Original Article

Effect of intrathecal dexmedetomidine versus intravenous dexmedetomidine on subarachnoid anesthesia with hyperbaric bupivacaine

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Abstract

Background and Aim: Alpha-2 agonists such as dexmedetomidine when given intravenously or intrathecally as an adjuvant potentiate subarachnoid anesthesia. We studied the difference in subarachnoid anesthesia when supplemented with either intrathecal or intravenous dexmedetomidine.

Material and Methods: Seventy-five patients posted for lower limb and infraumbilical procedures were enrolled for a prospective, randomized, double-blind, placebo-controlled study and divided into three groups: Group B (n = 25) received intravenous 20 mL 0.9%N aCl over 10 min followed by intrathecal 2.4 mL 0.5%bupivacaine + 0.2 mL sterile water; Group B_{DexIT} (n = 25) received intravenous 20 mL 0.9%N aCl over 10 min followed by intrathecal 2.4 mL 0.5%b upivacaine + 0.2 mL (5 μg) dexmedetomidine; Group B_{DexIV} (n = 25) received intravenous dexmedetomidine 1 μg/kg in 20 mL 0.9%N aCl over 10 min followed by intrathecal 2.4 mL 0.5%b upivacaine + 0.2 mL sterile water. Onset and recovery from motor and sensory blockade, and sedation score were recorded. Onset of sensory and motor blockade was assessed using Kruskal–Wallis test, whereas 2-segment regression and recovery was analyzed using ANOVA and *post hoc* Tukey's test to determine difference between the three groups. P value <0.05 was considered statistically significant.

Results: Although onset of sensory and motor block was similar in the three groups, motor recovery (modified Bromage scale 1) and two-segment sensory regression was prolonged in Group B_{DexIT} > Group B_{DexIV} > Group B ($P < 0.001$). Patients in Group B_{DexIT} and Group B_{DexIV} were sedated but easily arousable.

Conclusion: Intrathecal dexmedetomidine prolongs the effect of subarachnoid anesthesia with arousable sedation when compared with intravenous dexmedetomidine.

Keywords: Anesthesia, dexmedetomidine, subarachnoid

Introduction

Subarachnoid anesthesia is the most popular technique for lower abdominal and lower limb procedures.[1] Dexmedetomidine, a selective α-2 adrenergic agonist, through its synergistic action with local anaesthetics, prolongs the effect of subarachnoid anesthesia.[2-4] Studies have demonstrated that intrathecal as well as low-dose intravenous dexmedetomidine can prolong sensory and motor blockade during subarachnoid anesthesia without undesirable side effects.[4-11]

Several studies have compared the effect of intravenous with intrathecal dexmedetomidine on subarachnoid anesthesia.[12-14] Hence, we conducted a study to evaluate the effects of intrathecal versus intravenous dexmedetomidine on the sensory

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and motor block as well as hemodynamic stability and sedation in patients receiving subarachnoid anesthesia.

Material and Methods

The study was commenced after getting approval from the Departmental Dissertation Committee and the Institutional Ethics Committee. It was prospective, randomized, and double-blind in nature. Patients aged between 18 and 65 years of either gender undergoing elective infraumbilical or lower limb surgery under subarachnoid anesthesia belonging to American Society of Anesthesiologists Physical Status 1 or 2 were included in the study. Exclusion criteria included coagulopathy, hypovolemia, body mass index >35 kg/m^2, subarachnoid abnormalities, chronic use of sedatives or antidepressants, history of regular alcohol consumption, and local infection over lumbar spine.

A detailed preoperative evaluation of the patient was done on the day prior to surgery by one of the investigators. Written informed consent was obtained and all patients were kept nil per oral (6 h for solids and 3 h for clear fluids).

An anesthesiology faculty who was not otherwise involved in the study picked the lot and prepared the solutions to be administered intravenously and intrathecally. One investigator (blinded to the drug given intrathecally as well as intravenously) recorded the onset of sensory and motor blockade, maximum level of sensory and motor block, time for two-segment regression, time to recovery from sensory and motor blockade, hemodynamic parameters, and any complications arising during the study period.

