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Original Article

Epidural bupivacaine and dexmedetomidine versus bupivacaine and opioids for lower vascular surgery

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Abstract

Objective

The purpose of this study was to assess dexmedetomidine as an adjuvant to bupivacaine as a good alternative to other adjuvants like fentanyl in epidural anesthesia.

Patients and methods

Ninety patients between the age of 40 and 60 years with American Statistical Association status I–III planned for elective lower abdomen surgery were enrolled in a double-blind comparative study. Patients were randomized to one of three group: group A (n = 30) patients received bupivacaine, group B (n = 30) patients received bupivacaine and fentanyl, and group D (n = 30) patients received bupivacaine and dexmedetomidine.

Result

Regarding demographic data, no statistically significant difference was observed among the three groups. There was a statistically highly significant difference in onset of sensory block, time to achieve peak sensory level, two-segment regression time, and duration of sensory block among the three groups. In motor block, there was a statistically highly significant difference in onset of motor block and duration of motor block.

Conclusion

The use of dexmedetomidine as an adjuvant to bupivacaine was a good alternative to other adjuvants like fentanyl in epidural anesthesia, and dexmedetomidine had an edge over fentanyl as an adjuvant when used with bupivacaine in epidural anesthesia.

Keywords: Bupivacaine, dexmedetomidine, epidural, motor block, sensory block

Introduction

Epidural anesthesia is the most commonly used technique for providing not only perioperative surgical anesthesia but also postoperative analgesia in lower abdominal and limb surgeries.

Several adjuvant drugs have been used in combination with the epidural local anesthetic to improve the quality of motor block and prolong the duration of postoperative analgesia. These adjuvants include opioids such as morphine, fentanyl, and sufentanil; α-2 agonists such as clonidine and dexmedetomidine; magnesium sulfate; and neostigmine [1].

Opioids like fentanyl have been used traditionally as an adjuvant for epidural administration in combination with a lower dose of local anesthetic to achieve the desired anesthetic effect [2], but there is always a possibility of an increased incidence of pruritis, urinary retention, nausea, vomiting, and respiratory depression [3].

Many techniques and drug regimens have been tried to calm the patients and to eliminate the anxiety component during regional anesthesia [4]. The fear of surgery, the strange surroundings of the operation theater, the sight, and sound of sophisticated equipment, dynamicity of an 'operation'

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during regional anesthesia and the masked faces of so many strange personnel make the patient panic to a large extent [5]. α-2 adrenergic agonists have both analgesic and sedative properties when used as an adjuvant in regional anesthesia [6].

Dexmedetomidine is a highly selective α-2 adrenergic agonist with an affinity 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 hyperpolarization of nerve issues by altering transmembrane potential and ion conductance at locus coeruleus in the brain stem [7].

The stable hemodynamics and the decreased oxygen demand owing to enhanced sympathoadrenal stability make them very useful pharmacologic agents [8].

Dexmedetomidine does cause manageable hypotension and bradycardia, but the striking feature of this drug is the lack of opioid-related adverse effects like respiratory depression, pruritis, nausea, and vomiting [9].

Aim

The purpose of this study is to compare the onset and duration of sensory and motor block, as well as hemodynamic changes following epidural bupivacaine supplemented with dexmedetomidine and fentanyl in patients undergoing lower abdomen surgery.

Patients and methods

Patients were recruited between October 2015 and January 2018. Ninety patients between the age of 40 and 60 years with American Statistical Association (ASA) status I–III planned for elective lower abdominal surgery were enrolled in a double-blind comparative study after obtain approval and written informed consent from them.

Exclusion criteria

Patients with ASA physical status more than or equal to III, patients with contraindications to regional anesthesia, and patients with severe cardiac disease, bronchial asthma, chronic obstructive lung disease, history of sleep apnea, serum creatinine more than 200 μmol/l, and advanced liver disease were excluded from the study.

