Original Research Article

Indian Journal of Anesthesia and Analgesia
March – April 2020; 7(2): 493–499
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.7220.8

Single-dose Intravenous Dexmedetomidine as an Adjuvant for Prolongation of Spinal Anesthesia

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Abstract

Context: Dexmetedomidine is α_2 agonist used as adjuvant to spinal anesthesia for prolongation of sensory, motor block, postoperative analgesia. *Aims:* To study the effect of single-dose IV dexmetedomidine on hemodynamic profile, sensory-motor block prolongation, sedation. Methods and Material: 100 adult patients of ASA 1 and 2 posted for elective infraumbilical surgery were included. They were randomly divided into 2 groups. Group D received intravenous dexmtedomidine 0.5 μg/kg over 10 min slowly. Group M - 0.5 mg/kg over 10 mins. Both drugs were administered 15 min after spinal anaesthesia with 15 mg 0.5% intrathecal bupivacaine heavy. Vital data, duration of sensory and motor block, sensory regression, Ramsay Sedation score and side effects were evaluated. *Results:* Duration of sensory block in Group D was 308 ± 20 min prolonged than Group M 200 ± 15 min. Duration of two segment regression time in Group D – 140 ± 8 min more than Group M 120 ± 6 min. Ramsay sedation score was slightly more for Group D without any respiratory depression. Patients of both groups remained hemodynamically stable through out with minimal side-effects. *Conclusions:* Intravenous dexmetedomidine significantly augments the sensory and motor block of intrathecal bupivacaine providing excellent sedation.

Keywords: Dexmetedomidine; Midazolam; Motor and sensory block; Sensory regression, Sedation.

How to cite this article:
Divya N Kheskani, Heena S Chhanwal, Meshwa S Desai, et al. Single-dose Intravenous Dexmedetomidine as an Adjuvant for Prolongation of Spinal Anesthesia. Indian J Anesth Analg. 2020;7(2):493–499.

Introduction

Spinal anesthesia is unique form of regional anesthesia where many drugs as adjuvant agents can be added to suppliment and prolong sensory and motor blockade in large no of patients with less amount of drugs undergoing lower abdominal surgeries, sedation plays an important role as it provides anxiolysis and amnesia.[1–4]

In modern era anesthetists are fortunate to have agents that can be used intrathecally or intraveously to augment the duration and efficacy of block and we call them adjuvants. Epinephrine, magnesium sulphate, fentanyl, midazolam, clonidine were used until now and now-a-days dexmetedomidine is trending.

Dexmetedomidine is a selective alpha-2 agonist, newer congener of clonidine and is 8 times more selective. It was first introduced for short-time intensive care unit sedation in 1999. Since, then it is rapidly emerging drug now-a-days as an adjuvant to regional anesthesia, general anesthesia,

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Received on 07.12.2019, **Accepted on** 28.01.2020

MAC, premedication, postoperative sedation and analgesia. it induces cooperative sleep, does not disturb the sleep architecture or respiratory drive, thus proves as an excellent drug for sedation in intubated/nonintubated patients in critical care and icu short procedures.[5] Alpha-2 agonists are being increasingly used as adjuvants as they provide sedation, analgesia, hypnosis and sympatholysis without respiratory depression. Midazolam is among the currently available benzodiazapine with fast onset, short recovery time, hence wildely used sedative in spinal anesthesia and produces good sedation to counter act anxiety of patients.[6]

We conducted this randomized, prospective, double blinded clinical study to study the effect of single dose dexmetedomidine by administering it intravenously in association with spinal anesthesia and compared with midazolam

