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Fentanyl and Dexmedetomidine with Bupivacaine in Spinal Block for Post Operative Analgesia in lower limb Orthopaedic Surgery : A comparative study

Nigar Ali [1], Rajendra Gosavi [2], Deepak Phalgune [3]*

1 Senior resident, Dept. of Anaesthesia , Poona Hospital & Research Centre , Pune. India
2 Professor and HoD, Dept. of Anaesthesia, Poona Hospital & Research Centre, Pune.India
3 Research Consultant, Poona Hospital & Research Centre, Pune. India

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***Corresponding author:**

Email : dphalgune@gmail.com
Tel.: +91-09850434220
Fax No. : 020 24338477

ABSTRACT

Spinal anaesthesia with or without any adjuvant is the most commonly performed anaesthesia for almost all lower limb orthopaedic surgeries. Present study is aimed to compare analgesic efficacy between intrathecal fentanyl and intrathecal dexmedetomidine as an adjuvant to bupivacaine for unilateral lower limb orthopaedic surgeries. Ninety patients aged 18 to 60 years scheduled for lower limb open orthopaedic surgery were randomly allocated in two groups to receive the drugs intrathecally either fentanyl 25 µg or dexmedetomidine 5 µg. Pain was measured by VAS scores postoperatively at arrival in PACU and at intervals, for first 12 hours. At any time, if the score was ≥ 4, rescue analgesia was given in the form of Inj. Diclofenac 75 mg intravenously. Chi-square test was used for qualitative variables where as unpaired 't' test was used for quantitative variables. Mann-Whitney U test was used to compare the significance between VAS score . There was no significant differences with respect to mean age, sex distribution, mean weight and ASA distribution between two groups. Mean duration of sensory and motor block was significantly higher in Group dexmedetomidine as compared to Group fentanyl. Mean quantity of post operative rescue analgesia requirement was significantly less in Group dexmedetomidine as compared to Group fentanyl. Group dexmedetomidine has lower median VAS score. Intrathecal dexmedetomidine as an adjuvant to bupivacaine is useful in enhancing postoperative analgesia and also reduces requirement of total rescue analgesia.

INTRODUCTION

Adequate pain management is essential to facilitate rehabilitation and accelerate functional recovery, thus enabling patients to return to their normal activity more quickly. Intrathecal use of hyperbaric 0.5% bupivacaine is appropriate for surgeries of short duration and may lead to early analgesic intervention in the postoperative period.[1]

A number of adjuvants, such as clonidine and midazolam, and others have been studied to prolong the effect of spinal anaesthesia.[2,3] The addition of fentanyl to hyperbaric bupivacaine improves the quality of intraoperative and early postoperative subarachnoid block. Fentanyl produces many of its clinical effects rapidly after intrathecal administration. [4] Neuraxial administration of lipophilic opioids such as fentanyl and sufentanil tends to provide a rapid onset of analgesia. Their rapid clearance from cerebrospinal fluid may limit cephalic spread and the development of certain side effects such as delayed respiratory depression.[5] For intrathecal alpha agonist, most of literature is for clonidine and there are very few studies about intrathecal use of dexmedetomidine.[6]

Dexmedetomidine is a potent α2 agonist and is approximately eight-times more selective towards the α2 adrenergic receptor than clonidine. Dexmedetomidine is now emerging as an adjuvant to regional anaesthesia and analgesia, and now many evolving studies can build the evidence for its safe use in central neuraxial blocks.[7]

The additions of opioids to local anaesthetic solution have disadvantages, such as pruritus and respiratory depression.

Dexmedetomidine, a new highly selective α2-agonist, is under evaluation as a neuraxial adjuvant as it provides stable haemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects.[8-11] Based on earlier human studies, it is hypothesized that intrathecal 5 µg dexmedetomidine would produce more postoperative analgesic effect with hyperbaric bupivacaine in spinal anaesthesia with minimal side effects.[8-10] Till date, there has been only few studies comparing the addition of dexmedetomidine to hyperbaric bupivacaine, although various studies have compared dexmedetomidine and fentanyl with isobaric bupivacaine.

