www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 71.58
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i12.91

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Comparative Study of Bupivacaine alone versus Bupivacaine and Dexmedetomidine for Spinal Anesthesia in Hysterectomies

Authors
Lt Col (Dr) Krishna Prasad G V[1], Dr Sunil A[2], Lt Col (Dr) Abhinav Tewari[3], Lt Col (Dr) Ritu Grewal[4]
[1]Classified Specialist (Anaesthesiology), Military Hospital Jaipur, Rajasthan India
9024130145, Email: *drkaypee99@gmail.com*
[2]Anaesthesiologist, Railway Hospital Hubli, Karnataka
9789009727, Email: *sunnil0042@gmail.com*
[3,4]Classified Specialist (Anaesthesiology), Military Hospital Jaipur Rajasthan
Corresponding Author
Lt Col (Dr) Ritu Grewal
Classified Specialist (Anaesthesiology), Military Hospital Jaipur Rajasthan

Abstract
Introduction: *The efficacy of local anesthetics in spinal anesthesia can be enhanced by using adjuvants like fentanyl, morphine, tramadol and α2-agonists like clonidine, dexmeditomidine so as to improve the postoperative patient comfort and satisfaction.*
Aim: *The present study was designed to study the analgesic efficacy and side effects of adding dexmedetomidine to bupivacaine in spinal anesthesia for gynaecological surgeries i.e hysterectomies.*
Patients and Methods: *In a prospective, randomized, double-blind study, after taking their informed consent, 60 patients were randomly divided into two groups of 30 each. Sub arachnoid block was given with 12.5 mg of 0.5% hyperbaric bupivacaine in group I (n = 30) and with 12.5 mg of 0.5% hyperbaric bupivacaine plus 5 µg of dexmedetomidine in group II (n = 30). The two groups were compared with respect to hemodynamic parameters, onset of sensory block to T10 and regression to S1, time to achieve Bromage 3 and regression to Bromage 0, duration of analgesia, number of doses and type of rescue analgesia required, and complications occurring in 24 h.*
Results: *Significant difference was observed in relation to onset of sensory block [12.7 ± 1.015 min in group I and 6.84 ± 0.792 min in group II (P < 0.001)], total duration of sensory block [177.74 ± 28.573 min in group I and 353.36 ± 12.138 min in group II (P < 0.001)], total duration of motor block [146.94 ± 9.173 min in group I and 318.36 ± 9.374 min in group II (P < 0.001)], duration of analgesia [283.96 ± 11.165 min in group II and 126.34 ± 7.684 min in group I (P < 0.001)], and total number of doses of rescue analgesia required in 24 h [1.44 ± 0.501 in group II and 2.56 ± 0.675 in group I (P < 0.001)].*
Conclusion: *Addition of dexmedetomidine to bupivacaine in sub arachnoid block leads to early onset of sensory and motor block with prolonged duration, and patients remained pain free for a longer period with decreased demand for rescue analgesia in the postoperative period as compared with hyperbaric bupivacaine alone without addition of dexmeditomidine.*
Keywords: *bupivacaine, dexmedetomidine, intrathecal, subarachnoid block.*