Materials and Methods

We carried out prospective, double blind randomized study after approval of ethical committee. Written and informed consent was obtained from all the participating patients. We studied 100 adult patients of physical status American Society of Anesthesiologists ASA 1 and 2, of either sex aging from 25 to 60 years posted for elective infraumblical surgeries and randomly allocated into two groups. Patients excluded were, those refusing of giving consent, bleeding diathesis, infection at the puncture site, belonging to ASA 3 and 4 Patients on α_2 adrenergic receptors antagonists, calcium channel blockers, or angiotensin-converting enzyme inhibitors, Patients having cardiac rhythm abnormalities, Any drug allergy, pregnancy, lactating mother, obesity, Any major illness involving RS, CVS or CNS. All contraindication to spinal analgesia including, spinal deformity, patient on anticoagulants, preexisting neurological deficits in lower extremities were excluded. Preanesthesia examination was done preoperatively with a detailed history, general and systemic examinations, airway and back and spine were also examined. All routine laboratory investigations were done. Patients received 0.5 mg alprazolam tablet night prior to surgery and were kept nil by mouth on day of surgery. In the preoperative recovery room, peripheral IV line was secured with 18 g cannula and they were preloaded with 10 ml/kg of ringer lactate solution. Patients were then randomly allocated into either of two groups:

Group D: Intrathecal 0.5% bupivacaine heavy 3 ml, followed by infusion of intravenous dexmedetomidine 0.5 mcg/kg over 10 min.

Group M: Intrathecal 0.5% bupivacaine heavy 3 ml followed by infusion of midazolam 0.05 mg/kg over 10 mins.

Above study drugs were administered,15 min after spinal anesthesia with bupivacaine 0.5% 15 mg (n = 50 per group).

Preparation of Infusion

One ml of injection dexmedetomidine, will be diluted in 19 ml of normal saline; hence, the concentration of the drug in the solution is 5 μg/ml. Similarly for Group M: The infusion will be prepared by diluting 3 ml midazolam in 17 ml normal saline. Total infusion volume for each group is 20 ml.

These infusions were prepared by an independent senior resident who was not involved in the subsequent phases of the study. Thus, both the resident conducting the case as well as the patient were unaware of the assigned group in all the cases.

Standard monitoring was done, which includes noninvasive Blood Pressure (BP), electrocardiography, Heart Rate (HR), and Oxygen (O_2) saturation. All patients were supplemented with 4 L/min of O_2 by simple face (NRBM) mask. Subarachnoid block with 3 ml of 0.5% bupivacaine was performed in the L3–L4 interspace using a 25-gauge Quincke's spinal needle with the patient in sitting position.

After performing the spinal block vital signs were recorded at 0, 5 , 10 ,15 min initially, and every 30 min thereafter, 15 minutes after the subarachnoid block, dexmedetomidine group (Group D) received dexmedetomidine infusion 0.5 μg/kg over 10 min, and group (Group M) received midazolam 0.05 mg/kg (not more than 2.5 mg) infusion over 10 min.

Observations

Following variables were assessed:

Onset, height, duration, and regression of sensory block (two segment regression) by the loss of pinprick sensations. Before giving the study drug or placebo, the sensory level was recorded after giving the study drug Sensory block assessed every 2 min for the first 10 min and thereafter, every 5 min during surgery. In the Postanesthesia Care Unit (PACU), recorded every 15 min for the next 4 h or regression to S1 level, after which the patient

was shifted to the ward. The time of giving the intrathecal injection was considered as zero. Motor block was assessed by modified bromage scale:

0 No paralysis, able to flex hips/knees/ankles;

1 Able to move knees, unable to raise extended legs;

2 Able to flex knees, unable to flex knees;

3 Unable to move any part of the lower limb;

The level of sedation was evaluated using six point Ramsay Sedation Scale (RSS):

1. Patient fully awake and oriented;
2. Patient cooperative, drowsy and tranquil;
3. Patient asleep but responds to oral commands;
4. Asleep, but responds to light glabellar tap;
5. Asleep, sluggish response to light glabellar tap;
6. Asleep, no response.

Postoperative pain was assessed using Visual Analog Scale (VAS), every 15 min until the first analgesic given, and 4 hourly for the next 24 h, rescue analgesia will be given in the form of injection diclofenac sodium 75 mg Intramuscular (IM) when VAS score was more than 3.

For the purpose of this study, hypotension was considered Systolic BP of < 90 mm Hg and treated by foot end elevation, and fluid bolus of 300 to 500 ml. If such hypotension did not respond to this fluid administration, then injection mephentermine 5 mg IV was administered. If it did not respond to two repeated doses of mephentermine, then dopamine infusion was started to maintain the BP. Bradycardia for these cases was defined as HR < 50 beats/min (20% decrease from the baseline), and if persist treated with 0.6 mg of intravenous atropine.

