Spinal Anesthesia for Infra-umbilical Surgeries - A Prospective Randomized Study to evaluate the effectiveness of Dexmedetomidine as an adjuvant to Bupivacaine.

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ABSTRACT

Background: Spinal anesthesia is commonly used anesthetic modality worldwide but with the limitation of relatively short duration of action. However, the addition of adjuvants have increased the duration of sensory block with concomitant prolonged duration of post-operative analgesia.

Study design and Settings: This prospective randomized blind double study was conducted in the Department of Anesthesia, Pain and Critical Care at University Teaching Hospital.

Methodology: 60 patients irrespective of their age and gender were randomly divided into two groups of 30 each and received a total drug volume of 3 ml intra-theccally (IT) viz 2.5 ml of hyperbaric bupivacaine 0.5% mixed with 0.5 ml of normal saline in Group I and 0.5 ml of 5 mcg of dexmedetomidine in Group II respectively.

Results: The maximum height of sensory block achieved were dermatomes T 6.5 ± 1.43 in Group I and T 6.20 ± 1.28 in Group II (P value, 0.794) and the time required to achieve T10 level sensory block was 6.70 ± 0.98 minutes (min) in Group I and 5.50 ± 1.00 min in Group II (P value, 0.001). The time to achieve Bromage scale 3 was 15.70 ± 2.56 min in Group I and 8.55 ± 1.67 min in Group II (P value, < 0.001). The time of first rescue analgesic dose requested by patient was 196.75 ± 15.16 min in Group I and 359.50 ± 49.79 min in Group II (P value, 0.01).

Conclusions: Dexmedetomidine in doses of 5 mcg as an adjuvant to hyperbaric 0.5% bupivacaine IT produced a significantly quick onset and longer duration of motor and sensory block. In addition, it also resulted in prolonged postoperative analgesia. JMS 2018; 21 (2):95-100

Key words: Spinal Anesthesia, infra-umbilical surgeries, bupivacaine, dexmedetomidine, intrathecal, adjuvant, motor block, sensory block, Bromage scale, rescue analgesia, postoperative analgesia.

INTRODUCTION

Spinal anesthesia is popular and commonly used anesthetic modality for many surgical procedures worldwide with the advantages of awake patient, minimal drug cost and rapid patient turnover. These advantages are sometimes offset by relatively short duration of action and complaints of post-operative pain. Spinal anesthesia with hyperbaric bupivacaine is popular for longer procedures due to its prolonged duration. But there is still a need to intensify and increase the duration of sensory block, thereby prolonging the duration of post-operative analgesia without increasing the intensity and duration of motor blockade.^[1]

Central neuraxial opioids whether intrathecal (IT) or/and epidural (Ep) offers the benefit of selective analgesia without sensory or motor blockade. However, side effects

such as potentially catastrophic, delayed respiratory depression have prompted further research to develop non-opioid analgesics with lesser side effects. Several drugs such as midazolam, opioids, and alpha 2 adrenergic receptor agonists have been used as an adjuvant to local anesthetics.^[2,3]

Dexmedetomidine is a new highly selective, an alpha 2 adrenergic receptor agonist with alpha 2/alpha 1 selectivity ratio eight time higher than that of clonidine.^[4] IT dexmedetomidine as an adjuvant to spinal local anesthetics has been reported by various authors in literature but studies are scarce. IT alpha 2-adrenoceptor agonists produce analgesia by binding and depressing the release of pre-synaptic C-fiber neurotransmitters and also by hyperpolarization of post-synaptic dorsal horn neurons.^[5,6] This anti-nociceptive effect may explain the prolongation of the sensory block while prolongation of motor block may be due to the binding of alpha 2-adrenoceptor agonists to motor neurons in the dorsal horn.^[7]

Dexmedetomidine has been approved by Food and Drug

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Administration (FDA) in 1999 as a short term sedative and analgesic for mechanically ventilated intensive care unit (ICU) patients. Its use is often associated with a decrease in heart rate and blood pressure.^[8] A number of animal studies conducted using intrathecal dexmedetomidine at a dose range of 2.5–100 mcg did not report any neurologic deficits with its use.^[9-13] This drug is under evaluation as a neuraxial adjuvant as it provides stable hemodynamic conditions, good quality of intraoperative and postoperative analgesia with minimal side effects. Keeping in mind the multiple benefits of dexmedetomidine, we planned to use its beneficial aspects in patients undergoing infra-umbilical surgeries using it as an adjuvant to IT block with bupivacaine.