Patients were randomly allocated into one of the three groups using computer-generated random number table to receive 20 ml of intravenous test drug over 10 min as soon as the intravenous access was established and baseline vital signs recorded, and 2.4 mL of 0.5% hyperbaric bupivacaine with 0.2 mL of intrathecal test drug for subarachnoid block at the end of intravenous test drug infusion. Patients in Group B received 0.9% NaCl intravenously and 0.2 mL of sterile water intrathecally as test solutions. Those in Group B_{Dex}IT received 0.9% NaCl intravenously and 0.2 mL of dexmedetomidine (5 μg) intrathecally. Dexmedetomidine in this dilution was prepared by withdrawing 0.25 mL (25 μg) of dexmedetomidine from an ampoule of dexmedetomidine containing 100 μg/mL into an insulin syringe containing 10 divisions. This 25 μg of dexmedetomidine was then further diluted with sterile water to make up a total volume of 1 mL, i.e., 25 μg/mL or 2.5 μg/division. Two divisions of dexmedetomidine diluted thus (0.2 mL containing 5 μg) was then added to 2.4 mL of 0.5% hyperbaric bupivacaine.

Patients in Group B_{Dex}IV received dexmedetomidine 1 μg/kg (rounded to the nearest 10 μg) in 20 mL of 0.9% NaCl intravenously and 0.2 mL of sterile water intrathecally.

After shifting the patient to the operating room, electrocardiographic (ECG) monitoring of leads II and V_5, noninvasive blood pressure (NIBP), and pulse oximetry were established and the baseline vitals recorded. Intravenous access was secured with an 18 SWG intravenous cannula in the nondominant hand and an infusion of Ringer lactate started.

Patients were then administered subarachnoid anesthesia in left lateral decubitus position using a 25 SWG Quincke-Babcock needle in L_3–L_4 interspace. The study drug was injected intrathecally over a period of 10 s once free flow of clear cerebrospinal fluid was obtained. The study drug was prepared by the anesthesiology faculty not involved in the study and handed over to the anesthesiologist performing the subarachnoid anesthesia. The time of intrathecal drug injection was noted as time "0" and the patient was turned supine.

Ability to appreciate a cold swab was evaluated every 2 min along the midclavicular line on both sides. The higher of the two sides was taken as end point. Onset of analgesia at T_{10} was noted. The sensory level was checked every 2 min as described above until the level remained unchanged for four consecutive readings. This dermatomal level was noted as the highest level of analgesia. Sensory level was checked every 5 min till the end of 1 h, and every 15 min thereafter till two-segment regression (defined as recovery of sensory block by two segments from the highest level achieved in that patient) and sensory recovery (around S_2-S_4 segments) occur.

Motor blockade was assessed by modified Bromage scale at 2-min intervals till a modified Bromage scale score of 3 was obtained or till maximum motor blockade was achieved.[15] This time was noted as onset of motor blockade. The time at which modified Bromage scale 1 was obtained denoted recovery from motor blockade.

Sedation score was recorded every 15 min throughout the first 3 h using the six-point Ramsay Sedation Score.[16] as detailed below:

Ramsay Sedation Score[16]

- 1 - Anxious, agitated/restless or both
- 2 - Patient cooperative, oriented, and tranquil
- 3 - Patient responds to commands only
- 4 - Brisk response to light glabellar tap or loud auditory stimulus
- 5 - Sluggish response to light glabellar tap or loud auditory stimulus
- 6 – Patient shows no response.

Blood pressure and heart rate was recorded every 5 min for the first hour and every 15 min thereafter till complete sensory and motor recovery as defined above had been achieved. More than a 25% decrease in mean arterial pressure was treated with intravenous fluids and vasopressor (boluses of 3 mg of mephentermine). A heart rate <50/min was considered as bradycardia and treated at the discretion of the primary anesthesiologist. A respiratory rate <8/min or pulse oximetric values <95% on room air were taken as significant and nasal oxygen at 3–5 L/min was used as rescue. Incidence of adverse effects, such as nausea, vomiting, arterial desaturation, or pruritus, was noted.

