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Bupivacaine-Dexmedetomidine for Lumber Discectomy: Randomized Controlled Placebo Study

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Abstract

Background: Our purpose is to evaluate the efficacy of dexmedetomidine for spine surgery to improve the operative field, the onset and duration of sensory and motor block, the hemodynamic state.

Patients and Methods: Prospective randomized controlled placebo study include 50 patients undergoing lumbar discectomy for herniated disc under spinal anesthesia were randomly divided into two equal groups: Group B (25 patients) received 15 mg (3 ml) of hyperbaric bupivacaine plus 0.5 ml saline to a total volume of 3.5 ml and group D (25 patients) received 15 mg (3 ml) of bupivacaine supplemented with 3 µg of dexmedetomidine in 0.5 ml saline to a total volume 3.5 ml. The onset times to reach peak sensory levels, and the sensory regression times, were recorded. Time to first analgesic rescue, score of operative field, the level of sedation and postoperative complication were also recorded.

Results: Operative field was significantly better in D group (P<0.001). Patients in group D had rapid onset time of sensory block and significantly longer sensory regression time than patients in group B. The time of sensory regression to the S1 segment was 277.76 ± 8.02 min in group D and 239.70 ± 6.83 min in group B (P<0.001). The mean time of sensory regression of two segments was 129.13 ± 5.60 min in group D and 73.66 ± 4.62 min in group B (P<0.001). Highest sensory level was similar in both groups. The mean arterial pressure and heart rate were significantly different in both groups intra-operatively after 20 & 10 minutes respectively from intrathecal injection.

Conclusion: Dexmedetomidine when added to intrathecal bupivacaine improves the operative field, prolong the duration of the sensory block, and improves the quality of postoperative analgesia with minimal side effects with preserved hemodynamic stability and lack of sedation.

Keywords: Bupivacaine; Dexmedetomidine, Lumber discectomy; Spinal anesthesia

Introduction

Spinal block have rapid onset, good blockade, less failure rates and cost effectiveness, but its disadvantage are shorter duration of block and lack of postoperative analgesia. The use of intrathecal adjuvants aimed to prolonging the duration of anesthesia, improve success rate, patient satisfaction, simple resource compared with general anesthesia and faster recovery [1]. The adjuvant drugs to local anesthetics like intrathecal α_2-agonists are used [2]. They potentiate the action of local anesthetics and decrease the doses of local anesthetics [3]. Dexmedetomidine is α_2-adrenoreceptor agonist have an intravenous sedative and coanalgesic action. It has α_2/a_1 selectivity ratio which is eight times higher than that of clonidine [4]. They work by binding to presynaptic C-fibers and postsynaptic dorsal horn neurons [5]. Intrathecal α_2-receptor agonists have antinociceptive action for both somatic and visceral pain [6]. The use of intravenous dexmedetomidine resulted in a significant opioid-sparing effect as well as decrease requirements of inhalational anesthetics [7].

Some studies use dexmedetomidine as a hypotensive agent in posterior fixation for spine surgery [8]. Our purpose was to study efficacy of dexmedetomidine for spine surgery to improve the operative field, the duration of sensory block, the hemodynamic state and quality of postoperative analgesia.

Patients and Methods

This study was approved by Qena School of Medicine Ethical Committee (South Valley University, Qena, Egypt) and has been conducted in Qena university hospital between June 2013 and August 2014. Written informed consent was obtained from each patient pre-operatively.

Enrollment

Fifty patients (ASA I-II) between 20-60 years scheduled for one level lumbar discectomy for herniated lumbar disc under spinal anesthesia were included in the study. Exclusion criteria: treatment with α -adrenergic antagonists, dysrhythmia, allergic to study drugs, labile hypertension, an absolute contraindication for spinal anesthesia, coronary artery diseases, renal, hepatic or cerebral insufficiency.