METHODS

The present prospective double-blind randomized observational study was conducted in the Department of Anesthesiology, Pain and Critical Care of University teaching hospital in patients aged 18 years and above admitted for elective infra-umbilical surgeries belonging to ASA 1-4.

Following patients were included in the study like

- a) Patients undergoing infra-umbilical surgeries,
- b) Age $\geq$ 18 years,
- c) ASA grade 1 - 4.

Following patients were excluded from the study as per the exclusion criteria:

Exclusion Criteria

1. Patient refusal.
2. Patient allergic to study drugs.
3. History of mental illness.
4. Pregnancy.
5. Body weight more than 120 Kg.
6. Height less than 140 cm.
7. Patients on treatment with alpha-adrenergic antagonists.
8. Contraindications of spinal anesthesia, spine deformity, local infection at the site of injection, hypersensitivity to local anesthetic, shock, coagulation disorder, raised intracranial tension, neurological disorder.

On the day prior to surgery a detailed pre-anesthetic checkup was performed including general physical and

systemic examination. All the patients were explained about the anesthesia technique and written and informed consent was taken from the patient. The patients were kept NPO for 6 hours prior to surgery. All the patients were given oral tablets of Ranitidine 150 mg and Metachlorpromide 10 mg one hour prior to shifting to operating room (OR) with few sips of water.

Total of 60 patients were selected for the study and were randomized to either Group I or Group II using computer generated random sequence, allocating 30 patients in each group. All the patients irrespective of the group received the total volume of 3 ml IT drug containing 2.5 ml (12.5mg) hyperbaric 0.5% bupivacaine in addition to 0.5 ml fresh normal saline (NS) in Group I and 5 mcg dexmedetomidine (diluted to total volume of 0.5 ml in NS) in Group II respectively. After obtaining the written informed consent, patients were wheeled to operation theatre. The standard monitoring comprising of noninvasive blood pressure (NIBP), Digital pulse oximetry (SpO_2), Temperature (T) and electrocardiogram (ECG) was attached to measure perioperative parameters. IV line was secured with 18 G cannula preferably on left forearm to start IV fluids ringer lactate/normal saline as per patient's condition and 100% of oxygen was given through the oxygen mask at 5 L/min.

The patients were then placed in sitting position with the help of assistant. Under all aseptic precautions 27G Quincke spinal needle was inserted into lumbar spinal subarachnoid space preferably at L3-4 intervertebral space, a study solution was injected slowly after a free flow of CSF appeared.^[6] The study drug was prepared by an assistant anesthetist and was handed over in a 5 ml syringe without revealing the type of drug being given. Thus double blind study was maintained as both patient (subject) and investigator were unaware of the type of drug delivered IT. The punctured site was cleaned using chlorhexidine-alcohol solution and sealed with sterile gauge piece and micro-pore adhesive after the block. The patients were turned supine and soft pillow was kept under the head and upper shoulder. NIBP, heart rate (HR), SpO_2 and level of sensory and motor block were checked after every minute for 5 min for half hour and thereafter every 15 min till 3 hours then after every 30 minutes.