Hence, a study was undertaken to compare postoperative analgesic efficacy of fentanyl and dexmedetomidine, when added as an adjuvant to intrathecal hyperbaric bupivacaine in lower limb orthopaedic surgery.

MATERIALS AND METHODS

All the patients aged 18 to 60 years scheduled for lower limb open orthopaedic surgery in Poona Hospital & Research Centre, Pune between 1st September 2014 and 30th September 2015 under spinal anaesthesia and ready to participate in this study were included. .Permission was obtained from Institutional Ethics Committee (IEC) and Scientific Advisory Committee of the institution.

INCLUSION CRITERIA:

Patients posted for unilateral lower limb open orthopaedic surgery, ASA physical status class I and II, Age between 18-60 years of either sex.

EXCLUSION CRITERIA :

Patient posted for bilateral lower limb surgeries or orthopaedic surgeries like Arthroscopic surgeries , ASA physical status class III and IV, Emergency surgeries, Hypersensitivity to any of the drugs in the study, Contraindications to spinal anaesthesia like patient refusal, bleeding diathesis, Pregnancy.

Based on previously published study [12] , setting an alpha error at 0.05, and power at 80%, sample size of 45 in each group was calculated by formula.[13] In all 90 ASA (American Society of Anaesthesiologist) grade I and II patients scheduled for lower limb open orthopaedic surgery under spinal anaesthesia were included in this prospective, observational randomized study. They were randomly divided into two equal groups of 45 each, using computer generated randomization code.

The randomization code was provided to an anaesthetist who prepared the study medication. All other doctors, nurses and the patients were blind as to group assignment.

Group BF received 3 ml 0.5% hyperbaric bupivacaine and 25 µg fentanyl.

Group BD received 3 ml 0.5% hyperbaric bupivacaine and 5 µg dexmedetomidine.

PREANESTHETIC CHECK UP

The patients were evaluated for any systemic disease and laboratory investigations were recorded one day prior to surgery. The procedure of subarachnoid block was explained to the patient and written informed consent was obtained. The patients were educated about the visual analogue scale.

ANESTHETIC TECHNIQUE

Patients were asked for fasting for a period of 6 hours. Patients were shifted to OT table after accessing IV line. All patients were preloaded with 15 ml/kg Ringer's lactate, 15 minutes before the surgery and no premedication was given. Baseline vitals were recorded. The drug combinations were prepared by an anesthetist to whom randomization code was given, and various observations were made by a second anaesthesiologist who was involved after the procedure had been performed. Under strict aseptic precautions, using 25 gauge Quincke spinal needle, lumbar puncture was performed at L3-4 space. Once free flow of cerebrospinal fluid appeared, study solution was injected at a rate of 1 ml/10 s with direction of bevel of the needle cephalad. Intraoperatively no sedation or analgesia was given to any of the patient. Intra operatively Heart Rate(HR) , Mean Arterial Pressure(MAP) and SpO2 were monitored every 15 minutes till the end of surgery .On achieving T10 sensory blockade level, surgery was started. The time from intrathecal injection to sensory regression to S1 dermatome were noted. The duration of sensory blockade was taken as time from onset to time of return of pinprick sensation to S1 dermatome. Motor blockade was assessed by Bromage scale .The time interval between injection of the drug into the subarachnoid space, to the patient's inability to lift the straight extended leg was taken as onset time (Bromage 3). The duration of motor block was taken from time of injection to complete regression of motor block (ability to lift the extended leg) (Bromage 0).

- This was based on the following modified Bromage score.[14]
- The patient is able to move the hip, knee, and ankle, score = 0.
- The patient is unable to move the hip but is able to move the knee and ankle, score = 1.
- The patient is unable to move the hip and the knee but able to move the ankle, score =2.
- The patient is unable to move the hip, knee, or ankle, score = 3.