Introduction

Spinal anesthesia or subarachnoid block is a anesthetic technique that is widely used across the world for lower abdomen and lower limb surgeries[1]. Bupivacaine is long acting amide local anesthetic that has a prolonged duration of action and lower incidence of neurological complications like transient radicular symptoms, [2] but high doses of intrathecal bupivacaine may lead to myocardial depression, dysrythmias, and heart block[3]. Thus, to prolong the duration of action and to minimize the side effects of local anesthetics in subarachnoid block, various adjuvants are used[4]. The α2 adrenergic agonists clonidine and dexmedetomidine were more commonly used intrathecally [5,6]. The affinity of dexmedetomidine to α2-adrenergic receptors has been reported to be 10 times more when compared to that of clonidine, which makes it a more effective sedative and analgesic agent with a more stable pharmacodynamic profile[7]. In the past, most of the studies were done with dexmedetomidine being used as an adjuvant to hyperbaric bupivacaine for subarachnoid block in lower limb and urological surgeries. As gynaecological surgeries tend to be the painful among all types of surgeries and 70% of patients suffer from severe postoperative pain[8], the present study was done to evaluate the effect of adding dexmedetomidine to intrathecal bupivacaine on block characteristics and postoperative analgesia in patients undergoing hysterectomies. The primary aim was to study the onset and duration of sensory and motor block, duration of postoperative analgesia, and intraoperative hemodynamic parameters, and the secondary aim was to observe any complications or side effects of intrathecal dexmedetomidine and note the requirement of rescue analgesia in the immediate postoperative period.

Patients and Methods

In a prospective randomized double-blind study, 60 patients of ASA grade I and II in the age group of 40–60 years of females undergoing elective hysterectomies under spinal anesthesia at Military Hospital, Jaipur were recruited. Approval was taken from the institutional ethics committee of hospital. Patients with neurological disorders, coagulation disorders, allergy to the study drug, or unwillingness for spinal block, deformity or previous surgery of the spine were excluded from the study. Prior informed written consent of the patient was taken after explaining the procedure in detail. They were randomly allocated into two groups of 30 each — group I (n = 30) and group II (n = 30) — by means of a computer-generated table of random numbers by a person blinded to the procedures. Before surgery every patient was subjected to a detailed preanesthetic checkup. A visual analog scale (VAS) ranging from 0 to 10 was used to determine the level of analgesia in the postoperative period, with 0 indicating no pain and 10 indicating severe pain. A night before the surgery at 2200hrs all patients were given alprazolam (0.25 mg) orally in tablet form. The patients were not premedicated on the day of surgery. Preoperatively, pulse rate, noninvasive systolic and diastolic blood pressure, oxygen saturation, and respiratory rate of the patients were recorded. An intravenous line was started and patients were preloaded with Ringer lactate at 10 ml/kg body weight over 20 min. Under strict aseptic conditions, lumbar puncture was performed in sitting position with a 27-G Quinke spinal needle at the level of L3–L4 intervertebral space and the drug was given intrathecally. In group I, patients received 0.5% hyperbaric bupivacaine at 12.5 mg. In group II, patients received 0.5% hyperbaric bupivacaine at 12.5 mg along with 5 μg of dexmedetomidine. Immediately after administering the drug, the patients were made to lie supine and maintained the same position for 5 min before positioning for both abdominal and vaginal hysterectomies. The study drug was prepared by an anesthesiologist not involved in the study and block was performed by another anesthesiologist who also monitored the block characteristics. Continuous monitoring of hemodynamic parameters was done

