Dexmedetomidine as an Adjunct to Spinal Anesthesia in Urological Procedures

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ABSTRACT

Introduction: Patients undergoing urological procedures under spinal anaesthesia are usually elderly having comorbid conditions. Dexmedetomidine, the new highly selective α-2 agonists is being used as an adjuvant in spinal anaesthesia with improved quality of anaesthesia and analgesia and minimal side effects. The present study was designed to evaluate the effect of intrathecal dexmedetomidine to bupivacaine in spinal anesthesia for urological procedures.

Material and Methods: Sixty patients of ASA class I and II were randomly divided into two groups of thirty patients each. The control group received hyperbaric bupivacaine 15 mg + 0.5 ml normal saline (3.5 ml).The study group received hyperbaric bupivacaine 15 mg +10 mcg dexmedetomidine diluted in 0.5 ml normal saline (3.5ml).

Results: The time taken to reach the highest sensory level was 8.5 ± 0.5 minutes in control group while 6.2 ± 0.4 minutes in study group. The mean time to reach the bromage 3 was 10.1 ± 2.9 minutes in control group while 7.8 ± 1.9 minutes in study group. Time taken to sensory regression to S1 and duration of motor blockade was significantly higher (311 ± 36.6 min and 286 ± 34.2 min) in study group when compared to control group (230 ± 19.3 min and 197.9 ± 17.5 min). The duration of analgesia was significantly higher (339.7 ± 47.4 min) in study group as compared to control group (272.1 ± 39 min)

Conclusion: Addition of dexmeditomidine to hyperbaric bupivacaine in spinal anaesthesia results in early onset of sensory and motor block, prolongs duration of motor and sensory block, improves quality of intraoperative and post operative analgesia with good hemodynamic stability and minimal side effects.

Keywords: Bupivacaine, Dexmedetomidine, Intrathecal, TURP

INTRODUCTION

Transurethral resection of prostate and bladder tumours are routinely performed procedures. Most of these patients are elderly with associated co-morbidities. Subarachnoid block (SAB) is the most commonly used anesthetic technique in these patients as it has the advantages of rapid onset, superior blockade, less failure rates and cost effectiveness. Being technically easier, SAB provides the optimal operative conditions with minimal intra-operative blood loss.[1,2] However post operative pain control remains a concern as SAB using only local anaesthetic is associated with relatively short duration of action and thus early analgesic intervention is needed in the post operative period.

Neuroaxial adjuvants are used to prolong the effect of spinal anaesthesia, improved quality of analgesia and decrease the adverse effects associated with high doses of single local anaesthetic agents.[3] Dexmedetomidine, a newer α-2 adrenergic agonist has gained popularity because of its sedative, analgesic, sympatholytic, anaesthetic sparing and hemodynamic stabilising properties.[4] The use of intrathecal clonidine for post-operative analgesia alone[5] or co-administered with local anaesthetics[6] or opioids[7] has previously been studied. However the literature on intrathecal use of dexmedetomidine is relatively scarce.

Dexmedetomidine has 10 fold greater affinity to α-2 adrenergic receptors than clonidine and much less α-1 effects.[8] These properties make it more effective hypnotic, sedative and analgesic agent with a more favourable pharmacodynamic profile.[9] It seems to be a valuable adjuvant in regional anaesthesia and analgesia with better hemodynamic stability and minimal side effects.[10] However further studies are warranted to build the evidence for its safe use in central neuroaxial blocks in different patient groups.[11] This study was undertaken to compare the effects of dexmedetomidine in spinal anesthesia as an adjuvant to local anesthetics in patients undergoing different urological procedures.

MATERIAL AND METHODS

This prospective, randomized double blind controlled study was conducted in the Department of Anaesthesiology and Critical Care at Sheri-Kashmir Institute of Medical Sciences (SKIMS), Srinagar, Kashmir**.** After institutional ethical committee approval, sixty patients of ASA class I or II, scheduled for TURP or TURBT under spinal anaesthesia were selected for the study. Patients with contraindication to regional anaesthesia and advanced cardiac, renal and hepatic disease were excluded from the study. At preoperative visit, all patients were clinically evaluated and investigated for any comorbid condition. The study protocol was explained in detail and written informed consent was taken. The patients were advised to fast for 6hrs and no premedication was given.

In the operating room all patients were monitored for ECG, NIBP and SpO_2. An intravenous line was established with 16/18G cannula and all patients were preloaded with 500ml of Ringers lactate solution. Baseline heart rate, blood pressure and SPO_2 was recorded. Patients were taught how to express degree of pain on visual analogue scale (VAS), 0-10 scale, (0 = pain, 10

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How to cite this article: Mehmooda Akhter, Abdul Waheed Mir, Bilal Ahmad, Faroz Ahmad, Suhail Sidiq, Mohamad Akbar Shah, Sofi Khalid. Dexmedetomidine as an adjunct to spinal anesthesia in urological procedures. International Journal of Contemporary Medical Research 2017;4(1):154-158.