Preoperatively

The following routine investigation were done in all patients: ECG, complete blood count, coagulation profile, and liver and renal function tests. Intravenous access was established, and an infusion of ringer-lactate solution was started as a bolus of 500 ml in 15 min and then at a rate of 10 ml/kg/h. Monitors were connected, including pulse oximeter, noninvasive blood pressure, and ECG. Patients were put in lateral or sitting position, and under strict aseptic conditions, the back was painted and draped; the tip of lumbar spine was palpated, and L2–3 or L3–4 space was selected. The skin was infiltrated with ~2 ml of 1% lidocaine. The epidural space was identified by midline approach using 18-G Tuohy needle using a loss-of-resistance technique for air. An epidural catheter was then inserted into the epidural space, and the catheter was advanced into epidural 3–4 cm beyond the previously noted distance between the skin and epidural space. Patients were randomized to one of three group: group A ($n = 30$) patients received epidural bupivacaine 0.5% with a volume of 1 ml per segment, group B ($n = 30$) patients received epidural bupivacaine 0.5% 1 ml per segment with 25-μg fentanyl, and group C ($n = 30$) patients received epidural bupivacaine 0.5% 1 ml per segment with dexmedetomidine 0.5 μg/kg.

The following data were recorded:

(1) Sensory block is assessed bilateral at midclavicular line by pinprick test starting from time of injection considering zero and then every 15 min till discharge from Post-anesthesia care unit (PACU). The following were recorded: onset of sensory block at T10, time of two segments regression, and duration of sensory block.
(2) Motor block: Bromage Scale was used to assess the degree, onset, and duration of motor block at the same interval as sensory blockade, considering the time of epidural injection as zero time.
(3) Cardio-respiratory parameters such as heart rate (HR), mean arterial blood pressure (MAP), and O_2 saturation were monitored continuously and recorded every 5 min until 30 min, then at 10-min interval thereafter up to 60 min, then at 15-min interval for next hour, and finally at 30 min interval in the third hour.

Results

This study was conduct on 90 patients who underwent lower limb vascular surgery. Patients were divided into three groups:

(1) Group A ($n = 30$) receive bupivacaine.
(2) Group B ($n = 30$) receive bupivacaine+fentanyl.
(3) Group C ($n = 30$) receive bupivacaine+dexmedetomidine.

Demographic characteristics of patients

In the current study, as regarding demographic data, there was no statistically significant difference among the three groups ($P = 0.05$), as shown in Table 1.

Sensory block

There was a statistically highly significant difference in onset of sensory block, time to achieve peak sensory level, two-segment regression time, and duration of sensory block among the three groups ($P < 0.01$). Onset of sensory block and time to achieve peak sensory level were earlier in group B and group C as compared with group A ($P < 0.01$). The peak sensory level in group C was reached at 18.13 ± 2.80 min (T_5), which is higher, and earlier than that in group B at 21.50 ± 2.60 min (T_7) and that in group A at 24.43 ± 2.05 min (T_8). Two-segment regression time and duration of sensory block were prolonged in group B and group C as compared with group A. The difference was statistically highly significant ($P < 0.01$) (Table 2).

Motor block

In motor block, there was a statistically highly significant difference in onset of motor block and duration of motor block ($P < 0.01$).

Onset of motor block was significantly early in group B and group C as compared with group A ($P < 0.01$). Duration of motor block was prolonged in group B and group C as compared with group A, which was statistically highly significant ($P < 0.01$) as shown in Tables 3–5. Regarding the degree of motor block, there was a statistically significant difference among the three studied groups ($P < 0.01$), as shown in Table 4.

Hemodynamic data

Heart rate

Changes in the HR are shown in Tables 6.In the three study groups, the HR increased followed by gradual decrease. The initial increase in the HR was statistically insignificant in the three groups. There was a statistically significant difference in HR between the group A and group C at 25 min ($P < 0.05$) and highly significant difference between both group A and group C at the rest of the time intervals ($P < 0.01$).

Mean arterial blood pressure

There was a slight increase in MAP during epidural injection and slight decrease over 15 min after injection [Tables 7]. There was no statistically significant difference in the MAP among the three studied groups in the first 15 min ($P > 0.05$). Thereafter, there was a statistically highly significant difference in the MAP between group A and group C ($P < 0.01$).

O_2 saturation

O_2 saturation remained stable throughout the procedure. No statistical difference was found among the three groups, as shown in Table 8.