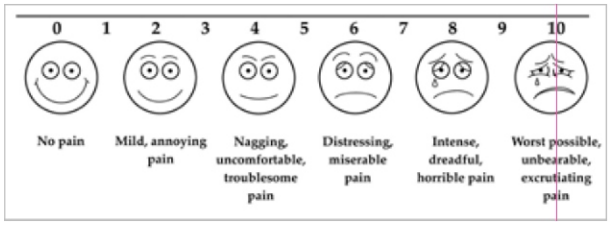
INTRAOPERATIVE PERIOD

HR < 50/ min was treated with 0.6 mg of IV Atropine. MAP < 60 mmHg was treated with bolus dose of 6 mg IV Ephedrine .Supplementary oxygen by mask was given to the patients who received above medication. Time of giving spinal block was noted .Time of onset of T10 sensory block was noted by pin prick method. Peak level of sensory block was noted using pin prick method. Time of onset of motor block was noted. Incision time was noted. Duration of motor block in minutes was recorded from the time of onset of the block to the time when the patient was able to lift the legs in bed against gravity, and was tested every 15 minutes. This was based on the modified Bromage score Duration of sensory block (time in minutes, it takes for sensory level to decrease to dermatomal level S1) was measured from the highest obtained sensory level every 15 minutes. All durations were calculated considering the time of spinal injection as time zero.

POSTOPERATIVE ASSESSMENT

Pain was assessed using “Visual Analogue Scale” (VAS) between 0 and 10 (0=no pain, 10=worst pain) for 12 hours postoperatively.

Patients were shifted to the postoperative ward and observed



VAS was graded as:
0 to 3 : no pain or mild pain
4 to 6 : moderate pain
7 to 10 : severe pain

till the administration of rescue analgesia or when VAS >4. Patient's pain was assessed using VAS at following times, on arrival in PACU when patient is awake and oriented (0 hour); thereafter, at 1, 2, 3, 4, 5, 6, 8, 10, 12 hours. Duration of analgesia (defined as the time from the spinal injection of drug to the first request for rescue analgesics) or VAS >4 was recorded. Rescue analgesics consisted of intravenous injection of diclofenac sodium 75 mg with a maximum daily dose of 150 mg. Rescue doses of diclofenac were recorded. Patients were discharged from post anaesthesia care unit after sensory regression to S1 dermatome and Bromage score 0.

Statistical analysis was done by using SPSS (Statistical package for social sciences) Version 20:0. Chi-square test was used for qualitative variables where as unpaired 't' test was used for quantitative variables. Mann-Whitney U test was used to compare the significance between VAS score in group BF and group BD. P-value < 0.05 was considered as significant.

RESULTS

Between 1st September 2014 and 30th September 2015 , 45 patients in each group were recruited for the study . There were no dropouts or failed spinal cases.

As shown in Table 1 the two groups were demographically comparable. There was no statistically significant differences with respect to mean age, sex distribution, mean weight and ASA distribution between the two groups.As depicted in Figure 1 , by using 2 independent sample t-test there was no statistically significant difference between mean heart rate at baseline to end of the surgery in group BF and group BD.As shown in Figure 2 by using 2 independent sample t-test there was no statistically significant difference between mean MAP at baseline to end of the surgery in group BF and group BD.As shown in Figure 3 by using 2 independent sample t-test there was no statistically significant difference between mean SpO2 at baseline to end of the surgery in group BF and group BD.

As depicted in table 2, mean duration of sensory and motor block was significantly higher in Group BD as compared to Group BF. Mean quantity of post operative rescue analgesia requirement was significantly less in Group BD as compared to Group BF. However, there was no statistically significant difference in mean duration of surgery in two groups.

