A Clinical Study on Effect of Dexmedetomidine Added to Spinal Hyperbaric Bupivacaine in Lower Abdominal Surgeries

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ABSTRACT

Introduction: Spinal anaesthesia is commonly used regional anaesthetic technique all over the world. This study investigates the effect of intrathecal administration of dexmedetomidine added to spinal hyperbaric bupivacaine on the duration of sensory and motor block and postoperative analgesic requirements in lower abdominal surgeries.

Material and Methods: Hundred adult patients posted for lower abdominal surgeries were randomized in two groups. Each patient was given 3.5 ml of drug solution intrathecally that consisted of 3 ml 0.5% hyperbaric bupivacaine and 0.5 ml containing 7.5 µg dexmedetomidine in Group D patients or normal saline in Group B patients. Intraoperative Heart rate, arterial blood pressure, sensory level, motor block, pain and level of sedation were assessed and continued up to 24 hours post spinal anesthesia for any complication during the procedure.

Results: Time to two segment regression, sensory regression to S1, regression of motor block to modified Bromage 0 and time to first rescue analgesic were significantly prolonged in dexmedetomidine group along with significantly decreased postoperative pain scores.

Conclusion: Intrathecal dexmedetomidine in doses of 7.5µg significantly prolong the anesthetic and analgesic effects of spinal hyperbaric bupivacaine.

Keywords: spinal anesthesia, adjuvant, dexmedetomidine, hyperbaric bupivacaine, lower abdominal surgeries

INTRODUCTION

Lower abdominal surgeries commonly performed under spinal anesthesia technique because of its rapid onset, less failure rates and cost effectiveness, but it has shorter duration of action and not much effective in view of postoperative analgesia. Many intrathecal adjuvents has been tried in past with the aim of prolonging the duration of block and to solve the purpose of post-operative analgesia. Clonidine an α2-adrenoreceptor as intrathecal adjuvent has been effectively used to increase the duration of spinal anesthesia using hyperbaric bupivacaine.1-3 Kanazi et al found that 3 µg dexmedetomidine and 30 µg clonidine are equipotent intrathecally when added to bupivacaine in patients undergoing urologic procedures. Dexmedetomidine is an α methylol derivative with a higher affinity for α2-adrenoreceptor than clonidine which has been started to be used as adjuvant to intrathecal hyperbaric bupivacaine.4-6 In humans the largest intrathecal dose used was 10 µg.6 In our institute we conducted a pilot study in which we used different doses of dexmedetomidine and came to a conclusion that 7.5µg will be appropriate for our study population. This prospective randomized double blinded controlled trial was aimed to investigate the effects of adding dexmedetomidine 7.5 µg to hyperbaric bupivacaine in patients scheduled for elective lower abdominal surgeries. The aim of the study was to determine the time to two segment sensory regression of spinal anesthesia. Time to sensory block to reach T10, sensory regression to S1, motor regression to modified Bromage scale 0, time to first rescue analgesic, verbal rating pain scores, sedation scores, postoperative analgesic use and occurrence of adverse effects were the objectives.

MATERIAL AND METHODS

The study was done after receiving the approval of the ethical-cum-screening committee and written informed consent was taken from all patients before initiation of the procedure. Using statistical formula appropriate for the design of the study as advised by statistician, 100 patients between age group 18 to 65 years with ASA physical status I and II undergoing elective lower abdominal surgeries were included as study population. Patients with ASA grading > 2, body mass index ≥30,hypersensitivity to any of the drugs which are to be used in the study, with contraindications for spinal anaesthesia were excluded from the study. All patients were randomly allocated into two equal groups (n=50). All the patients received equal volume of drug (3.5ml) containing 3 ml (15mg) hyperbaric bupivacaine hydrochloride. The study group [Group D (n=50)] received dexmedetomidine 7.5 µg in 0.5 ml 0.9% saline along with hyperbaric bupivacaine. The control group [Group "b"(n=50)] received an identical volume of 0.9% saline added to bupivacaine. On the preceding day of operation, relevant history and informed consent of the patient were taken and visual analogue scale was explained. All the patients were advised for overnight fasting. After arrival in the operating room, patient's identity and informed consent form were checked and all requisite monitors were attached. Preloading was done with Ringer Lactate solution (20ml/kg body weight) 30 minutes before the intrathecal drug administration to all patients. Premedication with pantoprazole and ondansetron were given. ECG, pulse oximetry, and non-invasive blood pressure were monitored and baseline values were recorded at the initiation of the procedure. Lumbar puncture was performed at L3-L4 interspace or L4-L5 interspace if it is difficult through a midline approach using a 25-gauge Quincke needle in sitting posture. All patients then laid on their back in supine position and received oxygen at 2L/

