intrathecal bupivacaine compared with bupivacaine alone.

Intrathecal dexamethasone as an analgesic could be explained by influencing prostaglandin production. Corticosteroids are capable of reducing prostaglandin synthesis by inhibition of phospholipase A2 through the production of calcium-dependent phospholipid-binding proteins called annexins, and by the inhibition of cyclooxygenases during inflammation (28).

The results of the current study regarding dexamethasone went in line with a study conducted by Bani-Hashem et al. (14) who reported an increase in the duration of sensory block associated with the addition of intrathecal dexamethasone.

CONCLUSION
It could be concluded that intrathecal dexametomidine is superior to both dexamethasone and bupivacaine alone regarding duration of analgesia and pain severity. Moreover, it has more rapid onset and longer duration of sensory blockade. No significant side effects were noted when compared to the remaining groups.

Financial support and sponsorship: Nil.
Conflict of interest: Nil.
REFERENCES


