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Evaluation of the effects of intrathecal bupivacaine-dexmedetomidine for lumbar spine fusion: a double blinded randomized controlled study

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Abstract. – OBJECTIVE: To evaluate the efficacy of intrathecal dexmedetomidine at improving the quality of the operative field, and prolonging the duration of sensory block, motor block, and postoperative analgesia during spinal surgery

PATIENTS AND METHODS: This prospective, double-blinded, randomized controlled study included 52 patients undergoing an instrumented one-level posterolateral lumbar spine fusion for lumbar spondylolisthesis under spinal anesthesia. The patients were randomized into two groups: group D (n = 26) received 15 mg of hyperbaric bupivacaine with 5 μg of dexmedetomidine, while group P (n = 26) received 15 mg of hyperbaric bupivacaine only. The operative field quality score, blood loss volume, and the surgeon's satisfaction with the procedure were recorded. The onset time of the sensory block, time to reach peak sensory level, sensory and motor regression times, time to the first requirement of analgesia, sedation level, hemodynamics, and all postoperative complications were also recorded.

RESULTS: The operative field quality and the surgeon's satisfaction scores (rated excellent) were significantly better in group D than in group P ($p < 0.0001$ and $p = 0.003$, respectively). Patients in group D had significantly longer sensory and motor regression times than patients in group P ($p < 0.0001$). The time to the first requirement of analgesia and the total dose of ketorolac was significantly longer and smaller, respectively, in group D than in group P ($p < 0.0001$).

CONCLUSIONS: Intrathecal bupivacaine-dexmedetomidine improved the quality of the operative field, prolonged the duration of the sensory and motor block, prolonged postoperative analgesia, and produced minimal side effects.

Key Words:
Bupivacaine, Dexmedetomidine, Spinal anesthesia.

Introduction

A spinal block for anesthesia has a rapid onset, produces an effective blockade, is associated with low failure rates, and is cost effective. The disadvantages of a spinal block include the short duration of the block and lack of postoperative analgesia. The use of intrathecal adjuvants to prolong the duration of anesthesia has increased the success rate and patient satisfaction while employing a more simple approach with a faster recovery than general anesthesia[1]. Owing to their sedative, analgesic, anesthetic-sparing, and hemodynamic stability properties, intrathecal α_2-agonists have been administered as adjuvant drugs to local anesthetics in order to prolong their effects and reduce doses[2,3]. Dexmedetomidine, a stereoisomer of medetomidine, is a highly selective α_2-adrenergic receptor agonist with a α_2/α_1 selectivity ratio eight times higher than that of clonidine[4]. This drug works by binding to presynaptic C-fibers and postsynaptic neurons in the dorsal horn[5]. Intrathecal α_2-receptor agonists possess antinociceptive action for both somatic and visceral pain[6]. The administration of intravenous dexmedetomidine results in a significant opioid-sparing effect, in addition to reducing the need for inhalational anesthetics[7].

Several studies[8] have investigated the administration of dexmedetomidine as a hypotensive agent in posterior fixation for spinal surgery. We aimed to investigate the efficacy of dexmedetomidine at improving the operative field quality and increasing the duration of the sensory block during spinal surgery. We also investigated the effects of dexmedetomidine on patient hemodynamics and the quality of postoperative analgesia.

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Patients and Methods

This prospective, randomized, double-blind, placebo-controlled clinical study was approved by the Ethics and Research Committee of Sohag Faculty of Medicine, Sohag University. It was conducted at Sohag University Hospital between August 2012 and July 2014. Written informed consent was obtained from each patient preoperatively. The study included 52 patients in the age range of 40-65 years.

Patients with an American Society of Anesthesiologists (ASA) physical status of I or II and scheduled for instrumented one-level posterolateral lumbar spine fusion for lumbar spondylolisthesis under spinal anesthesia were included in this study. Exclusion criteria comprised the following: an absolute contraindication for spinal anesthesia, known allergy to the study drugs, treatment with α-adrenergic antagonists, labile hypertension, cardiac dysrhythmia, coronary artery disease, renal or hepatic impairment, neurological disorders, and bleeding diathesis.