Results

There was no statistically significant difference in all subjects in Group D and Group C with respect to demographic profile that included patients age, sex, height, weight, ASA physical status and duration of surgery, (Table 1).

Table 1: Demographic Data

	Group D	Group M	*p* - Value
Age (years)	43 ± 9.4	42 ± 8.5	0.578
Height (cm)	145 ± 5	147 ± 5.2	0.0528
Weight (kg)	55 ± 5.4	53 ± 6.1	0.085
Duration of Surgery (min)	130 ± 15.4	133 ± 22	0.435
ASA Grade (1:2)	35:15	40:10	NS

The two segment regression time in Group D was 148 ± 8 min and Group M was 120 ± 6 min. with *p* - value being (< 0.0001) statistically highly significant, (Table 2). The duration of motor block was 230 ± 15 min in Group D and 160 ± 10 min in Group M with *p* - value being < 0.0001 statistically highly significant, (Table 2). Total duration of sensory block for Group D was prolonged (308 ± 20 min) than Group M (200 ± 15 min) with *p* - value < 0.0001 and difference is statistically highly significant, (Table 2).

Table 2: Spinal anesthesia parameters

	Group D	Group M	*p* - value
Duration of 2 Segment Regression (min)	148 ± 8	120 ± 6	< 0.0001
Duration of Motor block (min)	230 ± 15	160 ± 10	< 0.0001
Duration of Sensory block (Request for 1^{ST} rescue analgesia) (min)	308 ± 20	200 ± 15	< 0.0001

Sedation score was measured using modified Ramsay Sedation Score and was quite similar intraoperatively through out in both groups with dexmetedomidine having slightly higher scores and good sedation without any respiratory depression than Group M, (Table 3).

Table 3: Modified Ramsay sedation score (The time of giving the drug is taken as 0)

Time	Group D	Group M
0	2	2
15	3.64 ± 0.6	3.6 ± 0.3
30	4.3 ± 0.7	3.9 ± 0.7
45	4.6 ± 0.5	4.2 ± 0.5
60	4.6 ± 0.4	4.2 ± 0.4
75	4.56 ± 0.5	4.4 ± 0.2
90	4.4 ± 0.5	4.3 ± 0.2
120	4.2 ± 0.6	4.0 ± 0.4
180	3.2 ± 0.5	3.2 ± 0.2

Six (12%) patients of Group M had postoperative shivering which was managed, no patient in Group D had shivering (p - value 0.0112, not significant). While nausea occurred in 9 (18%) patients in Group D and 2 (4%) patients in Group M, p - value 0.1398. However, only 1 (2%) patient in Group D had vomitting (p - value 0.3197), (Table 4). Patients in both Groups D and M remained hemodynamically stable through out the surgery, (Figs. 1 and 2).

Table 4: Side-effects

	Group D	Group M	p - value
Shivering	0	6 (12%)	0.0112
Nausea	9 (18%)	4 (8%)	0.1398
Vomitting	1 (2%)	0	0.3197

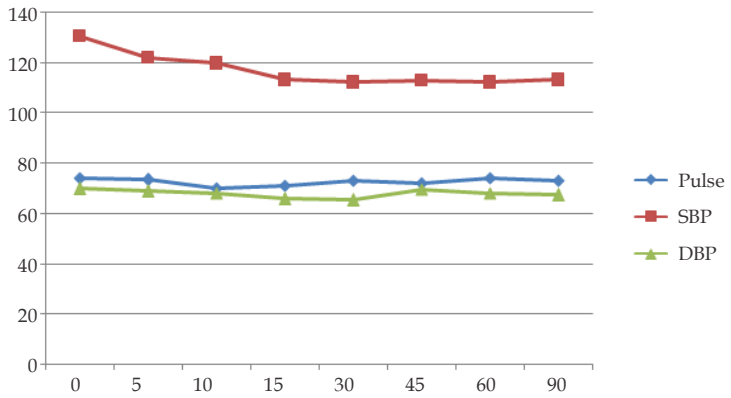

Fig. 1: Group D vitals (pulse, systolic blood pressure, diastolic blood pressure).

