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CLINICAL TRIAL

The effect of dexmedetomidine on spinal anesthesia quality and hemodynamic changes in patients undergoing inguinal hernia repair surgery: intravenous versus intrathecal

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Abstract

Purpose The aim of this study was to evaluate the quality of spinal anesthesia and hemodynamic parameters of intravenous versus intrathecal dexmedetomidine in patients undergoing inguinal hernia repair surgery under spinal anesthesia.

Methods Fifty male patients aged 18–70 years with ASA I and II were randomly divided into two groups of 25 patients receiving either intravenous (1 μg/kg infused during 10 min before blockade) or intrathecal (5 μg, added to local anesthetics) dexmedetomidine. The duration of analgesia, sensory and motor blockade levels, the score of pain intensity, post-operative analgesic usage and the level of sedation as well as hemodynamic changes, and complications were recorded.

Results The duration of analgesia in the intrathecal group was significantly longer than intravenous group (403.588 ± 93.706 vs. 274.048 ± 47.266 min; $P < 0.001$). Duration of the sensory and motor blockade were significantly longer in intrathecal than intravenous group (230.440 ± 26.494 vs. 181.400 ± 28.850 min; $P < 0.001$ for sensory block, and 253.800 ± 32.637 vs. 205.400 ± 30.921 min; $P < 0.001$ for motor block). The score of pain intensity was lower in the intrathecal group in the post-operative period (3.680 ± 1.680 vs. 5.520 ± 1.901; $P = 0.001$ and 2.360 ± 1.320 vs. 3.24 ± 1.69; $P = 0.041$, respectively, for the time 6 and 12). Ramsay sedation score was higher in the intravenous group during surgery but it was higher in intrathecal group during recovery room period ($P < 0.05$). Moreover, the incidence of bradycardia was significantly lower in the intrathecal group (0% vs. 36% respectively; $P = 0.002$).

Conclusion Administration of intrathecal dexmedetomidine along with local anesthetics can be recommended to increase the quality of spinal anesthesia with minimal complications.

Keywords Dexmedetomidine · Inguinal hernia · Spinal anesthesia

Introduction

Inguinal hernia is a common disease among men and women that affects approximately 25% of men and 2% of women during their lifetime [1]. Spinal anesthesia, as one of the most common neuraxial regional anesthesia techniques, is widely used in surgeries involving the lower extremities and lower abdomen, especially inguinal hernia. Spinal anesthesia is often considered by anesthetists as a less risky and more acceptable technique due to its rapid onset of action, more reliability, deep sensory and motor blockade as well as fewer complications [2]. The most commonly used drug for spinal anesthesia is bupivacaine, whose mechanism of action is through the blockade of voltage-gated sodium channel [3]. In recent years, a number of techniques have been proposed to prolong the duration of this type of anesthesia and improve the quality of the blockade with minimal complications. One of the techniques that can be mentioned is intravenous injection of various drugs or utilization of some drugs such as epinephrine, phenylephrine, opioids, and α2-adrenergic agonists as an adjunct to local anesthetics [4, 5]. However, addition of some adjunct drugs can be accompanied with lots of complications including hypotension, bradycardia, shivering, nausea and vomiting, excessive sedation, and itching. One of the commonly used new drugs in recent years is

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dexmedetomidine (Dex), which is a highly selective α2-adrenergic agonist with sedation, analgesic, and anesthetic effects [6]. Dex is eight times more potent and more selective to α2-adrenergic receptors (α2-AR) than clonidine. The intravenous administration of this drug prior to general anesthesia as a premedication induces perioperative sedation, analgesic effects, and hemodynamic stability. Moreover, it reduces the need for inhaled and intravenous anesthetic agents and analgesics [7, 8]. Dex exerts its effects on three α2 receptor subtypes, i.e., α2A, α2B, and α2C, in the brain and spinal cord. The activation of α2A and α2C receptors in the locus coeruleus leads to induction of sedation. Moreover, the activation of α2A and α2C receptors in the spinal cord directly reduces the level of pain by reducing the release of substance P [8].

