



## Clinical Evaluation of Intrathecal Dexmedetomidine as an Adjuvant to Bupivacaine in Patients of Abdominal Hysterectomy Under Spinal Anaesthesia

Authors

**Dr. Rajesh V Nagmothe<sup>1</sup>, Dr. Sanjay S Bule<sup>2</sup>, Dr. Sandhya A Bakshi<sup>3</sup>,  
Dr. A V Sangawar<sup>4</sup>, Dr. Naresh G Tirpude<sup>5</sup>**

<sup>1</sup>Assistant Professor, Department of anaesthesia, Government Medical College, Nagpur, Maharashtra.

<sup>2</sup>Associate Professor, Government Dental College, Nagpur, Maharashtra.

<sup>3</sup>Associate Professor, Department of anaesthesia, Government Medical College, Nagpur, Maharashtra.

<sup>4</sup>Professor, Department of anaesthesia, Government Medical College, Nagpur, Maharashtra.

<sup>5</sup>Professor & Head, Department of anaesthesia, Government Medical College, Nagpur, Maharashtra.

Corresponding Author

**Dr. Rajesh V Nagmothe**

44, Panchdeep nagar, Wardha Road, Near Redison Blu Hotel, Nagpur, Maharashtra.

Email: - [rajeshnagmothe@gmail.com](mailto:rajeshnagmothe@gmail.com), Phone No 9323602314

### Abstract

*This was a prospective randomized double blind study was conducted to evaluate Dexmedetomidine as an adjuvant with Bupivacaine (Bupivacaine 0.5% - Heavy for spinal anaesthesia) intrathecally in patient undergoing abdominal hysterectomy surgery.*

### Aim and Objectives:

- To evaluate the efficacy of Inj. Dexmedetomidine as an adjuvant to Inj. Bupivacaine (Heavy 0.5%) for Spinal anaesthesia.*
- To know the onset, duration & quality of sensory & motor block of spinal anaesthesia.*
- To know the hemodynamic stability & side effects of the drug under study.*

**Methods:** *A total of 60 female patients' age between 35-70 years classified as ASA grade I and II were randomly divided into two equal groups scheduled for abdominal hysterectomy under spinal anaesthesia. The dose of spinal anaesthesia drug in Group I was 3.5 ml Bupivacaine with 0.05 ml (5µg) Dexmedetomidine and in Group II was 3.5 ml Bupivacaine with 0.05 ml Normal Saline. The onset of sensory and motor block, duration of sensory and motor block, haemodynamic stability, quality of surgical anaesthesia, intraoperative complications, postoperative analgesia and side effects were recorded.*

**Results:** *In Group I, early onset of sensory and motor block was noted as compared to Group II. The duration of sensory and motor block was significantly longer in Group I than Group II. The hemodynamic stability was observed in Group I. The quality of anaesthesia was excellent in group I. The requirement of intraoperative sedation was significantly less in Group I when compared with Group II. The postoperative analgesia duration was significantly longer in Group I than Group II with minimal postoperative side effects.*

**Conclusions:** *Inj. Dexmedetomidine 5 µg seems to be an excellent alternative adjuvant with spinal Bupivacaine (Heavy 0.5%) to increase duration of postoperative analgesia of spinal anaesthesia in surgical procedure like abdominal hysterectomy.*

**Keywords:** *Dexmedetomidine (As adjuvant), Bupivacaine (Heavy), Abdominal hysterectomy, Sensory & motor blockade, Spinal anaesthesia.*

## Introduction

Abdominal (Lower abdominal) and lower limb surgeries may be performed under local, regional (spinal or epidural) or general anesthesia. The neuraxial blockade (spinal, Epidural or CSE) is the preferred mode of anesthesia <sup>[1]</sup>. Surgical skills/ methods and the anaesthetic techniques have evolved and improved drastically since last two decades. Many techniques and drug regimens, with partial or greater success, have been tried from time to time to calm and to eliminate the anxiety component of patients during regional anaesthesia <sup>[2-4]</sup>. Spinal block is still the first choice because of its rapid onset, superior blockade, negligible failure rates and cost-effectiveness <sup>[1]</sup>. The spinal anaesthesia technique is the widely used regional anaesthetic technique. However post-operative analgesia is a major concern associated with relatively short duration of action of spinal anaesthetics. Hence early rescue analgesic intervention is needed in post-operative period <sup>[5]</sup>. The advantages of subarachnoid block are limited by its short duration of action and side effects such as hypotension and bradycardia resulting due to sympathetic blockade <sup>[6, 7]</sup>.

