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SCIENTIFIC ARTICLE

Comparison of fentanyl and dexmedetomidine as an adjuvant to bupivacaine for unilateral spinal anesthesia in lower limb surgery: a randomized trial

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KEYWORDS
Bupivacaine;
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Unilateral spinal anesthesia

Abstract
Background and objectives: One of the disadvantages of unilateral spinal anesthesia is the short duration of post-operative analgesia, which can be addressed by adding adjuvants to local anesthetics. The aim of current study was to compare the effects of adding dexmedetomidine, fentanyl, or saline to bupivacaine on the properties of unilateral spinal anesthesia in patients undergoing calf surgery.
Methods: In this double-blind clinical trial, 90 patients who underwent elective calf surgery were randomly divided into three groups. The spinal anesthetic rate in each of the three groups was 1 mL bupivacaine 0.5% (5 mg). In groups BD, BF and BS, 5 μg of dexmedetomidine, 25 μg of fentanyl and 0.5 mL saline were added, respectively. The duration of the motor and sensory blocks in both limbs and the rate of pain during 24 h after surgery were calculated. Hemodynamic changes were also measured during anesthesia for up to 90 min.
Results: The duration of both of motor and sensory block was significantly longer in dependent limb in the BF (96 and 169 min) and BD (92 and 166 min) groups than the BS (84 and 157 min) group. Visual Analog Scale was significantly lower in the two groups of BF (1.4) and BD (1.3), within 24 h after surgery, than the BS (1.6) group.
Conclusions: The addition of fentanyl and dexmedetomidine to bupivacaine in unilateral spinal anesthesia can increase the duration of the motor and sensory block in dependent limb and prolong the duration of postoperative pain. However, fentanyl is more effective than dexmedetomidine.

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PALAVRAS-CHAVE
Bupivacaína;
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Fentanil;
Raquianestesia unilateral

Comparação de fentanil e dexmedetomidina como adjuvante à bupivacaína para raquianestesia unilateral em cirurgia de membros inferiores: estudo randômico

Resumo
Justificativa e objetivos: Uma das desvantagens da raquianestesia unilateral é a curta duração da analgesia pós-operatória, que pode ser abordada pela adição de adjuvantes aos anestésicos locais. O objetivo deste estudo foi comparar os efeitos da adição de dexmedetomidina, fentanil ou solução salina à bupivacaína sobre as propriedades da raquianestesia unilateral em pacientes submetidos à cirurgia de panturrilha.
Métodos: Neste ensaio clínico duplo-cego, 90 pacientes submetidos à cirurgia eletiva de panturrilha foram randomicamente divididos em três grupos. A quantidade de anestésico para a raquianestesia nos três grupos foi de 1 mL de bupivacaína a 0,5% (5 mg). Nos grupos BD, BF e BS, 5 μg de dexmedetomidina, 25 μg de fentanil e 0,5 mL de solução salina foram adicionados, respectivamente. Foram calculados a duração dos bloqueios motor e sensorial em ambos os membros e o escore de dor durante 24 horas após a cirurgia. As alterações hemodinâmicas também foram medidas durante a anestesia por até 90 minutos.
Resultados: A duração de ambos os bloqueios, motor e sensorial, foi significativamente maior no membro dependente nos grupos BF (96 e 169 min) e BD (92 e 166 min) que no grupo BS (84 e 157 min). Os escores da escala visual analógica foram significativamente menores nos grupos BF (1,4) e BD (1,3) que no grupo BS (1,6) nas 24 horas após a cirurgia.
Conclusões: A adição de fentanil e dexmedetomidina à bupivacaína em raquianestesia unilateral pode aumentar a duração dos bloqueios sensorial e motor no membro dependente e prolongar a duração da dor pós-operatória. Contudo, fentanil é mais eficaz que dexmedetomidina.