in the form readings at every 3 min for the first 30 min and thereafter every 5 min until the end of surgery. Episodes of intraoperative hypotension (decrease in systolic blood pressure by 20% from baseline or a systolic blood pressure lower than 90 mmHg) was recorded. Hypotension was treated with bolus administration of 250 ml lactated Ringer's solution over 10 min, or with intermittent doses of intravenous ephedrine hydrochloride at 6 mg if BP was not recovered with Ringer Lactate. Bradycardia (heart rate <50 beats/min or less than 10% of base line value) was treated with doses of atropine at 0.6 mg administered intravenously. The total duration of surgery was noted. Sensory block was assessed by loss of sensation to pinprick in the midline using a 22 G blunt hypodermic needle at 3-min intervals. Onset of sensory block to T10 dermatome, peak level of sensory block, and duration of sensory block (regression to S1 dermatome) were noted. The degree of motor block was assessed by means of the Bromage scale[9] every 3 min. The Bromage scale ranged from 0 to 3: 0, able to raise the whole lower limb at the hip; 1, able to flex the knee but unable to raise the leg at the hip; 2, able to planter flex the ankle but unable to flex the knee; and 3, no movement of the lower limb. Onset time to reach Bromage 3 and time taken for regression to Bromage 0 were noted. All durations were calculated by taking the time of subarachnoid block as time zero. Sedation was assessed every 5 min by means of the following scale[10]: 0, no sedation; 1, mild sedation, 2: moderate sedation; and 3, deep sedation. Postoperative follow-up was carried out for 24 h. Vital parameters, sedation scores, and postoperative analgesia (VAS) were monitored until 24 h. Analgesia was monitored using VAS scale both intraoperatively and postoperatively. During surgery if VAS was greater than 3, then incremental doses of ketofol (ketamine & propofol) slow intravenously was given as supplementary analgesia. In the postoperative period if VAS was greater than 3, then diclofenac sodium at 1.5 mg/kg body weight intramuscularly or if needed paracetamol 1gm slow intravenously was given as rescue analgesia. The time interval from spinal anaesthesia to the patient's demand for the first dose of rescue analgesia was taken as total duration of analgesia. The total dose of rescue analgesia was noted. The primary endpoint of our study was the time when the patient demanded the first dose of rescue analgesia. The quality of surgical analgesia was assessed and graded as follows: excellent, no supplementary drugs required; good, analgesic required; fair, more than one analgesic required; and poor, general anesthesia required. Any incidence of pruritus, nausea and vomiting, shivering, respiratory depression, urinary retention, transient neurological symptoms, and postdural puncture headache were recorded. Patients were monitored for sensory and motor block, postoperative analgesia, sedation, adverse effects, and complications for 24 h.

Statistical method: The data obtained were tabulated and analyzed using the statistical package for social science (SPSS 16.0 evaluation version, SPSS Inc., IBM, Chicago) and expressed as mean and SD and percentages. Patient characteristics (nonparametric data) were analyzed using the 'χ2-test' and Fisher's exact test, whereas intergroup comparison of parametric data was carried out using the Student 't' test'. The 'P' value was determined to evaluate the level of significance. P values less than 0.05 were considered significant at 5% significance level; P values less than 0.01 were considered significant at 1% significance level; and P values less than 0.001 were considered highly significant. Post-hoc power analysis was carried out using a Power and sample size calculator. The cutoff value for power analyses was taken as at least 80% ($\beta = 0.8$). The effective size/power of the study was calculated for the duration of analgesia ($\beta = 1$) and duration of motor block ($\beta = 1$) and determined as greater than 80%.

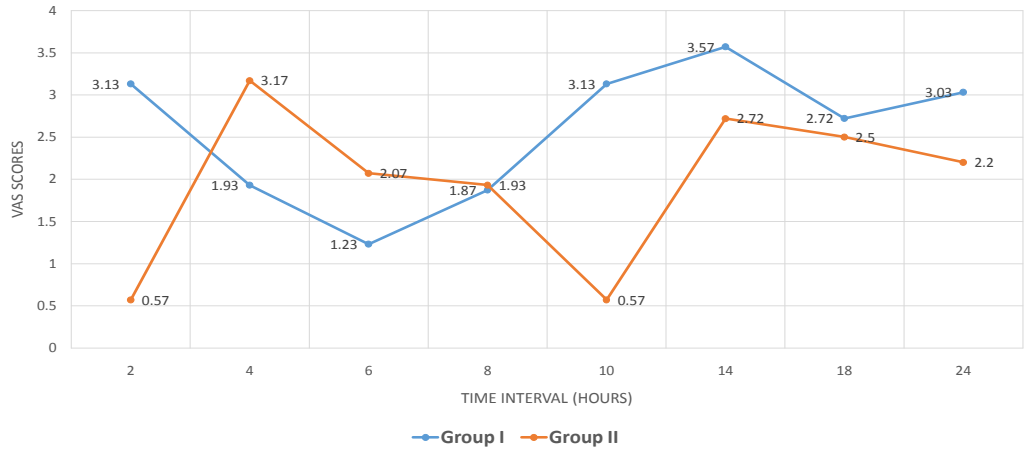
Results

Both groups were comparable with respect to age, weight, ASA grade, duration and type of surgery,

