Egyptian Journal of Anaesthesia (2014) **30**, 137–141

Egyptian Society of Anesthesiologists

Egyptian Journal of Anaesthesia

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Research Article

Comparative study of epidural morphine and epidural dexmedetomidine used as adjuvant to levobupivacaine in major abdominal surgery

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Received 27 May 2013; revised 17 November 2013; accepted 15 December 2013
Available online 7 January 2014

KEYWORDS

Levobupivacaine;
Morphine;
Dexmedetomidine;
Epidural anesthesia;
Major abdominal surgery

Abstract *Background:* A lot of researches have been done to find an adjuvant in regional anesthesia that inhibits pain without any side effects.
Aim: This study was conducted to evaluate the onset, extent and duration of sensory and motor block, and side effects of morphine and dexmedetomidine when used as adjuvants to levobupivacaine in epidural anesthesia in major abdominal surgery.
Materials and methods: A prospective randomized study was conducted on 60 patients classified as American Society of Anesthesiologists status I and status II who underwent abdominal surgery. Patients were randomly allocated into two groups; group I levobupivacaine morphine group (LM), group II: levobupivacaine dexmedetomidine group (LD), comprising of 30 patients each. Group I patients received 20 ml of 0.5% levobupivacaine (150 mg) and 0.005 % morphine. Group II patients received 20 ml of 0.5% levobupivacaine and 1.5 μg/kg dexmedetomidine. The onset, extent and duration of sensory and motor blocks, abdominal muscle relaxation, and side effects were recorded.
Results: There were no statistically significant differences between the two groups as regards onset of sensory block or sensory level achieved. Time to reach motor block was shorter in the LM group than the LD group. There were no significant differences between the time of total regression of sensory or motor black and abdominal muscle relaxation. As regards side effects, more patients in the LM group suffered from pruritis and more patients suffered from dry mouth in the LD group.
Conclusion: Dexmedetomidine is a good alternative to morphine as an adjuvant to levobupivacaine in epidural anesthesia in major abdominal surgeries.

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Peer review under responsibility of Egyptian Society of Anesthesiologists.

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1. Introduction

Major abdominal surgery may be done by using regional (spinal or epidural) or general anesthesia. Nowadays, regional (spinal or epidural) anesthesia is the preferable mode of anesthesia. Epidural anesthesia reduces the perioperative stress responses to surgery and improves surgical outcome [1]. Local anesthetics and opioids are the drugs most widely used in epidural anesthesia which is either by single injection or by infusion (see Tables 1–5).

Levobupivacaine is the isolated S(−) isomer of bupivacaine and is less cardiotoxic [2,3]. Dexmedetomidine is the selective α2-adrenoceptor agonist with analgesic potency, sedative properties and causes minimal respiratory depression when used as adjuvant to regional anesthesia [4–6].

The antinociceptive mechanisms of this drug when used in epidural anesthesia are spinally mediated as it has no analgesic effect when given systemically. It is highly lipid soluble and appears rapidly in CSF and has high binding affinity to α2 receptors in the spinal cord [7].

Morphine is the "gold standard" opioid for neuraxial analgesia during and after surgery [8,9]. This is because of its long action activity as it is water soluble and it crosses biological membranes as dural membrane slowly. Its analgesic effect is due to drug diffusion into cerebrospinal fluid (CSF) across the dural membrane and its binding to opioid receptors in the dorsal horn of the spinal cord and is also due to supraspinal action for both rostral spread in cerebrospinal fluid and systemic blood absorption of the drug [10,11].

Nowadays, the use of adjuvant with local anesthetics is essential as it prolongs the duration of work, gives better success rate and increases patient satisfaction.

This study makes a comparison between two adjuvants, one is opioid (morphine) and the other is α2 agonist (dexmedetomidine), used with levobupivacaine in major abdominal surgery as regards onset, extent, duration of block, muscle relaxation and side effects.

2. Patient and methods

After obtaining ethical committee approval and written informed consent, 60 ASA physical status I and status II patients aged 25–45 years, of both sexes, scheduled for abdominal surgery under epidural anesthesia were included in this study. Surgical procedures included colectomy, radical prostatectomy and abdominoperineal resection. Patients with history of uncontrolled hypertension, cardiac, respiratory, hepatic, neurological, neuromuscular disease; with allergy to the used drugs, contraindication or failure of epidural anesthesia were excluded from the study.

Patients were monitored by ECG, pulse oximetry (SPO2) and non-invasive blood pressure (NIBP).

After infusion of 500 ml of lactated Ringer's solution, patients were put in the sitting position. 3 ml of lidocaine was used to infiltrate the skin and subcutaneous tissues.

