The Effect of Adding Dexmedetomidine to Epidural Anesthesia for Lower Urinary Tract Surgeries


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Abstract

Background: Epidural anesthesia is a safe and inexpensive technique with the advantage of providing surgical anesthesia and prolonged postoperative pain relief. It is also an effective treatment of operative pain as it blunts autonomic, somatic and endocrine responses. This study showed the effect of adding dexmedetomidine to epidural bupivacaine in anesthesia for lower urinary tract surgeries, with respect to onset of action, potency, duration of the block and the total dose of bupivacaine consumption during surgery as well hemodynamic changes.

Methods: 40 patients, ASA I/II were enrolled into the study. All patients had epidural anesthesia and randomly allocated into one of two groups. Group C: (20 patients) the patient received 10ml of bupivacaine 0.5% and Group D: (20 patients): The patient received 10ml of bupivacaine 0.5% plus dexmedetomidine in a dose of 1 µg/kg diluted in 1ml normal saline. In both groups assessment was done after 10 minutes aiming to achieve T10 sensory level and G3 motor block. Otherwise incremental doses of 5ml bupivacaine 0.5% were given without additives.

Results: This study demonstrated that a more prolonged duration of action was recorded in the dexmedetomidine group. In addition, total dose consumption of the local anesthetic was lower than that of the control group. Hemodynamic variables were stable and there were no significant differences between groups.

Conclusion: Dexmedetomidine is effective as a useful adjuvant to local anesthetic for epidural anesthesia. It has a more prolonged duration of action and an increased potency of the block. The studied drug effectively decreased the total dose requirements of local anesthetic drugs. No significant side effects were observed throughout the study period.

Key Words: Epidural – Anesthesia – Dexmedetomidine.

Introduction

Epidural anesthesia is a safe and inexpensive technique with the advantage of providing surgical anesthesia and prolonged postoperative pain relief. It is also an effective treatment of operative pain as it blunts autonomic, somatic and endocrine responses. It has become a common practice to use polypharmacy approach for treatment of intra and postoperative pain, because no drug has yet been identified that specifically inhibits nociception without associated side effects [1]. Research continues concerning different techniques and drugs that could provide better surgical anesthesia and postoperative pain relief.

Dexmedetomidine is a new addition to the class of alpha-2 agonist which has got numerous beneficial effects when used through epidural route [2]. It acts on both pre and post synaptic sympathetic nerve terminal and central nervous system thereby decreasing the sympathetic outflow and nor-epinephrine release causing sedative, anti-anxiety, analgesic, sympatholytic and hemodynamic effects [3]. Dexmedetomidine does cause a manageable hypotension and bradycardia but the striking feature of this drug is the lack of opioid-related side effects like respiratory depression, pruritis, nausea, and vomiting [4].

Aim of work:

The main goal of our study is to show the efficacy of dexmedetomidine when added to 0.5% bupivacaine in epidural anesthesia for lower urinary tract surgery. The comparison will include onset time, duration, quality and dermatomal spread of epidural anesthesia.

Patients and Methods

The present study was a prospective randomized blind controlled study conducted for patients scheduled to undergo elective lower urinary tract surgeries in Kasr Al-Aini Hospital, Cairo University. After obtaining Institutional Ethics Committee
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approval and written informed consent, 40 patients ASA I/II were enrolled into the study.

Patient selection:
**Inclusion criteria:**
- ASA I, II patients.
- Aged 18-60 years old.
- Scheduled for lower urinary tract surgery (stone lower ureter, stone bladder, uretro-vesical implantation, varicocele, etc...).

**Exclusion criteria:**
Any contraindication to epidural anesthesia as;
- Patient refusal.
- Severe cardiac disease.
- Raised intracranial pressure or pre-existing neurological disorders, such as multiple sclerosis.
- Patients with coagulopathy due to liver or blood disease, therapeutic anti-coagulation.
- Inability to communicate and understand the aim of the project.
- Patients with history of allergic reaction to local anesthetics or opioids.
- Skin infection at injection site or systemic bacteraemia.

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 and all patients were premedicated with midazolam 2mg IV. Measurements of baseline hemodynamic parameters were recorded.