Due to the sedative and analgesic properties, Dex can prolong the duration of anesthesia and immobility in spinal anesthesia [9]. Moreover, its intravenous and intrathecal administration in surgeries under regional anesthesia is safe and has been proven to increase the duration of the blockade, increase post-operative analgesia, and has analgesic and sedative properties [5, 10–12]. Concerning about the best rout of applying Dex for these purposes is still under debate, as some studies are in favor of either intravenous [13, 14] or intrathecal rout [11, 15] for Dex administration. Since the quality of spinal anesthesia, the primary aim of this study was to evaluate the effect of Dex (intrathecal vs. intravenous) on the Ramsay sedation score during the surgery and recovery room in patients with inguinal hernia surgery under spinal anesthesia. Further aims were to evaluate any differences in hemodynamic stability, quality of spinal anesthesia, duration of analgesia, post-operative pain intensity, analgesic rescue medication, and complications.

Methods

The present prospective double-blind clinical trial was conducted on 50 male patients ($N = 25$ in each group) in Hormozgan University of Medical Sciences after obtaining the Ethics Committee approval with the following Code of Ethics HUMS.REC.1396.37 and registered at www.fa.irct.ir (IRCT20171030037093N23). The patients aged 18–70 years with ASA I and II were candidates for elective inguinal hernia repair surgery. Patients with emergency surgery, contraindication to spinal anesthesia, a history of sensitivity to anesthetic agents or Dex, chronic usage of analgesic drugs, patients with cardiac block or unstable cardiovascular disease, patients that receiving α2 agonists, and patients who failed blockade or required induction of general anesthesia were excluded from the study. A purposive method of sampling was carried out using a random block table.

Informed written consent was obtained from all the patients. Based on the sample size formula for comparing the two independent means with the confidence level of 95%, power of 80% and considering the standard deviation of Ramsay sedation score from previous studies [16] in Dex and control groups (0.30, 0.18, respectively) and the mean difference of 0.07 between the two groups (μ_1-$\mu_2 = 1.97$–1.90), the sample size in each group was calculated as 23 individuals and in order to account for a possible loss of up to two patients per group, 25 cases were assigned to each group (50 in total).

After setting up standard monitoring including NIBP, pulse oximetry, and ECG, the initial vital signs were measured and recorded. All the patients received a volume load of 10 ml/kg Ringer's Lactate solution before the blockade. Then, the patients were randomly assigned into two groups. The first group received intravenous Dex (Precedex™ 200 mcg/2 ml Hospira, Inc., Lake Forest, IL60045USA) [1 μg/kg diluted with normal saline (N/S) up to a total volume of 20 ml] during 10 min before the blockade, and the second group received intravenous 20 ml N/S via a syringe pump within 10 min before the blockade. Then, an anesthesiologist performed the spinal anesthesia in the sitting position with a 25G Quincke needle at L4–L5 space through the median approach. After observing transparent CSF, 2.5 ml (12.5 mg) of hyperbaric bupivacaine 0.5% (MYLAN 20 mg/4 ml S.A.S. 117 Allee' des parcs-69800 SAINT-PRIEST-FRANCE) was injected into the spinal canal. The administration of the drug to spinal canal was as follows: The patients in the first and second groups received bupivacaine (2.5 ml + 0.5 ml N/S) and bupivacaine plus 5 μg Dex (diluted in N/S up to the volume of 0.5 ml), respectively. Both groups received an equal volume of 3 ml. Then, the patients were positioned in the supine position. The level of anesthesia was checked using pin-prick, and surgery was allowed after sensory level fixation at Th10 level. The motor blockade level was also measured at the same time using the modified Bromage scale [10]. The sensory and motor blockade level was recorded in both groups. Moreover, the sensory and motor blockade level as well as the sedation level were measured every 10 min during the surgery. Furthermore, the recovery time of sensory blockade to two levels lower than the maximum level and recovery time of motor blockade to Bormage1 were recorded. The level of sedation was specified using the Ramsay sedation score [17]. All patients received equal intravenous fluid during the surgery (6 ml/kg/h of balanced salt solution).

