International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Dexmedetomidine as an Intrathecal Adjuvant in Spinal Anaesthesia: A Study

N Ratan Singh[1], Alem O Wapang [2], S Sarat Singh[3]

[1]Associate Professor, [2]PGT, [3]Professor;
Department of Anesthesiology, Regional Institute of Medical Sciences, Imphal, India.

Corresponding Author: N Ratan Singh

Received: 24/07/2015 *Revised: 13/08/2015* *Accepted: 14/08/2015*

ABSTRACT

Background: This study was conducted to evaluate the effect of 10 µg dexmedetomidine as intrathecal adjuvant in bupivacaine spinal anesthesia in terms of the onset and duration of sensory and motor blockade.
Methods: In this prospective, randomized, double-blinded study, 60 (sixty) patients undergoing elective lower abdominal and lower limb surgeries under spinal anaesthesia were randomly allocated into two groups to receive: Group D (n=30): 2.5ml (12.5mg) hyperbaric bupivacaine 0.5% plus 0.1ml (10µg) dexmedetomidine intrathecal and Group C (n= 30): 2.5ml (12.5 mg) hyperbaric bupivacaine 0.5% plus 0.1ml preservative free normal saline. Then, the onset and duration of sensory and motor blockade as well the side effects were studied and statistically analysed.
Results: The mean sensory onset time to reach T10 in Group D vs. Group C was 2.53±0.57 vs. 4.10±0.55 min ($p < 0.001$), and time to modified Bromage 3 was 3.60±0.62 vs. 5.37±0.56 respectively ($p < 0.001$). The difference in the motor regression to Modified Bromage 0 in both groups was significant ($p<0.001$) and the time to first analgesic request (TFAR-min) in the group D vs. Group C was 356.50±30.82 min vs. 158.00±12.42 min. ($p<0.001$). Haemodynamic stability was observed in the intraoperative period with only two cases of hypotension in group D and one case in group C ($p=2.069$) , and no significant side effects were observed in both the groups.
Conclusion: Considering the early onset and prolonged duration of sensory and motor block without associated significant hemodynamic changes, 10 µg intrathecal dexmedetomidine is an attractive adjuvant in spinal anesthesia.

Key words: Spinal anesthesia, bupivacaine, adjunct, dexmedetomidine.

INTRODUCTION

Spinal anesthesia is one of the most reliable and effective anaesthetic procedures for a variety of surgeries. However, it has the drawbacks of shorter duration of block and lack of postoperative analgesia. The 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. [1]

Intrathecal α2-receptor agonists are found to have antinociceptive action for both somatic and visceral pain. [2] In anesthetic practice, most clinical studies about

intrathecal a-2 adrenoreceptor agonists as adjuvants are related to clonidine. Dexmedetomidine, a highly selective α2-adrenergic agonist, has been used for premedication and as an adjunct to general anaesthesia. It reduces opioid and inhalational anaesthetics requirements. [3] It has been used intrathecally in animals and was found to be a very potent antinociceptive agent when given to rats. [2,4] Dexmedetomidine has been found to prolong analgesia when used as an adjuvant to local anaesthetics for subarachnoid block, epidural and caudal epidural blocks. Doses varying from 3 to 15 μg have been used as adjuvant to bupivacaine for spinal anaesthesia; however, there is no proper consensus regarding the dose of drug to be used for neuraxial blocks. [5] It provides stable hemodynamic conditions, good quality of intraoperative and prolonged postoperative analgesia with minimal side effects. [6-8] Intrathecal small dose of dexmedetomidine (3 μg) used in combination with bupivacaine in human beings for spinal anaesthesia have been shown to produce a shorter onset of motor block and a prolongation in the duration of motor and sensory block with haemodynamic stability and lack of sedation. [8]

Some workers observed that use of dexmedetomidine is associated with a decrease in heart rate and blood pressure. [9] This study was conducted to evaluate the effect of 10 μg dexmedetomidine as intrathecal adjuvant in bupivacaine spinal anesthesia in terms of the onset and duration of sensory and motor blockade as well the side effects in patients undergoing lower abdominal and lower extremity surgeries.