Statistical analysis

An interim statistical analysis was done (ANOVA) after collecting data for nine patients (3 in each group) in Phase I of the study. Aiming for a study power of 80% with an α-error of <0.05 for a 70 min difference in duration of analgesia (sensory recovery), the sample size was determined to be 23 patients in each group. We included 25 patients in each group for better validation of results.

Statistical analysis was done using SPSS Version 20. Onset of sensory and motor blockade was assessed using nonparametric test (Kruskal–Wallis test), whereas two-segment regression and recovery from sensory and motor blockade were analyzed using ANOVA and *post hoc* Tukey's test to determine difference between the three groups. P value <0.05 was considered statistically significant.

Results

The age, weight, height, and gender of patients were comparable in the three groups [Table 1]. There was no statistical significant difference in the time taken for sensory onset in the three groups [Table 2].

Maximum modified Bromage score (motor onset) observed was three in all three groups. There was no statistical difference between the groups with respect to onset of motor blockade [Table 2].

The mean two-segment regression time as depicted in Table 2 was longest in group receiving intrathecal dexmedetomidine along with hyperbaric bupivacaine (Group B_{Dex}IT) than in the other two groups. There was significant difference between Group B and Group B_{Dex}IT ($P < 0.001$) as well as between Group B and Group B_{Dex}IV ($P < 0.001$).

The mean time taken for sensory recovery to S_2-S_4 dermatomes was longer in the group receiving intrathecal dexmedetomidine among the three groups. There was a statistically significant difference between Group B and Group B_{Dex}IT, as well as between Group B and Group B_{Dex}IV ($P < 0.001$) [Table 2].

The mean time for motor recovery was longest in group receiving intrathecal dexmedetomidine. There was a statistically significant difference between Group B and Group B_{Dex}IT, as well as between Group B and Group B_{Dex}IV ($P < 0.001$) [Table 2].

Patients receiving dexmedetomidine by the intrathecal as well as the intravenous routes were more sedated as compared with the control group (Chi-square test; $P = 0.011$) [Table 3].

Patients experienced side effects such as hypotension and bradycardia as shown in Table 4. Other adverse effects, such as nausea, vomiting, desaturation, and pruritus, were not noticed in any patient.

Discussion

Dexmedetomidine is a highly lipophilic drug that gets rapidly absorbed into the cerebrospinal fluid and bind to alpha-2-adrenergic receptor of spinal cord to produce analgesia. It prolongs the duration of both sensory and motor blockade induced by local anesthetics irrespective of the route of administration whether epidural, caudal, or spinal.[17] Intravenous dexmedetomidine is also known to prolong the duration of sensory block of local anesthetics during spinal anesthesia and peripheral nerve block but the underlying mechanism of this effect is unclear.[18,19] The supra-spinal, direct analgesic, and/or vasoconstricting actions of dexmedetomidine are suggested to be involved in this mechanism.[19] Our study analyzed the sensorimotor effects of intrathecal versus intravenous dexmedetomidine on subarachnoid anesthesia. The dose of dexmedetomidine to be used intrathecally as well as intravenously was decided based on previous studies.[3,6,9] As per the review by Naaz *et al.* safe dose of intrathecal dexmedetomidine can be 0.1–0.2 μg/kg.[17] Kavya *et al.* found that intravenous dexmedetomidine given as bolus or bolus-plus-infusion prolongs both sensory and motor blockade of intrathecal hyberbaric bupivacaine without any untoward side effects.[20] Hence, we chose to give intravenous dexmedetomidine 1 μg/kg as bolus over 10 minutes prior to subarachnoid anesthesia. Only patients scheduled for infraumbilical and lower limb surgeries were included for the study so that they could be maintained in the supine position following administration of subarachnoid anesthesia. Assumption of any other position for surgery could have altered the spread of the local anaesthetic solution and confounded our results.