A 17 gauge Tuohy needle was used at T10–T12. After loss of resistance, the epidural catheter was advanced 3–4 cm into the epidural space. Any evidence of needle or catheter entry into an epidural vein or into the CSF excluded the patient from this study. A test dose of 3 ml of 2% lignocaine solution containing adrenaline 1: 200,000 was injected. After 4–6 min of injecting the test dose and excluding intravascular or subarachnoid injection, patients were allocated to one of two groups in a double blinded fashion based on computer-generated code, group I: levobupivacaine and morphine (LM) in which 20 ml of 0.5% levobupivacaine (150) and 0.005% morphine was administered in the epidural catheter, group II: levobupivacaine and dexmedetomidine (LD) in which 20 ml of 0.5% levobupivacaine (150 mg) and 1.5 μg/kg dexmedetomidine was administered in the epidural catheter. The drug syringes were prepared by an anesthetist not oriented with the idea of the study. Block was achieved for the surgery. Sensory block was assessed using the blunt end of a 27-gauge needle until an appropriate block was achieved. If an adequate sensory block was not achieved after 20 min from injection, an additional dose of 5 ml of 0.5% levobupivacaine was given. If no adequate sensory block was achieved after 30 min of injection, the patient was withdrawn from the study. Motor blockade was assessed by using the modified Bromage scale [12] (Bromage 0: The patient is able to move the hip, knee and ankle; Bromage 1: The patient is unable to move the hip but able to move the knee and the 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). The time to reach the peak sensory level and Bromage 3 motor block was recorded before surgery. The regression time for sensory and motor block was recorded in Post-anesthesia care unit (PACU). All durations were calculated from the time of epidural injection.

The overall quality of intra-operative muscle relaxation (poor, fair, good or excellent) was evaluated by the surgeon at the end of the surgery.

Table 1 Demographic data.

		Group I (n = 30)	Group II (n = 30)	t or chi-square	
				t/X^2	P-value
Age (yr)	Range	25.00–45.00	25.00–45.00	−1.63	0.11
	Mean (SD)	35.00(7.86)	38.33(7.99)		
Sex N (%)	Female	15.00(50)	14.00(46.67)	0.00	1.00
	Male	15.00(50)	16.00(53.33)		
Weight (kg)	Range	70.00–90.00	70.00–90.00	0.96	0.34
	Mean (SD)	80.54(8.44)	82.45(6.89)		
Height (cm)	Range	150.00–170.00	155.00–175.00	0.70	0.49
	Mean (SD)	162.11(5.49)	160.88(7.88)		
ASA N (%)	I	17.00(56.67)	18.00(60.00)	0.00	1.00
	II	13.00(43.33)	12.00(40.00)		

Table 2 Block characteristics.

		Group I (n = 30)	Group II (n = 30)	t or chi-square	
				t/X^2	P-value
Onset of sensory block		11.50(5.40)	12.60(5.90)	0.75	0.45
Time to reach maximum sensory level		20.30(5.60)	22.40(9.40)	1.05	0.30
Time to reach motor block		24.20(3.10)	27.30(2.10)	4.54	<0.001*
Time to regression of sensory		360.00(71.10)	390.00(87.60)	1.46	0.15
Time of total regression of motor block		420.00(89.70)	400.00(96.20)	0.83	0.41
Maximum sensory block level N (%)	T7	8.00(26.67)	6.00(20.00)	0.87	0.83
	T8	10.00(33.33)	9.00(30.00)		
	T9	7.00(23.33)	10.00(33.33)		
	T10	5.00(16.67)	5.00(16.67)		

Values presented as mean (SD).
* Means statistically significant.

Table 3 Degree of abdominal muscle relaxation.

	Group I (n = 30)		Group II (n = 30)		Total		Chi-square	
	N	%	N	%	N	%	X^2	P-value
Excellent	7.00	23.33	5.00	16.67	12.00	20.00	0.87	0.83
Good	10.00	33.33	10.00	33.33	20.00	33.33		
Fair	10.00	33.33	11.00	36.67	21.00	35.00		
Poor	3.00	10.00	5.00	16.67	8.00	13.33		

Table 4 Side effects observed in both groups.

	Group I (n = 30)		Group II (n = 30)		Total		Chi-square	
	N	%	N	%	N	%	X^2	P-value
Nausea	10	33.33	5	16.67	15	25.00	2.256	0.133
Vomiting	8	26.67	3	10.00	11	18.33	2.869	0.090
Pruritis	5	16.67	0	0.00	5	8.33	7.387	0.007*
Dry mouth	0	0.00	6	20.00	6	10.00	6.570	0.010*
Respiratory depression	0	0.00	0	0.00	0	0.00		

* Means statistically significant.

Table 5 Sedation score in both groups.

Sedation score	Group I (n = 30)		Group II (n = 30)		Total		Chi-square	
	N	%	N	%	N	%	X^2	P-value
1	5	16.67	3	10.00	8	13.33	1.83	0.40
2	15	50.00	12	40.00	27	45.00		
3	10	33.33	15	50.00	25	41.67		
4	0	0.00	0	0.00	0	0.00		
5	0	0.00	0	0.00	0	0.00		

The two groups were monitored preoperatively, intraoperatively for heart rate, non-invasive blood pressure and O_2 saturation (SpO_2). Hypotension was defined as systolic blood pressure <90 mmHg or $>30\%$ decrease in baseline values and was treated by fluids and vasopressors.