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minute through nasal prong. Surgeons then allowed to position the patients according to their convenience. After 2 minutes, every 2 minutes sensory nerve block was assessed bilaterally by using insensitivity to cold (when cotton swab soaked with alcohol was applied) in the midclavicular line. Motor blockade was assessed by using the modified Bromage scale bilaterally every 2 minutes. The intraoperative vitals that is heart rate (HR), NIBP and oxygen saturation were monitored and recorded at 15 minutes interval intraoperatively and 30 minutes interval postoperatively for next 8 hours. Any side effects in the form of severe hypotension, bradycardia, respiratory depression (SpO_2 <94%), nausea, vomiting, dizziness were also recorded. Systolic BP less than 90 mm of Hg was regarded as hypotension and treated with intravenous bolus administration of 500ml of Ringer Lactate over 10 minutes and if needed intravenous 3mg Mephenteramine and its multiplying doses were given accordingly. Bradycardia was defined as heart rate less than 50/minute and was treated with 0.6mg intravenous atropine. Intravenous midazolam at the dose of 0.5mg/kg was allowed if the patient is anxious. Time to reach T10 sensory block level, peak sensory block level, time to reach peak level of sensory block and time to achieve Bromage 3 motor block were recorded before surgery. The regression for sensory level by pin prick and motor block by Bromage scale was checked every 15 minutes in a post anaesthesia care room. Time of 2 sensory segment regressions from peak level, time to regress to S1 level, time to regain Bromage score 0 and time for 1st analgesic request were recorded. The level of sedation was evaluated intraopertively at 15 minutes interval and postoperatively at 30 minutes interval using Agitation scale. Durations were calculated from the point of intrathecal drug administration. Patients were discharged from the post anaesthesia care room after sensory block regresses to S1 dermatome level and motor block to Bromage 0. No analgesic drug was given in the immediate post-operative period until the patient requested for analgesia and time for first analgesia will be recorded. Intramuscular diclofenac sodium 1mg/kg body weight were used as rescue medication when patient complains of pain (VAS≥3). Any incidence of adverse effects in the intraoperative or immediate postoperative period were noted and again patients were followed up at 24 hours in the ward for incidence of nausea, vomiting or any other adverse

reaction. Postoperative nausea and vomiting was treated with 4mg of intravenous ondansetron as and when necessary.

STATISTICAL ANALYSIS

Data analysis was done using SPSS version 21 (Statistical Packages for the Social Sciences). N and median were used to represent Discrete categorical data whereas continuous data as mean ± Standard deviation. Differences in demographic, anaesthetic and post-operative data were tested by independent Student's t-test (continuous data) or by Chi-square test (categorical data). Most of collected data were of normal distribution and student 't' test was applied on them for statistical analysis. A p value less than 0.05 is taken as significant.

RESULTS

Demographic parameters (age, weight, height, sex ratio), ASA physical status, time to achieve T10 sensory block, time to achieve peak sensory block level, time to achieve Bromage 3 motor block were comparable between two groups with all insignificant p value (table-1).

Time taken by group B patients for 2 sensory segment regressions from the peak level was 88.38±6.21 minutes whereas in group-D patients this time was much higher with 133.58±18.8. The difference was significant as shown by unpaired student 't' test and the p value was <0.0001 which is extremely statistically significant. So it can be said that dexmedetomidine prolongs the 2 segment regression time when added with hyperbaric bupivacaine as an adjuvant (table-2).

Time taken by group-B patients for regression to S_1 segment level was 232.64±13.49 minutes. In group-D patients this time was higher (328±26.64 minutes).The parameters were compared with unpaired student 't' test and the two tailed p value was <0.0001. This difference is certainly statistically significant. So it can be said that dexmedetomidine prolongs the time for regression to S_1 level (table-3).