Patients were randomly assigned to receive either 15 mg (3 mL) of hyperbaric bupivacaine 0.5% with 5 μg of dexmedetomidine in 0.5 ml of saline (Group D, n = 26) or 15 mg (3 mL) of hyperbaric bupivacaine 0.5% with 0.5 ml of saline (Group P, n = 26). Randomization and enrollment were performed using sequentially numbered closed envelopes. Prior to administration of spinal anesthesia, all patients were premedicated with 0.015 mg/kg atropine intramuscularly and received lactated Ringer's solution 10 mL/kg, intravenously for volume preloading. Lumbar puncture was performed with the patient in a sitting position at the L3-L4 intervertebral disc space through a midline approach using a pencil point 25-gauge needle with the hole pointing upwards. Following the injection, all patients were placed in a supine position. Oxygen (3-5 L/min) was administered via a face mask or nasal prongs. The patients were moved to a prone position shortly after the establishment of the level of anesthesia. The anesthesiologist (R. A. S) performing the spinal block recorded the intraoperative data, while another anesthesiologist (E. I. D) followed the patients postoperatively until they were discharged from the post-anesthesia care unit (PACU). Both anesthesiologists were blinded to the patient group allocation. The same surgeon (M. A. W) performed all of the operations to ensure consistency in the estimation of the operative field quality. Data collection was performed by a separate investigator (A. A. M).

Data Collection and Measurements

The surgeon estimated the quality of the operative field using a pre-defined category scale adapted from Fromme et al[9]. The average category scale (ACS) is a 5-point scale. A score of 0, indicated that there was no bleeding, while a score of 1, indicated slight bleeding and no need for blood suctioning. A score of 2 indicated slight bleeding and occasional blood suctioning; the operative field was not threatened. A score of 3 indicated slight bleeding with the need for frequent blood suctioning; the operative field was threatened for few seconds after blood suctioning was discontinued. A score of 4 indicated moderate bleeding and a frequent requirement of blood suctioning; the operative field was directly threatened after blood suctioning stopped. A score of 5 indicated severe bleeding and the need for continuous blood suctioning. This score also indicated that blood appeared faster than it could be removed by suctioning, the operative field was severely threatened, and that surgery was not possible. The ideal ACS score for the quality of the operative field was pre-determined between 0 and 2. Volume of blood loss was measured from the suction apparatus. Surgeon satisfaction was scored on a 4-point scale as follows: 0, bad; 1, moderate; 2, good; and 3, excellent. The number of surgical procedures that satisfied the surgeon was recorded in each group. The peak level of sensory block was tested with a piece of gauze, soaked in iced saline, placed on each side of the mid-thoracic line every 2 min until it became fixed after four consecutive tests, every 10 min during surgery up to 30 min, and then every 15 min until discharge from the PACU. Motor block was assessed using a modified Bromage scale (0, the patient is able to move the hip, knee, and ankle; 1, hip is blocked but the knee and ankle can be moved by the patient; 2, hip and knee are blocked but the ankle can be moved by the patient; 3, hip, knee, and ankle are blocked). The time taken to reach the T10 dermatome, peak sensory level, sensory regression of two-dermatomes, and sensory regression to the S1 dermatome was recorded. The time of intrathecal injection was recorded as the baseline. Patients were discharged from the PACU after sensory regression to the S1 dermatome and at a Bromage scale of 0.

Mean arterial pressure (MAP), heart rate (HR), and oxygen saturation (S_PO_2%) were monitored preoperatively, intraoperatively, and in the

Table I. Patient demographic and hemodynamic data.

	Group D (n = 26)	Group P (n = 26)	*p*-value*
Age (y)	53.04 ± 10.41	51.32 ± 9.65	0.654
Sex (M/W)	17/8	18/9	0.765
Weight (kg)	84.06 ± 6.02	82.86 ± 6.18	0.399
Height (cm)	174.86 ± 5.56	171.4 ± 5.49	0.619
MAP (mmHg)	87.15 ± 4.53	89.15 ± 2.53	0.428
HR (beats/min)	96.72 ± 2.42	98.45 ± 1.46	0.294

M/W = men/women; MAP = mean arterial pressure; HR = heart rate. Data are presented as mean ± standard deviation. Group D = dexmedetomidine administration; Group P = placebo. *$p < 0.05$ denotes statistical significance.

PACU. MAP, HR, and S_PO_2 were recorded as baseline values, every 2 min for the first 10 min after intrathecal injection and then every 5 min until discharge from the PACU. Hypotension was considered if the systolic blood pressure (SBP) decreased by > 30% from baseline, and was treated with 5 mg of intravenous ephedrine and a rapid intravenous infusion of lactated Ringer's solution. Bradycardia was considered if the HR decreased to < 50 beats/min and was treated with intravenous atropine (0.4-0.6 mg). The time to the first requirement of analgesia and the total dose of ketorolac (in mg) over 24 h were recorded. Intraoperative and postoperative side effects, including nausea and vomiting, were also recorded.