and baseline hemodynamic parameters (Table 1). The surgeries were hysterectomies both vaginal and abdominal. The number of patients under each type of surgery was comparable in both groups (Table 2). The sensory and motor block characteristics are shown in Table 3. The mean time required for onset of sensory block to T10 dermatome in group II (6.84 ± 0.792 min) was more rapid than that in group I (12.7 ± 1.015 min) and the difference was statistically highly significant (P < 0.001). The maximum upper level of sensory block achieved in group I was T 6– T8 dermatome with a median value of T6 and that in group II was T5–T8 dermatome with a median of T6 dermatome, which was comparable in the two groups. However, the maximum level of sensory block was achieved earlier in group II (7.94 ± 0.712 min) as compared with group I (18.26 ± 1.015 min) and the difference was highly significant (P < 0.001). Even the mean time taken for regression of sensory block to S1 dermatome was prolonged in group II (353.36 ± 12.138 min) as compared with group I (177.74 ± 28.573 min) and the difference was highly significant (P < 0.001). Complete motor block was achieved earlier in group II as compared with group I. The mean time taken for onset of complete motor block (Bromage 3) was less in group II (9.856 ± 0.7115 min) as compared with group I (19.100 ± 2.9433 min) (P < 0.001). The total duration of motor block in group II (318.36 ± 9.374 min) was prolonged as compared with group I (146.94 ± 9.173 min) (P < 0.001). Patients remained pain free for a longer period in group II and the requirement for the first dose of rescue analgesia was also delayed as compared with group I. VAS scores were less than 3 in both groups during the intraoperative period and none of the patients required supplementary analgesia. In group I, VAS started increasing and was more than 3 in the second and third hour postoperatively and the first dose of rescue analgesia (injectable diclofenac) was given. Thereafter, VAS decreased to less than 3 and patients were pain free. VAS again increased to more than 3 in the 10th hour and intravenous paracetamol was given. The second dose of injectable diclofenac was given in the 14th hour. In group II, VAS increased to more than 3 in the fourth and fifth hour and the first dose of injectable diclofenac was given. Thereafter, VAS decreased to less than 3 and the patient demanded the second dose of rescue analgesia in the 16th and 17th hour. None of the patients in this group required injectable paracetamol. At the 24th hour VAS was higher in group I (3.03 ± 1.21) as compared with group II (2.20 ± 0.48) (Fig. 1). The total duration of analgesia was prolonged in group II (283.96 ± 11.165 min) compared with group I (126.34 ± 7.684 min) (P < 0.001). The total number of rescue analgesia doses required at 24 h postoperatively was also significantly less in group II (1.44 ± 0.501) compared with group I (2.56 ± 0.675), as shown in Table 2.

