A Randomized Control Study to Compare Intrathecal Dexmedetomidine Used as Adjuvant to Intrathecal Bupivacaine with Intrathecal Bupivacaine Alone in Orthopedic Surgeries

ANTONY A. FAHMY, M.Sc.; MOHAMED K. ABOULGHATE, M.D.; SHEREEN M. AMIN, M.D. and AHMED R. ABD EL-HAKIM, M.D.

The Departments of Anaesthesia, Pain and Intensive Care, Faculty of Medicine, Cairo University

Abstract

Background: Regional techniques especially Spinal anesthesia are used in orthopedic surgeries commonly. It has many advantages over general anaesthesia as adequate analgesia in the perioperative period and it has less complications, also, it provides more successful blockade with less failure rate than epidural block. The main disadvantage is the shorter duration of block and lack of postoperative analgesia.

One of the means to overcome this drawback is adding an adjuvant to the block so as to speed the onset and prolong the duration of the block. Many drugs had been used including clonidine, benzodiazepines and lately dexmedetomidine has been used for this purpose too.

Methods: 60 patients, ASA I/II were enrolled into the study. All patients had spinal anesthesia and randomly allocated into one of two groups. Group C: (30 patients): The patient received 15mg of bupivacaine 0.5% plus 0.4ml saline, Group D: (30 patients): The patient received 15mg of bupivacaine 0.5% plus 0.1ml dexmedetomidine (10 mcg) plus 0.3ml saline.

In both groups assessment was done for time to reach T10 dermatome, time to peak sensory level, time to reach complete motor block (Bromage 3), regression to S1 dermatome and time for motor recovery.

Results: This study demonstrated that a more rapid onset of action of the spinal block was achieved in the dexmedetomidine group, with prolonged duration of both sensory and motor block. Hemodynamic variables were stable and there were no significant differences between both groups.

Conclusion: Finally, it is concluded that Dexmedetomidine (10mcg) is effective as useful adjuvant to the local anesthetic for spinal anesthesia. Dexmedetomidine is associated with a faster onset of action and longer postoperative sensory and motor block. Dexmedetomidine also reduce intraoperative shivering with no significant side effects.

Key Words: Spinal anesthesia – Adjuvants – Bupivacaine and dexmedetomidine.

Introduction

DEXMEDETOMIDINE is a highly selective α2-adrenoreceptor agonist recently introduced to anesthesia. It produces dose-dependent sedation, anxiolysis, and analgesia (involving spinal and supraspinal sites) without respiratory depression. α2-agonists are known to reduce anesthetic requirements. Activation of α2-adrenoceptors in the brain and spinal cord inhibits neuronal firing causing hypotension, bradycardia, sedation, and analgesia. In general, presynaptic activation of the α2-adrenoceptor inhibits the release of norepinephrine terminating the propagation of pain signals. Postsynaptic activation of α2-adrenoceptors in the central nervous system inhibits sympathetic activity and thus can decrease blood pressure and heart rate. Administration of an α2-agonist via an intrathecal or epidural route provides an analgesic effect in postoperative pain without severe sedation [1,2].

Dexmedetomidine has been approved as a short-term sedative for adult intubated patients in the ICU. Given its well-documented beneficial effects of anxiolysis, sedation, analgesia, and sympatholysis with minimal respiratory depression, it also has been used in various other clinical scenarios as an adjuvant to local anesthetics in epidural and intrathecal anesthesia [3].

The use of dexmedetomidine has dramatically increased. This highly selective α2 agonist has a set of unique effects that include titrated sedation, sympatholysis, and analgesia without significant respiratory depression [4].

Aim of the work:

This prospective randomized controlled study is conducted to evaluate the onset and duration of sensory and motor block as well as perioperative
analgesia, adverse effects and effectiveness of dexmedetomidine given intrathecally with 0.5% hyperbaric bupivacaine for spinal anesthesia.

**Patients and Methods**

The present study was a prospective randomized blind controlled study conducted for patients scheduled to undergo elective lower limb orthopedic surgeries under spinal anesthesia in Kasr Al-Aini Hospital, Cairo University during 2014. After obtaining Institutional Ethics Committee approval and written informed consent, 60 patients ASA I/II were enrolled into the study.

**Inclusion criteria:** ASA I, II patients, aged 18-45 years old, height 160-190cm, weight 50-90kg., Scheduled for lower limb surgery (knee arthroscopy, Tibial fractures, Femur fractures, etc...).

**Exclusion criteria:** Any contraindication to spinal anesthesia (patient refusal, severe cardiac disease, severe labile hypertension, raised intracranial pressure or pre-existing neurological disorders, such as multiple sclerosis), patients with coagulopathy due to liver or blood disease, therapeutically coagulopathy, inability to communicate and understand the aim of the project, patients with history of allergic reaction to local anesthetics or benzodiazepines, skin infection at injection site or systemic bacteremia and failure of the block and need for general anesthesia.