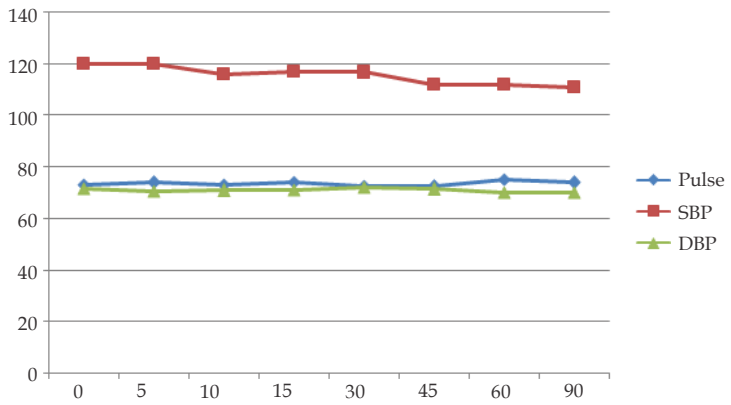

Fig. 2: Group M vitals (pulse, systolic blood pressure, diastolic blood pressure).

Discussion

Subarachnoid block causes sympatholysis whish is hallmark feature of central neuraxial blockade. the hemodynamic stability was attained after 15 mins of giving intrathecal bupivacaine, after which we administered intravenous dexmetedomidine and midazolam slowly over 10 mins.

Jyotsna Kubre et al. in her study entitled "Single dose IV dexmetedomidine prolongs spinal anesthesia with hyperbaric bupivacaine" administered intravenous dexmetedomidine 45 mins after the intrathecal bupivacaine.[7]

In our study, patients of both groups Group D and Group M remained vitally stable through out the surgery. The decrease in heart rate was more evident in Group D as compared to Group M and was not statistically significant. This is due to the postsynaptic activation of α_2 adenoreceptors in CNS, that results in decrease in sympathetic activity and circulatory levels of catecholamines.[8,9] Similar observation was made by Jyotsna et al. and Group D had decrease in heart rate in her study.[7]

Aantaa R, Jaakola ML in their study "A comparison of dexmetedomidine an alpha-2 adenoreceptor agonist and midazolam as a premedication intramuscularly for minor gynecological surgeries" and observed that bradycardia was caused by dexmetedmodine but it was longlasting when given as premedication.[10]

In other studies, continuous infusion was administered throughout the procedure, hypotension and bradycardia remained intraopertively as well as postoperatively which lead to increase consumption of other drugs to treat these effects.[11-13]

Henceforth, when peak hemodynamic effects of intrathecal subarachnoid block were settled, in our study, single-dose intravenous dexmetedomidine was given slowly to overcome these complications. In both groups of our study there was decrease in BP which was clinically and stastically not significant, normally dexmetedomidine does not have any direct effect on heart rate. Although it causes a dose dependent increase in coronary vascular resistance and O_2 extraction but the demand/supply ratio is unaltered. It shows biphasic response occurs after administration of bolus 1 microgram/kg causing transient rise in BP and reflex decrease in heart rate. This initial response is due to effect of B adenoreceptor stimulation of vascular smooth muscle[14] in our study as we administered the drug slowly over 10 mins there was stabilization of Heart Rate and BP 10–15% below the baseline value.

This result was very-well supported by Mamta Mahobia et al. as they had similar timing and conclusion.[7] However, Tekin M, in his research "effect of dexmetedomidine IV on duration of spinal anesthesia with prilocine "found no significant diffrence in MAP in dexmetedomidine group.[11]

In our research, the duration of 2 segment regression in Group D pt. was 148 ± 8 min and Group M was 120 ± 6 min, p - value < 0.0001 being statistically highly significant. The total duration of sensory block was prolonged in Group D 308 ± 20 min than Group M 200 ± 18 min. The total duration of motor block in Group D was 230 ± 15 mins and group M 160 ± 10 mins. These prolonged effects in patients of Group D can be explained by the fact that the site of action of dexmetedomidine is locus cerulus and is mediated by hyperpolarization of nonadrenergic neurons and inhibits noradrenaline release and thus inhibits activity of descending medullospinal noradrenergic pathways.[15]