In recent years, use of intrathecal adjuvants has gained popularity with the aim of prolonging the duration of block, better success rate, patient satisfaction, decreased resource utilization compared with general anesthesia and faster recovery <sup>[8]</sup>. Dexmedetomidine, a highly selective  $\alpha_2$  adrenergic agonist has evolved as a panacea for various applications and procedures in the perioperative and critical care settings <sup>[9]</sup>. It was

first used intrathecally in humans for transurethral resection of prostate. It provides stable hemodynamic condition, good quality of intra-operative analgesia and prolonged post-operative analgesia with minimal side effects <sup>[10-12]</sup>. It is also emerging as a valuable adjunct to regional anesthesia and analgesia, where gradually evolving studies can build the evidence for its safe use in central neuraxial blocks <sup>[13]</sup>. Based on earlier human studies, it is hypothesized that 'Intrathecal Dexmedetomidine' would produce more postoperative analgesic effect with hyperbaric bupivacaine in spinal anaesthesia with minimal side effects <sup>[7, 10-12]</sup>.

Therefore, present study was undertaken to evaluate and compare the characteristics of subarachnoid blockade, hemodynamic stability, quality of surgical anesthesia, intraoperative complications, postoperative analgesia and side effects of intrathecal Dexmedetomidine as an adjuvant to Bupivacaine (0.5% hyperbaric) versus Bupivacaine (0.5% hyperbaric) in patients of abdominal hysterectomy.

## Materials and Methods

This is a prospective, randomized double blind study that included a total of 60 female patients. The study was conducted in the department of Anaesthesiology at tertiary care centre (Government Medical College & Hospital) following approval of study by institutional ethical committee. A written informed consent was obtained from all patients posted for abdominal hysterectomy planned under subarachnoid block/ spinal; anesthesia.

**Inclusion Criteria-** ASA grades I & II with the age, weight and height between 35-70 years, 40 to 70 kgs and 145 to 170 cms respectively.

**Exclusion criteria-** Patients with a known history of drug allergy, heart block/ dysrhythmia, therapy with adrenergic receptor antagonist, calcium channel blocker, and/ or ACE inhibitor, obesity (weight > 120 kgs), uncontrolled HT/DM/IHD, contraindications to spinal anaesthesia like skin infection at site of lumbar puncture, CNS diseases like brain tumor, syphilis, meningitis, spinal cord and peripheral nerve diseases like poliomyelitis, multiple sclerosis, post traumatic vertebral injuries, bleeding and clotting disorders.

Sixty patients were divided into two equal groups of 30 patients in each group using the sealed envelope technique.

**Group I-** To receive 3.5 ml Inj. Bupivacaine (0.5% hyperbaric/ heavy) and 0.05ml=5µg Dexmedetomidine (Strength- Inj. Dexmedetomidine-100 mcg/ml, 0.05 ml of Inj. Dexmedetomidine is taken using insulin syringe & added to 3.5 ml Bupivacaine).

**Group II-** To receive 3.5 ml Bupivacaine (0.5% hyperbaric/ heavy) & 0.05 ml normal saline using insulin syringe. The medication was prepared by third party (anesthesiologist) so that both patients and investigator were blinded. A detail history, thorough general and systemic examination and all relevant investigations were done of all patients undergoing abdominal hysterectomy. The Patients were kept nil by mouth for 6 hours prior to the spinal anesthesia procedure.