Group-B patients took 184.2±6.65 minutes to regain Bromage score 0 and group-D patients took 281±14.03 minutes (table-4). Unpaired student 't' test was done and p value was <0.0001 which is which is considered to highly statistically significant. So group-D patients took significantly longer time than group-B patients to regain Bromage 0 score. This concludes that motor blockade was also prolonged in dexmedetomidine group than in

	Group B	Group D	p value
Age(years)	42.86 ± 10.35	39.9 ± 8.41	0.119
Weight(kgs)	59.28 ± 6.67	58.52 ± 5.77	0.543
Height(cms)	155.82 ± 5.92	156.98 ± 5.39	0.308
Sex(male/female)	25/25	25/25	1
ASA(I/II)	38/12	34/16	0.504
Time to achieve T10 sensory block	5.8±2.4	6±1.5	0.618
Time to achieve peak sensory block level	13.5±1.4	13.9±1.5	0.171
Time to achieve Bromage 3 motor block	7.84±2.23	7.42±1.84	0.306
Table-1: Demographic parameters, asa status, time to achieve t10, peak sensory block level, bromage 3 motor block			

Time of 2 segment regression from peak level				
Group B		Group C		p Value (Student 't' test)
Mean	Std. dev.	Mean	Std. dev.	<0.0001
88.38	6.21	133.58	18.8	
Table-2: Two segment regressions from peak level				

Regression of spinal anaesthesia				
Group B		Group D		p Value (Student 't' test)
Mean	Std. dev.	Mean	Std. dev.	<0.0001
232.64	13.49	328.65	26.64	
Table-3: Time to regress to s_1 segment				

bupivacaine only group.

Similarly, the duration of analgesia was significantly different among the groups. Group D had a significantly longer time to first analgesic requirement than group B. On an average group-B patients required inj. diclofenac sodium after 157.7±9.32 minutes whereas group-D patients requested it much later i.e. after 253.3±8.18 minutes (table-5). When compared with unpaired student 't' test this difference was extremely significant with a very low p value of <0.0001. So the conclusion is that dexmedetomidine when used as an adjuvant with hyperbaric bupivacaine it increases the time of post-operative analgesia.

The incidences of different side effects were low in the perioperative period up to a period of 24 hours and they were comparable between all the groups (table-6). The data was compared with fisher's exact probability test and p values were all very high i.e. statistically Insignificant.

DISCUSSION

$\alpha2$-agonist when administered via intrathecal route produces an analgesic effect in postoperative pain without causing significant sedation. It is considered to be due to the sparing of supraspinal CNS sites which causes profound analgesia without significant sedation. Most of the clinical studies has used clonidine as intrathecal $\alpha2$- adrenoceptor agonists and concluded a synergetic effect with local anaesthetics[7,2,8,9]

Dexmedetomidine is also an $\alpha2$-adrenoreceptor agonist which has about ten times higher affinity for $\alpha2$-adrenoreceptor than clonidine.[10,11] Intrathecal dexmedetomidine produces its analgesic effect by inhibition of C-fibers transmitters release together with hyperpolarization of post-synaptic dorsal horn neurons.[12] The prolongation of motor effect might be caused by direct impairment of excitatory amino acid release from spinal interneurons.[13]

Intrathecal 5 μg and 10 μg dexmedetomidine were used in previous studies with insignificant effect on blood pressure or heart rate.[14,15] $\alpha2$ agonists produce sedative effect by acting on $\alpha2$-adrenergic receptors in locus ceruleus.[12,11] It is unlikely for intrathecal 7.5 μg of dexmedetomidine to produce significant increase in sedation score as a previous study which used 10 μg of intrathecal dexmedetomidine in patients undergoing transurethral resection of prostate was unable to do the same.[14]

In our study we compared the duration of sensory and motor block in the two groups of patients, Group B was given Intrathecal bupivacaine alone and group D was given intrathecal bupivacaine plus dexmedetomidine. Intrathecal 7.5 μg of dexmedetomidine provided significant increase in the sensory and motor block of spinal anesthesia in addition to prolonged postoperative analgesia. Highest dose of intrathecal dexmedetomidine used in animal studies was 100 μg.[16] Konakci and colleagues[17] reported white matter injury in rats when high dose epidural dexmedetomidine (6μg/kg) was used alone; however, subsequently Brummett and coworkers[18] demonstrated no injury and a protective effect when doses of 26-40 μg/kg were used perineurally.