As shown in Table 3, by using Mann-Whitney U test p-value < 0.05, therefore there was statistically significant difference between median VAS score at post operative 2 hours to 8 hours and 12th hour in group BF and group BD. Group BD has lower median VAS score.

DISCUSSION

Orthopaedic lower limb surgeries are very painful . Various techniques like local infiltration block, spinal, epidural or general anaesthesia can be used. Epidural and spinal anaesthesia is most commonly used technique because of rapid onset, less failure, easy administration as compared to general anaesthesia. Various drugs like neostigmine,[15]morphine,[16] midazolam, [17] and magnesium sulphate[18] have been tried intrathecally to improve quality of spinal anaesthesia in the form of faster onset and prolonged duration of sensory and motor block with postoperative analgesia.

Table 1. : Demographic profile

Demographic characteristic	Group BF (N = 45)	Group BD (N = 45)	p value
Mean age in years (SD)	41.67 (± 11.29)	42.07(± 9.89)	0.858
Gender , no (%)			
Male	35(77.78)	33(73.33)	
Female	10(22.22)	12(26.67)	0.807
Mean weight in kg (SD)	58.60(± 6.46)	59.40(± 6.72)	0.567
ASA Grade (%)			
I	32(71.11)	31(68.89)	
II	13(28.89)	14(31.11)	0.999

Table 2. : Post operative comparison between group BF and group BD

Post operative block characteristic	Group BF (N = 45)	Group BD (N = 45)	p value
Duration of surgery in min (SD)	125.44(± 15.49)	127.09(± 15.79)	0.619
Mean duration of sensory block in min(SD)	178.68(± 14.19)	329(± 14.06)	<0.001
Mean duration of motor block in min(SD))	147.51(± 10.38)	254.71(± 7.48)	<0.001
Mean quantity of rescue analgesia required in 12 hours post operative (SD)	73.88(± 5.21)	70.55(± 9.86)	0.045

Table 3. : Comparison of VAS between group BF and group BD postoperatively

	Group BF			Group BD			p value
	Min	Max	Median	Min	Max	Median	
1 h	0	0	0	0	0	0	0.999
2 h	0	2	0	0	0	0	0.001*
3 h	0	3	2	0	0	0	< 0.001*
4 h	1	4	2	0	3	0	< 0.001*
5 h	0	5	3	0	3	0	< 0.001*
6 h	0	5	4	0	4	2	0.002*
8 h	0	1	0	0	5	3	< 0.001*
10 h	1	2	2	0	5	4	0.172
12 h	1	2	1	0	4	0	< 0.001*

Statistically Significant

Intrathecal α2 adrenoceptor agonists analgesic action is a result of depression of the release of C-fiber transmitters and hyperpolarization of postsynaptic dorsal horn neurons.[19] Local anesthetic agents act by blocking sodium channels. The prolongation of the effect may result from synergism between local anaesthetic and α2 adrenoceptor agonist, whereas the prolongation of the motor block of spinal anaesthetics may result from the binding of α2 adrenoceptor agonists to motor neurons in the dorsal horn. [20] Intrathecal α2 receptor agonists have been found to have antinociceptive actions for both somatic and visceral pain.[8] Fentanyl is a lipophilic μ receptor agonist opioid. Intrathecally, fentanyl exerts its effect by combining with opioid receptors in the dorsal horn of the spinal cord and may have a supraspinal spread and action.[21] Most of the clinical experience is gained by the use of intrathecal α2 adrenoceptor agonists has been described with clonidine. [22-25] There has