Discussion

In the present study, the three groups were compared with respect to demographic feature such as age, sex, and ASA type, and there were no significant differences observed

Table 1: The demographic characteristics of the patients in the three groups

	Group A ($n=30$)	Group B ($n=30$)	Group C ($n=30$)	One-way ANOVA test	
				F/χ^2*	P
Age (years)					
Mean±SD	34.17±8.42	34.87±8.09	33.77±8.39	0.135	0.874
Range	20-46	21-46	21-46		
Sex [n (%)]					
Female	12 (40.0)	7 (23.3)	10 (33.3)	1.933	0.380*
Male	18 (60.0)	23 (76.7)	20 (66.7)		
ASA [n (%)]					
I	24 (80.0)	16 (53.3)	21 (70.0)	4.986	0.083*
II	6 (20.0)	14 (46.7)	9 (30.0)		
BW (kg)					
Mean±SD	81.93±7.53	82.60±6.53	82.87±8.59	0.120	0.887
Range	(70-98)	(67-93)	(67-99)		
Height (cm)					
Mean±SD	171.13±4.78	172.57±5.26	171.90±5.68	0.559	0.574
Range	165-181	165-182	165-182		

*Not significant; ANOVA, analysis of variance; ASA, American Statistical Association; BW, Body Weight.

Table 2: Assessment of sensory blockade

	Group A (mean±SD)	Group B (mean±SD)	Group C (mean±SD)	One-way ANOVA test		P_1	P_2	P_3
				F/t*	P			
Onset of sensory analgesia at T_{10}	15.10±2.20	13.73±2.15	11.63±1.27	24.752	0.000	0.018	0.000	0.000
Time to T_9	19.53±2.11	17.37±2.03	13.50±1.87	69.671	0.000	0.000	0.000	0.000
Time to T_8	24.43±2.05	20.30±2.71	15.57±1.38	132.062	0.000	0.000	0.000	0.000
Time of two-segment regression	86.67±9.91	105.60±7.30	130.13±6.02	227.816	0.000	0.000	0.000	0.000
Duration of sensory block	259.00±30.94	284.20±28.94	305.27±29.33	18.189	0.000	0.002	0.000	0.007

ANOVA, analysis of variance.

Table 3: Onset of motor block

	Group A (mean±SD)	Group B (mean±SD)	Group C (mean±SD)	One-way ANOVA test		P_1	P_2	P_3
				F	P			
Onset of motor block (time to Bromage 1)	17.20±2.25	15.93±2.00	13.87±2.10	18.940	0.000	0.025	0.000	0.000

Table 4: Degree of motor block

Degree of motor block	Group A (mean±SD)	Group B (mean±SD)	Group C (mean±SD)	One-way ANOVA		P_1	P_2	P_3
				F	*P*			
0 min	0.00±0.00	0.00±0.00	0.00±0.00	-	-	-	-	-
5 min	0.00±0.00	0.00±0.00	0.00±0.00	-	-	-	-	-
10 min	0.17±0.38	0.23±0.43	0.37±0.49	1.640	0.200	-	-	-
15 min	0.67±0.48	0.83±0.70	1.43±0.50	15.048	0.000	0.286	0.000	0.000
20 min	0.83±0.38	1.17±0.38	1.53±0.51	20.251	0.000	0.001	0.000	0.002
25 min	0.93±0.25	1.23±0.43	1.60±0.50	20.159	0.000	0.002	0.000	0.003
30 min	1.00±0.00	1.23±0.43	1.60±0.50	19.000	0.000	0.004	0.000	0.003
45 min	1.00±0.00	1.20±0.41	1.60±0.50	20.300	0.000	0.009	0.000	0.001
60 min	1.00±0.00	1.20±0.41	1.60±0.50	20.300	0.000	0.009	0.000	0.001
75 min	1.00±0.00	1.20±0.41	1.60±0.50	20.300	0.000	0.009	0.000	0.001
90 min	1.00±0.00	1.17±0.38	1.60±0.50	22.026	0.000	0.019	0.000	0.000
105 min	1.00±0.00	1.17±0.38	1.60±0.50	22.026	0.000	0.019	0.000	0.000
120 min	1.00±0.00	1.13±0.43	1.37±0.49	7.231	0.001	0.098	0.000	0.056
135 min	0.43±0.50	0.87±0.43	1.37±0.49	28.756	0.000	0.001	0.000	0.000
150 min	0.23±0.43	0.33±0.48	1.23±0.43	45.500	0.000	0.399	0.000	0.000
165 min	0.10±0.31	0.23±	1.13±0.35	71.494	0.000	0.171	0.000	0.000
180 min	0.00±0.00	0.00±0.00	0.60±0.56	34.043	0.000	1.000	0.000	0.000

ANOVA, analysis of variance.