Introduction

Spinal anesthesia is one of the most common anesthetic procedures in lower limb surgery. Some of the advantages of this method include patient's wakefulness during surgery, rapid onset of effect, low failure rate, low-dose drug, desirable sensory and motor blocks and affordability.[1] Despite the advantages of spinal anesthesia, it has side effects such as hypotension, bradycardia, nausea, vomiting and shivering. To reduce the side effects of conventional spinal anesthesia, it is possible to lay the patient in the lateral position, rotate the bevel of needle to the bottom and inject the hyperbaric local anesthetics slowly so that the turbulent movement of the local anesthetics in the CSF can be avoided and the spinal anesthesia can be restricted to one side.[2] This method is especially appropriate for patients with low cardiovascular reserve, hypovolemia, elderly patients and traumatic patients. It reduces hemodynamic, respiratory and systemic side effects of conventional spinal anesthesia. In unilateral spinal anesthesia, the lowest possible dose of local anesthetics is used. It is therefore likely that the analgesic effects and the quality of the sensory and motor blocks are reduced. To overcome this defect, some adjuvants can be added to local anesthetics. One of the drugs traditionally used for this purpose is opioid and in particular fentanyl which has side effects such as itching and respiratory depression.[3] Dexmedetomidine is an Alpha2 agonist which has recently been increasingly popular. It is added to the local anesthetics as an adjuvant for regional blocks. According to the studies, intrathecal dexmedetomidine has improved the properties of the block.[4] It also plays an important role in alleviating the visceral pain by stimulating Alpha2-Adrenergic Receptors (α2-ARs) in the posterior spinal cord.[5] This study aimed to compare the effects of bupivacaine–saline, bupivacaine–dexmedetomidine and bupivacaine–fentanyl on the properties of unilateral spinal block in calf surgery patients.

Methods

After approval by Kurdistan University of Medical Sciences Ethics committee, registration of study in Iranian Registry of Clinical Trail (IRCT20161031030601N2), and given informed consent, this double blind, and parallel clinical trial was conducted in accordance with the Helsinki Declaration on 90 patients with American Society of Anesthesiologist physical status I or II, aged 18–70 which posted for elective calf surgery in Kawsar Hospital, Sanandaj, Iran from February to July 2018.

Patients with contraindication of the spinal block, history of dyspnea, diabetes, renal or hepatic disease, history of addiction, alcoholism and antiepileptic or analgesics drug intake were excluded from the study. In addition, patients who had pain during the procedure due to insufficiency of the anesthesia and needed systemic analgesics during surgery, were also excluded from the study. An anesthesiologist who was not involved in collecting data's, enrolled participants to study, and randomly allocated them into three

groups using a computerized random number table. The patient was visited and evaluated day before the surgery and received information about the procedure of anesthesia.

On the day of surgery, all patients were fast. After the patients were laid on the operating bed, standard cardiac monitoring (ECG), Noninvasive Blood Pressure (NIBP) and Pulse Oximetry (SpO2) were performed using a multiparameter monitoring system. In addition, Heart Rate (HR), peripheral blood oxygen saturation (SpO_2), and mean arterial pressure (MAP) were recorded. Having fixed the 18G venous cannula, all patients were injected with 5 mL.kg^{-1} Ringer fluid. None of the patients were given premedication.

The spinal anesthesia technique was similar in all patients as follows: The patients were put in the lateral position and the limb that was to be operated was put on the lower side. After Prep and Drep, a 25 G Quincke spinal needle was used to inject the drug to L3–L4 or L4–L5 interspace level at 0.2 mL.s^{-1} speed. While injecting the drug, the bevel of the needle was pointed down. All patients received oxygen at 5–6 L.min^{-1} via face mask during anesthesia. The local anesthetic dosage was similar in all patients and included 1 mL of bupivacaine 0.5% (5 mg). Accordingly, 25 μg fentanyl, 5 μg of dexmedetomidine and 0.5 mL of saline were added to the Bupivacaine–Fentanyl (BF), Bupivacaine–Dexmedetomidine (BD), and the Bupivacaine–Saline (BS) groups, respectively.