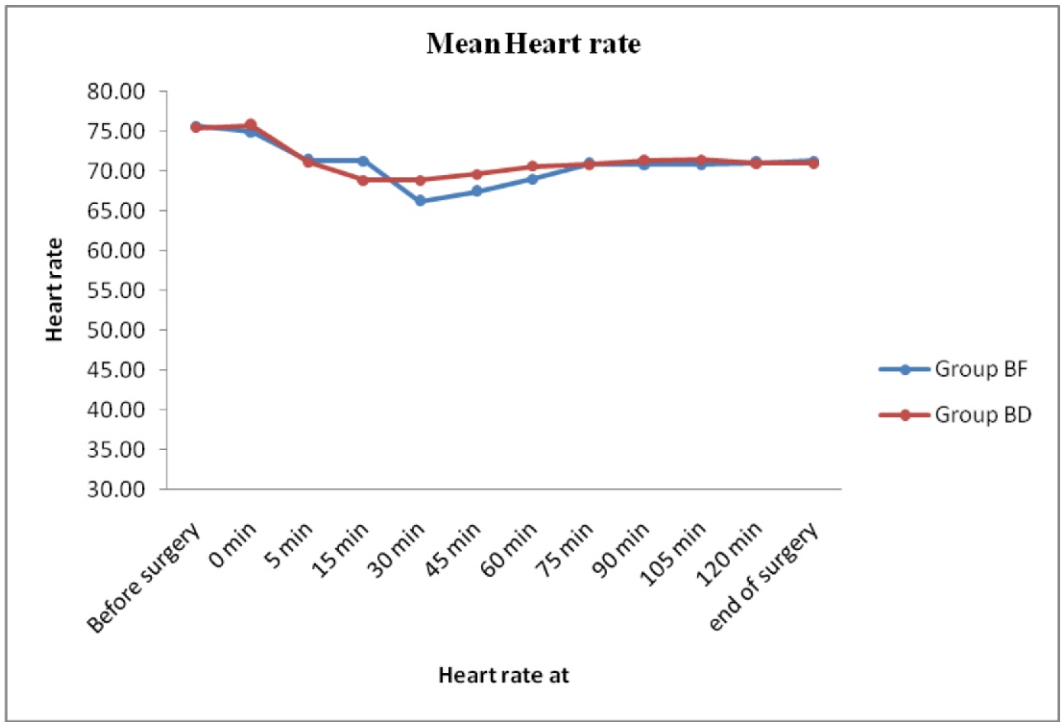


Figure 1 : Line diagram showing changing heart rate between group BF and BD throughout the surger.