In humans the largest epidural dose used was 2μg/kg[19] and the largest intrathecal dose used was 10 μg[14] though neurological adverse events have not been reported. The population involved includes young otherwise healthy patients and the effect in older patients with cardiovascular comorbidities are yet to

Time to regress to bromage 0 motor block				
Group B		**Group D**		**p Value (Student 't' test)**
Mean	Std. dev.	Mean	Std. dev.	<0.0001
184.2	6.65	281.4	14.03	

Table-4: Time to regress to bromage 0 motor block

Time to first analgesic requirement				
Group B		**Group D**		**p Value (Student 't' test)**
Mean	Std. dev.	Mean	Std. dev.	<0.0001
157.7	9.32	253.3	8.18	

Table-5: Time to first analgesic requirement

Incidence of side effects			
	Group B	**Group D**	**p Value**
Bradycardia	3	5	0.715
Hypotension	3	8	0.199
Nausea and vomiting	3	2	1
Post dural puncture headache	2	3	1
Arrhythmia	0	0	1
Sedation	0	0	1
Respiratory depression	0	0	1

Table-6: Incidence of side effects

be investigated. In our study, the patients administered 7.5μg intrathecal dexmedetomidine reported prolonged duration of sensory and motor block.

Rampal Singh et al[20] in 2012 compared intrathecal clonidine and dexmedetomidine with intrathecal hyperbaric bupivacaine and concluded the higher efficacy of dexmedetomidine to produce longer duration of sensory and motor blockade. They did not find any increase in side effects. Gupta R et al[21] compared the duration of motor and sensory blockade and haemodynamic stability on adding dexmedetomidine with hyperbaric bupivacaine in patients who underwent lower abdominal surgeries and reported similar findings. Our study has shown similar results.

Thus, dexmedetomidine a newer $\alpha2$ agonist seems to be a good adjuvant when added to spinal hyperbaric bupivacaine. Dexmedetomidine with bupivacaine provide prolonged sensory and motor blockade, haemodynamic stability, minimal side effects and excellent intraoperative and postoperative analgesia.

CONCLUSION

Our conclusion from the study is that dexmedetomidine as intrathecal adjuvant significantly prolongs the sensory and motor blockade of intrathecal hyperbaric bupivacaine without altering the onset of spinal anaesthesia. Patients who receive dexmedetomidine had reduced postoperative pain scores and a longer analgesic duration than those who received spinal bupivacaine alone. Also there is no hemodynamic instability or increased side effects when dexmedetomidine is added to spinal hyperbaric bupivacaine.

REFERENCES

1.   Fogarty DJ, Carabine UA, Milligan KR: Comparison of the analgesic effects of intrathecal clonidine and intrathecal morphine after spinal anaesthesia in patients undergoing total hip replacement. Br J Anaesth. 1993;71:661-4.

2. Strebel S, Gurzeler JA, Schneider MC, Aeschbach A, Kindler CH. Small-dose intrathecal clonidine and isobaric bupivacaine for orthopedic surgery: a dose-response study. AnesthAnalg. 2004;99:1231-8.

3. Van Tuijl I, GiezemanMJ,Braithwaite SA, Hennis PJ, Kalkman CJ, van Klei WA. Intrathecal lowdosehyperbaric bupivacaine-clonidine combination in outpatient knee arthroscopy: a randomized controlled trial. ActaAnaesthesiol Scand. 2008;52:343-9.

4. Al-Ghanem S M., Massad IM., Al-Mustafa M M., Al-Zaben K R.,Qudaisat I Y, Qatawneh A M, Abu-Ali H M. Effect of Adding Dexmedetomidine versus Fentanyl to Intrathecal Bupivacaine on Spinal Block Characteristics in Gynecological Procedures: A Double Blind Controlled Study American Journal of Applied Sciences. 2009;6:882-887.