All patients were monitored intra-operatively using: An ECG with S-T segment analysis, 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 an epidural anesthesia; Patients were assumed lateral or 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 L2-3 or L3-4 space was selected. The skin was infiltrated with about 2ml of 1% lidocaine. The epidural space was identified through a midline approach by an 18 gauge Tuohy’s needle, using loss-of-resistance technique, an epidural catheter was then inserted into the epidural space, the catheter was advanced 3-4cm beyond the previously-noted distance between the skin and epidural space and a test dose of 3ml Lidocaine 2% was injected. Thereafter, activation of epidural anesthesia was done as follows;

**Group C (control group):** (20 patients):
The patient received 1 1ml of bupivacaine 0.5% as a bolus dose initially.

**Group D (dexmedetomidine group):** (20 patients):
The patient received 10 ml of bupivacaine 0.5% plus 1ml of dexmedetomidine in a dose of 1 µg/kg diluted in normal saline as a bolus dose initially.

In both groups, assessment was done after 10 minutes aiming to achieve T 10 sensory level and G3 motor block. Otherwise incremental doses of 5ml bupivacaine 0.5% were given without additives to achieve the desired level. Top ups were given everytime when two segment regression of the sensory level occurred at a dose equal to one third of the corresponding initial dose.

Data collected:
The following data were collected from the study patients:
- Onset, detected by time needed to achieve sensory block level at T10 and motor block grade 3 by modified Bromage score will be measured in all groups. Bromage score is a range from 0 to 3 [0=No motor block; 1=Partial block, ability to flex the knee; 2=Almost complete block, only plantar flexion of the ankle possible; 3=Complete block, no voluntary movement of the limb possible]. Sensory block level, using warm-cold temperature discrimination and pin-prick test.
- Duration of the block by measuring time to two segment regression.
• **Vital signs:** Blood pressure and heart rate [Hypotension (defined as a decrease of more than 20% from the baseline mean arterial blood pressure (MAP), severe hypotension (defined as a decrease in MAP more than 30% of baseline value) and bradycardia (defined as a heart rate <55bpm). 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 0.5mg IV.

• **Potency of the block:** At the end of the operation, assessed by visual analogue scale 'VAS': Value range from 0 (no pain) to 10 (worst pain imaginable).

• **Total dose of local anesthetic needed.**

• The onset of post-operative pain and the recovery of sensory and motor blocks were estimated.

• Patients were also evaluated for the side-effects related to epidural drugs:

• Drowsiness: Was defined as a state of impaired awareness associated with a desire or inclination to sleep, it was graded on a 4-point rank drowsiness score (0): Awake and alert, (1): Mildly sedated, easily aroused; (2): Moderately sedated, aroused by shaking, (3): Deeply sedated, difficult to be aroused by physical stimulation.

• Nausea and vomiting: Was evaluated on a 3-point ordinal scale (0=none, 1=nausea, 2= vomiting).

**Statistical analysis:**

Collected data were presented as mean ±SD, numbers and percentages as appropriate. Demographic data were compared using Chi-square test, Fischer exact test or unpaired t-tests as appropriate. Numerical Data were compared by using Univariate two-group repeated measures analysis of variance (ANOVA) with post-hoc Dunnett's test for further comparisons against baseline values. Mann-Whitney U-test was used when data were skewed. Statistical analysis was performed using SPSS (Version 20, 2011). p-value <0.05 was considered statistically significant.

**Sample size and method of randomization:**

Randomization was done using computer-generated algorithm. Concealment was performed using sequentially numbered opaque sealed envelopes.

Sample size calculation showed that 20 patients in each group were adequate to detect a moderate effect size (f=0.75). Assuming alpha error of 0.05, beta error of 0.2 and statistical power of 80%.

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**Results**

**I- Demographic data:**

Fourty patients were enrolled in the study. All of them were male patients with a mean age of 38.4±10.6 years; Thirty two (80%) patients were ASA I and eight (20%) patients were ASA II. Five patients were hypertensive and 3 patients were diabetics, controlled with medications. Average duration of surgery was about 2.5-3.5 hours in all groups. There was no statistical difference between the two groups as regard age, body mass index, duration or type of surgeries that included lower ureteric stones, stone bladder, varicocele and uretro-vesical operations (Table 1).