In our study, the time taken for onset of sensory blockade was not significantly shortened by the use of dexmedetomidine.

However, Harsoor *et al.* reported a faster onset of sensory block in dexmedetomidine group compared with control group (66 vs. 129.6 s).[21]

The onset of motor blockade was also found to be comparable in all three groups as was the case in other studies.[12-14] The mean time for two-segment regression of sensory blockade was significantly prolonged in our study. This is similar to other studies.[11,21,22] Duration of analgesia was taken as sensory recovery at S_2-S_4 dermatomes. Sensory recovery was prolonged with the use of intrathecal as well as intravenous dexmedetomidine which is in agreement with the findings in earlier studies.[12-14] The intrathecal route was found to prolong the duration of analgesia even more as compared with the intravenous route. Motor blockade was significantly prolonged in both the groups receiving dexmedetomidine, with the prolongation being more with intrathecal dexmedetomidine. Similar prolongation was observed in other studies.[13,14] However, some studies reported no significant prolongation of duration of motor blockade.[12] This difference could be attributed to the different end points that were taken to indicate recovery from motor blockade.

A meta-analysis conducted by Niu *et al.* concluded that dexmedetomidine prolonged the duration of subarachnoid anesthesia and improved postoperative analgesia while at the same time not increasing the incidence of hypotension and other adverse events.[23] The meta-analysis also noted that there was a greater need for using atropine to reverse bradycardia when dexmedetomidine was used in the context of subarachnoid anesthesia. The database analyzed had a high degree of heterogenicity caused by different doses of dexmedetomidine and bupivacaine used for different types of surgical procedures. There was no unified method of delivering the drug and the criteria used to define sensory and motor recovery were different. Our study comparing intrathecal with intravenous dexmedetomidine concluded that motor blockade was significantly prolonged with both intrathecal dexmedetomidine as well as intravenous dexmedetomidine with the prolongation being more with intrathecal dexmedetomidine which correlates with a study done by Hamed *et al.*[13]

Patients receiving dexmedetomidine had a Ramsay sedation score of 3 or 4 with no respiratory depression and were easily arousable. Such finding was also documented by Abdallah *et al.* who failed to detect any serious complication with respect to sedation in the postoperative period attributable to the use of dexmedetomidine as an adjunct to subarachnoid anesthesia.[22]

Hemodynamic response following dexmedetomidine depends on the dose and speed of intravenous infusion. Higher doses of dexmedetomidine are associated with bradycardia and decreased cardiac output. Bearing this in mind, we administered dexmedetomidine as a slow intravenous infusion over 10 min. This could possibly explain why we had a low incidence of bradycardia and hypotension following intravenous dexmedetomidine. Even these few instances were easily treated with intravenous atropine and/or intravenous mephentermine. A study by Abdallah *et al.* also reported a 3.7-fold increase in transient reversible bradycardia in patients receiving intravenous dexmedetomidine, with the incidence being higher when the initial loading dose was administered over a short duration of time.[15]

There was no significant difference in terms of hypotension as seen in various trials, which was summarized in a meta-analysis by Abdallah *et al.*[21] The incidence reported was 14%, 17%, 23%, and 27% with infusion doses of 0.25, 0.5, 1, and 2 μg/kg, respectively.

In comparison to some recent studies evaluating the effect of two different route of dexmedetomidine on subarachnoid

Table 1: Demographic data

Parameters	Group B	Group B_{Dex}IT	Group B_{Dex}IV
Age (years) Mean±SD	49.71±14.196	44.19±12.17	47.27±13.44
Weight (kg) Mean±SD	62.42±7.336	64.12±11.45	63.20±10.751
Height (cm) Mean±SD	161±8.11	166.38±8.73	161.96±8.97
Male/Female	23/2	21/4	21/4

Group B: Group bupivacaine, Group B_{Dex}IT: Group bupivacaine with intrathecal dexmedetomidine, Group B_{Dex}IV: Group bupivacaine with intravenous dexmedetomidine