5. Kanazi GE, Aouad MT, Jabbour-Khoury SI, Al JazzarMD,Alameddine MM, Al-YamanR, Bulbul M, Baraka AS. Effect of lowdose dexmedetomidine or clonidine on the characteristics of bupivacaine spinal block.ActaAnaesthesiol Scand. 2006;50:222-7.

6. Al-Mustafa MM, Abu-HalawehSA,Aloweidi AS, MurshidiMM,Ammari BA, Awwad ZM, Al-Edwan GM, Ramsay MA. Effect of dexmedetomidine added to spinal bupivacaine for urological procedures.Saudi Med J. 2009; 30:365-70.

7. Niemi L. Effects of intrathecalClonidine on duration of Bupivacaine spinal anaesthesia, haemodynamics, and postoperative analgesia in patients undergoing knee arthroscopy. ActaAnaesthesiolScand. 1994;38:724–8.

8. Cao JP, Miao XY, Liu J, Shi XY. An evaluation of intrathecal Bupivacaine combined with intrathecal or intravenous Clonidine in children undergoing orthopedic surgery: a randomized double-blinded study. Paediatr Anaesth. 2001; 21:399-405.

9. Gecaj-Gashi A, Terziqi H, Pervorfi T, Kryeziu A. Intrathecal Clonidine added to small dose Bupivacaine prolongs postoperative analgesia in patients undergoing transurethral surgery. Can UrolAssoc J. 2012;6:25-9.

10. Asano Toshio, Dohi Shuji, Ohta, Shuichiro, Shimonaka Hiroyuki, Iida Hiroki. Antinociception by Epidural and Systemic α2¬Adrenoceptor Agonists and Their Binding Affinity in Rat Spinal Cord and Brain. Anesthesia and Analgesia. 2000;90:400-407.

11. Coursin D B, Coursin D B, Maccioli GA. Dexmedetomidine. Current Opinion in Critical Care. 2001;7:221–226.

12. Correa-Sales C, Rabin BC, Maze M. A hypnotic response to dexmedetomidine, an alpha 2 agonist, is mediated in the locus coeruleus in rats. Anesthesiology. 1992;76:948-52.

13. Palmeri A, Wiesendanger M. Concomitant depression of locus coeruleus neurons and of flexor reflexes by an alpha 2-adrenergic agonist in rats: a possible mechanism for an alpha 2-mediated muscle relaxation.Neuroscience. 1990; 34:177-87.

14. 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.

15. Al-Ghanem S M, Massad IM, Al-Mustafa MM, Al-Zaben KR, Qudaisat IY, Qatawneh AM et al. Effect of adding dexmedetomidine versus fentanyl to intrathecal bupivacaine on spinal block characteristics in gynaecological procedures-a double blind controlled study. Am J Applied Sci. 2009;6:882-7.

16. EisenachJ,ShaferS,BucklinB,CarswellJ.Pharmacokinetics and pharmacodynamics of intraspinaldexmedetomidin in sheep. Anesthesiology. 1994; 80:1349—59.

17. Konakci S, Adanir T, Yilmaz G, Rezanko T. The efficacy and neurotoxicity of dexmedetomidine administered via the epidural route. Eur J Anaesthesiol. 2008;25:403-9.

18. Brummett CM, Norat MA, Palmisano JM, Lydic R. Perineural administration of dexmedetomidine in combination with bupivacaine enhances sensory and motor blockade in sciatic nerve block without inducing neurotoxicity in rat. Anesthesiology. 2008;109:502-11.

19. Maroof M, Khan SA, Jain D, Khan RM, Maroof S M. Evaluation of effect of dexmedetomidinee in reducing shivering following epidural anesthesia. Anesthesiology. 2004;101:A495.

20. Singh and shukla: Randomized, controlled study to compare the effect of intrathecal clonidine and dexmedetomidine on sensory analgesia and motor block of hyperbaric bupivacaine. Indian Journal Of Fundamental And Applied Life Sciences. 2012;2:24-33.

21. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kumar S et al. Dexmedetomidine as an intrathecal adjuvant for post-operative analgesia. Indian J Anaesth. 2011;55:347-51.

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