Table 5: Duration of motor block

	Group A (mean±SD)	Group B (mean±SD)	Group C (mean±SD)	One-way ANOVA test		P_1	P_2	P_3
				F	*P*			
Duration of motor block (time to Bromage 0)	150.13±16.95	162.87±16.61	204.07±18.17	80.060	0.000	0.005	0.000	0.000

ANOVA, analysis of variance.

Table 6: Heart rate changes in the three groups

	L group (mean±SD)	LF group (mean±SD)	LD group (mean±SD)	One-way ANOVA test		P_1	P_2	P_3
				F	*P*			
HR 0	84.63±6.65	84.10±6.05	83.40±6.55	0.278	0.758	-	-	-
HR 5	82.13±5.41	81.40±5.04	81.07±4.32	0.366	0.694	-	-	-
HR 10	81.00±4.19	80.20±6.02	80.63±5.35	0.175	0.840	-	-	-
HR 15	80.00±5.01	78.23±4.66	76.77±5.38	3.114	0.049	0.163	0.019	0.264
HR 20	79.00±5.43	77.87±5.96	75.50±4.76	3.273	0.043	0.445	0.010	0.095
HR 25	78.60±5.67	77.03±5.12	74.03±6.13	3.352	0.035	0.614	0.021	0.124
HR 30	78.40±6.70	76.03±5.94	74.20±5.73	3.531	0.034	0.153	0.012	0.228
HR 40	78.00±6.29	76.00±4.60	74.00±4.76	4.321	0.016	0.165	0.007	0.103
HR 50	77.00±5.76	75.67±5.79	73.03±5.68	3.703	0.029	0.375	0.009	0.081
HR 60	76.13±5.52	74.53±5.41	72.53±5.13	3.650	0.006	0.314	0.001	0.087
HR 75	75.07±5.00	73.10±6.00	71.23±6.74	3.171	0.018	0.135	0.011	0.091
HR 90	74.57±6.25	72.03±5.79	70.07±6.43	4.020	0.021	0.109	0.008	0.218
HR 105	76.33±6.24	73.87±5.76	71.37±6.55	4.826	0.010	0.117	0.004	0.122
HR 120	78.03±5.65	75.70±6.42	72.70±5.11	6.483	0.002	0.140	0.000	0.050
HR 150	78.97±5.93	77.93±4.40	75.93±4.17	3.678	0.001	0.150	0.000	0.312
HR 180	81.07±5.99	79.87±4.89	77.13±6.29	3.684	0.029	0.421	0.010	0.069

ANOVA, analysis of variance; HR, heart rate.

among the three groups. Addition of dexmedetomidine to levobupivacaine as an adjuvant resulted in an earlier onset (11.63 ± 1.27 min) of sensory analgesia at T_{10} as compared with the addition of fentanyl (13.73 ± 2.15 min) and bupivacaine without adjuvant (15.10 ± 2.20 min). Dexmedetomidine not only provided a higher dermatomal spread but also helped in achieving the maximum sensory anesthetic level in a shorter period at T_5 (18.13 ± 2.80 min) compared with fentanyl at T_7 (21.50 ± 2.60 min) and bupivacaine alone at T_8 (24.43 ± 2.05 min). Dexmedetomidine