**Preoperatively the following routine investigations were done for all patients:**

- Complete Blood Count (CBC), blood grouping, coagulation profile: Prothrombin Time (PT), Prothrombin Concentration (PC), Partial Thromboplastin Time (PTT), International Normalized Ratio (INR), Bleeding Time (BT), Clotting Time (CT), Random Blood Sugar (RBS), blood urea, serum creatinine, Alanine Aminotransferase (ALT), Aspartate aminotransferase (AST), blood-albumin, bilirubin total and direct, Electrocardiogram (ECG) for patients aged >40 years, X-ray chest, serum electrolytes if necessary.

**Anesthetic procedure:**

Upon arrival to the operating theatre, venous access was secured using an 18G venous cannula with no premedication given. Measurements of baseline hemodynamic parameters were recorded.

All patients were monitored intra-operatively using: An ECG, non-invasive blood pressure, and pulse oximetry. An infusion of Ringer's lactate solution was started as a bolus of 500ml in 15min.

All patients had spinal anesthesia; patients were put in sitting position. Under strict aseptic precautions, the back was sterilized using povidone iodine at the site of insertion, tips of lumbar spine were palpated and L3-4 space was selected. The skin was infiltrated with about 2ml of 1% lignocaine. Lumbar puncture was performed at the L3-L4 level through a midline approach using a 25G spinal needle.

**Using closed envelopes random numbers, patients were allocated into two groups:**

- **Group C (control group):** (30 patients): The patient received 15mg hyperbaric bupivacaine and 0.4ml normal saline as control.
- **Group D (dexmedetomidine group):** (30 patients): The patient received 15mg hyperbaric bupivacaine and 0.1ml (10 µg) DXM (Precedex® by Hospira), and 0.3ml saline.

After intrathecal injection, patients were positioned in supine position and oxygen 4L/min was given through a face mask. The anesthesiologist performing the block didn't know the study drug used and recorded the intraoperative data. Sensory block was assessed bilaterally by using loss of sensation to cold with alcohol gauze in the mid-clavicular line.

**Motor blockade was assessed by using the modified Bromage scale:**

- Bromage 0, the patient is able to move the hip, knee and ankle.
- Bromage 1, the patient is unable to move the 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.
- Bromage 3, the patient is unable to move the hip, knee and ankle.

**Data collected:** We measured the time to reach T 10 dermatome sensory block, time to reach peak sensory block level, time to reach Bromage 3 motor block was recorded, the recovery time from sensory and motor block were recorded in a Post Anesthesia Care Unit (PACU).

**Sedation:** Was assessed using modified Ramsay sedation score:

- Grade 1: Anxious, agitated and restless.
- Grade 2: Cooperative, oriented and tranquil.
- Grade 3: Responds to commands only.
- Grade 4: Brisk response to light glabellar tap or loud noise.
Grade 5: Sluggish response to light glabellar tap or loud noise.

Grade 6: No response.

Vital signs: Blood pressure and heart rate [Hypotension (defined as a decrease of more than 30% from the baseline Mean Arterial Blood Pressure (MAP), or systolic blood pressure less than 90 mmHg and bradycardia (defined as a heart rate <60bpm). Hypotension will be managed with an IV bolus of 250ml of crystalloids and if severe, 9-12mg of ephedrine will be given. Bradycardia will be managed with atropine 0.5mgIV. Patients were also evaluated for the presence of nausea and vomiting.

Results

Demographic data: Sixty patients were enrolled in the study. All of them were male patients with a mean age of 31.4±6.3 years; six patients (10%) were diabetics and one patient was asthmatic, controlled with medications. Average duration of surgery was about one hour in all groups. There was no statistical difference between the groups as regard age, body mass index, duration of surgeries that included knee arthroscopy, Tibial fractures, Pott's fractures and femur fractures.

Characteristics of the block:

• Onset to T10 dermatome: There was a more rapid onset of the block in patients of the dexmedetomidine group (1.71min. ±0.81) when compared to the control group (2.92min. ±0.93). This difference was statistically significant (p-value <0.01).

• Time to peak sensory level: The time to reach peak sensory level was faster in patients of the dexmedetomidine group (3.01min. ±1.2) when compared to the control group (5.52min. ±1.39). This difference was statistically significant (p-value <0.01).

• Time to reach Bromage 3 motor block: The time to reach bromage 3 motor block was more rapid in patients of the dexmedetomidine group (2.8min. ±1.16) when compared to the control group (4.72min. ±1.82). This difference was statistically significant (p-value <0.01).

• Regression to S1 dermatome: The time passed for regression to S1 was more prolonged in patients of the dexmedetomidine group (228min. ±27) when compared to the control group (179 min. ±19). This difference was statistically significant (p-value <0.01).

• Recovery of motor power: There was a statistically significant difference (p-value <0.01) reported between dexmedetomidine group (197min. ±18) when compared to the control group (175min. ±18).