All patients were received orally Tab. Diazepam 10 mg and Tab. Ranitidine 150 mg 12 hours prior

the surgery (at night hours prior the surgery). In the operation theatre, standard multiparamonitor (with ECG, NIBP and SpO<sub>2</sub> parameters) was attached to all patients. The baseline parameters e.g. ECG, pulse rate, blood pressure and SpO<sub>2</sub> were recorded. After preloading the patients with Lactated Ringer's solution 10 mL/ kg, patient, lumbar puncture was performed in lateral position at L3-4 level with Quincke type point 25 G spinal needle. Group I 30 patients received 3.5 ml Inj. Bupivacaine (0.5% hyperbaric/ heavy) and 0.05ml=5µg Dexmedetomidine (Strength- Inj. Dexmedetomidine-100 mcg/ml, 0.05 ml of Inj. Dexmedetomidine is taken using insulin syringe & added to 3.5 ml Bupivacaine) & Group II patients received 3.5 ml volume of (0.5% hyperbaric) Bupivacaine with 0.05 ml normal saline. After spinal injection of drug, patient was made to lie supine for period of 20 minutes. In cases where there was decrease in oxygen saturation < 90%, oxygen supplementation was done (2-3 L/min) via a oxygen mask.

Hypotension was defined as a decrease of systolic blood pressure by more than 30% from baseline or a fall below 90 mm/ Hg, and was treated with incremental doses of Inj. Mephentermine 3- 6 mg IV and fluid as per need. Bradycardia was defined as heart rate < 50 b.p.m., and was treated with Inj. atropine 0.3–0.6 mg IV. The intraoperative occurrence of nausea, vomiting, shivering, pruritus, respiratory depression, sedation (using Ramsay Sedation Scale), hypotension and other side-effects were noted during the study. Sensory level was assessed by loss of pin prick sensation using 23G hypodermic

needle and dermatomes level were tested every 2 min. until the highest level had stabilized by consecutive tests. On achieving T- 6 sensory blockade level, surgeon was allowed to start the surgery. Sensory level testing was then conducted every 10 min. until the point of two segment regression of the block was observed. Further sensory level testing was performed at 20 min. intervals until the recovery of L1 dermatome. The surgeon, patient, and the observing anesthesiologist were blinded to the patient group. Data of the highest dermatome level of sensory blockade, the time to reach this level from the time of injection, time to L1 level sensory regression, and incidence of side effects were noted. Onset of motor block (by modified Bromage scale) was tested every 2 min. until the highest level had stabilized.

**Modified Bromage scale (mbs) is scored as follows:**

**Bromage- 0:** Patients is able to move hip, knee & ankle; **Bromage- 1:** Patients is unable to move hip, but able to move knee & ankle; **Bromage- 2:** Patient is unable to move hip & knee but able to move ankle; **Bromage- 3:** Patient is unable to move hip, knee & ankle. **All durations were calculated considering the time of 'spinal injection' as time 'zero' [13].** The time taken for the onset of motor blockade and the duration of motor blockade were noted. The time required for movement & raising of ankle from the injection of drug was taken as duration of motor blockade.

**Statistical Analysis**

Data was analyzed using computer statistical analysis program SSPO. Data expressed as mean and standard deviation. Chi-square test or Fisher's test was used wherever appropriate. P-value < 0.05 was considered significant.

**Observations and Results**

The demographic profiles of patients in both the groups were comparable with regards to age, weight and height. The distribution as per ASA status was similar in both the groups and mean duration of surgery was comparable in both the groups and statistically non significant ( $p > 0.05$ ), [Table 1].

The Group I had early onset of sensory block ( $1.86 \pm 0.86$  min.) as compared to Group II ( $2.97 \pm 0.85$  min.). The time required to achieve T10 dermatome level was significantly less in Group I ( $3.7 \pm 1.60$  min.) than in Group II ( $7.83 \pm 1.62$  min.). The time to reach maximum sensory block was shorter in Group I ( $8.8 \pm 2.09$ ) as compared to Group II ( $12.56 \pm 2.78$  min.). Both the groups had comparable maximum sensory level that is (T5.) in Group I and (T5-6.) in Group II. The mean duration of sensory block was longer in Group I ( $307.83 \pm 55.66$ ) than Group II ( $187.16 \pm 21.16$  min.), [Table 2]. Whereas the mean time for onset of motor block in group 1 ( $2 \pm 0.74$  min.) was shorter than that in Group II ( $5.63 \pm 1.80$ ) while the duration of motor block was more prolonged in Group I ( $281.5 \pm 56.75$ ) as compared to that in Group II ( $170.16 \pm 22.64$ ) which was statistically significant. ( $P < 0.05$ ), [Table 3].