Table 7: Mean blood pressure in the three groups

	Group A (mean±SD)	Group B (mean±SD)	Group C (mean±SD)	One-way ANOVA test		P_1	P_2	P_3
				F	*P*			
MABP 0	90.07±5.77	90.10±5.93	90.40±7.14	0.025	0.975	-	-	-
MABP 5	82.13±7.57	80.27±7.63	80.07±7.43	0.685	0.507	-	-	-
MABP 10	81.00±6.73	80.93±7.08	79.40±7.52	0.485	0.617	-	-	-
MABP 15	79.73±7.21	77.20±5.86	74.67±5.27	5.062	0.008	0.141	0.003	0.084
MABP 20	79.00±6.96	76.50±7.50	74.20±4.93	4.022	0.021	0.186	0.003	0.166
MABP 25	78.00±5.93	76.07±7.35	74.00±4.94	3.173	0.047	0.267	0.006	0.206
MABP 30	77.37±6.15	75.00±6.43	73.00±4.92	4.158	0.019	0.151	0.004	0.181
MABP 40	77.97±6.25	75.37±5.54	73.20±4.87	5.403	0.006	0.058	0.002	0.181
MABP 50	78.17±5.91	75.3±6.37	73.97±5.79	3.803	0.026	0.069	0.008	0.394
MABP 60	78.50±5.65	75.70±5.64	72.77±5.69	7.697	0.001	0.059	0.000	0.058
MABP 75	78.90±5.87	76.37±4.52	73.93±4.62	7.272	0.001	0.056	0.000	0.065
MABP 90	79.30±6.13	77.03±3.87	74.57±4.52	6.911	0.002	0.079	0.000	0.056
MABP 105	79.20±6.19	77.00±3.79	75.27±3.99	5.100	0.008	0.078	0.002	0.164
MABP 120	79.40±5.80	77.30±3.23	75.60±3.40	5.864	0.004	0.062	0.001	0.130
MABP 150	82.73±6.82	79.43±5.87	76.33±7.35	6.827	0.002	0.060	0.000	0.077
MABP 180	83.53±8.00	82.97±7.01	83.13±8.49	0.041	0.960	-	-	-

ANOVA, analysis of variance; MABP, mean arterial blood pressure.

Table 8: O_2 saturation changes in the three groups

	L group (mean±SD)	LF group (mean±SD)	LD group (mean±SD)	One-way ANOVA test	
				F	*P*
SpO_2 0	97.27±1.39	97.53±1.41	97.10±1.30	0.770	0.466
SpO_2 5	97.10±1.03	97.70±1.32	97.57±1.55	1.723	0.185
SpO_2 10	97.43±1.36	97.60±1.33	97.80±1.24	0.589	0.557
SpO_2 15	97.60±1.35	97.00±1.34	97.70±1.37	2.345	0.102
SpO_2 20	97.63±1.30	97.47±1.31	97.50±1.20	0.145	0.865
SpO_2 25	97.00±1.15	96.37±0.85	97.00±1.39	3.035	0.053
SpO_2 30	97.03±1.40	96.77±1.01	96.67±1.42	0.647	0.526
SpO_2 40	96.23±0.90	96.00±1.05	96.10±1.06	0.406	0.667
SpO_2 50	96.00±0.95	95.93±0.79	95.63±0.621	1.816	0.169
SpO_2 60	95.67±0.96	95.80±1.13	96.00±1.23	0.684	0.507
SpO_2 75	96.93±1.34	96.07±1.64	96.80±1.50	2.922	0.059
SpO_2 90	96.53±1.48	95.97±1.67	95.50±1.74	3.013	0.054
SpO_2 105	95.77±1.70	95.60±1.22	95.83±1.05	0.238	0.789
SpO_2 120	96.33±1.12	96.07±1.02	96.40±1.30	0.702	0.499
SpO_2 150	98.03±1.00	98.07±0.94	98.00±0.98	0.035	0.966
SpO_2 180	97.20±0.93	97.23±0.82	97.43±0.94	0.598	0.552

ANOVA, analysis of variance; SpO_2, O_2 saturation.

provided prolonged time to two-segmental dermatomal regression in group C (130.13 ± 6.02 min) as compared with group B (105.60 ± 7.30 min) and group A (86.67 ± 9.91 min); prolonged the duration of sensory block, which was 305.27 ± 29.33 min in group C compared with 284.20 ± 28.94 min in group B and 259.00 ± 30.94 min in group A; and prolonged the duration of effective analgesia, which was 330.00 ± 18.61 min in group C as compared with group B, which was (305.23 ± 16.13 min) and group A, which was 272.03 ± 18.36 min. As a result, the number of patients requiring rescue analgesia was comparatively fewer (zero patients) in group C than in group B (two patients) and group A (six patients).

In agreement with our study, Milligan *et al.* [10] opined that patients undergoing total hip replacement, the addition of the α-2 adrenergic agonist clonidine to epidural infusions of bupivacaine significantly improved postoperative analgesia.