Similar to BS group, the volume of the drug injected into the BF and BD groups reached 1.5 mL by adding normal saline. The sterilized drug was prepared by an anesthetist nurse who had read the patient's grouping on a computerized sheet. According to the patient group, she prepared the spinal anesthetic drug without mentioning the name of the group and the name of the drug. The anesthesiologist that carried out the spinal block, did not know the content of the drug which is supposed to be injected.

Having injected the drug, the needle was removed and patients remained in the lateral position for 15 min and then were turned to the supine position. The injector then monitored the patient and evaluated the outcomes of the study. Both of patients, and outcome evaluator were blinded to patient groups.

The primary outcome of the study included the duration of the sensory and motor blocks in the dependent limb. The duration of the sensory block was measured based on the time interval from the start of the block to sensory block regression to the S5 dermatome using loss of pressure sense with pinprick test. The duration of the motor block was measured based on the block start time to the block regression to the grade one. The motor blockade was assessed using Bromage scale[6] as follows: (1) free movement of legs and feet; (2) just able to flex knees with free movement of feet; (3) unable to flex knees, but with free movement of feet; (4) unable to move legs or feet.

The post-operative analgesia and changes in blood pressure and heart rate were measured over time. The post-operative pain was also measured using Visual Analog Scale (VAS) 24 h after surgery at 6 h intervals. The mean arterial blood pressure and heart rate were measured at 0 (baseline), 5, 10, 15, 30, 60, and 90 min.

Patients were also monitored during surgery and recovery from hypotension, bradycardia, shivering, and nausea or vomiting. Hypotension was defined as MAP drop (more than 30% baseline) or SBP $\leq$ 90 mmHg and bradycardia as heart rate (less than 30% baseline) or HR $\leq$ 40 min. In the case of bradycardia and hypotension, Ephedrine (5 mg) and atropine (0.5 mg) were used as rescue drugs respectively. In the case of severe shivering, meperidine (25 mg) was taken, while in case of vomiting or severe nausea, 2 mg of intravenous ondansetron was taken. Patients who had a VAS $\geq$ 4 were injected with meperidine 0.5 mg.kg^{-1} (up to 50 mg). Furthermore, the total dosages of needed systemic analgesics to relieve the patient's pain in 24 h were recorded.

Statistics

The sample size was calculated based on the detection of 30% differences in duration of sensory block between dexmedetomidine–bupivacaine and plain bupivacaine after unilateral spinal anesthesia in previous investigation[7] given 95% confidence level and 99% test power, 30 patients per group were required. The software STATA 12 was used to analyze the data. Demographic data and duration of surgery was evaluated using One-Way ANOVA and Chi square test. Having estimating the concentration and dispersion indices for quantitative variables and the frequency distribution table for qualitative variables Kruskal–Wallis and Mann–Whitney test were used to examine the sensory and motor block. Hemodynamic changes during anesthesia were analyzed with repeated measures test. The significance level was $p < 0.05$ in all phases.

Results

Of the 114 patients that participated in the study, 94 were divided into 3 groups, and the collected data of 90 patients were analyzed (30 in each groups). Flowchart of participants in the 3 groups presented in Fig. 1. There were no significant differences between the 3 groups in terms of age, sex, weight and duration of surgery (Table 1). The duration of motor block in dependent limb was significantly higher in the BF Group (95 min) than the BS and BD Groups (84 and 92 min), respectively ($p = 0.001$). Likewise, the duration of the sensory block in dependent limb was significantly higher in the BF and BD Groups than BS Group. All patients showed some degree of sensory block in the symmetric area for non-surgery limb in all three groups, and duration of sensory block regression to S5 dermatome did not differ significantly between the three groups in independent limb. The motor block in non-surgery limb was not significantly different in the three groups ($p = 0.116$) (Table 2). VAS was significantly lower in the BF and BD Groups than the BS Group in 6, 12 and 24 h after surgery ($p = 0.016$) (Table 2). According to the Repeated Measure groups and in relation to baseline values at different times were not statistically significant. Incidence of spinal anesthesia side effects, in the BS, BD, and BF Groups for hypotension (3.3%, 6.6% and 6.6%), bradycardia (0% in all three groups), shivering (3.3%, 0% and 0%), and nausea or vomiting (6.6%, 6.6% and 10% respectively) were similar in the patients, and there was no significant difference between the 3 groups ($p > 0.05$).