MATERIALS AND METHODS

In this prospective, randomized, double-blinded study, 60 (sixty) patients of ASA [10] physical status I and II aged 18-60 years of both sexes, scheduled for elective lower limb surgeries under spinal anaesthesia were included after obtaining informed written consent and institutional ethical committee approval. Based on previous studies, [1] it was calculated that a sample size of 30 patients would be required per group to demonstrate a clinically significant difference among the groups, at $\alpha = 0.05$ with a power $(1-\beta)$ of 80%.

Patients were randomly allocated into two groups by a computer generated randomization chart to receive the drugs during the study as follows: Group D (n=30): received 2.5ml (12.5mg) hyperbaric bupivacaine 0.5% plus 0.1ml(10μg) dexmedetomidine intrathecal and Group C (n=30): received 2.5ml (12.5 mg) hyperbaric bupivacaine 0.5% plus 0.1ml preservative free normal saline intrathecal as control.

Exclusion criteria were-infection at the site of injection, post spinal surgeries, spinal deformity, neurological disorder, coagulopathy, hypovolemia or bradycardia, hypertension, patients on adrenergic receptor blockers, history of hypersensitivity to the study drugs, refusal by the patient.

On arrival in the operating room, preloading was done with lactated Ringer's solution (15mL/kg) after pre-anaesthetic evaluations. The patients were monitored with electrocardiogram (ECG), pulse oximetry (SpO2) and non-invasive blood pressure (NIBP). Under full aseptic conditions in the sitting position, lumbar puncture was performed at the level of L3-L4 through a midline approach using a 25-gauge Quincke spinal needle (Spinocan, B Braun Medical, Melsungen, Germany). The investigator performing the block and collecting the data was blinded to the study drug. After performing the spinal block, patients were positioned in the supine position and received 4L/min of oxygen via a face mask. The heart rate, mean arterial blood pressure and oxygen saturation were

monitored in the baseline and every 15 minutes until the end of surgery.

The time of intrathecal injection was taken as time "0" (zero) ; the sensory block levels were assessed bilaterally by pin-prick sensation using a blunt 25-guage needle along the mid-clavicular line every 2 minutes until the highest level had stabilized for four consecutive tests, and then every 10 minutes until the point of two segment regression of the block. Further testing was performed at 30 minutes interval until the recovery of S1 dermatome. The time to reach the T10 dermatome sensory block, the peak sensory block level, a two-dermatome regression and sensory regression to the S1 dermatome were recorded.

Motor blockade were assessed by using the Modified Bromage Scale: [11] (Bromage 0-able to move hip, knee and ankle; Bromage 1-unable to move the hip, but is able to move the knee and ankle; Bromage 2-unable to move the hip and knee but is able to move the ankle; Bromage 3-unable to move the hip, knee and ankle). Motor blockade were assessed every 2 min. before the onset of the surgery and then every 15 minutes thereafter. The times to reach modified Bromage 3 motor blockade and regression to modified Bromage Scale 0 were noted.

Intraoperative side-effects like nausea/vomiting, hypotension, bradycardia or respiratory depression and shivering were recorded. Hypotension, defined as a decrease in systolic blood pressure >30% from baseline values, was corrected with fluids or injection mephentermine intravenously.

The parameters were recorded and statistical analysis was performed using statistical package for social sciences (SPSS) version 16.0 for windows and compared between the groups using chi square test for categorical variables, independent't' test for continuous variables wherever appropriate; p-value of < 0.05 was considered statistically significant.

RESULTS

The demographic profile viz. patients' age, sex, weight, height and ASA physical classification were similar and no significant difference ($p>0.05$) was observed between the groups (Table 1).

As shown in Table 2, The mean sensory onset time to reach T10 in Group D vs. Group C was 2.53±0.57 vs. 4.10±0.55 min respectively ($p <0.001$), and the motor onset to modified Bromage 3 was 3.60±0.62 vs. 5.37±0.56 respectively ($p <0.001$). The time to reach peak sensory block (TPSBL) and the time to two segment regression (TTSR) in group D and group C were 9.83±1.23 min vs. 13.07±1.36 min ($p <0.001$); and 132.33±12.51 min vs. 97.67±10.06 min respectively (($p <0.001$). The difference in the motor regression to Modified Bromage 0 in both groups was significant and the time to first analgesic request (TFAR) in the group D vs. Group C was 356.50±30.82 min vs. 158.00±12.42 min. ($p<0.001$).