= most severe pain)

Subarachnoid block was performed in sitting position under strict aseptic technique through midline approach between L2-L3 or L3-L4 intervertebral space using 25G Quincke's spinal needle. After free flow of CSF, 15 mg of 0.5% hyperbaric bupivacaine with 0.5 ml of normal saline or 15 mg of 0.5% hyperbaric bupivacaine with 10 mcg of dexmeditomidine, diluted in 0.5 ml normal saline, was injected into subarachnoid space (Total volume 3.5ml in each group). The total volume of dexmedetomidine solution was measured using insulin syringe. The preparation of the drugs was carried out by a person not involved in the study and both patient and the observer remained blind from the preparation of drug till the end of the study. After intrathecal injection, patients were positioned in lithotomy position and oxygen 2-6 L/min was given through the face mask. Vital signs (heart rate, blood pressure and arterial oxygen saturation) were recorded at 5 minute intervals during surgery and at 15 minute intervals in the recovery till the patient was shifted to the ward.

The level of sensory block was assessed after subarachnoid injection by pin prick method at 3 minutes interval for 30 minutes and every 15 minutes thereafter until regression of the block to S1 segment. The onset of sensory block was taken from the time of intrathecal injection to the absence of pin prick sensation and the duration of sensory block from the time of intrathecal injection till regression of level to S1.The motor block was assessed according to the modified bromage scale.[12] (Bromage 0: The patient is able to move the hip, knee and ankle. Bromage 1: The patient is unable to move the hip but is able to move the knee and ankle. Bromage 2: The patient is unable to move hip and the knee but is able to move the ankle. Bromage 3: The patient is unable to move hip, knee and ankle. The measurements were performed at 3, 6,9, 12 and 15 minutes after intrathecal injection and subsequently after every 15 minutes until no motor block was detected. The onset and duration of motor block was recorded.

Analgesia was assessed by Visual Analogue Scale (VAS) 0 to 10 cm score from no pain to worst pain on marked paper strip at 15, 30, 60 minutes during surgery and thereafter at 4-hourly intervals for 24 hours during the post operative period. Patients with VAS score above or equal to 4 received rescue analgesia in the form of intravenous Ketorolac 0.5 mg/kg in the post operative period. Time of first rescue analgesic required and VAS score at that time was noted. Quality of analgesia was assessed and compared in both the groups (0 - No pain relief,1 - Poor pain relief, 3 - Fair pain relief, 4 - Good pain relief, 5 - Excellent pain relief).The level of sedation was assessed intra and post-operatively every 15 minutes using Ramsay Sedation Scale.[13]

The incidence of side effects like hypotension, bradycardia, nausea and vomiting was recorded. Hypotension was taken as a decrease in systolic pressure >30% of the baseline value or SBP of <90mmHg,which was treated with crystalloid boluses and intravenous boluses of ephedrine (6mg).Bradycardia was taken as a pulse rate of <50beats/min and was treated with iv atropine (0.6mg).

The data obtained was analyzed statistically using analysis of variance (ANOVA) and students 't' test. A value of <0.05 was considered statistically significant.

RESULTS

The two groups were comparable in demographic parameters like age, weight, ASA status as depicted in Table 1.

Hemodynamic parameters heart rate, SBP and DBP were comparable between the two groups when observed at base line, immediately after intrathecal injection and at 5, 10, 15, 20, 25, 30, 40, 50, 60 minutes, till end of surgery.

The time taken to reach the highest sensory level was 8.5 ± 0.5 minutes in control group while 6.2 ± 0.4 minutes in study group. The mean time to reach the bromage 3 was 10.1 ± 2.9 minutes in control group while 7.8 ± 1.9 minutes in study group. Time taken to sensory regression to S1 and duration of motor blockade was significantly higher (311 ± 36.6 minutes and 286 ± 34.2 minutes) in study group when compared to control group (230 ± 19.3 minutes and 197.9 ± 17.5 minutes).The sedation score between two groups was insignificant as shown in Table 2.

The duration of analgesia was significantly higher (339.7 ±47.4 minutes) in study group as compared to control group (272.1 ± 39 minutes) as show in Table 3.

There was a statistically significant prolongation of the duration of analgesia in the study group.

The incidence of side effects like bradycardia, hypotension, nausea and vomiting was comparable between the two groups as depicted in Table 4.