The above-mentioned criteria were also measured and recorded not only in the operating room but also in the recovery room. The patients' hemodynamic parameters including Heart Rate (HR), Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), Mean Arterial Pressure (MAP), and Saturation of peripheral O_2 (Spo2) were measured and recorded during the surgery and in the recovery room every 10 and

15 min, respectively. Hypotension (SBP < 90 mmHg or a decrease in arterial pressure of greater than 20% from baseline) was treated with intravenous ephedrine 5 mg. Moreover, bradycardia (HR <50 beats/min) was also treated with atropine 0.6 mg. The incidence rate of hypotension and bradycardia as well as the employed doses of ephedrine and atropine was recorded in each group.

The patients' pain score of the two groups was measured and recorded in the recovery room (t_1), and at 6, 12, and 24 h in the post-operative period (t_6, t_{12} and t_{24}). To do so, visual analog scale (VAS) score, which is a horizontal continuous 10-cm line with the anchors "no pain" at the left side and "extreme pain" at the right side was used. In the mentioned scale, the scores of 1–3, 4–7, and 8–10 represent mild, moderate, and severe pain, respectively. In the case of VAS > 3 and at the patient's request, 25 mg of pethidine was administered. Moreover, the duration of analgesia (the time interval between the onset of block and patient's first request), the number of requests, and the dosage of the administered drug were recorded during 24 h in the post-operative period. In addition, complications such as nausea and vomiting, shivering, and hypoxia (Spo2 < 90%) were also recorded during the recovery room.

All of the mentioned data was recorded in a two-part questionnaire by an anesthesiologist assistant who did not know the study groups and drug prescriptions.

Statistical analysis

Data analysis was performed by SPSS software using mean ± standard deviation, independent samples *t* test, Chi-square test, Mann-Whitney *U* test, Friedman test, Fisher's exact test, and ANOVA. There was no adjustment of *P* values for multiple testing.

Results

Spinal anesthesia was successful in all patients, and the study was completed by all patients. Patients in both groups ($N = 25$) were similar in terms of demographic profile and no significant difference was observed between the two groups (Table 1).

There was no significant difference in the level of sensory (Th6, Th8, Th10) and motor (Th10, Th11, Th12) blockade ($P = 1.00$, $P = 0.667$, respectively). Also, duration of the recovery time of sensory and motor blockade and the duration of analgesia in the intrathecal group were significantly longer than those of the intravenous group ($P < 0.001$) (Table 2).

The patients' pain score was measured in this study at the first hour of arrival in the recovery room (t_1) as well as at t_6, t_{12}, and t_{24} in the post-operative period. According to the Friedman test, there was a significant difference between the intravenous and intrathecal groups at 6 and 12 h in the post-operative period in this regard. The pain level in the intrathecal group was less than that of the intravenous group ($P = 0.001$, $P = 0.041$, respectively). Moreover, there was no significant difference between the two groups at t_1 ($P = 0.317$) and t_{24} ($P = 0.296$) (Fig. 1).

Table 1 Patient demographics data

Characteristics	Intravenous ($n = 25$)	Intrathecal ($n = 25$)	*P* value
Age (year)	47.240 ± 16.024	44.920 ± 18.457	0.637*
Weight (kg)	64.840 ± 8.596	63.840 ± 10.597	0.716*
Height (cm)	171.360 ± 5.446	171.400 ± 54.838	0.980*
ASA I/II	16/9	15/10	0.771**

Values are presented as mean ± SD or numbers

*Used of independent sample *t* test

**Used of Fisher exact test

There was no significant difference in the mean values of SBP, DBP, MAP, HR, and Spo2 between the two groups at different time periods. Moreover, following hypotension, eight and three patients in the intravenous and intrathecal groups received ephedrine with the mean dose of 8.125 ± 5.303 and 5.000 ± 0.000 mg, respectively. According to the Mann-Whitney test, there was no significant difference between the two groups in this regard ($p = 0.241$). With respect to bradycardia, 9 (36%) and 0 (0%) patients in the intravenous and intrathecal groups had bradycardia, respectively. According to Fisher's exact test, there was a significant difference between the two groups in this regard ($P = 0.002$).

The two groups indicated a significant difference in terms of the sedation level according to the results of Friedman test (compare the level of sedation over the time) ($P < 0.05$). The level of sedation during the surgery was higher in the intravenous group as compared with the intrathecal group; however, the level of sedation during the recovery room was higher in the intrathecal group (Fig. 2).