Table 3, shows the incidence of various side effects in the two groups such as nausea, vomiting, respiratory depression, shivering and any need for intraoperative analgesic supplementation. There were two cases hypotension in group D and one case of hypotension in the control group (2/30 vs. 1/30; $p=2.069$) were observed. Shivering was seen as a side effect in a case in the control group (1/30; $p=2.02$).

The patients in both the groups remained haemodynamically stable intraoperatively and no significant changes were observed in the heart rate and mean arterial pressure at different time intervals in both the groups (Fig. 1).

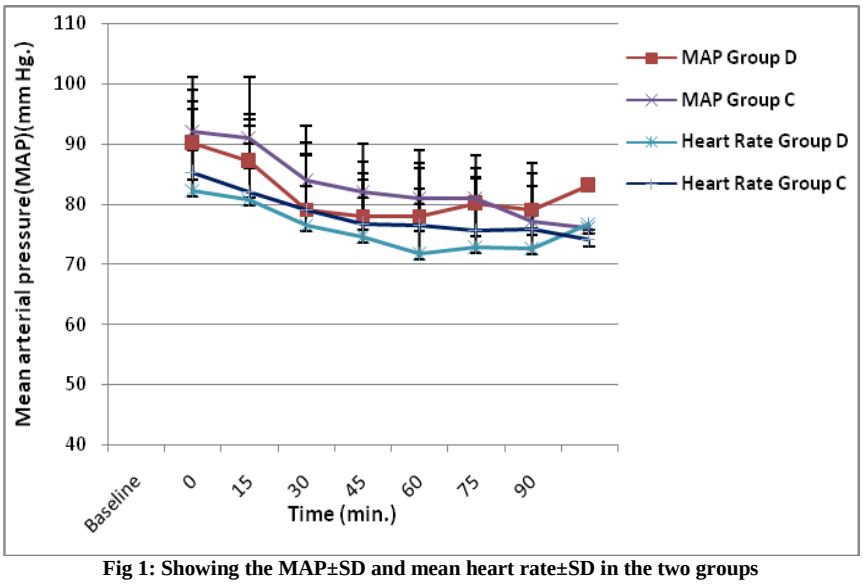

Fig 1: Showing the MAP±SD and mean heart rate±SD in the two groups

Table 1: Demographic profile

Parameters	Group D (n=30) (Mean±SD)	Group C (n=30) (Mean±SD)	p-value
Age (years)	35.93±14.38	34.80±10.82	0.731
Sex(M: F)	10:20	12:18	0.721
Weight (kg)	53.90±7.55	54.30±8.60	0.849
Height (cm)	160.67±5.85	159.40±6.34	0.425
ASA (I:II)	26:4	27:3	0.894

Table 2: Showing the characteristics of the spinal block in the groups.

Parameters	Group D (n=30) (mean±SD)	Group C (n=30) (mean±SD)	*p value*
Sensory onset to reach T_{10}(min.)	2.53±0.57	4.10±0.55	<0.001
Motor onset to modified Bromage 3(min.)	3.60±0.62	5.37±0.56	<0.001
Peak sensory block level(PSBL*)	T4-4;T512; T6-11; T7-3;T8-0	T4-0;T5-; T6-18; T7-6;T8-1	0.032
Time to peak sensory block(TPSBL-min)**	9.83±1.23	13.07±1.36	<0.001
Time to two segment regression(TTSR-min)***	132.33±12.51	97.67±10.06	<0.001
Sensory regression to S_1(min)	339.00±21.06	175.50±11.25	<0.001
Motor regression to Modified Bromage 0	306.50±19.57	148.50±12.05	<0.001
Time to first analgesic request(TFAR-min)****	356.50±30.82	158.00±12.42	<0.001

(p <0.05, considered significant)* PSBL- peak sensory block level;** TPSBL- time to peak sensory block level;***TTSR-Time to Two Segment Regression;****TFAR -Time to First Analgesic Request

Table 3: Side effects

Side effects	Group D (n= 30)	Group C (n= 30)	p value
Bradycardia	0	0	NA
Hypotension	2(6.7%)	1(3.3%)	2.069
Nausea	0	0	NA
Vomiting	0	0	NA
Respiratory depression	0	0	NA
Shivering	0	1(3.3)	2.02