The meperidine used as rescue drug for pain relief in 24 h was comparable in 3 groups (23.2 $\pm$ 7 mg, 24.9 $\pm$ 7 mg and 22.9 $\pm$ 9 mg in BS, BD and BF groups, respectively and

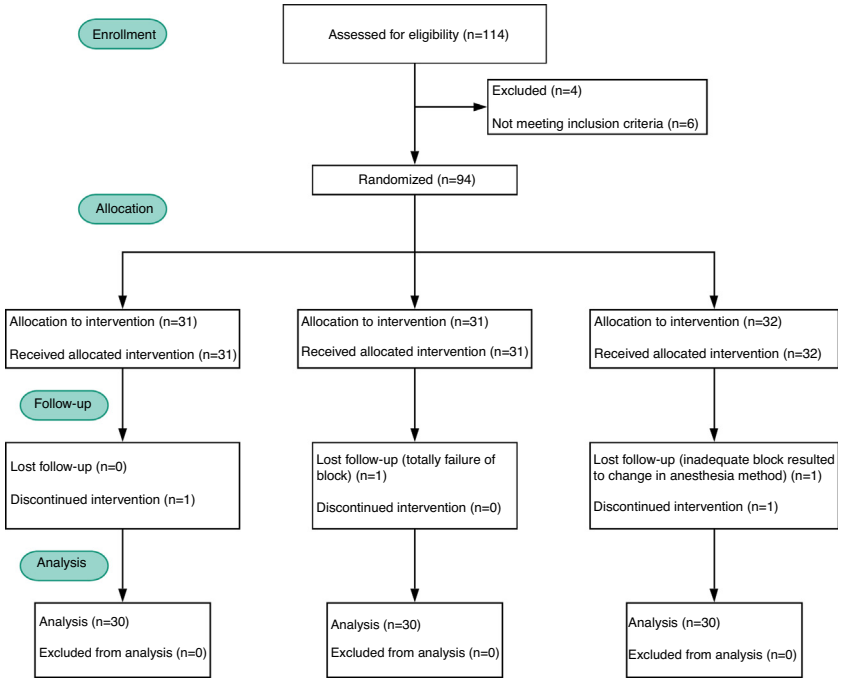

Figure 1 Flow diagram of participants in the three groups of study.

Table 1 Data related to patients and duration of surgery.

Variable	Bupivacaine–Saline (n = 30)	Bupivacaine–Fentanyl (n = 30)	Bupivacaine–Dexmedetomidine (n = 30)	p-value
Age (year) mean ± SD	40.63 ± 14.59	34.7 ± 15.6	39.6 ± 13.9	0.279[a]
Weight (kg) mean ± SD	76.6 ± 5.5	73.5 ± 11.13	74.6 ± 11.32	0.436[a]
Duration of surgery (min)	57.87 ± 8.8	56.2 ± 11.53	59.7 ± 11.7	0.134[a]
Sex (M/F)	22 (73.3%)/8 (26.7%)	23 (76.7%)/7 (23.3%)	25 (83.3%)/5 (16.7%)	0.638[b]

Values are expressed as mean ± SD or number of patient (%).
[a] One-Way ANOVA test were used to compare the variables among three groups.
[b] Chi square test were used to compare sex in three groups.

there was no significant difference between the 3 groups (p = 0.092).

Discussion

Unilateral spinal anesthesia is a simple and safe technique for unilateral surgery of the lower abdomen and lower limbs. In this method, the minimum dose of local anesthetics is used and adjuvants can be used to improve the block quality and prolong the duration of analgesia. Therefore selecting different compounds and appropriate doses of adjuvants added to local anesthetics is a vital process that affects the duration and termination of the sensory and motor blocks, as well as spinal complications.[8] So adjuvants should be selected with great care.