RESULTS

The surgeries performed in this study were all infra-umbilical surgeries like appendectomies, mesh hernioplasties, ileostomies and colostomies. (Table 1)

Table 1: Type of surgeries performed

Type of Surgeries	Group I, N (%)	Group II, N (%)
Mesh Hernioplasties	7/30 (23%)	9/30 (30%)
Appendectomies	8/30 (26%)	6/30 (20%)
Colostomies	7/30 (23%)	8/30 (26)
Ileostomies	8/30 (26%)	7/30 (23%)
Total	30(100%)	30(100%)

N = Number of cases; % = Percentage of cases

The maximum height of sensory block achieved was T6.5 ± 1.43 dermatome in Group I and T6.20 ± 1.28 dermatome in Group II with statistically non-significant P value of 0.794 > 0.05. (Table2)

Table 2: Maximum height of Sensory block achieved

Highest Sensory Level	Group I (N)	Group II (N)	P Value
T 4	0	3	0.752
T 6	9	12	
T 8	8	5	
T 10	13	10	
Total	30	30	
Mean Height of T sensory block Achieved (Mean ± SD)	6.5 ± 1.43	6.20 ± 1.28	0.794

SD = Standard Deviation; T = Thoracic level; N = number of cases

The time required to achieve T10 level sensory block was 6.70 ± 0.98 min in Group I and 5.50 ± 1.00 min in Group II with statistically significant P value of 0.001. (Table 3)

Table 3: Temporal characteristics of Sensory Blocks.

	Group I (Mean ± SD)	Group II (Mean ± SD)	P Value
Time to reach T10 Sensory level (Min)	6.70 ± 0.98	5.70 ± 1.03	0.001
Time to reach highest sensory level (Min)	14.60 ± 0.94	13.20 ± 2.68	0.235
Time to 2 segment Regression (Min)	100.00 ± 29.82	157.50 ± 19.09	<0.001
Time to S1 Regression (Min)	188.00 ± 20.93	328.75 ± 51.17	<0.001

SD = Standard Deviation; T = Thoracic level; S = Sacral Level; Min = Minutes

The time required to reach peak sensory block level was 14.60 ± 0.94 min in Group I and 14.45 ± 3.52 min in Group II with P value of > 0.05 (statistically insignificant). (Table3)

The two segments regression time was 100.00 ± 29.82 min in Group I and 133.75 ± 20.06 min in Group II with P value

of < 0.05 (statistically significant). (Table3)

The time to regression to S1 dermatome was 188.00 ± 20.93 min in Group I and 328.75 ± 51.17 min in Group II with P value of < 0.05 (statistically significant). Complete recovery of sensory function was observed in all studied patients. (Table3)

All patients achieved Bromage scale 3 motor block. The time to reach Bromage scale 3 was 15.70 ± 2.56 min in Group I and 8.55 ± 1.67 min in Group II with a P value of < 0.001 (statistically significant). The regression time to reach Bromage scale 0 was 162.25 ± 16.02 min in Group I and 267.25 ± 30.20 min in Group II with a P value was < 0.0001 (statistically significant). (Table 4)

Table 4: Temporal Characteristics of Motor Block

	Group I Mean ± SD	Group II Mean ± SD	P Value
Time to reach Bromage Score 3 (Min)	15.70 ± 2.56	8.55 ± 1.67	<0.001
Regression time to Bromage Score 0 (Min)	162.25 ± 16.02	267.25 ± 30.20	<0.001
Time for first pain medication/ rescue analgesia (Min)	196.75 ± 15.16	359.50 ± 49.79	<0.001

SD = Standard Deviation; Min = Minutes

The time of first rescue analgesic dose requested by patient was 196.75 ± 15.16 min in Group I and 359.50 ± 49.79 min in Group II with a P value of < 0.05 (statistically significant). (Table 4).

Both the groups were comparable with respect to SpO₂ (P value > 0.05). (Table 5)

Table 5: Peri-operative Hemodynamic and Oximetry parameters.