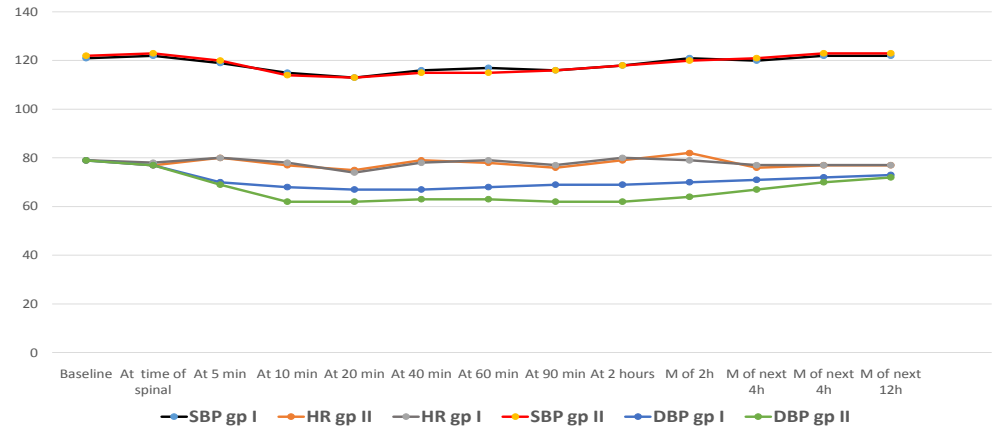
Hemodynamic parameters remained stable and were comparable in both groups at all measured intervals (Fig. 2). Three patients in group I and four patients in group II had hypotension, which was treated by giving fluids intravenously. None of the patients required injectable ephedrine hydrochloride. Bradycardia occurred only in one patient in each group, which was treated with atropine (0.6 mg intravenously). The sedation score was comparable in both groups at all intervals for 24 h. Most of the patients in group I (22patients) and group II (20 patients) had a sedation score of 0; seven patients in group I and nine patients in group II had a sedation score of 1; and only one patient in group II had a sedation score of 2. No patient had respiratory depression, pruritus, postdural puncture headache, or transient neurological deficits in the postoperative period. Incidence of nausea and vomiting was also comparable in both groups. Only one patient in each group had nausea, which was relieved without any intervention. The quality of surgical analgesia was excellent in all patients in both groups and none of the patients required any supplementary analgesia during the intraoperative period.

Figure 1



Mean VAS score of Group B and D during the study period. Values are expressed as mean +/- SD. VAS-Visual Analog Scale.

Figure 2



Line diagram showing mean systolic and diastolic BP(in mmHg) and mean heart rate(in beats/min) at various time intervals

Table 1: Demographic parameters in the two groups

Parameters	Group I (N=30)	Group II (N=30)	P value
Age(Years)	40.3 +/- 9.95	40.4 +/- 10.47	0.946 (NS)
Weight(Kg)	65.78 +/- 9.27	62.06 +/- 5.59	0.017(NS)
Duration of surgery(Min)	86.18 +/- 31.7	79.80 +/- 28.9	0.296 (NS)
Pulse rate(/min)	79.00 +/- 8.57	78.74 +/- 10.0	0.89 (NS)
Systolic BP(mmHg)	124.54 +/- 8.86	124.88 +/- 8.51	0.84 (NS)
Diastolic BP(mmHg)	77.40 +/- 12.59	78.04 +/- 8.28	0.359 (NS)
Respiratory rate(/min)	13.10 +/- 0.78	12.94 +/- 0.76	0.306 (NS)

Values are expressed as mean +/- SD or number of pts.All parameters were comparable in both gps;Gp I,Bupivacaine;Gp II,Dexmedetomidine;NS,Not significant

Table 2: Number of patients under each type of surgery in Gp I and Gp II

Type of surgery	Gp I (N=30)	Gp II (N=30)	P Value
Abdominal Hysterectomy	08(26.6)	09(30)	0.790(NS)
Vaginal Hysterectomy	22(73.33)	21(70)	0.81(NS)

Data is presented as no of patients and percentage. There was no significant difference between the two groups regarding types of surgeries performed; NS,Not significant.

Table 3 - Characteristics of motor and sensory block in group I and group II

Time(In mins)	Group I (N=30)	Group II (N=30)	P value(significance level)
Onset of sensory block to T10 dermatome	12.7 +/- 1.015 min	6.84 +/- 0.792 min	P < 0.001 (HS)
Maximum level of sensory block	T11 dermatome	T11 dermatome	P = 0.016 (HS)
Time to maximum sensory block	18.26 +/- 1.015 min	7.94 +/- 0.712 min	P < 0.001 (HS)
Time to regression to S1 dermatome	177.74 +/- 28.57 min	353.36 +/- 12.13 min	P < 0.001 (HS)
Time to onset of motor block(Brom age 3)	19.10 +/- 2.943 min	9.88 +/- 0.7115 min	P < 0.001 (HS)
Total duration of motor block	146.94 +/- 9.713 min	318.36 +/- 9.374 min	P < 0.001 (HS)
Duration of analgesia	126.34 +/- 7.684 min	283.96 +/- 11.165 min	P < 0.001 (HS)
Number of doses of rescue analgesia	2.56 +/- 0.675	1.44 +/- 0.501	P < 0.001 (HS)