At various time of surgery there is no significant difference has been found in systolic blood pressure (SBP) of both the groups, [Figure 1]. The mean values of mean arterial pressure (MAP) and heart rate (HR) were comparable between the two groups throughout the intraoperative and postoperative periods, [Figures 2 and 3]. Significantly less incidence of bradycardia and hypotension was noted in Group I than Group II, [Figure 4]. The Group I provided excellent quality

of anaesthesia as well as requirement of intraoperative sedative drugs was significantly reduced in Group I when compared with Group 2. The time to rescue analgesic was significantly longer in Dexmedetomidine + Bupivacaine Group as compared to Bupivacaine group with minimal postoperative side effects i.e. less incidence of nausea, vomiting, shivering & no incidence of respiratory depression, deep intra operative sedation (Ramsay sedation scale >4), [Table 4].

**Table No. 1** Demographic data and Duration of surgery

Variable	Group – I (n = 30)	Group -II (n = 30)	“p”
Age ( yrs)	50.33 ± 05.83	48.96 ± 07.92	0.4500 (> 0.05)
Weight (kgs)	56.40 ± 05.92	56.90 ± 05.42	0.7343 (>0.05)
Height ( cms)	160.56 ± 05.13	161.13 ± 04.78	0.6598 (>0.05)
Duration of surgery (min)	90.66 ± 15.18	88.33 ± 14.93	-0.5508 (>0.05)

Above data indicates that Group I and Groups II are statistically comparable with regard to age, weight, height and duration of surgery of patients.

**Table No. 2** Sensory block

S.N.	Character of spinal block	Group- I	Group- II	P value
1	Onset of sensory block (Min.) - Time to reach L1	1.86 ± 0.86	2.97 ± 0.85	0.000, HS
2	Time to reach T 10 (Min.)	3.7 ± 1.60	7.83 ± 1.62	0.000, HS
3	Time to reach Max Sensory block (Min.)	8.8 ± 2.09	12.56 ± 2.78	0.000, HS
4	Max. Sensory level	5.5 ± 1.43	5.5 ± 1.53	0.6038, NS
5	Duration of sensory block (Min.)	307.83 ± 55.66	187.16 ± 21.16	0.000, HS

Data are Mean and ± SD

**Table No. 3** Motor block

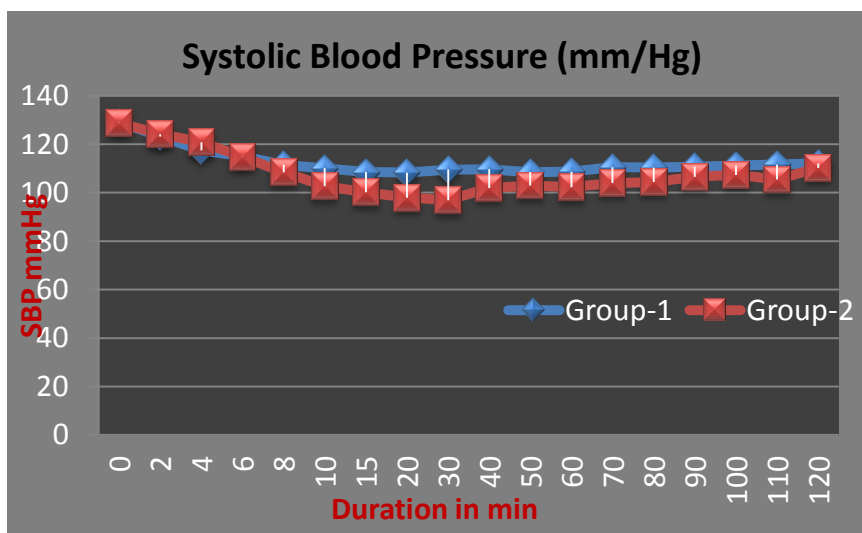
SN	Character of motor block	Group- I (Study Gr.)	Group-II (Control Gr.)	P Value
1	Onset of motor block (Min.)	02 ± 00.74	05.63 ± 01.80	0.000 , HS
2	Duration of motor block (Min.)	281.5 ± 56.75	170.16 ± 22.64	0.000 , HS