DISCUSSION

The results from the our study show that the duration of

Demographic Characteristics						
		Group I		Group II		p value
		n	%	n	%	
Age (yr)	≤ 50	3	10.0	2	6.7	0.478 (NS)
	51 to 60	7	23.3	9	30.0	
	61 to 70	13	43.3	9	30.0	
	> 70	7	23.3	10	33.3	
	Mean ± SD	62.8 ± 9.4 (46, 81)		64.6 ± 9.7 (47, 82)		
Gender	Male	30	100.0	30	100.0	1.000 (NS)
Operation	TURP	22	73.3	21	70.0	0.776 (NS)
	TURBT	8	26.7	9	30.0	
ASA	I	20	66.7	19	63.3	0.788 (NS)
	II	10	33.3	11	36.7	
NS:Non-significant.						

Table-1: Comparison of age, gender and ASA status in the two groups.

	Group I	Group II	P value
	Mean ± SD	Mean ± SD	
Time taken to reach highest sensory level (minutes)	8.5 ± 0.5	6.2 ± 0.4	0.000 (S*)
Sensory regression to S1 (minutes)	230 ± 19.3 (185,285)	311.0 ± 36.6 (245,385)	0.000 (S*)
Time from injection to bromage III (minutes)	10.1 ± 2.9	7.8 ± 1.9	0.000 (S*)
Duration of grade III motor block (minutes)	197.9 ± 17.5 (172,252)	286 ± 34.2 (242,367)	0.000 (S*)
Sedation Score	0.5 ± 0.6	0.7 ± 0.7	0.317 (NS)
S*:Statistically significant; NS:Non significant			

Table-2: Characteristics of spinal block.

VAS Score			
	Group I	Group II	p value
15 min	0.0 ± 0.0(0,0)	0.0 ± 0.0(0,0)	-
30 min	0.0 ± 0.0(0,0)	0.0 ± 0.0(0,0)	-
1 hour	0.0 ± 0.0(0,0)	0.0 ± 0.0(0,0)	-
4 hours	3.7 ± 1.2(1,6)	1.8 ± 1.2(0,4)	0.000 (S*)
8 hours	2.6 ± 2.5(0,7)	5.1 ± 1.7(1,7)	0.000 (S*)
12 hours	2.5 ± 1.1(1,5)	1.9 ± 0.8(1,3)	0.015 (S*)
16 hours	0.9 ± 0.8(0,2)	1.2 ± 0.8(0,2)	0.175 (NS)
24 hours	0.9 ± 0.8(0,2)	0.6 ± 0.8(0,2)	0.082 (NS)
Time from injection to Ist complaint of pain	272.1 ± 39.0 (220,395)	339.7 ± 47.4 (255,505)	0.000 (S*)
S*: Significant; NS: Not significant.			

Table-3: Comparison of pain score and time from injection to first complaint of pain in the two groups.

Side effects					
	Control		Study		p value
	n	%	n	%	
Nausea and Vomiting	3	10.0	4	13.3	0.690 (NS)
Shivering	1	3.3	2	6.7	0.557 (NS)
Pruritus	3	10.0	2	6.7	0.643 (NS)
Respiratory Distress	3	10.0	2	6.7	0.643 (NS)
NS: Not significant.					

Table-4: Comparison of side effects in the two groups.

sensory and motor blockade was significantly prolonged in dexmedetomidine group. The mechanism by which intrathecal α-2 adrenergic agonists prolong the motor and sensory block of local anaesthetic is not clear. It may be an additive or synergistic effect secondary to the different mechanism of action of the local anaesthetic and α-2 adrenergic agonists.[14] The local anaesthetics act by blocking sodium channels, whereas α-2 adrenergic agonists act by binding to pre synaptic C fibres and post synaptic dorsal horn neurons. Intrathecal α-2 adrenergic agonists produce anaesthesia by depressing the release of C fibre transmitters and by hyperpolarisation of post synaptic dorsal horn neurons.[15] This antinociceptive effect may explain the prolongation of sensory block while prolongation of the motor block of spinal anaesthetics may result from the binding of α-2 adrenergic agonists to motor neurons in dorsal horn.[16]

Our results are in accordance with the study conducted by Mohammad M Al Mustafa et al[17] in which they found that dexmedetomidine has a dose dependent effect on the regression of sensory and motor block when used as an adjuvant to bupivacaine in spinal anaesthesia. Subhi M. Al Ghanem[10] and colleagues compared the duration of sensory and motor block between the two groups receiving dexmedetomidine 5 mcg (D group) and fentanyl 25 mcg (F group).The duration of sensory as well as motor blockade was significantly more in D group as compared to F group. G.E Kanazi[18] also showed prolonged sensory and motor blockade in dexmeditomidine group as compared to clonidine group and reported that dexmedetomidine affinity to α-2 adrenoceptor agonists is 10 times more as compared to clonidine.