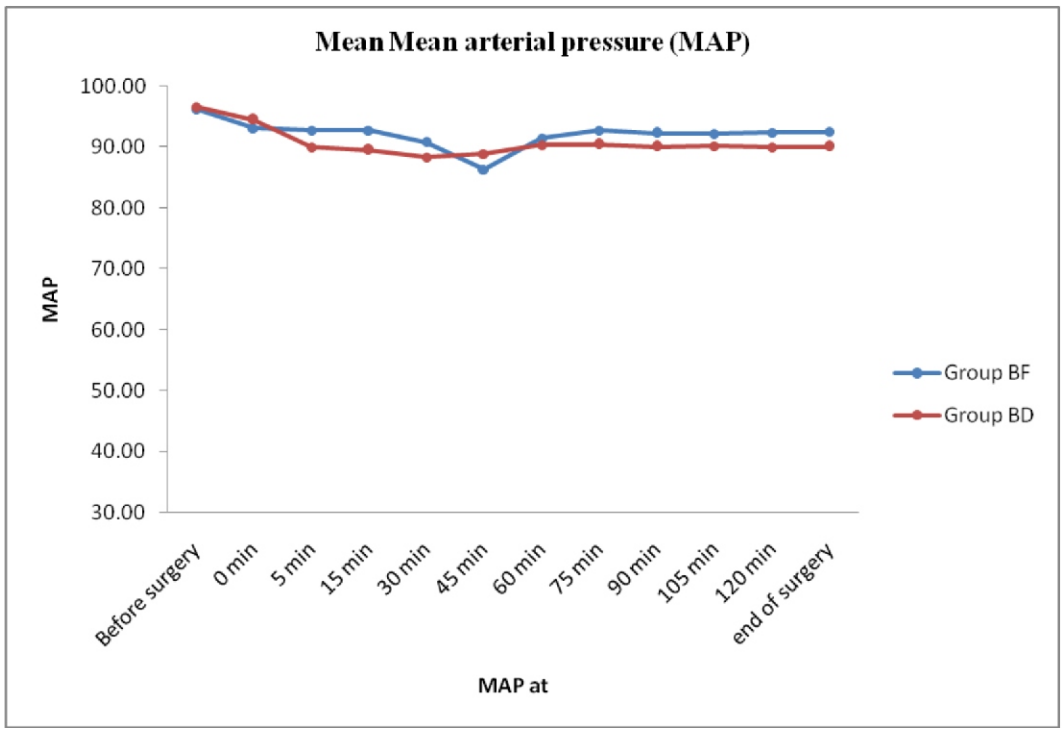


Figure 2 : Line diagram showing the change in mean arterial pressure between group BF and group BD throughout the surgery

been a need for clinical studies related to intrathecal dexmedetomidine to prove its efficacy, safety, and the suitable dose for supplementation to spinal local anaesthetics. In our study, the intrathecal dose of dexmedetomidine selected was based on previous human studies wherein no neurotoxic effects have been observed. [8-10]

The present study was conducted to compare the addition of either dexmedetomidine or fentanyl to intrathecal bupivacaine as regards the hemodynamic effects, postoperative analgesia (i.e. time from IT injection till demand for rescue analgesic or VRS > 4) , and adverse effects of either drug. Kanazi et al[10] *reported* that 3 g dexmedetomidine or 30 g clonidine added to 13 mg spinal

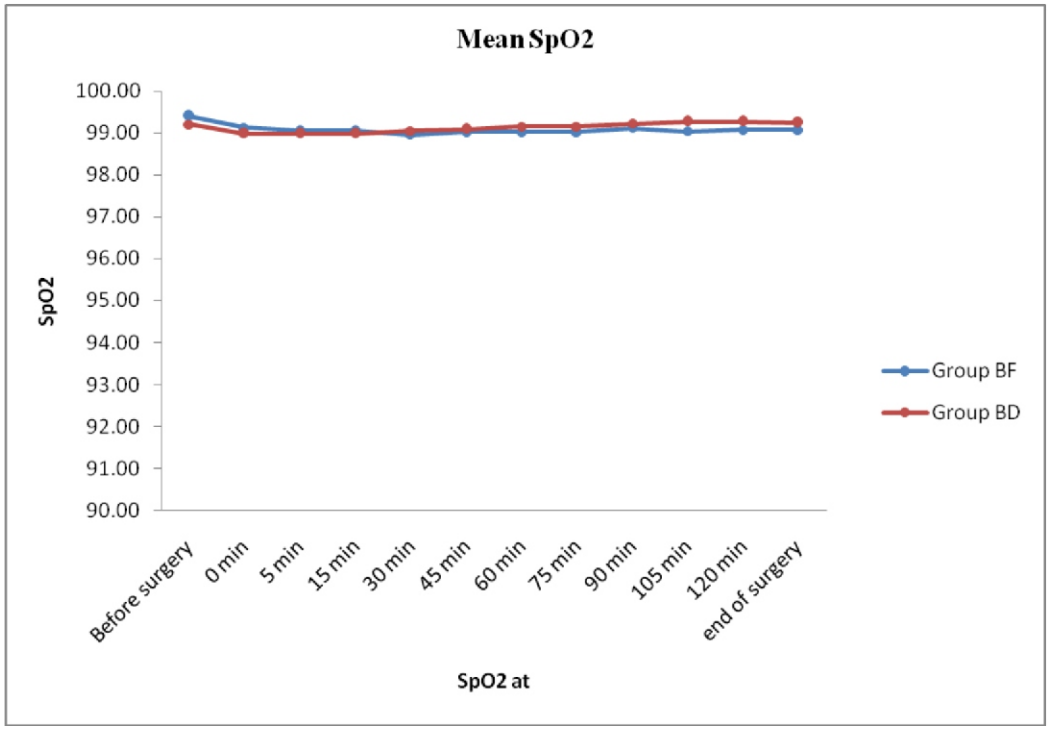


Figure 3 : Line diagram showing changes in SpO2 between group BF and group BD throughout the surgery