Data are Mean and ± SD

**Table No. 4** Postoperative side effects

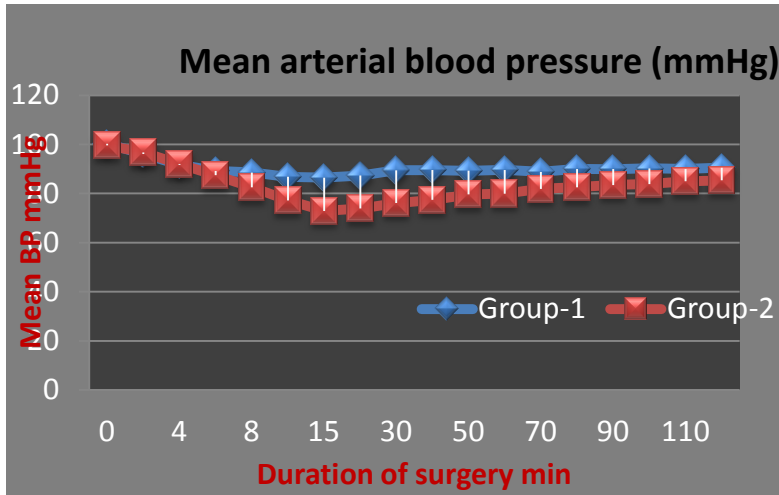
SN	Criteria	Group- I	Group- II	P- Value
1	Hypotension	6	14	<0.05-HS
2	Bradycardia	6	9	>0.05 NS
3	Nausea	1	2	>0.05 NS
4	Vomiting	0	1	>0.05 NS
5	Pruritus	0	0	-
6	Shivering	2	4	>0.05 NS
7	Intraoperative sedation (Ramsay Sedation scale > 4)	0	0	-
8	Respiratory Depression	0	0	-

**Fig. No. 1-** Diagrammatic Representation of MEAN SYSTOLIC BLOOD PRESSURE (Mean SBP)



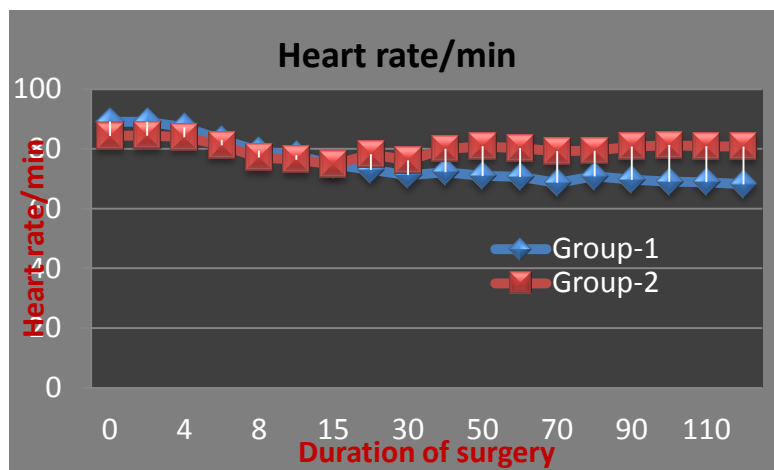
Above figure indicates comparison between two groups with regards to mean systolic blood pressure (SBP)