The duration of analgesia was 339 ± 47 minutes in dexmedetomidine group compared to 272 ± 39 minutes in plain bupivacaine group. The analgesia provided by addition of dexmedetomidine not only covered intraoperative period but also extended to postoperative period and the demand of rescue analgesia in first 24 hours was much reduced. The quality of intra-operative anaesthesia as well as postoperative analgesia was better in the study group. It is thought that intrathecal dexmeditomidine produces its analgesic effect by inhibiting the release of C- fibre transmitters and by hyperpolarisation of post synaptic dorsal horn neurons.[15] Intrathecal α-2 receptor agonists have been found to have antinociceptic action for both somatic and visceral pain.[10]

Our results are comparable to the study conducted by Mohammad AA[19] who reported that dexmeditomidine 5 mcg given intrathecal improves quality and the duration of postoperative analgesia and also provides an analgesic sparing effect in patients undergoing major abdominal cancer surgeries. Rajni Gupta et al[20] in her study reported that 5 mcg dexmeditomidine is an excellent alternative as an adjuvant to spinal ropivacaine in long surgical procedures with excellent quality of postoperative analgesia with minimal side effects. Subhi Al Ghanem[10] also reported a statistically significant analgesic effect of intrathecal dexmeditomidine when compared to intrathecal fentanyl bupivacaine combination.

The average maximum level of sensory block achieved was comparable between dexmedetomidine and control group. The time taken to reach the highest sensory level was significantly lower in study group. The onset of grade III motor block was also found to be less in study group. Kim et al[21] observed that the patients in dexmedetomidine group demonstrated a shorter time to reach the peak sympathetic and sensory block level compared to patients in control group.

Subhi Al Ghanam et al[10] observed that the onset of bromage 3 motor block and time taken to achieve peak sensory level was not different between dexmeditomidine and fentanyl group. The possible explanation may be that we used a higher dose of

dexmedetomidine and we injected a large volume of drug into the subarachnoid space.

The hemodynamic variables were comparable between the two groups. Two patients in dexmedetomidine group and one patient in control group developed bradycardia requiring treatment with atropine 0.6 mg, however the difference was statistically insignificant. There was no significant difference when systolic and diastolic BP was compared between the two groups. Intrathecal dexmedetomidine did not potentiate the effect of bupivacaine on blood pressure. This may be explained by the mechanism that, local anaesthetics affect the blood pressure by decreasing sympathetic outflow. Sympathetic blockade produced by bupivacaine is nearly maximum.[22] This might explain the observation that 150 mcg of clonidine added to a high dose of bupivacaine (15 mg or more) did not decrease the blood pressure compared with bupivacaine alone[6] but when added to a small dose of bupivacaine[22] (5mg) or used alone as a sole analgesic[5,23] resulted in a greater reduction in blood pressure in comparison to bupivacaine alone or saline respectively. Our results are in agreement with study conducted by Hala EA et al,[24] who found that adding 10 micrograms or 15 micrograms of dexmeditomidine to 15 mg of bupivacaine didn't have any significant effect on blood pressure or heart rate.

While comparing the sedation scores, we observed a statistically insignificant difference between the study and control group. α-2 agonists produce sedative effect by acting on alpha adrenergic receptors in locus coeruleus.[25] The lack of increase in the sedation scores is in agreement with the study conducted by Mohammad M. Al Mustafa[17] who utilised 10 micrograms of intrathecal dexmeditomidine for TURP patients, and all the patients in the study as well as control group had sedation score of 2. The study conducted by G.E Kanazi[18] also reported no statistically significant difference in sedation score.

Our results are contradictory to the study conducted by Hala EA et al,[24] who found that intrathecal dexmeditomidine has a dose dependent sedative effect. They reported that sedation scores were significantly higher when 15 micrograms of dexmedetomidine were used. The results may be attributed to its systemic absorption and vascular redistribution to higher centres or cephalad migration in CSF. The sedation scores were statistically insignificant, when they used 5 and 10 micrograms of dexmedetomidine. This may explain the probable reason of low sedation scores in our study.

A potential limitation of our study was that we used a set dose (10 mcg) of dexmedetomidine, though different doses need to be compared so that an optimal dose could be obtained with excellent quality of intraoperative anaesthesia and postoperative analgesia with minimal side effects. Also prolonged duration of motor blockade may be undesirable for short term surgical procedures.

CONCLUSION

To conclude 10 mcg dexmeditomidine as an adjuvant to intrathecal bupivacaine provides good quality of anaesthesia, prolonged analgesia, hemodynamically stable conditions with minimal side effects. We endorse its use especially when prolongation of spinal anaesthesia is desired where it can replace epidural or general anaesthesia.

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Source of Support: Nil; **Conflict of Interest:** None

Submitted: 23-12-2016; **Published online**: 03-02-2017