Study design

This was randomized; double blind, placebo-controlled clinical study. Randomization and enrollment to Dexmedetomidine or placebo was done by closed envelop by (A.M.). Collection of data was performed by the other physician (R.S.). Drug preparation (Dexmedetomidine 3 μg or saline) was done by the resident not involved in the study. Group B (25 patients) received 15 mg (3 ml) of hyperbaric bupivacaine 0.5%+0.5 ml saline to total volume 3.5 ml and group D (25 patients) received 15 mg (3 ml) of hyperbaric bupivacaine 0.5% supplemented with 3 μg of dexmedetomidine in 0.5 ml to total volume 3.5 ml. All patients were pre-medicated with 0.01 mg/kg atropine I.M. 30 min before shifting to operation room. Intravenous (i.v.) catheter was inserted for patient preload with Lactated Ringer's solution 15 ml/Kg. Lumbar puncture was performed with the patient in the sitting position at the L3-L4 level through a midline approach using a pencil point 25-gauge needle with the hole pointing upwards. Following injection, all patients were lying supine. Oxygen (2 L/min) was administered via a face mask. The patients were put in prone position just the level of anesthesia was established. The anesthesiologists performing the block recorded the intra-operative data and a 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. The same surgeon performed all operations to ensure the assessment of surgical field [9].

Data collection and measurement

Intraoperative scale for assessment of surgical field:

0 - No bleeding

1 - Slight bleeding – no suctioning of blood required

2 - Slight bleeding - occasional suctioning required but not threatened the operative field.

3 - Slight-bleeding – frequent suctioning of blood was required that threatens the operative field a few seconds after suctioning.

4 - Moderate bleeding - frequent suctioning of blood was required which threatens the operative field directly after suctioning.

5 - Sever bleeding - continuous suctioning of blood was required which severely threatened the operative field make the surgery not possible. Surgeon satisfaction was represented as satisfied or unsatisfied and number of satisfied surgeons was calculated in each group. The sensory blockade was assessed intra-operatively every 5 min to 30 min, and then every 15 min until discharge from the PACU. The sensory level was assessed by pinprick sensation using a blunt 25-gauge needle along the mid-clavicular line bilaterally. Motor block was assessed using a modified Bromage scale (0, no motor block; 1, hip blocked; 2, hip and knee blocked; 3, hip, knee, and ankle blocked). The times to reach the T10 dermatome, the highest dermatomal level (peak sensory level), a two-dermatome regression and regression to the S1 dermatome were recorded. All durations were calculated considering the time of intrathecal injection as time zero. Patients were discharged from the PACU after sensory regression to the S1 segment. The mean arterial pressure (MAP), heart rate (HR) and SPO_2 (%) were recorded as baseline values, every minute for the first 10 min after intrathecal injection, and then every 5 min until discharge from the PACU. Hypotension was defined as a decrease in systolic blood pressure by 30% from baseline, or a systolic blood pressure lower than 90 mmHg. Hypotension was treated with 6 mg of intravenous ephedrine and a bolus administration of 250 ml of lactated Ringer's solution over 10 min. Ephedrine at 6 mg and lactated Ringer's solution at 250 ml were repeated if the blood pressure remained low. Bradycardia was defined as HR <50 beats/min, and was treated with 0.5 mg of intravenous atropine. The total blood loss was measured from the suction apparatus. The visual analog score (VAS) pain scale between 0 and 10 (0=no pain, 10=the most severe pain) was assessed initially every 1 hour for 6 hours, then every 2 hours for next 24 hours. When VAS pain score was ≥ 3 rescue doses of analgesics Ketorolac 30 mg was administered intravenously and the time to first analgesic rescue were recorded. Patients who developed intra-operative or post-operative nausea or vomiting were recorded.