Values are expressed as mean SD.Group I-Bupivacaine and Group II- Dexmedetomidine;HS-Highly significant; NS-Not significant

Discussion

The α2-adrenergic agonist dexmedetomidine is being increasingly used in anesthesia and critical care as it decreases the sympathetic tone and attenuates the neuroendocrine and hemodynamic responses to anesthesia and surgery. It also reduces opioid requirement both intraoperatively and postoperatively and results in prolonged postoperative analgesia[11]. When dexmedeto-midine is used as an adjuvant to bupivacaine in subarachnoid block, the prolongation of sensory and motor block occurs in a dose-dependent manner; that is, as the dose of dexmedetomidine is increased, the duration of sensory and motor block and postoperative analgesia is also prolonged. In previous studies, it was observed that 10 μg of dexmedetomidine produces early onset and prolonged duration of sensory and motor block and prolonged postoperative analgesia as compared with 5 μg of dexmedetomidine[12]. The postoperative analgesia is even more prolonged with 15 μg of dexmedetomidine, which may be beneficial in patients undergoing lengthy and complex surgeries, but this dose leads to higher sedation scores, which may be undesirable[13]. In the present study, we selected 5 μg dexmedetomidine as an intrathecal adjuvant to bupivacaine, with the aim of achieving prolonged postoperative analgesia with minimal side effects. The primary outcome of the present study was faster onset and prolonged duration of sensory and motor block and prolonged postoperative analgesia with addition of 5 μg of dexmedetomidine to 12.5 mg of 0.5% hyperbaric bupivacaine in spinal block. The secondary outcome was less requirement of rescue analgesia in the postoperative period, with no significant side effects and complications associated with addition of dexmedetomidine to bupivacaine. Evidence suggests that dexmedetomidine when combined with spinal bupivacaine prolongs the sensory block by depressing the release of C-fibre