According to the results of the present study, the addition of both fentanyl and dexmedetomidine to bupivacaine in unilateral spinal anesthesia increased the duration of motor block in the dependent limb and this increase was significantly higher in the fentanyl group than in the dexmedetomidine group. Several studies on the addition of fentanyl and dexmedetomidine to bupivacaine in bilateral spinal anesthesia, the effects of these adjuvants on the duration of the motor and sensory blocks, and on postoperative analgesia have been conducted. Gupta et al.[9] used a combination of bupivacaine 12.5 mg plus 5 μg of dexmedetomidine or 12.5 mg of bupivacaine plus 25 μg of fentanyl in the spinal anesthesia for lower abdominal surgery in two groups consisting of 30 patients and concluded that the addition of dexmedetomidine increased the duration of the motor block as compared with the fentanyl. Also, the regression time of the sensory block to the S1 dermatome was longer in the dexmedetomidine group as compared with the fentanyl. It was concluded that dexmedetomidine significantly increased the duration of motor and sensory blocks and

Table 2 Characteristics of block in two limbs and Visual Analog Scale (VAS) in three study groups.

Variable	Bupivacaine–Saline ($n = 30$)	Bupivacaine–Fentanyl ($n = 30$)	Bupivacaine–Dexmedetomidine ($n = 30$)	Intergroup significance
Duration of any degree of Motor block in dependent limb (min)	84 ± 10	95 ± 5	92 ± 12	*p*-Value (BF–BD): 0.135 *p*-Value (BD–BS) = 0.001[a] *p*-Value (BF–BS) = 0.000[a]
Duration of any degree of Motor block in independent limb (min)	41 ± 7	43 ± 5	43 ± 11	*p*-Value (BS–BD): 0.116 *p*-Value (BD–BF) = 0.976 *p*-Value (BF–BS) = 0.123
Intensity of Motor block in independent limb (Bromage), *n* (%)				0.093
1	0 (0)	0 (0)	0 (0)	
2	29 (26.6)	26 (86.6)	26 (86.6)	
3	1 (3.3)	4 (13.3)	4 (13.3)	
4	0 (0)	0 (0)	0 (0)	
Duration of any degree of Sensory block in dependent limb (min)	157 ± 31	169 ± 14	166 ± 18	Kruskal–Wallis; *p*-value: 0.001 Mann–Whitney; *p*-Value (BS–BF): 0.003[a] *p*-Value (BS–BD): 0.012[a] *p*-Value (BF–BD): 0.42
Duration of any degree of Sensory block in independent limb (min)	78 ± 88	82 ± 12	84 ± 19	Kruskal–Wallis; *p*-value: 0.576 Mann–Whitney; *p*-Value (BS–BF): 0.643 *p*-Value (BS–BD): 0.287 *p*-Value (BF–BD): 0.921
Maximum level of sensory block in dependent limb, *n* (%)				0.71
T6	1 (3.3%)	1 (3.3%)	0 (0)	
T8	4 (13.3%)	3 (10%)	4 (13.3%)	
T10	22 (73.3%)	23 (76.6%)	22 (73.3%)	
T12	3 (10%)	3 (10%)	4 (13.3%)	
Maximum level of sensory block in independent limb, *n* (%)				0.43
T8	0 (0)	0 (0)	0 (0)	
T10	1 (3.3%)	0 (0%)	1 (3.3%)	
T12	12 (40%)	14 (46.6%)	11 (36.6%)	
L1	17 (56.6%)	16 (53.3%)	18 (60%)	
VAS				Kruskal–Wallis
6 h	3.8 ± 0.4	3.4 ± 0.8	3.2 ± 0.9	*p*-Value (BS–BF) = 0.045[a]
12 h	3.7 ± 1.2	3.3 ± 1.3	3.1 ± 1.1	*p*-Value (BS–BD) = 0.016[a]
24 h	1.6 ± 0.4	1.4 ± 0.6	1.3 ± 0.4	*p*-Value (BF–BD) = 0.318

Values are expressed as mean ± SD or number of patient (%).