		Group I Mean ± SD	Group II Mean ± SD	P Value
Pre-operative/ SAB Parameters	Heart Rate (beats per min.)	88.25 ± 10.42	86.30 ± 6.38	0.427
	SBP (mmHg)	122.00 ± 3.61	121.50 ± 4.98	0.652
	DBP (mmHg)	78.45 ± 5.43	75.65 ± 7.10	0.152
	SpO ₂ (%)	99.60 ± 0.40	99.75 ± 0.25	0.65
Intra-operative Parameters	Heart Rate (beats per min.)	93.65 ± 6.65	95.00 ± 7.03	0.233
	SBP (mmHg)	117.55 ± 5.48	115.95 ± 5.76	0.330
	DBP (mmHg)	83.30 ± 6.85	81.85 ± 5.83	0.092
	SpO ₂ (%)	99.70 ± 0.30	99.80 ± 0.20	0.70
Post-operative/P ACU Parameters	Heart Rate (beats per min.)	77.75 ± 11.74	73.10 ± 8.97	0.263
	SBP (mmHg)	116.15 ± 2.94	118.25 ± 4.45	0.204
	DBP (mmHg)	71.85 ± 4.63	69.65 ± 3.84	0.220
	SpO ₂ (%)	98.70 ± 1.30	98.80 ± 1.20	0.71

SD = Standard Deviation; Min = Minutes; SBP = Systolic blood pressure; DBP = Diastolic blood pressure; mmHg = millimeters of Mercury (Pressure); SpO₂ (%) = Digital Pulse oximetry in percent

Hemodynamically, no significant differences were observed in systolic, diastolic, mean arterial blood pressures and HR between the control group (Group I) and study groups (Group II) throughout the perioperative period with a P value of > 0.05 (statistically insignificant). (Table 5)

Two patients each in Group II and one patient in Group I developed hypotension (30% below baseline) and hence required vasopressor (Phenylephrine) in doses of 100 mcg IV push and intravenous fluids in Group II whereas patient in Group I was treated with intravenous fluids only. None of the patients in either of the groups developed any bradycardia during the study period. (Table 6)

Table 6: Side effect profile among the patients

Side effects & Management	Group I N (%)	Group II N (%)	P Value
Bradycardia	0 (0.0%)	0 (0.0%)	-
Atropine IV	0 (0.0%)	0 (0.0%)	
Hypotension	1 (5.0%)	2 (10.0%)	0.804
Phenylephrine IV	0 (0.0%)	1 (5.0%)	0.596

Rescue analgesia dose requirement in first 24 hours was significantly less in Group II as compared to Group I (P value < 0.001). (Table 7)

Table 7: Number of rescue analgesic doses (diclofenac) used during first 24 hours

		Group I	Group II	P Value
Time for the first Rescue Analgesia (Min)	Mean $\pm$ SD	196.75 $\pm$ 15.16	359.50 $\pm$ 49.79	0.01
Number of rescue analgesic doses (diclofenac) used	0	0	9	< 0.001
	1	1	15	
	2	13	3	
	3	16	3	
	TOTAL	30	21	

SD = Standard Deviation; Min = Minutes

DISCUSSION

Spinal anesthesia is effective in the management of perioperative pain which extends into the initial post-operative period. In order to maximize post-operative pain free period numerous techniques and newer drugs have been tried as adjuvants to local anesthetics used IT.

Median peak sensory level achieved was T6 and the highest level of sensory block achieved was T4 in both of our studied groups. The mean time to achieve maximum sensory block was 6.20 ± 1.28 min in Group II (dexmedetomidine) and 6.5 ± 1.43 min in Group I (bupivacaine) was comparable (P value, 0.794). The present

study was comparable with studies conducted by *Kanazi GE et al*,^[4] *Hala EA et al*.^[14] It was concluded that there was no significant difference in maximum height of sensory block achieved in any of the groups. Hence all the infra-umbilical surgeries could be performed with complete intraoperative analgesia under spinal anesthesia.

The mean time to reach the T10 level in group I was 6.70 ± 0.98 min which was comparable to 6.57 ± 4.9 min observed in the study of *Saxena H et al*^[15] wherein they used bupivacaine 12.5 mg. The mean time to reach T10 in group II was rapid 5.70 ± 1.03 min. So the surgical incision could be given earlier in group II as compared to group I. The results were comparable to the studies conducted by *Kanazi GE et al*,^[4] *Hala EA et al*.^[14]

The mean time to achieve highest level of sensory block was 13.20 ± 2.68 min in Group II and 14.60 ± 0.94 min in Group I, was comparable (P value, 0.235).