As the level of patient's pain score was more than 3 , a dose of 25 mg pethidine was administered, in this regard 22 (88%) patients in the intravenous group and 18 (72%) patients in the intrathecal group received the average doses of 35.227 ± 12.581 and 29.167 ± 9.587 mg pethidine, respectively. These findings showed no significant difference between two groups according to Mann-Whitney U test ($P = 0.100$).

Moreover, there was no significant difference in the incidence of shivering as well as nausea and vomiting in the two groups ($P = 0.463$ and $P = 0.417$, respectively). Furthermore, hypoxia (Spo2 < 90%) was not observed in the patients.

Discussion

The results of the present study indicated that the level of sensory and motor blockade between the two groups were

Table 2 Comparison of the levels of sensory and motor block, the recovery time of sensory and motor blockade, and duration of analgesia between two groups

Variables	Intravenous ($n = 25$)	Intrathecal ($n = 25$)	P value
Sensory block			
Th_6	2(8%)	3(12%)	1.00*
Th_8	3(12%)	3(12%)	
Th_{10}	20(80%)	19(76%)	
Motor block			
Th_{10}	2(8%)	3(12%)	0.667*
Th_{11}	0(0%)	1(4%)	
Th_{12}	23(92%)	21(84%)	
Recovery time of sensory block (minutes)	181.400 ± 28.850	230.440 ± 26.494	< 0.001**
Recovery time of motor block (minutes)	205.400 ± 30.921	253.800 ± 32.637	< 0.001**
Duration of analgesia (minutes)	274.048 ± 47.266	403.588 ± 93.706	< 0.001**

Values are presented as mean ± SD or *n* (%)

"Th" is defined as thoracic dermatome

*Used of Chi-Square test

**Used of independent sample *t* test

not different; however, the duration of sensory and motor blockade in the intrathecal group were significantly longer than intravenous group. Moreover, the duration of analgesia in the intrathecal group was significantly longer than the intravenous group. The mentioned findings are consistent with those of Afifi et al. [11]; however, they are in contrast with the results of Elgebaly et al. [13] which revealed that recovery time of motor and sensory blockade and the duration of analgesia in the intravenous group was longer than those of the intrathecal group. It should be noted that this study was performed on patients with severe preeclampsia undergoing cesarean section. The desired level of anesthesia was higher than Th7 in the mentioned study, while the level of Th10 anesthesia was acceptable in the present study.

The results of the present study regarding the patients' pain score in the recovery and then in the surgical ward during the first 24 h indicated that pain intensity especially at t_6 and t_{12} was significantly lower in the intrathecal group as compared with the intravenous group (3.680 versus 5.520 at t_6 and 2.360 versus 3.240 at t_{12}, respectively) which may be due to the effect of Dex on inhibition of pain receptors at the spinal cord. Moreover, its systemic absorption through the action on supra-spinal site and peripheral tissues may be involved in the reduction of pain, which is also in line with the findings presented by Gupta et al., Afifi et al., and Kim J et al. [9, 11, 18]; however, they are in contrast with the results of Elgebaly et al. study [13] which was performed on patients with severe

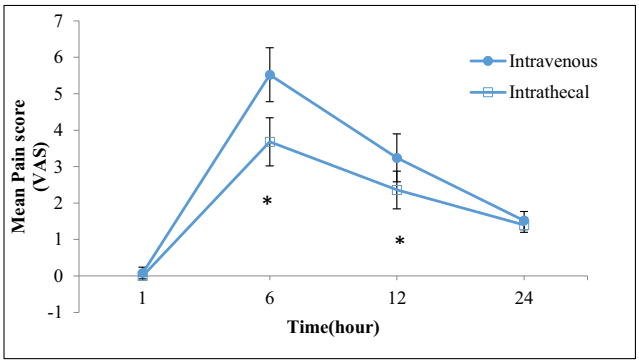

Fig. 1 Evaluation of pain score (VAS) between two groups in post-operative period. Comparison of pain score in intravenous and intrathecal groups at the first hour in the recovery room (t_1) as well as at t_6, t_{12}, and t_{24}in the post-operative period (25 patients in each group, data are expressed as mean±SD).*Significant difference between intravenous and intrathecal (according to Mann-Whitney U test) at $t_6$and t_{12}(P=0.001, P=0.041, respectively)