Table 2: Sensorimotor parameters following subarachnoid anesthesia

Parameter	Group B (*n*=25)	Group B_{Dex}IT (*n*=25)	Group B_{Dex}IV (*n*=25)	*P*
Onset of sensory blockade at T10 dermatomal level (min) Median (Interquartile range)	2 (2,4)	2 (2,4)	2 (2,4)	0.057
Onset of motor blockade (min) Median (Interquartile range)	4 (2,6)	4 (2,6)	4 (2,6)	0.186
Two-segment regression Mean±SD (min)	106.04±31.34	194.23±42.70	174.60±31.32	<0.001
Sensory recovery to S2 to S4 dermatomes Mean±SD (min)	189.29±46.07	315.92±63.14	247.48±46.39	<0.001
Motor recovery Mean±SD (min)	208.67±50.2	344.38±57.77	272.52±53.57	<0.001

Group B: Group bupivacaine, Group BDexIT: Group bupivacaine with intrathecal dexmedetomidine, Group BDexIV: Group bupivacaine with intravenous dexmedetomidine

Table 3: Ramsay sedation score

Group	Sedation score 2	Sedation score 3 or 4
Group B (n=25)	16	9
Group BDexIT (n=25)	11	14
Group BDexIV (n=25)	6	19

Chi-square test; P=0.011

Table 4: Adverse effects

Group	Bradycardia	Hypotension
Group B	0	4
Group B_{Dex}IT	0	3
Group B_{Dex}IV	4	2
Total	4	9

anesthesia, our study is unique in its methodology and doses of dexmedetomidine used.[12-14] We studied that addition of intrathecal dexmedetomidine (5 μg) or intravenous dexmedetomidine infusion (1 μg/kg) given over 10 min just prior to subarachnoid anesthesia with 2.4 mL of 0.5% hyperbaric bupivacaine prolongs both the duration of sensory and motor blockade, with the intrathecal route producing greater prolongation than the intravenous route. Dexmedetomidine through either route produces sedation from which the patients are easily arousable. Intravenous dexmedetomidine produces a low incidence of bradycardia that is easily treatable. Thus, this study facilitates us to choose the best route and dose of dexmedetomidine supplementation for subarachnoid anesthesia depending on the anesthetic requirement and resources available.

Conclusion

We conclude that while both intrathecal and intravenous dexmedetomidine prolong the sensorimotor effect of subarachnoid anesthesia with reasonable hemodynamic stability and arousable sedation, intrathecal dexmedetomidine produces greater prolongation of motor and sensory block than intravenous dexmedetomidine.

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Conflicts of interest
There are no conflicts of interest.