<table>
<thead>
<tr>
<th>Table (1): Demographic data. (Data are presented as mean ±S).</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control (n=20)</strong></td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
</tr>
<tr>
<td>ASA:</td>
</tr>
<tr>
<td>I</td>
</tr>
<tr>
<td>II</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
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**II- Characteristics of the epidural block:**

• **Onset of block:**

There was no statistical significance between the dexmedetomidine groups compared to the control group regarding onset of the block (p-value>0.05). [(Table 2) & Fig. (1)].

• **Time to two-segment regression:**

This time was more prolonged in patients of the dexmedetomidine group when compared with the control group and this prolongation was statistically significant (p-values were 0.03). [(Table 2) & Fig. (2)].

• **Total dose:**

There was statistically significant difference reported between the dexmedetomidine group and the control group as the total dose was much higher in the latter group (p-value=0.02). [(Table 2) & Fig. (3)].

• **Onset of post-operative pain:**

This time was more prolonged in patients of the dexmedetomidine group when compared with the control group and this prolongation was statistically significant (p-values were 0.03). [(Table 2) & Fig. (4)].
### Recovery of motor power:
There was statistically significant difference reported between the dexmedetomidine group and the control group and this prolongation was statistically significant ($p$-values were 0.03). [[Table 2] & Fig. (5)].

**Table (2): Characteristics of the epidural Block. Data are means±SD.**

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>Dex (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset of block (min)</td>
<td>17.8±3.02</td>
<td>18.8±3.19</td>
</tr>
<tr>
<td>Time to two-segment regression (min)</td>
<td>82.8±6.38</td>
<td>96.3±5.59*</td>
</tr>
<tr>
<td>Total dose (ml)</td>
<td>29.5±3.94</td>
<td>22.3±2.55*</td>
</tr>
<tr>
<td>Onset of post-operative pain (min)</td>
<td>182±8.8</td>
<td>235.5±21.4*</td>
</tr>
<tr>
<td>Recovery of motor power (min)</td>
<td>131±13.34</td>
<td>157.8±25.1*</td>
</tr>
</tbody>
</table>

*: Significant $p$-value <0.05 vs. the control group (One-way anova).

### Potency of the block assessed by VAS:
At the end of the surgical procedures, all patients were asked about their analgesia experience. There was no statistical significance between the two groups as regard potency of the block, and visual analogue scale was <3 in all the study patients.
III- Hemodynamics:

Comparing mean arterial blood pressure in the intra-operative period revealed statistically significant lower MAP in each group at the 10 minutes reading compared to its baseline values, however there were no statistically significant differences observed while comparing the study groups with each others. Also there were no significant MAP changes in each group at the successive readings compared to their baseline values (Table 3).

Table (3): MAP measurements throughout the study period.

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>Dex (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>92.5±5.96</td>
<td>90±6.07</td>
</tr>
<tr>
<td>MAP at 10min</td>
<td>86.5±6.3#</td>
<td>85.8±4.9#</td>
</tr>
<tr>
<td>MAP at 30min</td>
<td>87±8.7.52</td>
<td>88±5.64</td>
</tr>
<tr>
<td>MAP at 60min</td>
<td>88±8.4±7.3</td>
<td>88±4.55</td>
</tr>
<tr>
<td>MAP at 90min</td>
<td>84±7.54</td>
<td>86±5.15</td>
</tr>
<tr>
<td>MAP at 120min</td>
<td>88±7.46</td>
<td>84±9.27</td>
</tr>
<tr>
<td>MAP at 150min</td>
<td>89±6.7</td>
<td>84±4.67</td>
</tr>
<tr>
<td>MAP at 180min</td>
<td>89±7.34</td>
<td>82±5.45</td>
</tr>
</tbody>
</table>

*: Significant p-value <0.05 vs. the corresponding measurement in the control group (One-way anova).
#: Significant p-value <0.05 vs. baseline measurement in the same group (repeated measures anova).

Regarding heart rate, no statistical significance was noted neither inside each group nor in between the study groups (Table 4).