Sedation was assessed by Ramsay sedation scale (RSS) as follows [10]:

- Patient is anxious and agitated or restless, or both.
- Patient is co-operative, oriented and tranquil.
- Patient responds to commands only.
- Patient exhibits brisk response to light glabellar tap or loud auditory stimulus.
- Patient exhibits sluggish response to light glabellar tap or loud auditory stimulus.
- Patient exhibits no response.

Outcomes

The primary outcome measure was the improvement operative field in dexmedetomidine group. The secondary outcome measures were time to sensory regression of two segments (min), time of sensory regression to S1 segment, time to first analgesic rescue and Total dose of ketorolac in mg over 24 hr.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 16.0 (IBM, Chicago, IL). A sample size of 24 patients in each group was determined through power analysis (α=0.05; β=0.80) to detect an increase of 30 min in the time of a two dermatome sensory regression. Data are presented as mean ± SD, or numbers as appropriate. Patient characteristics were analyzed using the independent two sample t-test. Peak sensory block levels were compared using the Mann–Whitney U-test. The linear mixed model (post-hoc: Bonferroni correction) was used for comparison of MAP and HR between the two groups. p values of <0.05 were considered significant.

Results

In our study fifty patients were enrolled. The demographic data did not differ between the two study groups (Table 1). The spinal technique was easy in all patients and recovery from spinal block was uneventful.

Primary outcome

Operative field was statistically significance in dexmedetomidine group with comparison to placebo group (2.56 ± 0.97 placebo and 1.60 ± 0.62 group D) P<0.001(Table 2).

Parameters	Groups		t-test	P- value
	Group B n = 25	Group D n = 25		
Age (years)	34.13 ± 10.45	37.23 ± 9.49	1.897	0.056
Sex (M:F)	17:8	16:9	1.222	0.423
Weight (kg)	72.86 ± 6.18	74.06 ± 6.02	1.471	0.152
Height (cm)	175.4 ± 5.49	171.86 ± 5.56	0.503	0.619
MBP (mmHg)	87.15 ± 2.53	89.15 ± 4.53	0.346	0.428
HR (beats/min)	97.45 ± 1.46	94.72 ± 2.42	0.423	0.294
M:F: Male : Female; MBP: Mean arterial Blood Pressure; HR: Heart Rate Data are presented as mean ± standard deviation.				

Table 1: Patients' criteria.

Secondary outcome

The differences between the groups in the mean times to reach T10 sensory block (group B, 4.78 ± 0.43 min; group D, 4.83 ± 0.43 min) and the peak sensory level (group B, 10.13 ± 0.91 min; group D, 10.01 ± 0.84 min) did not reach statistical significance (P=0.325 and P=0.217 respectively). The regression times of the two segments were highly significantly different between groups B and D (P<0.0001). The regression times to the S1 segment were highly significantly different between groups B and D (Table 2).

The peripheral oxygen saturation was greater than 96% at all times in both groups with no statistically different between them with a value of 99.63 ± 0.49 % in group D compared to 99.43 ± 1.86 % in group B with p value=0.553. As regard to intraoperative blood loss, patients in group D were significantly losses blood lower than those in group B with a volume of 137.20 ± 70.54 to 300.63 ± 96.49 ml respectively with p value<0.0001 (Table 2). Surgeon was significantly more satisfied in group D (23 satisfied 92%) in comparison to group B (15 60%) p value<0.003 (Table 2).

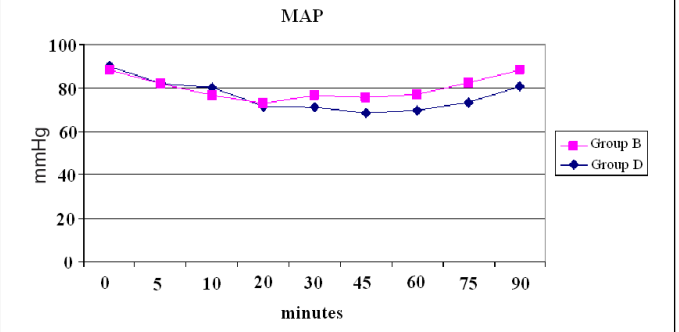

Figure 1: Mean arterial blood pressure (MAP). Patients in dexmedetomidine (DEX) achieved lower MAP after 20 minutes. All the values depicted are means at the corresponding time points.