The sedation level was evaluated using the clinical observational method of the modified Observer's Assessment of Alertness/Sedation scale (OAA/S) as follows: 5, rapid response to sound spoken in normal tone (awake and alert); 4, lethargic response to sound spoken in normal tone; 3, responds only after sound is spoken repeatedly or loudly; 2, responds only after mild stimulation or shaking; and 1, does not respond to mild stimulation or shaking (asleep/unarousable)[10].

After 24 h postoperatively, patients were asked to rate their overall satisfaction with the control of their pain (0, inadequate; 1, fair; 2, good; or 3, excellent).

Outcome Variables

The primary outcome variable was the change in the quality of the operative field in group D. The secondary outcome variables comprised volume of blood loss, surgeon's satisfaction, number of surgical procedures satisfying the surgeon, time to sensory regression of two segments, time of sensory regression to the S1 segment, time to the first requirement of analgesia and the total dose of ketorolac, and patient's satisfaction with the control of their pain during the first 24 h postoperatively.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences version 16.0 (SPSS IBM, Chicago, IL, USA). A sample size of 26 patients in each group was required for a 0.05 level of significance and a power of 80% was required to detect a 30 min increase in the time of regression of two sensory dermatomes. Data were presented as mean ± standard deviation, number, and percentage, as appropriate. Qualitative data were compared between groups by the Chi-Square test, while quantitative data were compared using the *t*-test and analysis of variance. The level of statistical significance was considered at $p < 0.05$.

Results

A total of 52 patients were enrolled in this study. Patient demographic data did not differ between the two study groups (Table I). The spinal technique was performed with ease in all patients and the recovery from the spinal block was uneventful.

Primary Outcome

The mean ACS score for the quality of the operative field was significantly lower in group D than in group P ($p < 0.0001$) (Table II).

Secondary Outcomes

The patients in group D experienced significantly less intraoperative blood loss than those in group P ($p < 0.0001$) (Table II). The surgeon was significantly more satisfied with the procedure

Table II. Average category scale (ACS) for quality of the operative field, volume of blood loss, surgeon's satisfaction score, and number of procedures satisfying the surgeon.

	Group D (n = 26)	Group P (n = 26)	*p*-value*
ACS of operative field	1.62 ± 0.59	2.61 ± 0.96	< 0.0001
Blood loss (ml)	148.20 ± 70.54	312.63 ± 96.49	< 0.0001
Surgeon's satisfaction score:			
Bad	1 (3.8%)	5 (19.2%)	0.08
Moderate	2 (7.7%)	11 42.3%)	0.03
Good	12 (46.2%)	8 (30.8%)	0.25
Excellent	11 (42.3%)	2 (7.7%)	0.003
Number of procedures satisfying the surgeon	23 (88.5%)	10 (38.5%)	< 0.0001

Data are presented as the mean ± standard deviation or number (%). Group D = dexmedetomidine administration; Group P = placebo. *$p < 0.05$ statistically significant.

for patients in group D compared with those in group P (excellent score; $p = 0.003$) and the number of procedures satisfying the surgeon was significantly greater in group D than in group P ($p < 0.0001$) (Table II).

Differences in the mean time to reach a T10 sensory level and the time to reach the highest sensory level were not statistically significant between the two groups (Table III). The sensory regression times of two segments and of the S1 segment were significantly longer in group D than in group P ($p < 0.0001$) (Table III). The time to return to a modified Bromage scale of 0 was significantly longer in group D than in group P ($p < 0.0001$) (Table III). The peripheral oxygen saturation exceeded 97% at all times in both groups, with no significant difference between them (Table III).

Intraoperatively, MAP was significantly lower in group D than in group P 20 min after intrathecal injection ($p < 0.05$) (Figure 1). Two patients in group D required a 5-mg dose of ephedrine. Similarly, HR showed a significant reduction in group D 10 min after the intrathecal injection compared with group P ($p < 0.05$) (Figure 2). Three patients in group D required 0.5 mg atropine. In all of these patients, there were no further changes in mean MAP or HR after 90 and 75 min, respectively. The time to the first requirement of analgesia was significantly longer in group D compared with group P ($p < 0.0001$) (Table III). Total dose of ketorolac during the first 24 h postoperatively was smaller in group D than in group P ($p < 0.0001$) (Table III). The sedation score was in the range of 1-2 in both groups, with a median of zero. Intraoperative and

Table III. Spinal blockade characteristics.