Jyotsna et al., study also concluded that the duration of sensory blockade was prolonged in dexmetedomidine group 341.7 ± 20.8 min as compared to control group 329 ± 22.1. The 2 dermatomal regression time was also prolonged 115.5 ± 8.8 as compared to control group 95.8 ± 14 min. The motor block was also augmented in Group D 278 ± 11 min as compared to control group - 250 ± 14.8 min.[7]

Bajwa S et al. who reviewed "Dexmetedomidine: An adjuvant making large roads into clinical practice," had similar observations that dexmetedomidine as an adjuvant in neuraxial anesthesia prolongs the sensory and motor blockade with more intense and good postoperative analgesia.[15,16]

Honge et al.[13] who admisintered intravenous dexmetedomidine as an adjuvant to regional anesthesia with hyperbaric bupivacaine observed that complete resolution of motor and sensory blockade was significantly prolonged in Dexmetdomidine group and the findings of our present study corroborate the result.

We assessed sedation by modified ramsay sedation score which was quite similar intraoperatively through out in both groups, Group D has slightly higher scores and good sedation without any respiratory depression than Group M. Evidences suggests that of the 3 major receptor subtypes α_2A, α_2B and α_2C in CNS, α_2A and α_2C predominate in CNS and are responsible for

sedative, analgesic and sympatholytic components of agonist action.[17]

Dexmetedomidine induced sedation is called "Cooperative sedation" as it does not cause much respiratory depression with wide safety margins, sleep induced with it has rapid eye movement and is easily arousable.[18] However, the sedation induced by drugs acting on GABA system such as midazolam or propofol that produce clouding of Conciousness.[7] Rekha Kumaru, Ani Kumar concluded that Ramsay Sedation Score was significantly higher in dexmetedomidine group as compared to control group. Mustafa et al. l noted that the median sedation score was 4 in dexmetedomidine gorup in their study.[13]

In our study, none of the patients of Group D had shivering as compared to Group M patients where 6 (12%) had postoperative shivering (*p* - value 0.0112). The incidense of nausea was in 9 (18%) patients in Group D and 4 (8%) patients in Group M and vomitting was observed in only 1 patient in Group D.

Venn RM et al. in their study "Pharmacokinetics of dexmetedomidine infusions for sedation of postoperative patients requiring intensive care" had similar observations.[20] Elvan EG et al. carried out a study to observe the incidence of postoperative shivering in patients undergoing elective abdominal hysterectomy. His study results proved that intraoperative infusion of dexmtedomidine prevented postoperative shivering.[21]

A study entitled "A balanced anesthesia with dexmtedomidine decreases postoperative nausea and vomitting after laprosocopic surgery" was done by Massad IM et el. He concluded that on combining dexmetedomidine to other anesthetic agents for patients posted for general anesthesia, there was significant decrease in insidence of postoperative nausea and vomiting.[22] All these findings are similar to our study and thus strengthen our results.

Conclusion

We concluded that dexmetedomidine is superior to midazolam as it provides arousable sedation, analgesia, hypnosis and sympatholysis without causing respiratory depression. Single-dose IV dexmetedomidine 0.5 microgram/kg given slowly prolongs the durations of sensory and motor blockade.

Midazolam is a nearly ideal supplement providing sedation with effective anxiolysis, fast onset, short recovery time, predictable depth of anesthesia, with minimal side-effects and no evidence of accumulation.

Acknowledgment: Nil.

Conflict of Interest: Nil.