References

1. Brull R, Macfarlane AJR, Chan VWS. Spinal, epidural, and caudal anesthesia. In: Miller RD, editor. Miller's Anesthesia. 8th ed. Philadelphia: Elsevier Saunders; 2015. p. 1684.
2. Afonso J, Reis F. Dexmedetomidine: Current role in anesthesia and intensive care. Rev Bras Anestesiol 2012;62:118-33.
3. Reddy VS, Shaik NA, Donthu B, Sannala VK, Jangam V. Intravenous dexmedetomidine versus clonidine for prolongation of bupivacaine spinal anesthesia and analgesia: A randomized doubleblind study. J Anaesthesiol Clin Pharmacol 2013;29:342-7.
4. Annamalai A, Singh S, Singh A, Mahrous DE. Can intravenous dexmedetomidine prolong bupivacaine intrathecal spinal anesthesia? J Anesth Clin Res 2013;4:1-5.
5. Songir S, Kumar J, Saraf S, Waindeskar V, Khan P, Gaikwad M. Study of the effect of intrathecal dexmedetomidine as an adjuvant in spinal anesthesia for gynecological surgery. Int J Med Res Rev 2016;4:602-7.
6. Nethra SS, Sathesha M, Aanchal D, Dongare PA, Harsoor SS, Devikarani D. Intrathecal dexmedetomidine as adjuvant for spinal anesthesia for perianal ambulatory surgeries: A randomised double-blind controlled study. Indian J Anaesth 2015;59:177-81.
7. Singh AK, Singh Y, Jain G, Verma RK. Comparison of two different doses of intrathecal dexmedetomidine as adjuvant with isobaric ropivacaine in lower abdominal surgery. Anesth Essays Res 2015;9:343-7.
8. Shaikh SI, Dattatri R. Dexmedetomidine as an adjuvant to hyperbaric spinal bupivacaine for infra-umbilical procedures: A dose related study. Anaesth Pain Intensive Care 2014;18:180-5.
9. Kubre J, Sethi A, Mahobia M, Bindal D, Narang N, Saxena A. Single dose intravenous dexmedetomidine prolongs spinal anesthesia with hyperbaric bupivacaine. Anesth Essays Res 2016;10:273-7.
10. Gupta K, Tiwari V, Gupta PK, Pandey MN, Agarwal S, Arora A. Prolongation of subarachnoid block by intravenous dexmedetomidine for sub umbilical surgical procedures: A prospective control study. Anesth Essays Res 2014;8:175-8.
11. Lee MH, Ko JH, Kim EM, Cheung MH, Choi YR, Choi EM. The effects of intravenous dexmedetomidine on spinal anesthesia: Comparison of different dose of dexmedetomidine. Korean J Anesthesiol 2014;67:252-7.
12. Magdy H, Mohsen M, Saleh M. The effect of intrathecal compared with intravenous dexmedetomidine as an adjuvant to spinal bupivacaine anesthesia for cesarean section. Ain-Shams J Anesthesiol 2015;8:93-9.
13. Hamed AMS, Talaat SM. Effect of intravenous versus intrathecal low-dose dexmedetomidine on spinal block in lower limb orthopedic surgery. Ain-Shams J Anesthesiol 2014;07:205-10.
14. Afifi MH, Mohammed AM, Abdullah SI, Ellisy KE. Intrathecal versus intravenous dexmedetomidine in characteristics of bupivacaine spinal block in lower abdominal surgery. Menoufia Med J 2016;29:523-9.
15. Brull R, Macfarlane AJR, Chan VWS. Spinal, epidural, and caudal anesthesia. In: Miller RD, editor. Miller's Anesthesia. 8th ed. Philadelphia: Elsevier Saunders; 2015. p. 1703.
16. Shah PN, Dongre V, Patil V, Pandya S, Mungantiwar A, Choulwar A. Comparison of post-operative ICU sedation between dexmedetomidine and propofol in Indian population. Indian J Crit Care Med 2014;18:291-6.
17. Naaz S, Ozair E. Dexmedetomidine in current anaesthesia practice- A review. J Clin Diagn Res 2014;8:GE01-4.
18. Grewal A. Dexmedetomidine: New avenues. J Anaesth Clin Pharmacol 2011;27:297-302.
19. Ebert TJ, Hall JE, Barney JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology 2000;93:382-94.
20. Kavya UR, Laxmi S, Ramkumar V. Effect of intravenous dexmedetomidine administered as bolus or as bolus-plus-infusion on subarachnoid anesthesia with hyperbaric bupivacaine. J Anaesthesiol Clin Pharmacol 2018;34:46-50.
21. Harsoor SS, Rani DD, Yalamuru B, Sudheesh K, Nethra SS. Effect of supplementation of low dose intravenous dexmedetomidine on characteristics of spinal anesthesia with hyperbaric bupivacaine. Indian J Anaesth 2013;57:265-9.
22. Abdallah FW, Abrishami A, Brull R. The facilitatory effects of intravenous dexmedetomidine on the duration of spinal anesthesia: A systematic review and meta-analysis. Anesth Analg 2013;117:271-8.
23. Niu XY, Ding XB, Guo T, Chen MH, Fu SK, Li Q. Effects of intravenous and intrathecal dexmedetomidine in spinal anesthesia: A meta-analysis. CNS Neurosci Ther 2013;9:897-904.