	Group P (n = 26)	Group D (n = 26)	*p*-value*
Duration of surgery (min)	72.16 ± 9.98	71.83 ± 9.51	0.805
Onset of sensory block (min)	3.76 ± 0.77	3.950 ± 0.78	0.542
Time to reach T10 sensory level	4.88 ± 0.43	4.93 ± 0.43	0.325
Time to reach highest sensory level (min)	9.81 ± 0.84	9.83 ± 0.91	0.217
Time of sensory regression of two segments (min)	139.13 ± 5.60	83.66 ± 4.62	< 0.0001
Time of sensory regression to the S1segment (min)	286.76 ± 8.02	2248.70 ± 6.83	< 0.0001
Time to reach modified BRS3 (min)	7.84 ± 0.66	8.14 ± 0.82	0.295
Time to return to modified BRS0 (min)	244 ± 77.58	138 ± 37.28	< 0.0001
SPO_2 (%)	99.63 ± 0.49	99.43 ± 1.86	0.553
Time to the first requirement of analgesia (min)	399.63 ± 6.93	269.26 ± 9.26	< 0.0001
Total dose of ketorolac in mg over 24 h	45.86 ± 4.95	75.00 ± 6.65	< 0.0001

Data are presented as the mean ± standard deviation or number (%). BRS: Bromage scale; SPO_2: oxygen saturation. Group D = dexmedetomidine administration; Group P = placebo. *$p < 0.05$ denotes statistical significance.

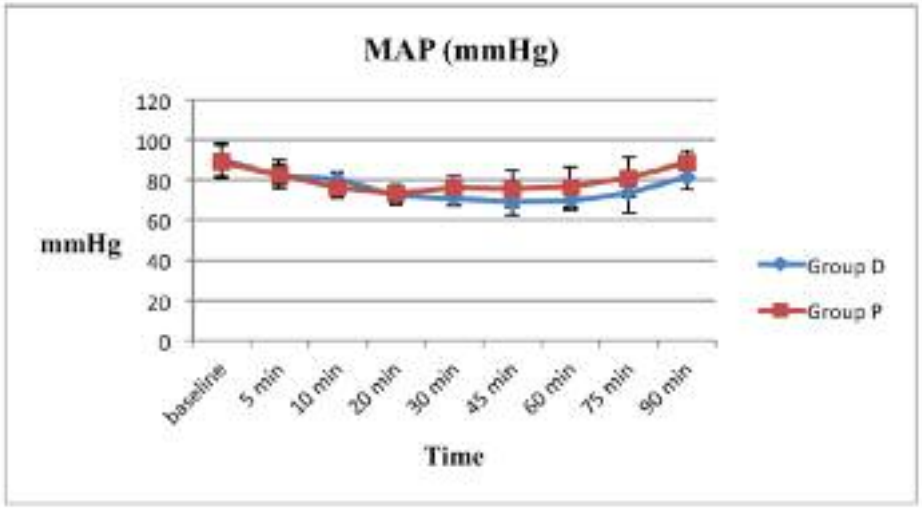

Figure 1. Mean arterial pressure (MAP). Data are presented as means ± standard deviation Group D = dexmedetomidine administration; Group P = placebo.

postoperative nausea or vomiting was not recorded in either group. Four patients experienced shivering in group P; however, no shivering was recorded in group D. Patients in group D were more satisfied with their control of pain than those in group P (Table IV).

Discussion

Spinal surgeries are known to present a risk of substantial blood loss during the course of the procedure. Surgical visualization may be difficult in a bloody operative field. Alongside the introduction of new anesthetic agents and monitoring techniques, a commonly utilized technique to limit blood loss and improve visualization of the operative field during spinal surgery is controlled hypotension[8]. Dexmedetomidine was previously reported to provide a good surgical field and reduce blood loss during controlled hypotension for tympanoplasty, septoplasty, and maxillofacial surgery[11-13]. In the present study, we observed an improved hemodynamic state and clearer operative field, with less blood loss in patients in the dexmedetomidine group compared with those in the placebo group. These results are in agreement with the results of Jamaliya et al[8] who reported that patients in a dexmedetomidine group achieved target MAP with improved HR control and less blood loss compared with patients in a nitroglycerine group. The mechanism by which intrathecal α_2-adrenergic receptor agonists prolong the sensory and motor block of local anesthetics is not well understood. Systemic absorption is not the cause, since the addition of intrathecal clonidine to bupivacaine spinal anesthesia is not altered by the plasma level of bupivacaine[14]. Intrathecal α_2-adrenergic receptor agonists provide analgesia by depressing the release of C-fiber transmitters and by hyperpolarizing postsynaptic neurons in the dorsal horn[5,15]. These effects may explain the prolongation of the sen-

Table IV Patient pain control satisfaction scores.