DISCUSSION

The mechanism of prolongation of the motor and sensory block of local anaesthetics by intrathecal a2-adrenoceptor agonists like dexmedetomidine is not well understood. The mechanism may be an additive or synergistic effect secondary to the different mechanisms of action of the

local anaesthetic and the a2-adrenoceptor agonist. Several workers are of the opinion that a2-adrenoceptor agonists act by binding to pre-synaptic C fibers and post-synaptic dorsal horn neurons and the local anaesthetics act by blocking sodium channels. Intrathecal a2-adrenoceptor agonists produce analgesia by depressing the release of C-fiber transmitters and by hyperpolarization of post-synaptic dorsal horn neurons. [12-16]

In a study by Kanazi et al. [8] who used 3 μg of dexmedetomidine, the mean times to reach T10 sensory block was 9.7 ± 4.2 min in the control group compared to 8.6 ± 3.7 min in group D; while the time to reach Bromage 3 motor block was 13.2 ± 5.6 min in group D and 20.7 ± 10.3 min in the control group. However, the sensory onset to reach T_{10} (min) and the motor onset to modified Bromage 3(min) were 2.53±0.57 min and 3.60±0.62 respectively in dexmedetomidine group in our study, which could be explained by the difference in the dose of the dexmedetomidine in these studies. Interestingly, Al-Mustafa et al. [7] studied isobaric bupivacaine with 10 μg intrathecal dexmedetomidine, and observed that the mean time of sensory block to reach the T10 dermatome was 4.7 +/- 2.0 min and the mean time to reach Bromage 3 scale was 10.4 +/- 3.4 min. This may be due to the difference in the baricity of the bupivacaine in their study.

In our study, the sensory regression to S_1 (339.00±21.06 min.) and motor regression to Modified Bromage 0 (306.50±19.57min.) and TFAR (356.50±30.82min.), were significantly longer compared to the control group ($p<0.001$). These may be favourably compared with the findings of Eid et al. [17] where intrathecal 10 μg of dexmedetomidine provided significant increase in the sensory and motor block of spinal anesthesia in addition to prolonged postoperative analgesia.

Some workers observed that use of dexmedetomidine is associated with a decrease in heart rate and blood pressure. [9] However, studies conducted by Al-Ghanem et al. [6] and Al-Mustafa et al. [7] revealed prolongation of spinal block by intrathecal 5 μg and 10 μg dexmedetomidine with no significant effect on blood pressure or heart rate. The findings were in concurrence with those of our study where no changes in the haemodynamics were observed. Similar observations were also made by Kanazi et al. [8] who observed that the addition of dexmedetomidine or clonidine to bupivacaine did not cause a significant decrease in the blood pressure intra-operatively or post-operatively.

No significant side effects were observed in the present study other than two (2) cases of hypotension in group D and a case in the control group. Similar observations were made by Shukla et al. [1] Intrathecal local anaesthetics block the sympathetic outflow and reduce the blood pressure and the sympathetic block is usually near-maximal with the doses used for spinal anesthesia. The addition of a low dose of α_2-agonist to a high dose of local anaesthetics does not further affect the near-maximal sympatholysis. [12] Interestingly, Gupta et al. [18] observed only two cases of bradycardia (HR <50/ min) in dexmedetomidine group (5 μg). The absence of shivering as side effect in the dexmedetomidine in the present study could be because of the anti-shivering properties of α2-adrenergic agents. [19]

CONCLUSION

Considering the early onset and prolonged duration of sensory and motor block without associated significant hemodynamic changes, 10 μg intrathecal dexmedetomidine is an attractive adjuvant in

spinal anesthesia. However, further studies may be taken up using varied doses of intrathecal dexmedetomidine.