[a] Kruskal–Wallis test and Mann–Whitney test were used to compare variables among 3 groups.

diminished the need for analgesic within 24 h as compared with the fentanyl. Saadalla and Khalifa[10] divided 60 patients into 3 groups in a study and spinal anesthesia was completed with 15 mg bupivacaine in each group. Accordingly, 10 mcg of dexmedetomidine, 25 μg of fentanyl and 0.5 mL of saline were added to each group, respectively. They concluded that the addition of 10 μg of dexmedetomidine prolonged the duration of the sensory and motor blocks as compared with 25 μg of fentanyl and further reduced the need for analgesic drugs within 24 h after surgery.

The results of these two studies are not consistent with our study. The reason for this inconsistency in the results is not known because in both studies, the dosage of fentanyl added was similar to the present study. In addition, the dosage of dexmedetomidine was similar with the present study in the first study but it was higher than the present study in the next study. Fentanyl binds to the opioid receptors in the brain and spinal cord and inhibits the release of the nociceptive transmitter of substance P.

In addition to increasing the duration of the regional block, combining fentanyl with local anesthetics increases the quality of the block.[11] The effects of intrathecal fentanyl can be attributed to its combination with opioid receptors in the dorsal horn of spinal cord.[12] While the mechanism by which α2-ARs increase the sensory and motor blocks of the local anesthetics is yet to be well understood, and at optimum, it is subjective. There may be a synergistic or secondary additive effect between the mechanisms of local anesthetics and α2-ARs but this behavior cannot be attributed to a change in the systemic absorption of local anesthetics because the plasma levels of bupivacaine did not change when it was added to the intrathecal clonidine.[13] Additionally, α2-ARs act by binding to the pre-synaptic C fibers and post-syntactic neurons of the posterior horn.

Accordingly, α2-AR agonists produce analgesia by suppressing the secretion of fiber C transmitters and using the hyperpolarization of post-syntactic neurons of the posterior horn.[14] It is probable that prolonging the motor block of the spinal anesthetics results from the binding of the α2-AR agonists to the motor neurons in the posterior horn,[13,14] while local anesthetics act by blocking the sodium channels.

According to the results of the present study, the duration of the sensory block was longer in BF and BD groups in compare with BS group. Nayagam et al.[15] evaluated the effect of adding both fentanyl and dexmedetomidine on the properties of the block. In their study conducted on 150 patients, fentanyl and dexmedetomidine were added to low dose of bupivacaine in lower abdominal surgery while the patients were placed in the lateral position and turned later to Trendelenburg position.

According to their results, the effects of fentanyl and dexmedetomidine on sensory block during spinal anesthesia showed no difference.[15] These results were not in agreement with the results of the present study. The results of current study showed that keeping patients in the lateral position for 15 min did not completely prevent the sensory and motor blocks in the upper side, although the depth of the block was minor and the duration of the block in the independent limb were significantly shorter than the lower limb.

Therefore, we were unsuccessful in achieving a complete unilateral anesthesia. Tekye and Alipour[16] were able to perform successful unilateral spinal anesthesia in 94% of patients by injecting a 1.5 mL of 0.5% bupivacaine and placing them in lateral position for 20 min. These results are not in agreement with the results of the present study. These differences may be attributed to the type of drugs used. Although, the base of intrathecal injected drug was 1 mL of 0.5% heavy bupivacaine in the present study, however, the volume of primary drug was increased to 1.5 mL by adding 0.5 mL saline. This could change the baricity of bupivacaine and close that from hyperbaric to an isobaric drug. Kuusniemi et al.[17] believe that hyperbaric bupivacaine is more effective than isobaric bupivacaine in achieving unilateral spinal anesthesia, although this argument was disregarded by the results of Van Tuijl et al.[18] They injected 5 mg of hyperbaric bupivacaine with 15 and 30 μg of clonidine and concluded that less than 50% of patients who received 15 mcg of clonidine and 30% of patients who received 30 mcg of clonidine were classified as unilateral spinal anesthesia and the rest were bilateral.[18]

The second influential factor is the patient's position. The patient's position affects the distribution of the drugs, as soon as the intrathecal drugs are injected. The longer the patient in the lateral position, the higher the probability of achieving success in unilateral spinal anesthesia. Since the distance between the neural roots in the lumbar is about 10–15 cm, even by injecting hyperbaric drugs and the patient being in the lateral position, the drug can distribute to upward for 30–60 min.