References

1. Kamibayashi T, Maze M. Clinical uses of alpha2 -adrenergic agonists. Anesthesiology 2000;93:1345–359.
2. Saxena H, Singh S, Ghildiyal S. Low-dose intrathecal clonidine with bupivicaine improves onset and duration of block with hemodynamic stability. Internet J Anesthesiol 2009;23:1.
3. Thakur A, Bhardwaj M, Kaur K, et al. Intrathecal clonidine as an adjuvant to hyperbaric bupivacaine in patients undergoing inguinal herniorrhaphy: A randomized double-blinded study. J Anesthesiol Clin Pharmacol 2013;29:66–70.
4. Sethi BS, Samuel M, Sreevastava D. Efficacy of analgesic effects of low-dose intrathecal clonidine as adjuvant to bupivacaine. Indian J Anesth. 2007;51:415–19.
5. Eren G, Cukurova Z, Demir G, et al. Comparison of dexmedetomidine and three different doses of midazolam in preoperative sedation. J Anesthesiol Clin Pharmacol 2011;27:367–72.
6. Midazolam in Spinal Anesthesia—Intrathecal or Intravenous? By Beyazit Zencirci Submitted: September 13th 2013 (Reviewed: June 12th 2014 Published: September 3rd 2014); DOI: 10.5772/58750.
7. Kubre Jyotsna, Sethi Ashish. Single-dose intravenous dexmedetomidine prolongs spinal anesthesia with hyperbaric bupivacaine, Anesth Essays Res 2016 May–Aug;10(2):273–77. doi: 10.4103/0259-1162.174465 PMCID: PMC4864683PMID: 27212760
8. Yazbek-Karam VG, Aouad MM. Perioperative uses of dexmedetomidine. Middle East J Anaesthesiol. 2006;18:1043–58. [PubMed] [Google Scholar]
9. Arain SR, Ebert TJ. The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation. AnesthAnalg. 2002;95:461–6. [PubMed] [Google Scholar]
10. Aantaa R, Jaakola ML, Kallio A, et al. A comparison of dexmedetomidine, and alpha 2-adrenoceptor agonist, and midazolam as IM premedication for minor gynecological surgery. Br J Anesth 1991;67:402–09.
11. Tekin M, Kati I, Tomak Y, et al. Effect of dexmedetomidine IV on the duration of spinal anesthesia with prilocaine: A double-blind, prospective study in adult surgical patients. Curr Ther Res 2007;68:313–24.

12. Hong JY, Kim WO, Yoon Y, et al. Effects of intravenous dexmedetomidine on low-dose bupivacaine spinal anesthesia in elderly patients. Acta Anesthesiol Scand 2012;56:382–87.
13. Al-Mustafa MM, Badran IZ, Abu-Ali HM, et al. Intravenous dexmedetomidine prolongs bupivacaine spinal analgesia. Middle East J Anesthesiol 2009;20:225–31.
14. Patel CR, Engineer SR, Shah BJ, et al. Effect of intravenous infusion of dexmedetomidine on perioperative hemodynamic changes and postoperative recovery: A study with entropy analysis. Indian J Anesth 2012;56:542–46.
15. Bajwa S, Kulshrestha A. Dexmedetomidine: An adjuvant making large inroads into clinical practice. Ann Med Health Sci Res 2013;3:475–83.
16. Mannion S. Sedation, spinal anesthesia and older patients. J Postgrad Med 2007;53:155.
17. Nelson LE, Lu J, Guo T, et al. The alpha 2-adrenoceptor agonist dexmedetomidine converges on an endogenous sleep-promoting pathway to exert its sedative effects. Anesthesiology 2003 Feb;98(2):428–36.
18. Venn RM, Hell J, Grounds RM. Respiratory effects of dexmedetomidine in the surgical patient requiring intensive care. Crit Care 2000;4:302–308.
19. Kumari Rekha, Kumar Anil. Intravenous dexmedetomidine as an adjunct to subarachnoid block: A simple effective method of better perioperative efficacy. J Anesthesiol Clin Pharmacol 2017 Apr–Jun;33(2):203–208. doi: 10.4103/joacp.JOACP_367_15 PMCID: PMC5520593.PMID: 28781446
20. Venn RM, Karol MD, Grounds RM. Pharmacokinetics of dexmedetomidine infusions for sedation of postoperative patients requiring intensive caret. Br J Anesth 2002;88:669–75.
21. Elvan EG, Oç B, Uzun S, et al. Dexmedetomidine and postoperative shivering in patients undergoing elective abdominal hysterectomy. Eur J Anesthesiol 2008;25:357–64.
22. Massad IM, Mohsen WA, Basha AS, et al. A balanced anesthesia with dexmedetomidine decreases postoperative nausea and vomiting after laparoscopic surgery. Saudi Med J 2009;30:153741.