REFERENCES

1. Shukla D, Verma A, Agarwal A, Pandey HD, Tyagi C. Comparative study of intrathecal dexmedetomidine with intrathecal magnesium sulphate used as adjuvants to bupivacaine. J Anaesthesiol Clin Pharmacol.2011; 27(4): 495-99
2. Kalso E, Poyhia R, Rosenberg P. Spinal antinociception by dexmedetomidine, a highly selective a2 –adrenergic agonist. Pharmacol Toxicol.1991; 68:140-43.
3. Martin E, Ramsay G, Mantz J, Sum-Ping ST. The role of the alpha2-adrenreceptor agonist dexmedeto-midine in post-surgical sedation in the intensive care unit. J Intensive Care Med. 2003; 18:29-34.
4. Asano T, Dohi S, Ohta S, Shimonaka H, Iida H. Antinociception by epidural and systemic alpha 2 adrenoreceptor agonists and their binding affinity in rat spinal cord and brain. Anesth Analg.2000; 90:400-7.
5. Sudheesh K, Harsoor SS. Dexmedetomidine in anaesthesia practice: A wonder drug? Ind J Anesth 2011; 55(4):323-24.
6. Al-Ghanem SM, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM, Abu-Ali HM. Effect of Adding Dexmedetomidine versus Fentanyl to Intrathecal Bupivacaine on Spinal Block Characteristics in Gynecological Procedures: A Double Blind Controlled Study. Am J Appl Sci 2009;6:882-7.
7. Al-Mustafa MM, Abu-Halaweh SA, Aloweidi AS, Murshidi MM, Ammari BA, Awwad ZM, et al. Effect of dexmedetomidine added to spinal bupivacaine for urological procedure. Saudi Med J. 2009; 30:365-70.
8. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al Jazzar MD, Alameddine MM, Al-Yaman R, et al. Effect of low-dose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block. Acta Anesthesiol Scand. 2006; 50:222-7.
9. Venn RM, Grounds RM. Comparison between dexmedeto-midine and propofol for sedation in the intensive care unit: Patient and clinician perceptions. Br J Anaesth. 2001; 87:684-90.
10. Fischer SP, Bader AM, Sweitzer B. Perioperative evaluation, In: Miller RD, editor. Miller's Anesthesia 7th ed. Philadelphia: Churchill Livingstone Elsevier; 2010.p.1002.
11. Bromage PR. A comparison of the hydrochloride and carbon-dioxide salts of lidocaine and prilocaine in epidural analgesia. Acta Anaesthesiol Scand 1965; 16: 55-69.
12. Eisanach JC, De Kock M, Klimscha W. α2 adrenergic agonists for regional anesthesia. Anesthesiology 1996; 85: 655-74.
13. Lawhead RG, Blaxall HS, Bylund BD. Alpha-2A is the predominant α-2 adrenergic receptor subtype in human spinal cord. Anesthesiology 1992; 77: 983-91.
14. Smith MS, Schumbra UB, Wilson KH et al. Alpha 2 adrenergic receptor in human spinal cord: specific localized expression of mRNA encoding alpha-2 adrenergic receptor subtypes at four distinct levels. Brain Res 1995; 34: 109-17.
15. Yaksh TL, Jage J, Takano Y. Pharmacokinetics and

pharmacodynamics of medullar agents. The spinal actions of α -2 adrenergic agonists as analgesics. In: Atikenhead, AR, Benad, G, Brown, BR, editors. Baillieres Clinical Anaesthesiology.Vol.7.No.3. London: Bailliere Tindall; 1993:597-614.
16. Fairbanke CA, Wilcox GL. Spinal antinociceptive synergism between morphine and clonidine persists in mice made acutely or chronically tolerant to morphine. J Pharmacol Exp Ther 1999; 288: 1107-16.
17. Eid HEA, Shafie MA, Youssef H. Dose-Related Prolongation of Hyperbaric Bupivacaine spinal anesthesia by dexmedetomidine. Ain Shams J Anesthesiol. 2011; 4(2): 83-95.
18. Gupta R, Verma R, Bogra J, Kohli M, Raman R, and Kushwaha JK. A Comparative study of intrathecal dexmedetomidine and fentanyl as adjuvants to Bupivacaine. Anaesthesiol Clin Pharmacol. 2011; 27(3): 339-43.
19. Talke P, Tayefeh F, Sessler DI, et al. Dexmedetomidine does not alter sweating threshold but comparably and linearly decreases the vasoconstriction and shivering thresholds. Anesthesiology 1997; 87: 835-41.

How to cite this article: Singh NR, Wapang AO, Singh SS. Dexmedetomidine as an intrathecal adjuvant in spinal anaesthesia: a study. Int J Health Sci Res. 2015; 5(9):146-152.

****