transmitters and by hyperpolarization of postsynaptic dorsal horn neurons. Motor block prolongation by dexmedetomidine may result from binding these agents to motor neurons in the dorsal horn of the spinal cord[7]. In the present study, both groups were comparable with respect to demographic profile, duration and type of surgery, and baseline hemodynamic parameters. In group II, onset of sensory block to T10 dermatome was more rapid, maximum level of sensory block at T6 dermatome was achieved earlier, and regression to S1 dermatome was delayed as compared with group I. When 12.5 mg of 0.5% hyperbaric bupivacaine was used in subarachnoid block, the time to reach T10 dermatome was 9.5 ± 3 min [12]. With addition of 5μg dexmedetomidine as an adjuvant to 12.5 mg of 0.5% bupivacaine the time to reach T10 dermatome was decreased to 7.7 ± 3.3 min [13]. Maximum sensory level achieved was T6 dermatome in other studies also, using either bupivacaine alone or dexmedetomidine as an additive to bupivacaine [12–13]. It was observed that time to reach maximum sensory level that is T6 dermatome was 21.9±3.6 min when 10 mg of 0.5% bupivacaine was used in spinal anesthesia, which coincides with the present study[14]. However, with the addition of 5 μg dexmedetomidine to 10 mg of 0.5% hyperbaric bupivacaine, the time taken to reach maximum sensory level was 19.9 ± 2.99 min[14], which was slightly more as compared with the present study. This difference may be due to the fact that the dose of bupivacaine and dexmedetomidine used in the above study is less as compared with the present study. Another study was conducted in which 12 mg of 0.5% hyperbaric bupivacaine was given intrathecally and it was found that time required to reach maximum sensory level was 20.2 ± 8.4 min[15], which is in accordance with the present study. In the present study it was observed that maximum sensory level achieved was similar in both the groups that is T6 dermatome but this was achieved earlier in group II as compared with group I. It has an added advantage because, if the sensory block is achieved earlier at T6 dermatome, surgery can also be started earlier in group II as compared with group I. Previously it was also observed that time taken for regression of sensory block to S1 dermatome was delayed with the addition of dexmedetomidine to bupivacaine[12,16–18], which is in accordance with the present study. Complete motor blockade was achieved earlier and the duration of motor block was more prolonged in group II as compared with group I. Previous studies also concluded that, with addition of dexmedetomidine to bupivacaine intrathecally, onset of motor block is achieved earlier and duration is more prolonged [12,13,19,20]. Duration of analgesia was prolonged in group II as compared with group I. Addition of dexmedetomidine to intrathecal bupivacaine produced prolonged postoperative analgesia, and requirement of rescue analgesia in the postoperative period was also decreased [13,16–19]. In the present study, no sedative was given during premedication, and thus most of the patients had sedation score in the range of 0 and 1 at all measured intervals in both groups. It has also been observed earlier that addition of low-dose dexmedetomidine to intrathecal bupivacaine does not lead to higher sedation scores [12,13]. Patients remained hemodynamically stable in both groups at all measured intervals for 24 h. Dexmedetomidine as an adjuvant to bupivacaine does not produce any significant hemodynamic changes and vitals remained stable both intraoperatively and postoperatively[16–18]. Incidence of side effects and complication was comparable between the two groups, which is in accordance with previous studies[13,19].. The effect of intravenous and intrathecal dexmedetomidine on block characteristics and postoperative analgesia was observed. It was concluded that addition of dexmedetomidine leads to prolonged duration of spinal anesthesia and improved postoperative analgesia without increasing the incidence of hypotension and any other adverse effects[21]. One of the limitations of the present study is that the population enrolled comprised

healthy patients of ASA grade I and II and therefore the effect of dexmedetomidine as an adjuvant in patients with cardiovascular comorbidities is yet to be investigated. Although no major side effects or complications were observed in the present study, further studies are required to rule out any short term or long-term adverse effects of intrathecal dexmedetomidine. We have used 5 µg of dexmedetomidine as an adjuvant to spinal anesthesia in the present study. Therefore, further clinical studies are required to prove its efficacy and safety with varying dosages for supplementation of spinal anesthesia. Effect of adding dexmedetomidine to other local anesthetics like ropivacaine or levobupivacaine in other neuraxial block needs further research. Dexmedetomidine appears to have promising applications as an intrathecal adjuvant. However, more randomized controlled trials are needed to be conducted before this can be put into clinical practice safely.

Conclusion

Dexmedetomidine produces early onset and prolonged duration of sensory and motor block as well as prolonged postoperative analgesia resulting in lesser requirement of rescue analgesics in the postoperative period without any serious side effects when used as an adjuvant to intrathecal bupivacaine.

Conflicts interest: There are no conflicts of interest.