	Group D (n = 26)	Group P (n = 26)	*p*-value*
Excellent (%)	20 (76.9%)	12 (46.2%)	0.02
Good (%)	3 (11.6%)	5 (19.2%)	0.44
Fair (%)	2 (7.7%)	4 (15.4%)	0.39
Inadequate (%)	1 (3.8)	5 (19.2%)	0.08

Data are presented as numbers (%). Group D = dexmedetomidine administration; Group P = placebo. *$p < 0.05$ statistically significant.

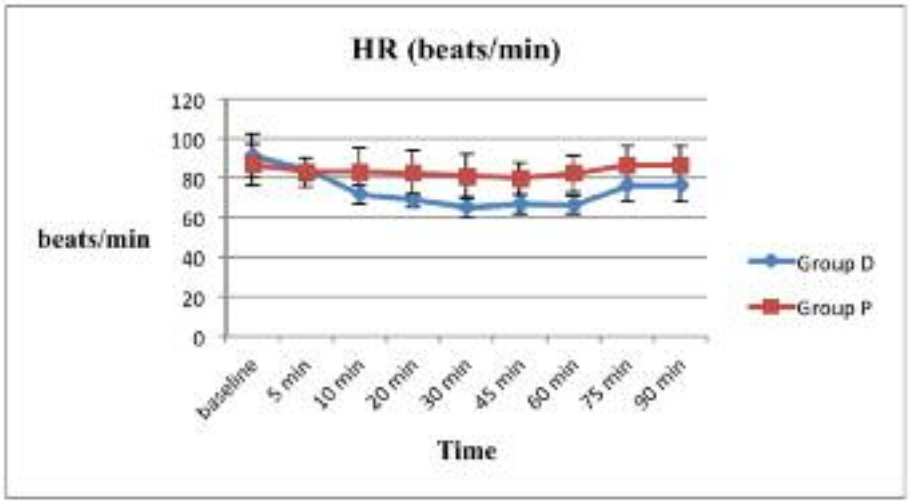

Figure 2. Mean heart rate (HR). Data are presented as means ± standard deviation. Group D = dexmedetomidine administration; Group P = placebo.

sory block when α_2-adrenergic receptor agonists are added to spinal anesthetics. The prolongation of the motor block of spinal anesthetics may result from the binding of α_2-adrenergic receptor agonists to motor neurons in the dorsal horn[16]. Our results demonstrated that a combination of 15 mg of intrathecal bupivacaine with 5 μg of dexmedetomidine significantly prolonged both the sensory and the motor block, compared with bupivacaine alone. In agreement with our results, Kanazi et al[17] reported that a supplementation of a bupivacaine (12 mg) spinal block with a low dose of dexmedetomidine (3 μg) produced significantly longer sensory and motor blocks than bupivacaine alone.

We recorded prolonged postoperative analgesia in the dexmedetomidine group; the time to the first postoperative analgesic requirement was longer in group D than in group P. Our findings are in accordance with those of Gurbet et al[18] who reported a reduction in perioperative analgesic requirement due to intraoperative infusion of dexmedetomidine. The analgesic effects of dexmedetomidine have been previously described in various settings and populations[19-21].

The favorable hemodynamic profile induced by dexmedetomidine can be attributed to the sympatholytic effects of α_2-adrenergic receptor agonists[22]. Alpha2 adrenergic receptors are located in blood vessels, where they mediate vasoconstriction, and on sympathetic terminals, where they inhibit the release of norepinephrine[23]. At lower doses, dexmedetomidine decreases the sympathetic outflow, resulting in reduced HR and cardiac output[24]. In the present study, MAP was chosen as a parameter to quantify hypotension because it is a true measure of tissue perfusion[25]. We found that the addition of dexmedetomidine to bupivacaine caused a significant reduction in MAP and HR intraoperatively. In agreement with these results, Al-Ghanem et al[26] observed a reduction in the HR and MAP occurred 25-30 min after spinal injection of dexmedetomidine. In our study, no patients in the dexmedetomidine group experienced shivering, in comparison with four patients in the control group. This is because α_2-adrenergic agents have an anti-shivering effect, as referred by Talke et al[27].

Conclusions

Our study showed that, in combination with 5 μg intrathecal bupivacaine, dexmedetomidine improved the quality of the operative field, prolonged the duration of the sensory block, and improved the quality of postoperative analgesia, with minimal side effects. Furthermore, dexmedetomidine preserved hemodynamic stability and did not cause sedation.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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