**Fig. No. 2** Diagrammatic Representation of MEAN ARTERIAL BLOOD PRESSURE (mm/Hg)



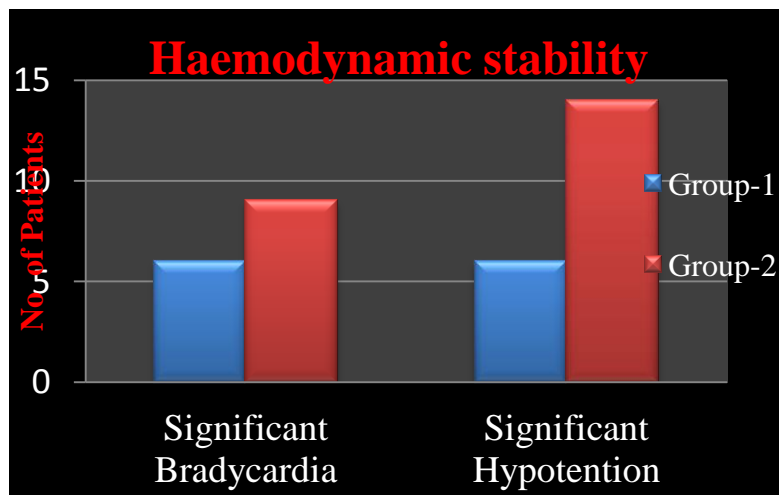
The study groups i.e. group 1 and groups 2 were statistically comparable with regard to mean arterial blood pressure (mm/Hg)

**Fig. No. 3** Diagrammatic presentation of MEAN HEART RATE ( Mean HR)



Above figure represents comparison between two groups with regards to mean heart rate (HR)

**Fig. No. 4** Diagrammatic presentation of HAEMODYNAMIC STABILITY



Above figure represent the comparison of Haemodynamic stability between two groups.

## Discussion

A revolution has occurred in the management of post-operative pain since the understanding of its neurobiology and pharmacology of the available drugs for the control of pain <sup>[14]</sup>. Various drugs have been used as adjuvants along with local anesthetics in the subarachnoid space with the aim of improving the duration of post-operative analgesia <sup>[15]</sup>. Various techniques like local infiltration block, spinal, epidural or general anaesthesia can be used in cases of abdominal hysterectomy. Because of its rapid onset, less failure rate, technically easy administration and economical than general anaesthesia, the spinal anaesthesia is most commonly used technique in developing country like India <sup>[5]</sup>. Local anesthetics are commonly used for intrathecal anesthesia, but the major problem is the relatively short duration of action, thus early analgesic intervention is needed in the postoperative period. A number of adjuvants, such as Clonidine, Dexmedetomidine and Midazolam, and others have been studied to prolong the effect of spinal anesthesia <sup>[16, 17]</sup>.

The use of Dexmedetomidine has been studied as an epidural adjunct by various authors who have observed its synergism with local anesthetics. It was observed to prolong the motor/ sensory block duration time and postoperative analgesia without any additional morbidity <sup>[18, 19]</sup>. The mechanism by which intrathecal  $\alpha 2$  - adrenoceptor agonists prolong the motor and sensory block of local anesthetics is not well known. They act by binding to presynaptic C-fibers and postsynaptic dorsal horn neurons. Their analgesic action is a result of depression of the release of C-fiber transmitters

and hyper-polarisation of postsynaptic dorsal horn neurons <sup>[20]</sup>. Local anesthetic agents act by blocking sodium channels. The prolongation of effect may be the result of synergism between local anesthetic and  $\alpha 2$  - adrenoceptor agonist, while the prolongation of the motor block of spinal anesthetics may result from the binding of  $\alpha 2$  -adrenoceptor agonists to motor neurons in the dorsal horn <sup>[21]</sup>. The faster onset of action of local anaesthetics, rapid establishment of both sensory and motor blockade, prolonged duration of analgesia into the post-operative period, dose-sparing action of local anaesthetics and stable cardiovascular parameters makes these agents a very effective adjuvant in regional anaesthesia <sup>[22-26]</sup>. Dexmedetomidine has been found to prolong analgesia when used as an adjuvant to local anaesthetics for subarachnoid, epidural and caudal epidural block. However, there is no proper consensus regarding the dose of drug to be used for neuraxial blocks <sup>[27]</sup>.