The mean time to two segment regression in Group II was delayed 157.50 ± 19.09 min as compared to 100.00 ± 29.82 min in Group I, was statistically significant (P value, < 0.001). This observation was comparable with the studies conducted by *Kanazi GE et al*,^[4] *Hala EA et al*,^[14] *Sethi BS et al*.^[16] Hence our study proves that time of regression is prolonged in dexmedetomidine Group II.

Dexmedetomidine as an adjuvant to IT hyperbaric bupivacaine 0.5% significantly prolonged the time of regression to S1 in Group II as compared to Group I (328.75 ± 51.17 min v/s 188.00 ± 20.93 min; P value, < 0.001). This observation was comparable with the studies conducted by *Al-Mustafa MM et al*.^[17]

The duration of analgesia was longer in Group II (304.50 ± 30.82 min) as compared to Group I (196.75 ± 15.16 min) and the observations were comparable to the studies conducted by *Hala EA et al*,^[14] *Sethi BS et al*.^[16] Hence we concluded that addition of dexmedetomidine as an adjuvant to IT bupivacaine significantly prolongs the duration of analgesia.

The mean time to reach Bromage scale 3 motor block was significantly shorter in Group II than in Group I (8.55 ± 1.67 min v/s 15.70 ± 2.56 min; P value < 0.001), suggesting the significance of dexmedetomidine as IT adjuvant to bupivacaine in achieving maximum motor block earlier. Similar observations were made by *Kanazi GE et al*,^[4] *Al-Mustafa MM et al*,^[17] *Gupta R et al*^[18] in their study.

The mean regression time to reach Bromage scale 0 was 162.25 ± 16.02 min in Group I as compared to $267.25 \pm$

30.20 min in Group II with P value of <0.0001 (statistically significant) suggesting prolonged loss of motor response in group II. Similar results were observed by *Kanazi GE et al*,^[4] *Al-Mustafa MM et al*,^[17] *Kim JE et al*^[19] in their study.

The mean time for rescue analgesia was significantly earlier in Group I (196.75 ± 15.16 min) as compared to Group II that did not require analgesics for about 359.50 ± 49.79 min (P value <0.001).

Dexmedetomidine when used IT with hyperbaric bupivacaine, significantly reduced the requirement of rescue analgesics (diclofenac) injection for pain relief in 24 hours in postoperative period as compared to bupivacaine alone. VAS score was less than 4 throughout the duration of surgery.

Hemodynamically patients were stable in both the groups. Hypotension was noted in patients of both the Groups and was comparable, which was statistically not significant (P value > 0.05). Hypotension, were treated with injection phenylephrine and intravenous fluids with no further complications. *Kanazi GE et al*^[4] and *Al Ghanem SM et al*^[20] also observed that dexmedetomidine added to IT bupivacaine produced a similar prolongation in the duration of the motor and sensory block, with preservation of hemodynamic stability. Bradycardia and hypotension are most common side effect of IT Alpha adrenergic receptor agonists.^[4,21]

The SpO₂ and RR in both groups were comparable at different time intervals (P value, > 0.05). No sedation or respiratory depression was noted in any of the patient. No other complications like dizziness, fatigue, pruritus, tremors, headache etc. were observed in any group.

After analyzing the results obtained in our study it is evident that the use of 5mcg of dexmedetomidine as an adjuvant to hyperbaric bupivacaine IT in infra-umbilical surgeries is beneficial in several aspects. These include shorter onset of motor block and longer duration of sensory and motor block with prolonged post-operative analgesia with minimum use of rescue analgesics without any significant hemodynamic instability. Further it was observed that dexmedetomidine as an adjuvant to bupivacaine was better in prolongation of motor and sensory block, postoperative analgesia as compared to bupivacaine alone.^[22]

CONCLUSION

Neuraxial blockade with a local anesthetics provides analgesia limited to the initial postoperative period but

adjuvant like dexmedetomidine in doses of 5 mcg added to hyperbaric bupivacaine IT extends its benefits not only perioperatively but provides prolonged postoperative analgesia and produces a significantly quick onset and longer duration of motor and sensory block in comparison to bupivacaine alone.

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