References

1. Koller C. On the use of cocaine for producing anaesthesia on the eye . Lancet 1 884; 2:990.
2. Casati A , Fanelli G, B eccaria P, Aldegheri G, Berti M, Senatore R, Torri G. Block distribution and cardiovascular effects of unilateral spinal anaesthesia by 0.5% hyperbaric bupivacaine. A clinical comparison with bilateral spinal block. Minerva Anestesiol 1998; 64:307–312.
3. Albright GA Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. Anesthesiolo gy 1979; 51:285–287.
4. Buvanendran A, Kroin JS Useful adjuvants for postoperative pain management. Best Pract Res Clin Anaesthe siol 2007; 21:31–49.
5. Bouaziz H, Hewitt C, Eisenach JC. Subarachnoid neostigmine potentiation of alpha-2-adrenergic agonist analgesia, dexmedetomidine vs clonidine. Reg Anesth 1995; 20:121–127.
6. Glynn C, Dawson D, Sanders R. A double-blind comparison between epidural morphine and epidural clonidine in patients with chronic noncancer pain. Pa in 1988; 34:123–128 .
7. Kalso EA, Poyhia R, Rosenberg PH. Spinal antinociception by dexmedet-omidine, a highly selective alpha 2-adrenergic agonist. Pharmacol Toxic ol 1991; 68:140–143.
8. Sommer M, de Rijke JM, Van Kleef M, Kessels AG, Peters ML, Geurts JW, et al. The prevalence of postoperative pain in a sample of 1490 surgical patients. Eur J Anesth esiol. 2008; 25:267–274.
9. Bromage PR. Epidural Analgesia. Philadelphia: WB Saunders; 1978:144. Available at: http://www.soap.org/media/newsletters/spring2003 / research_column.htm
10. American Society of Anesthesiologists Continuum of depth of sedation: definition of general anesthesia and levels of sedation/analgesia. Available at: http://en.wikipedia.org/wiki/Sedation. [Last accessed on 2010 Nov 29].
11. Kalso E. Effect of intrathecal morphine, injected with bupivacaine, on pain after orthopedic surgery. Br J A naes th 1983; 55:415 –422.
12. Al-Mustafa MM, Abu-H alaweh SA, A loweidi AS, Murshidi MM, Ammari BA,

Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures. Saudi Med J 2009; 30:365–370.

13. Hala EA, Shafie MA, Youssef H. Dose-related prolongation of hyperbaric bupivacaine spinal anaesthesia by dexmedetomidine. Ain Shams J Anae sthesiol. 2011; 4:83–95.
14. Ibrahim FA. A comparative study of adding intrathecal dexmedetomidine versus sufentanil to heavy bupivacaine for postoperative analgesia in patients undergoing inguinal hernia repair. Benha Med J 2009; 26 :207–217.
15. Kanazi GE, Aoua d MT, Jabbour- Khoury SI, Al Ja zzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anaesthesiol Scan d. 2 006; 50: 222–227.
16. Mahendr u V, Tewar i A, Katya l S, Grewal A, Singh MR, Katyal R. A comparison of intrathecal dexmedeto-midine, clonidine, and fentanyl as adjuvants to hyperbaric bupivacaine for lower limb surgery: a double blind controlled study. J Anaesthesiol Clin Pharmac ol.2013; 29:496–502.
17. Solanki SL, Bharti N, Batra YK, Jain A, Kumar P, Nikhar SA. The analgesic effect of intrathecal dexmedetomidine or clonidine, with bupivacaine, in trauma patients undergoing lower limb surgery: a randomised, doubleblind study. Anaesth Intensive Care 2013; 41:51–56.
18. Kim JE, Kim NY, Lee HS, Kil HK. Effects of intrathecal dexmedetomidine on low dose bupivacaine spinal anaesthesia in elderly patients undergoing transuretheral prostatectomy. Biol Phar m Bull 2013; 36:959–965.
19. Kaur M, Katyal S, Kathuria S, Singh P. A comparative evaluation of intrathecal bupivacaine alone, sufentanil or butorp-hanol in combination with bupivacaine for endoscopic urological surgery. Saudi J Anae sth 2011; 5:202–207.
20. Dahlgren G, Hulstrand C, Jakobsson J, Norman M, Eriksson EW, Martin H. Intrathecal sufentanil, fentanyl or placebo added to bupivacaine for caesarean section. Anaesth A nalg 1997; 85:1288–1293.
21. Niu XY, Ding XB, Guo T, Chen MH, Fu SK, Li Q. Effects of intravenous and intrathecal dexmedetomidine in spinal anesthesia: a meta-analysis. CNS Neurosci Ther 2013; 19:897–904.