MAP was significantly lower in group D than group B after 20 minutes from intrathecal injection p value<0.05 (Figure 1) two patients in group D required 6 mg dose of ephedrine. In a similar pattern, HR showed significant increase in group B compared to group D, three patients in group D respond to 0.5 mg atropine. In all these patients there were no further changes in blood pressure or heart rate (Figure 1 and 2). VAS values were less than 3 (1.60 ± 0.62 in group D compared to 2.56 ± 0.97 in group B) the whole intraoperative period. Time to first analgesic rescue was significantly longer in group D in comparison to group B (389.63 ± 6.93and 259.26 ± 9.26) with p value<0.0001 (Table 2). Total dose of ketorolac was less in group D (45.86 ± 4.95) compared to group B (75.00 ± 6.65) with p value<0.0001 (Table 2). The level of sedation scores were in the range of 1-2 in both groups with a median of zero. No intraoperative or postoperative nausea or vomiting was recorded in both groups. Four patients have shivering in control group but no shivering was recorded in group D.

Parameters	Groups		t-test	P-value
	Group B n = 25	Group D n = 25		
Duration of surgery (min)	66.83 ± 9.51	67.16 ± 9.98	0.249	0.805
Onset of sensory block (min)	3.26 ± 0.78	3.40 ± 0.77	1	0.542
Time to reach T10 sensory level	4.78 ± 0.43	4.83 ± 0.43	0.616	0.325
Time to reach highest sensory level (min)	10.13 ± 0.91	10.01 ± 0.84	1.26	0.217
Sensory regression of two segment (min)	73.66 ± 4.62	129.13 ± 5.60	40.75	<0.0001
Sensory regression to S1 segment (min)	239.70 ± 6.83	277.76 ± 8.02	19.54	<0.0001
Time to reach modified BRS3	7.14 ± 0.82	6.84 ± 0.66	0.315	0.295
Time to return to modified BRS0	129 ± 7.28	134 ± 7.58	1.26	0.517
Score of operative field	2.56 ± 0.97	1.60 ± 0.62	5.124	<0.001
Surgeon satisfaction: satisfied n (%)	15 (60%)	23 (92%)	4.097	0.003
SPO_2 (%)	99.43 ± 1.86	99.63 ± 0.49	0.6	0.553
Blood loss (ml)	300.63 ± 96.49	137.20 ± 70.54	7.456	<0.0001
Time to first analgesic rescue (min)	259.26 ± 9.26	389.63 ± 6.93	75.68	<0.0001
Total dose of ketorolac in mg over 24 hr	75.00 ± 6.65	45.86 ± 4.95	15.25	<0.0001
BRS: Bromage Scale; SPO_2: Oxygen Saturation Data are presented as mean ± standard deviation.				

Table 2: Characteristics of spinal anesthesia.

Discussion

Dexmedetomidine is a highly selective α_2-adrenergic agonist which has been used for premedication and as an adjuvant to general anesthesia; it decreases opioid and inhalational anesthetics demands

[11]. Spinal surgeries were infamous for the tremendous blood losses during the course of surgery. This could make the surgical visualization difficult in bloody operative field. With the newer anesthetic agents, drugs, and monitoring techniques introduced to control this problem, a commonly used technique is controlled hypotension to limit blood loss and improve visualization of the operative field during spinal surgery [8].