Table (4): Heart rate measurements throughout the study period.

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>Dex (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>80.8±9.77</td>
<td>79±6.61</td>
</tr>
<tr>
<td>HR at 10min</td>
<td>83±6.5</td>
<td>78±5.68</td>
</tr>
<tr>
<td>HR at 30min</td>
<td>85±8.8</td>
<td>80±7.99</td>
</tr>
<tr>
<td>HR at 60min</td>
<td>83±8.6</td>
<td>77±8.76</td>
</tr>
<tr>
<td>HR at 90min</td>
<td>83±11.4</td>
<td>78±7.34</td>
</tr>
<tr>
<td>HR at 120min</td>
<td>82±7.65</td>
<td>81±7.58</td>
</tr>
<tr>
<td>HR at 150min</td>
<td>81.8±7.6</td>
<td>80±3.5.49</td>
</tr>
<tr>
<td>HR at 180min</td>
<td>83±8.66</td>
<td>81±7.76</td>
</tr>
</tbody>
</table>

*: Significant p-value <0.05 vs. the corresponding measurement of the control group (One-way anova).
#: Significant p-value <0.05 vs. baseline measurement in the same group (repeated measures anova).

There was no statistical difference between both groups as regard side effects like nausea, vomiting, or drowsiness (Table 5).

Table (5): Side effects; data are presented as number (frequency).

<table>
<thead>
<tr>
<th></th>
<th>Control (n=20)</th>
<th>Dex (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>3 (15%)</td>
<td>3 (15%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2 (10%)</td>
<td>1 (5%)</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>0 (0.0%)</td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>

Discussion

Epidural anesthesia is a safe and inexpensive technique with the advantage of providing surgical anesthesia and prolonged postoperative pain relief. It is an effective treatment of operative pain as it blunts autonomic, somatic and endocrine responses. It has become a common practice to use polypharmacy approach for treatment of intra and postoperative pain, because no drug has yet been identified that specifically inhibits nociception without associated side effects [1].

Dexmedetomidine is a new addition to the class of alpha-2 agonist which has got numerous beneficial effects when used through epidural route [2]. It acts on both pre and post synaptic sympathetic nerve terminal and central nervous system thereby decreasing the sympathetic outflow and noradrenaline release causing sedative, anti-anxiety, analgesic, sympatholytic and hemodynamic effects [3]. Dexmedetomidine does cause a manageable hypotension and bradycardia but the striking feature of this drug is the lack of opioid-related side effects like respiratory depression, pruritus, nausea, and vomiting [4].

The present study was designed to assess the effect of adding dexmedetomidine to bupivacaine in epidural anesthesia for lower urinary tract surgeries.

When compared, in respect to age, BMI, duration of surgery and gender, there were no statistically significant differences observed between the study groups, (p-value >0.05).

Hemodynamic variables including mean arterial blood pressure and heart rate were stable although the operative period, and there were no clinically significant differences between the study groups, with the exception of a decrease in the mean blood pressure in both groups at the 10 minutes readings, (from 92.5±5.9mmHg to 90.5±6.07 in the control group, p-value=0.03. From 90.6±7.1 to 85.8±4.9mmHg in dexmedetomidine group p-value=0.03). This can be explained by the vasodilatation of resistance and capacitance vessels, resulting from the block of the sympathetic outflow by the epidural local anesthetic, causing relative hypovolemia with a consequent drop in blood pressure.

In contrast to the present study, Jit, et al., 2011 [5]. Found that the mean arterial pressure (MAP) decreased from the baseline with a maximum decline at 30-50 minutes after the epidural injection of dexmedetomidine to epidural ropivacaine, but it never went below 65mmHg. They reported that a negative chronotropic effect was exhibited ap-
proximately 30-35 minutes after the epidural injection of these drugs. Postoperatively, HR and MAP remained stable. The decrease in HR caused by α-2 agonist can again be explained on the basis of their central action whereby they decrease sympathetic outflow and nor-epinephrine release.

In this study, as regard the onset of action of the block, a T10 sensory level and a G3 motor block by Bromage scale were reached in the dexmedetomidine group with no significant difference was detected compared to the control group (p-value >0.05).