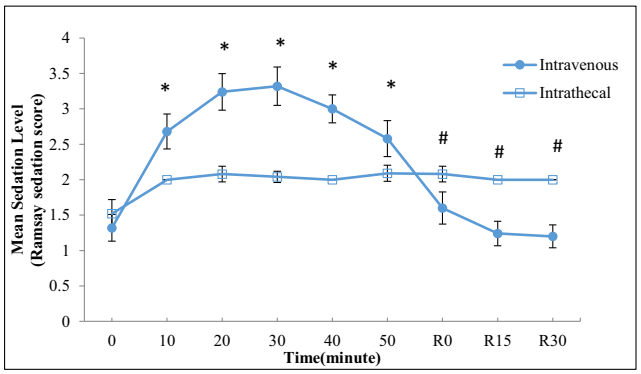

Fig. 2 Evaluation of sedation level (Ramsay sedation score) between two groups during the surgery and recovery room. Comparison of sedation level between intravenous and intrathecal groups ($n = 25$, data are expressed as mean± SD). * According to Mann-Whitney *U* test, there was significant difference between intravenous and intrathecal groups during the surgery ($P < 0.05$). # According to Mann-Whitney U test, there was significant difference between intrathecal and intravenous groups during recovery time ($P < 0.05$). Time 0–50: Ramsay sedation score during the surgery (every 10 min) and R0-R30: Ramsay sedation score in recovery room (every 15 min). R0: Ramsay sedation score when patients entered the recovery room, R15: Ramsay sedation score at the time of 15 min at recovery room, R30: Ramsay sedation score at the time of 30 min at recovery room

preeclampsia undergoing cesarean section. The higher level of sensory blockade, physiological changes of pregnancy, the need for local anesthetic, and different gender may be the possible justifications for the mentioned finding in Elgebaly et al. study [13].

One of the complications of intrathecal anesthesia is hypotension and bradycardia. The prevalence of hypotension in spinal anesthesia has been reported to be 30–35% [2]. Hypotension usually occurs as a result of sympathetic blockade and decreases in venous return or decreases in systemic vascular resistance. In addition, Dex can reduce the blood pressure and HR due to its binding to α2 receptors in the locus coeruleus, decreasing the release of norepinephrine, and inhibiting the sympathetic activity. Considering the mentioned points, hemodynamic changes in two groups at different times were evaluated in the present study. The findings revealed that SBP, DBP, MAP, and Spo2 were not significantly different between the two groups in most of the study periods. The mentioned findings were similar to the results of previous studies [9, 11, 18, 19]. Moreover, following the hypotension, 8 (32%) and 3 (12%) cases in the intravenous and intrathecal groups received ephedrine, respectively (the mean dose of 8.125 ± 5.303 mg and 5.000 ± 0.000 mg, respectively). There was no significant difference between the two groups in this regard.

In various studies, the incidence of bradycardia after spinal anesthesia was reported to be 10–15%, and the incidence of bradycardia after Dex infusion was 25% [20]. Stimulation of the brain and spinal receptors postpones neuronal stimulation and evacuation and induces hypotension, bradycardia, sedation, and analgesia [13]. The findings of the present study also indicated that the heart rate in the intravenous group was significantly lower than that of the intrathecal group, especially at 40 and 50 min during the surgery. Overall, the incidence of bradycardia in the intravenous group was 30%, while no cases of bradycardia requiring treatment were observed in the intrathecal group. The mentioned finding demonstrates a statistically significant difference between two groups in this regard, which is in agreement with the findings of Afifi et al. and Xin-Yin N et al. [5, 11]. However, the presented findings were in contrast with those of Magdy et al. [19] which indicated no difference between the two techniques of intrathecal and intravenous on patients undergoing cesarean section. Elgebaly et al. [13] focused on patients with severe preeclampsia and revealed that reduction of MAP and HR in the intrathecal group was higher than that of intravenous group, which is not consistent with the findings of the present study. A number of possible causes of bradycardia can be the effects of drug on α2 receptors and inhibition of the release of norepinephrine and sympathetic nervous system [21].