Comparing systolic and diastolic arterial blood pressures in the intra-operative period revealed statistically significant lower systolic and diastolic pressures in each group at the 10 minutes reading compared to its baseline values, however there were no statistically significant differences observed while comparing the two study groups with each other. Also there were no significant changes in each group at the successive readings compared to their baseline values. Regarding heart rate, Comparing in the intra-operative period revealed statistically significant bradycardia in each group at the 20 minutes reading when compared to its baseline values, however there were no statistically significant differences observed while comparing the two study groups with each other. Regarding side effects, there was a remarkable statistically significant decrease in shivering when comparing the control group (56.7%) with the Dexmedetomidine group (23.3%) (p-value <0.05).

There was no statistical difference between the two groups as regarding other side effects like nausea, vomiting, pruritus, and headache.

Discussion

In this study we tried to compare the adjuvant effect of adding dexmedetomidine to bupivacaine in orthopedic surgeries in adults.

Each group consisted of 30 patients, randomly allocated for bupivacaine (15mg) alone as control, and bupivacaine (15mg) plus dexmedetomidine (10 µg).

When comparing the demographic data in the two groups involved in the study, in respect to age, body mass index, duration of surgery and gender, there were no statistically significant differences observed between the study groups.

For estimation of the onset of the block we recorded three measurements, which are the time for the anesthetic to reach T10 sensory level, time to reach the peak sensory level and time to reach Bromage Grade 3 (G3). As regard the onset of the block, we found that this was achieved more rapidly in patients of the dexmedetomidine group when compared to the control group. For estimation of duration of block, we measured the time taken to regression of sensory level to S1 dermatome and
regression of motor block to Bromage grade zero. We found that the time passed for regression to S1 was more prolonged in patients of the dexmedetomidine group when compared to the control group (p-value <0.01), this difference was statistically significant, also, the time passed to reach Bromage zero was found more prolonged in the dexmedetomidine group when compared to the control group (p-value <0.01).

We also assessed the degree of sedation by using modified Ramsay sedation score, but we found no difference in sedation degree.

These observed results agreed with a study similar to ours done by Samantaray et al., [5] where they compared dexmedetomidine (5mcg) and midazolam (2mg) added to intrathecal bupivacaine in 60 patients scheduled for endourological procedures. It was found that addition of dexmedetomidine significantly prolongs the duration of effective analgesia in comparison to placebo (0.9% normal saline) with no side effects, on contrary to our study they found no difference in speed of onset and they noted increased level of sedation in dexmedetomidine group.

The difference in speed of onset of block maybe attributed to the used doses of the drugs as we used double their dose (dexmedetomidine 10mcg).

We also found that Li et al., [6] compared different adjuvants added to bupivacaine in intrathecal block including dexmedetomidine.

In this study, similar results were found as regards the onset of the block and duration of analgesia and motor block, it was significantly higher in dexmedetomidine group when compared to bupivacaine group. On the contrary to this study they observed increased level of sedation in dexmedetomidine group.

Sun et al., [7] and Kim et al., [8] found similar results with dexmedetomidine when compared to placebo (normal saline) regarding duration of sensory block. However, they disagree with this study when they examined the duration of motor block. Sun Y et al., found no difference in the duration of the motor block when compared to bupivacaine alone. On the contrary to this study they found some degree of sedation with dexmedetomidine adjuvant.

Nayagam et al., [9] and Gupta et al., [10] and Mahendru et al., [11] and Shukla et al., [12] found comparable results to this study as regards the duration of the block and minimal side effects caused by the addition of dexmedetomidine.

One meta-analysis done by Niu et al., [13] done on 412 patients from MEDLINE, EMBASE and the Cochrane compared dexmedetomidine to placebo. It deduced that dexmedetomidine prolongs spinal anesthesia duration and improves post-operative analgesia which is equivalent to the findings in this study.

A study done by Knazi et al., [14] agreed with this study as regards the absence of sedation with intrathecal dexmedetomidine. However, the used dose was far smaller (3mcg versus 10mcg).

Limitations of this study included, difficulty to standardize the pain variable as it is a subjective phenomenon associated with a wide variability of responses among the individuals. What may be tolerable for one person may be intolerable for another. Under these circumstances it is difficult to assess and grade the pain in the same manner which can lead to a lot of unwanted bias.

Difference in type of surgery may also lead to variations in duration of analgesia, as endoscopic surgeries are less painful than open surgical techniques. This can be negated in future studies by selecting similar type of patients undergoing same operative procedure.

We didn't focus on post-operative side effects as post-operative nausea and vomiting, we only observed intraoperative side effect and that may give under estimation of adjuvants role in preventing post-operative complications.

Our used dose of dexmedetomidine (10g g) is based on average doses used in previous literature, more studies should be done to compare different doses of the same drug to identify the appropriate dose for intrathecal route.

Conclusion:

Finally, it is concluded that Dexmedetomidine (10mcg) is effective as useful adjuvants to the local anesthetic for intrathecal anesthesia. Dexmedetomidine is associated with a faster onset of action and longer postoperative sensory and motor block.

References