Same results were noted by Jit, et al., 2011 [5]. Concerning the evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries.

In the present study; Regarding the time to two-segment regression, the onset of post-operative pain and the recovery time of motor power; they were all longer in the dexmedetomidine group in comparison to the control group. (p-values <0.05).

The time to two segments regression was 96.3 ± 5.59 minutes in the dexmedetomidine groups compared to 82.8±6.38 minutes in the control group (p-value 0.02).

The onset of post-operative pain (guided by visual analogue scale more than 3) was 235.5 ±21.4 minutes in the dexmedetomidine groups compared to 182±8.8 minutes in the control group. (p-value 0.02).

The recovery of motor power was after 157.8 ± 25.1 minutes in the dexmedetomidine groups compared to 131 ±13.34 minutes in the control group (p-value 0.02).

Total dose of local anesthetic given during the surgical procedure was by far, lower in the dexmedetomidine group compared to the control group. Average of 29.5±3.94ml of local anesthetic were given to patients in the control group versus 22.3 ± 2.55ml for the dexmedetomidine group (p-value 0.02).

In line to our study also, Jit, et al. [8] have done a comparative evaluation of dexmedetomidine and fentanyl for epidural analgesia in lower limb orthopedic surgeries where one hundred patients, aged 21-56 years, ASA physical status I and II undergoing lower limb orthopedic surgery were enrolled into that study. Patients were randomly allocated to receive either ropivacaine with dexmedetomidine (RD) or ropivacaine with Fentanyl (RF). The authors reported that postoperative analgesia was prolonged significantly in the RD group (366±24.4 vs. 300±16.9 minutes) and a lower local anesthetic dose consumption was detected (77±14.3 vs. 104±18.9ml) for epidural top-ups during the first 24-hours, postoperatively.

α-2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anesthesia [6]. Dexmedetomidine is a highly selective α2 adrenergic agonist with an affinity of eight times greater than clonidine. The anesthetic and the analgesic requirement get reduced to a huge extent by the use of these two adjuvants because of their analgesic properties and augmentation of local anesthetic effects as they cause hyperpolarisation of nerve tissues by altering transmembrane potential and ion conductance at locus coeruleus in the brainstem [6]. The stable hemodynamics and the decreased oxygen demand due to enhanced sympathoadrenal stability make them very useful pharmacologic agents [7].

Limitations of the study includes, 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. This can be negated in future studies by selecting similar type of patients undergoing same operative procedure. Generalization of use of these drugs in major operations and for postoperative pain management may be tried later on. Also different doses of adjuvants in each group should be studied separately in future studies.

Conclusion:

Finally, it is concluded that, dexmedetomidine is effective as useful adjuvant to the local anesthetic for epidural anesthesia. It is associated with a more prolonged duration of action and an increased potency of the block.

It also effectively decreased the total dose requirements of the local anesthetic. No significant side effects were observed during the study.

References

الملخص العربي

يعتبر التخدير النصفي للجزء الجراحический من الجراحة قطعية أمرًا غير مكلف، ويدعم فكرة أن استخدامها أثناء الانتظار الجراحية للتحريج أو القضاء على إحتمالات النزيف.

وقد أصبحت هذه الدراسة نقطة تأسيسية حيث تتقدم الدراسات القصيرة والبدنية بالإضافة إلى ذلك تحدث تذكرة تأثير النزيف بأفضل حال.

هذا وقد أظهرت هذه الدراسة أن هذا العقار يفيد عند إضافة عقار الديميتوميدين إلى عقار البيبريفاكان أن يؤثر على سرعة عمل المخدر النصفي بالإضافة إلى مدى انتشاره وعدم ثباته.

وقد أظهرت هذه الدراسة أن هذا العقار يفيد عند إضافة عقار الديميتوميدين إلى عقار البيبريفاكان حيث أنه يقوم بإطلالة عمل المخدر وفقطة.

كما أنه نتائج هذه الدراسة تأتي إلى التقليل من كمية المخدر اللازمة لعمل التخدير النصفي، وجدير بالذكر أنه لم يتم ملاحظة أعراض جانبية لهذا العقار أثناء الدراسة الحالية.