Another reason for difference between the results of the present study and the previous study is the method of examining the sensory and motor blocks. We used the Pinprick test in the S5 dermatome for evaluating the sensory block regression, and the modified Bromage scale (1–4) for motor block evaluation. While in other studies, the Bromage scale (0–5) was used to evaluate the motor block. Perhaps none of these two used scales in the present study were sufficient to carry out surgery in the dependent limb. So, anesthesia has been practically unilateral, despite some degree of sensory and motor blocks in the upper limb. Furthermore, the results of the present study showed that during the 24 h after surgery, the pain was lower in the BD and BF groups than the BS group. In a study by Safari et al.,[7] the addition of dexmedetomidine to bupivacaine caused less postoperative pain than saline.

In a study on 84 patients who underwent cesarean section, Li et al.[19] reported that the addition of dexmedetomidine to bupivacaine resulted in an efficient analgesia after surgery as compared with fentanyl or clonidine. The results of these two studies are in agreement with the findings of the present study. It has been found that α2 intrathecal receptors have anti-nociceptive function on both somatic and visceral pain.[8] Dexmedetomidine affects these receptors by its analgesic effects. The analgesic effects of intrathecal dexmedetomidine are facilitated by hyperpolarization of non-adrenergic neurons which suppress neuronal stimulation in the locus coeruleus. This process results in the activation of the α2-AR switch, causing the suppression of epinephrine secretion and inhibition of its activity in the descending spinal noradrenergic route. The suppression of the activity in the noradrenergic pathway, which decreases the nociceptive transmitter, may terminate the pain.[20] The results of present study showed that unilateral spinal anesthesia with

bupivacaine and the addition of add-ons of dexmedetomidine and fentanyl did not significantly change the parameters of MAP and HR.

The results of most studies[9,11,19] in this area are in agreement with the findings of the present study, while Safari et al.[7] showed that heart rate and blood pressure were higher in the dexmedetomidine group than in the fentanyl and saline groups. This difference can probably be attributed to the type of patients selected in the latter study, which was performed on addicted patients. The hemodynamic stability of the unilateral spinal anesthesia is because of the low dosage of bupivacaine and the limited block of sympathetic system. In this study, the lack of control group for bilateral spinal anesthesia was an evident limitation which could have been helpful in comparing the duration of the sensory and motor blocks, the analgesics, and the hemodynamic changes of the unilateral and bilateral spinal anesthesia. In the present study the adequacy of the sensory block for independent limb surgery was not thoroughly investigated. Although all patients in this study showed some degree of sensory and motor blocks in the upper limb, it seems that this degree of block was not adequate for surgery. Furthermore, the sensory block level was not studied. This could have helped in determining whether a dose of 5 mg of bupivacaine in a unilateral spinal is enough for surgery in which level, and distribute to what level? Our patients underwent elective calf surgery that required low levels of sensory block.

Limitation

Thought, meperidine is not a popular drug for post-operative analgesia; however, due to shortage of other opioid analgesics in our center, the only two drugs that were available for post-operative pain relief were morphine sulfate and meperidine. This study was designed in such a way that we used meperidine for post-operative analgesia. The rational for choosing meperidine was based on its vagolytic properties and lack of histamine release in compare to morphine sulfate.

Conclusion

Based on study results, it can be concluded that the addition of dexmedetomidine and fentanyl to bupivacaine in unilateral spinal anesthesia can increase the duration of motor and sensory blocks in the dependent limb and prolong the duration of postoperative analgesia.

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Conflicts of interest

The authors declare no conflicts of interest.

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