Kanazi et al <sup>[12]</sup> used a small doses of intrathecal Dexmedetomidine (3 $\mu$ g) in combination with Bupivacaine in humans have been shown to shorten the onset of motor block and prolong the duration of motor and sensory block with hemodynamic stability and lack of sedation. Al-Mustafa et al <sup>[11]</sup> studied effect of Dexmedetomidine 5 and 10  $\mu$ g with Bupivacaine in urological procedures and found that Dexmedetomidine prolongs the duration of spinal anesthesia in a dose-dependent manner. Although Fyनेface-Ogan et al., <sup>[28]</sup> reported that a single shot of 2.5  $\mu$ g Dexmedetomidine with 2.5 mg hyperbaric Bupivacaine in combination



significantly prolonged sensory block in laboring women. In our study, intrathecal 5 µg Dexmedetomidine when added to 3.5 ml hyperbaric Bupivacaine shows early onset of sensory and motor block by Bupivacaine for patients undergoing abdominal or vaginal hysterectomy. This is in agreement with studies done by Hala E A Eid, et al<sup>[29]</sup> and Mohamad M Al Mustafa et al.<sup>[11]</sup> Prolongation of duration of sensory and motor block with use of Dexmedetomidine as adjuvant to Bupivacaine in spinal anaesthesia observed in present study correlates with finding of Rajani Gupta et al<sup>[7]</sup>, Mohamad M Al Mustafa et al.<sup>[11]</sup>

A lower dose (2.5 µg) of intrathecal Dexmedetomidine with 2.5 mg hyperbaric Bupivacaine was used previously and the patients remained hemodynamically stable<sup>[28]</sup>. Although, previous studies revealed prolongation of spinal block by intrathecal 5 µg and 10 µg Dexmedetomidine with no significant effect on blood pressure or heart rate<sup>[7,11,27,30]</sup>. In our study, there was significantly less incidence of hypotension with use of Dexmedetomidine as compared with Bupivacaine alone does not support the observation of Hala E A Eid et al<sup>[29]</sup> because the dose of Bupivacaine used in reference study was quite less (2.5 ml) as compared to 3.5 ml in present study.

Various drugs like Neostigmine<sup>[30]</sup>, Ketamine<sup>[31]</sup>, Morphine<sup>[32]</sup>, Midazolam<sup>[33]</sup> and Magnesium sulphate<sup>[34]</sup> 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 post-operative analgesia. In

our study, 5 µg Dexmedetomidine when added to 3.5 ml hyperbaric Bupivacaine produced excellent quality of anesthesia as compared to control group.

Although sedation can be attributed to its action is at locus ceruleus and in promoting natural sleep pathways. Requirement of intraoperative sedation was significantly reduced in the present study with the use of Dexmedetomidine. These findings were correlating with the findings of Rajani Gupta et al. Fukushima et al<sup>[35]</sup> administered 2 µg/kg epidural Dexmedetomidine for postoperative analgesia in humans but did not report neurologic deficits. The results of Al-Ghanem et al.,<sup>[10]</sup> Al-Moustafa et al.,<sup>[11]</sup> and Eid et al.,<sup>[36]</sup> when they used different doses of Dexmedetomidine (5 µg, 10 µg and 15 µg, respectively) intrathecally, they found that its effect on duration of postoperative analgesia is dose dependent and the onset of sensory block to reach T10 dermatomes was shorter with the use of Dexmedetomidine. We had a similar result in our study when adding only 5 µg Dexmedetomidine to 3.5 ml hyperbaric Bupivacaine to spinal anesthesia.

The α 2 agonist also have anti shivering property as observe by Burhanettin Usta et al<sup>[37]</sup> In present study there was less incidence of nausea, vomiting, shivering & no incidence of respiratory depression, deep intra operative sedation (Ramsay sedation scale > 4). Post operative analgesia was significantly longer in Dexmedetomidine + Bupivacaine (Group I) as compared to Bupivacaine + Normal saline group (Control Group II). This finding was in concordance with observations of Rajani Gupta et al.<sup>[7]</sup>

## Conclusion

From observations of present study, it may be concluded that 5 µg Dexmedetomidine seems to be an attractive adjuvant to Bupivacaine for spinal anaesthesia in surgical procedure like abdominal hysterectomy. It provides early onset & prolonged duration of sensory & motor block with satisfactory surgical anaesthesia, hemodynamic stability, minimal side effects and longer duration of postoperative analgesia.

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