bupivacaine produced same duration of sensory and motor block with minimal side effects in urological surgical patients. On the basis of this, we assumed that 3-5 g of dexmedetomidine is equipotent to 30-45 g clonidine when used for supplementation of spinal bupivacaine.

In the present study , there was no significant difference in the mean values of heart rate and MAP between the two groups. Our results were comparable to the study conducted by Kanazi et al[10] who studied 3 µg of dexmedetomidine when added to intrathecal bupivacaine produced no significant difference between mean values of mean arterial pressure (MAP) and heart rate (HR), compared to 30µg of clonidine intrathecally. Present study is also comparable to the study conducted by Mahendru et al[26] who concluded that the mean values of mean arterial pressure (MAP) and heart rate (HR) were comparable between the four groups throughout the intraoperative and postoperative period, when 5 µg of dexmedetomidine used intrathecally, compared to intrathecal 25 µg of fentanyl and 30 µg of clonidine, as an adjuvant to bupivacaine in spinal block.However , studies conducted by El-Attar et al [27] and Abdelhamid and El-Lakany [28] reported significant decrease in the heart rate and mean arterial pressure in the dexmedetomidine group as compared to 5 µg dexmedetomidine with hyperbaric bupivacaine only.

The most significant side effects reported about the use of intrathecal α2 adrenoceptor agonists are bradycardia and hypotension. In the present study, these side effects were not significant probably because we used small dose of intrathecal dexmedetomidine and fentanyl with low dose local anesthetics. These doses of adjuvants used in our study did not affect the near maximal sympatholysis caused by local anaesthetics.As regards arterial oxygen saturation, there was no significant difference between the two groups through out the surgery, which may be due to the following reasons: firstly, the dose of local anaesthetic used while designing the study, which was kept to minimal possible levels with noninvolvement of the intercostal muscles and/or diaphragm during motor blockade. Secondly, supplemental oxygen administration through a face-mask throughout the procedure. This was in agreement with the research by Shukla et al [18]who studied 10 µg of dexmedetomidine and 50 mg of magnesium sulfate to 3 ml of bupivacaine and found no significant difference in mean arterial oxygen saturation.

With regards to duration of sensory and motor blockade group BD had significantly longer mean sensory and motor block durations as compared with BF group. This was in agreement with the studies conducted by Mahendru et al[26] and Al-Ghanem et al [8] who reported significantly prolonged mean durations of sensory and motor blocks. Kanazi et al, [10] and Al-Mustafa et al [9] also reported the effect of dexmedetomidine on spinal bupivacaine for urological procedures and observed dose-dependent prolongation of motor and sensory blockade when increasing the dose of dexmedetomidine from 5 to 10 µg.The time to first analgesic request was significantly longer in group BD in comparison with groups BF. There was significantly reduced 12 hour requirements of total analgesics in group BD compared with groups BF. The results were similar to that reported by Mahendru et al[26] , Gupta et al [29] and Al-Mustafa et al .[9]

As regards the VAS, similar to our current study, Gupta et al [29] and Mahendru et al [26] reported lower VAS values in the dexmedetomidine group compared with the bupivacaine group.

CONCLUSION

Using dexmedetomidine as an adjuvant to intrathecal bupivacaine compared with fentanyl was associated with prolonged durations of both sensory and motor blockade. Postoperatively Dexmedetomidine was associated with prolonged analgesia. Total analgesic consumption was less with Dexmedetomidine.

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