Tachycardia was defined as heart rate >100/min. Bradycardia was defined as heart rate <55/min and was treated by 0.5 mg of atropine injection. Intraoperative nausea, vomiting, pruritus, sedation or any other side effects were recorded.

Sedation was assessed by sedation score (1: alert and awake, 2: arousable to verbal command, 3: arousable with gentle tactile stimulation, 4: arousable with vigorous shaking, 5: unarousable).

3. Statistical methods

Data were presented as mean ± SD. t-test was used to compare the two groups for quantitative data and chi-square test was used for qualitative data by SPSS V18. Value of $P < 0.05$ was considered statistically significant. The primary outcome upon which we calculated the sample size was the time to reach motor block. We made a pilot study from group

I and group II (5 cases from each group) and we found the difference between 2 means 1.7 by SD from group I 2.8 and SD from group II 2.6. We found the minimal sample size was 54 by α (type I error) 0.05 and β (type II error) 0.1 with power of test 90%.

4. Results

There was no statistically significant difference between the two groups in any of the demographic data.

There was no statistical significance between the two groups as regards the onset of sensory block, time to total regression of motor or sensory block or maximum sensory block level. Time to reach total motor block was significantly shorter in the (LM) group than the (LD) group.

There was no statistically significant difference between the two groups in the degree of muscle relaxation.

There was no statistically significant difference as regards nausea vomiting or respiratory depression. However, 5 patients (16.6%) in the LM group suffered from pruritis while no patient suffered from it in the LD group, and 6 patients (20%) suffered from dry mouth in the LD group while no patient suffered from it in the LM group.

There was no statistically significant difference between the two groups as regards sedation score.

No remarkable changes in the hemodynamic variables were recorded in both groups.

5. Discussion

Nowadays, a lot of adjuvants are used with local anesthetics in the epidural anesthesia. The aim of these adjuvants is to fasten and prolong the sensory and motor block and produce more sedation and analgesia. In this study, morphine was compared with dexmedetomidine (α2 agonist) as adjuvants to levobupivacaine in epidural anesthesia. Opioids are often combined with epidural local anesthetics to improve the quality of analgesia and decrease local anesthetic requirements and motor blockade [13]. Morphine represents the ''gold standard'' opioid for neuraxial analgesia in the major surgeries [8,9]. Dexmedetomidine, a highly selective α2 adrenoceptor agonist, is used in combination with local anesthetics for sedation and analgesia. Dexmedetomidine when combined with spinal bupivacaine prolongs the sensory block by depressing the release of c-fiber transmitter and by hyperpolarization of post-synaptic dorsal horn neurons [14]. Motor block prolongation by α2-adrenoceptor agonists may result from binding of these agonists to motor neurons in the dorsal horn of the spinal cord [15].

This study was the first study to compare morphine and dexmedetomidine as adjuvants to levobupivacaine in epidural anesthesia. In this study, it was found that both of them were alike in the onset and duration of sensory and motor block, but morphine gave faster motor block. Both of them were comparable in the time of regression of sensory and motor block and abdominal muscle relaxation degree.

As regards side effects, more patients suffered from pruritis in the levobupivacaine morphine group and more patients suffered from dry mouth in the levobupivacaine dexmedetomidine group. There was no difference in the sedation score between the two groups. All the side effects were well tolerated by the patients.

Kanazi and colleagues [16] found in their study that the supplementation of bupivacaine with a low dose dexmedetomidine produced significantly longer sensory and motor blocks than bupivacaine alone, and they found that dexmedetomidine produced a significantly shorter onset of motor block but in comparison with bupivacaine alone and in our study morphine accelerated the onset of motor block when added to levobupivacaine other than dexmedetomidine. On the other hand, Gupta and associates [17] found that there was no difference in the onset time to Bromage 3 motor block on comparing intrathecal bupivacaine dexmedetomidine with intrathecal bupivacaine fentanyl but the regression to Bromage 0 motor block was significantly slower on adding dexmedetomidine. A study done by Odette and Lesley [18] on dogs showed that epidural bupivacaine dexmedetomidine group had a slower return of motor function than bupivacaine morphine group, which is different from our study that showed no statistical difference between the two groups in time to total regression of motor block.

Al-Mustafa et al. [19] and Al-Ghanem et al. [20] used dexmedetomidine but as an intrathecal adjuvant to bupivacaine and found that its effect was dose-dependent and that its use accelerated the onset of sensory block to reach T10 dermatome.

Bajwa and his team [21] showed in their study that dexmedetomidine was a better adjuvant than clonidine in epidural anesthesia for patient comfort, superior sedative and anxiolytic properties, intra-operative and postoperative analgesia.

Crews et al. [22] found in their study that the use of continuous levobupivacaine in addition to morphine via a thoracic epidural catheter produced a segmental sensory block and excellent analgesia.

6. Conclusion

The use of dexmedetomidine as an adjuvant to levobupivacaine seems to be a good alternative to the use of morphine in epidural anesthesia in major abdominal surgery. Both of them provide adequate sensory, motor block and abdominal muscle relaxation. Their side effects are well tolerated by the patients. Further studies may be needed to confirm this result.

Conflict of interest

No conflict of interest.

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