The sedation in the regional anesthesia is of great significance to obtain patient's satisfaction and reduce patient's anxiety during surgery. One of the main reasons for block failure and patients' dissatisfaction during regional anesthesia is inadequate sedation [22]. The results of this study showed that the sedation score during surgery was significantly higher in the intravenous group as compared with the intrathecal group; however, the level of sedation during recovery room was higher in the intrathecal group, which was consistent with Afifi et al. [11] study regarding the level of sedation during surgery and was in line with Magdy et al. [19] study regarding the level of sedation during the recovery room. However, Elgebaly et al. [13] study revealed no significant difference between the two groups in terms of the level of sedation.

The possible mechanism of sedation induction can be the binding of drug to α2 receptors in the locus coeruleus and its central effects on brain and brain stem. Moreover, the drug can be rapidly absorbed into the Cerebro Spinal Fluid (CSF) and exerts its effects on α2 receptors in the spinal cord [11, 12, 19].

Evaluation of the complications of intrathecal anesthesia revealed that the incidence of nausea and vomiting was within the range of 2–18% and 0–7%, respectively [20]. The results of the present study showed that the rate of nausea and vomiting was 20% and 8% in the two groups, respectively. The mentioned finding was indicative of no significant difference between the two groups in this regard, which was consistent with the results of other studies [5, 11, 19]. Moreover, the incidence of shivering in the intravenous and intrathecal groups was 24% and 12%, respectively, which did not show any significant difference.

Conclusion

This study revealed that the duration of analgesia and the duration of the sensory and motor blockade in the intrathecal group were significantly longer than those of the intravenous group. Besides, the findings of the present study revealed some interesting results regarding the effect of intrathecal vs. intravenous Dex administration on the Ramsay sedation score. In this study, sedation was acceptable in both groups and Ramsay sedation score was higher in the intravenous group during the surgery but it was higher in the intrathecal group during the recovery room period. Moreover, the intensity of pain score and bradycardia was significantly lower in the intrathecal group. Therefore, according to the mentioned findings, it can be concluded that the use of intrathecal Dex, compared to intravenous Dex, reached better outcome. Hence, intrathecal Dex administration can be recommended in this regard.

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Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

Informed consent Informed consent to participate was obtained from all participants.

Ethical approval All procedures performed in this study were in accordance with the ethical standards and the study was done after obtaining the Ethics Committee approval with the following Code of Ethics HUMS.REC.1396.37 and IRCT code IRCT20171030037093N23. Implementation of the research project and possible complications were explained to the patients and they were included in the study after obtaining written informed consent from each patient in accordance with the Helsinki declaration.