Regarding the motor block in the current study, addition of dexmedetomidine to bupivacaine resulted in an earlier onset (13.87 ± 2.10 min) of motor block as compared with the addition of fentanyl (15.93 ± 2.00 min) and bupivacaine without adjuvant (17.20 ± 2.25 min), with statistically highly significant differences among the three groups ($P < 0.01$); moreover, it prolonged the duration of motor block, which was 150.13 ± 16.95 min in group A, 162.87 ± 16.61 min in group B, and 204.07 ± 18.17 min in group C, with statistically highly significant differences among the three groups ($P < 0.01$). In the current study, when the degrees of motor block over time were compared, a statistically highly significant difference was found among the three groups ($P < 0.01$).

In agreement of our finding, Zeng *et al.* [11] in their study found that low-dose epidural dexmedetomidine improved thoracic epidural anesthesia for nephrectomy.

There was a statistical difference in hemodynamic parameters in the three groups. There was a statistically significant difference in HR between group A and group C at 25 min ($P < 0.05$) and highly significant difference between both group A and group C at the rest of time intervals ($P < 0.01$). There was a slight increase in MAP during epidural injection and slight decrease over 15 min after injection. There was no statistically significant difference in the MAP between the three studied groups in the first 15 min ($P > 0.05$), then there was statistically highly significant difference in the MAP between group A and group C ($P < 0.01$). The HR and blood pressure were significantly lower in the group C over time but without clinical consequences.

Wallet *et al.* [12] in their study found that the addition of clonidine to epidural levobupivacaine and sufentanil for patients controlled epidural analgesia in labor. Blood pressure was significantly lower in the clonidine group over time but without clinical consequence.

Conclusion

The use of dexmedetomidine as an adjuvant to bupivacaine was a good alternative to other adjuvants like fentanyl in epidural anesthesia. Both fentanyl and dexmedetomidine provided adequate sensory and motor block, but dexmedetomidine had an edge over fentanyl as adjuvant when used with bupivacaine in epidural anesthesia.

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Conflicts of interest

There are no conflicts of interest.

References

1. Jabalameli M, Pakzadmoghadam H. Adding different doses of intrathecal magnesium sulfate for spinal anaesthesia in caesarean section. A prospective double blind randomized trials. Adv Biomed Res 2012; 1:7.
2. Benzon HT, Wong HY, Belavic AM, Goodman I, Mitchell D, Lefheit T, Locicero J. A randomized double-blind comparison of epidural fentanyl infusion versus patient controlled analgesia with morphine for postthoracotomy pain. Anesth Analg 1993; 76:316–322.
3. Lorenzini C, Moreira LB, Ferreira MB. Efficacy of ropivacaine compared with ropivacaine plus sufentanil for postoperative analgesia after major knee surgery. Anaesthesia 2002; 57:424–428.
4. Hohener D, Blmenthal S, Borgeat A. Sedation and regional anaesthesia in the adult patient. Br J Anaesth 2008; 100:8–16.
5. Badner NH, Nielson WR, Munk S. Preoperative anxiety: detection and contributing factors. Can J Anaesth 1990; 37:444–447.
6. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic and Analgesic properties of small dose dexmedetomidine infusions. Anesth Analg 2000; 90:699–705.
7. Correa-Sales C. A hypnotic response to dexmedrtomedine, an alpha-2 agonist, is mediated in the Locus Coeruleus in rats. Anesthesiology 1992; 76:948–952.
8. Buerkle H. Peripheral anti-nociceptive action of alpha-2 agonists. Best Pract Res Clin Anaesthesiol 2000; 14:411–418.
9. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care 2000; 4:302–308.
10. Milligan KR, Convery PN, Weir P. The efficacy and safety of epidural infusions of levobupivacaine with and without clonidine for postoperative pain relief in patients undergoing total hip replacement. Anesth Analg 2000; 91:393–397.
11. Zeng XZ, Xu YM, Cui XG. Low dose epidural dexmedetomidine improves thoracic epidural anaesthesia for nephrectomy. Anaesth Intensive Care 2014; 42:185–190.
12. Wallet F, Clement JH, Bouret C. Effectts of a continuous low-dose clonidine epidural regimen on pain, satisfaction and adverse events during labour. Eur J Anaesthesiol 2010; 27:441–447.