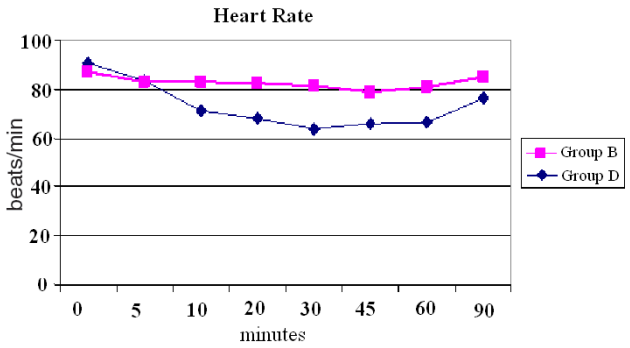

Figure 2: heart rate (HR). Patients in dexmedetomidine (DEX) have lower HR than placebo group. All the values depicted are means at the corresponding time points.

In our study group D achieved VAS score of 1.60 ± 0.62 compared to 2.56 ± 0.97 in group B with p value<0.0001, during hypotensive period for quality of surgical field with little bleeding that did not traverse the visual clarity during the surgery. In concordance with our results, Goksu et al. [12] and Guven et al. [13] reported good hemodynamic state, visual analog scale for pain and clear surgical field with less side effects in Dexmedetomidine group than placebo group under either local anesthesia or conscious sedation respectively [12,13]. Our results showed that the combination of 15 mg of intrathecal bupivacaine with a low dose of 3 μg of dexmedetomidine insignificantly shortened the onset of sensory block while prolonged it when compared with bupivacaine alone. The mechanism is not well known by which intrathecal α_2-adrenoceptor agonists prolong the sensory block of local anesthetics. Systemic absorption is not the cause, as the addition of intrathecal clonidine to bupivacaine spinal anesthesia was not altered the plasma level of bupivacaine [14,15]. This study demonstrated prolonged postoperative analgesia in dexmedetomidine group, the first time of postoperatively analgesic rescue was highly significant different in both groups recorded 389.63 ± 6.93 minutes for group D compared to 259.26 ± 9.26 minutes in group B (P<0.0001). In accordance with Gurbet et al. [16] who stated that intraoperative infusion of dexmedetomidine reduces perioperative analgesic requirements. Also the analgesic effects of dexmedetomidine had been appreciated in various setting and various populations [17-19]. Our results showed that the sensory block was significantly prolonged in the dexmedetomidine group in comparison to the control group, which confirm that the intrathecal doses of dexmedetomidine used in our study prolonged the sensory block. MAP was chosen as a parameter to quantify hypotension as it is the true measure of tissue perfusion [20]. We adopted a conservative approach in terms of limiting the target MAP to 65-70 mmHg so as to minimize the risk of compromising the perfusion of spinal cord tissue resulting in neurological deficit. Chiesa et al. [21] showed that a perioperative hypotension with MAP<70 mmHg was a risk factor for developing spinal cord ischemia. In our patients, the addition of dexmedetomidine to bupivacaine causes a significant decrease in the MAP and HR intra-operatively. Similar result was recorded that the effect of single dose of 0.5 μg/kg dexmedetomidine administered 10 min before induction of anesthesia and reported significant reduction in MAP and HR [22,23]. Al-Ghanem et al. [9] have reported the use of dexmedetomidine to be associated with a decrease in heart rate and mean blood pressure. The central and peripheral sympatholytic action of dexmedetomidine is mediated by α_2-adrenergic receptor and is manifested by dose-dependent decrease in arterial blood pressure, heart rate, [9]. In our study no patients have shivering in dexmedetomidine group in comparison to four patients in the control group because α_2-adrenergic agents have antishivering property as observed by Talk et al. [11,24].

Conclusion

In conclusion, our report shows that Dexmedetomidine when added to intrathecal bupivacaine at a dose of 3 μg improved the operative field, prolonged the duration of the sensory block, and improved the quality of postoperative analgesia with minimal side effects with preserved hemodynamic stability and lack of sedation. It is recommended to perform more studies to evaluate the effect of dexmedetomidine with different doses with larger sample size for maximum duration of analgesia without drawbacks.

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