References

1. Petersen L, Millikan KW (2015) Inguinal hernia. In: Saclarides TJ, Myers JA, Millikan KW (eds) Common surgical diseases: an algorithmic approach to problem solving. Springer New York, New York, pp 229–231
2. Khosravi F, Alishahi M, Khanchemehr Y, Jarineshin H (2019) A comparison between the effects of preloading with Ringer's solution and Voluven on hemodynamic changes in patients undergoing elective cesarean section under spinal anesthesia. Med Arch 73:44–48
3. Farzi F, Mirmansouri A, Naderi Nabi B et al (2017) Comparing the effect of adding fentanyl, Sufentanil, and placebo with Intrathecal bupivacaine on duration of analgesia and complications of spinal anesthesia in patients undergoing cesarean section. Anesth Pain Med 7(5):e12738
4. Amer MM, Rashwan DA, Shaker MA (2015) Comparative study of two doses of Intrathecal Dexmedetomidine versus fentanyl as adjuvant to hyperbaric bupivacaine spinal anesthesia. Med Sci 3: 2450–2464
5. Niu X-Y, Ding X-B, Guo T, Chen MH, Fu SK, Li Q (2013) Effects of intravenous and Intrathecal Dexmedetomidine in spinal anesthesia: a meta-analysis. CNS Neurosci Ther 19:897–904. https://doi.org/10.1111/cns.12172
6. Jarineshin H, Abdolahzade Baghaei A, Fekrat F, Kargar A, Abdi N, Navabipour S, Zare A, Akhlaghi H (2015) Comparison of two different doses of dexmedetomidine in attenuating cardiovascular responses during laryngoscopy and endotracheal intubation: a double blind, randomized, clinical trial study. J Med Life 8:45–51
7. Khan ZP, Munday IT, Jones RM, Thornton C, Mant TG, Amin D (1999) Effects of dexmedetomidine on isoflurane requirements in healthy volunteers. 1: pharmacodynamic and pharmacokinetic interactions. Br J Anaesth 83:372–380. https://doi.org/10.1093/bja/83.3.372
8. Manne GR, Upadhyay MR, Swadia VN (2014) Effects of low dose dexmedetomidine infusion on haemodynamic stress response, sedation and post-operative analgesia requirement in patients undergoing laparoscopic cholecystectomy. Indian J Anaesth 58:726
9. Kim JE, Kim NY, Lee HS, Kil HK (2013) Effects of intrathecal dexmedetomidine on low-dose bupivacaine spinal anesthesia in elderly patients undergoing transurethral prostatectomy. Biol Pharm Bull 36:959–965. https://doi.org/10.1248/bpb.b12-01067
10. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS et al (2009) Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J 30:365–370
11. Afifi MH, Mohammed AM, Abdullah SI, Ellisy KE (2016) Intrathecal versus intravenous dexmedetomidine in characteristics of bupivacaine spinal block in lower abdominal surgery. Menoufia Med J 29:523–529
12. Jarineshin H, Fekrat F, Kermanshah AK (2016) Treatment of postoperative pain in pediatric operations: comparing the efficiency of bupivacaine, bupivacaine-dexmedetomidine and bupivacaine-fentanyl for caudal block. Anesthesiol Pain Med 6:5e39495. https://doi.org/10.5812/aapm.39495
13. Elgebaly AS (2018) Evaluation the effects of intravenous vs. spinal dexmedetomidine during anesthesia for cesarean sections with severe pre-eclampsia. J Anesth Clin Res 9:801. https://doi.org/10.4172/2155-6148.1000801
14. Kaya FN, Yavascaoglu B, Turker G, Yildirim A, Gurbet A, Mogol EB, Ozcan B (2010) Intravenous dexmedetomidine, but not midazolam, prolongs bupivacaine spinal anesthesia. Can J Anesth 57: 39–45
15. Ashour FH, Abdellah AS, El Sayed RM (2018) Intrathecal versus intravenous infusion of dexmedetomidine during subarachnoid block in lower abdominal surgeries. Sci J Al-Azhar Med Fac Girls 2:237
16. Tarıkçı Kılıç E, Aydın G (2018) Effects of dexmedetomidine infusion during spinal anesthesia on hemodynamics and sedation. Libyan Med 13(1):1436845. https://doi.org/10.1080/19932820.2018.1436845
17. Park SH, Shin YD, Yu HJ et al (2014) Comparison of two dosing schedules of intravenous dexmedetomidine in elderly patients during spinal anesthesia. Korean J Anesthesiol 66:371
18. Gupta R, Bogra J, Verma R, Kohli M, Kushwaha JK, Kumar S (2011) Dexmedetomidine as an intrathecal adjuvant for postoperative analgesia. Indian J Anaesth 55:347–351
19. Magdy H, Mohsen M, Saleh M (2015) The effect of intrathecal compared with intravenous dexmedetomidine as an adjuvant to spinal bupivacaine anesthesia for cesarean section. Ain Shams J Anaesthesiol 8:93–99
20. Elcıcek K, Tekın M, Katı I (2010) The effects of intravenous dexmedetomidine on spinal hyperbaric ropivacaine anesthesia. J Anesth 24:544–548
21. Gertler R, Brown HC, Mitchell DH, Silvius EN (2001) Dexmedetomidine: a novel sedative-analgesic agent. Proc (Bayl Univ Med Cen) 14:13–21. https://doi.org/10.1080/08998280.2001.11927725
22. Miller RD, Pardo M (2011) Basics of anesthesia e-book. Elsevier Health Sciences

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