Effects of intravenous dexmedetomidine on spinal anesthesia and sedation – A comparison of two different maintenance infusions

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Introduction

Adequate sedation during surgery under spinal anesthesia is of utmost importance to relieve patient anxiety, stress and increase the satisfaction of both the surgeon and patient.

Dexmedetomidine, a centrally acting α-2 adrenoceptor agonist, provides titratable level of sedation without causing respiratory depression.[1] It has analgesic properties and predictable sympatholytic effects.[2-4] Additionally, a bolus dose of dexmedetomidine prior to subarachnoid block (SAB) has been shown to have a favourable effect in prolonging the duration of spinal anesthesia.[5]

A bolus dose of 1 microgram/kilogram (mcg/kg) dexmedetomidine followed by three different continuous infusions 0.25, 0.5 and 0.75 mcg/kg/hour (mcg/kg/h) was
studied by Song et al. and they found 0.25 mcg/kg/h had the least effect on hemodynamics. Harsoor et al. concluded that 0.5 mcg/kg bolus as well as maintenance hastened and prolonged SAB along with adequate sedation as compared to control group whereas Hong et al. concluded that 1 mcg/kg bolus of dexmedetomidine prior to SAB, prolonged the same but the incidence of bradycardia needing treatment was higher. As per previous literature, the average duration for two segment regression of SAB with heavy bupivacaine is approximately 55 min. A 10% increase in the time taken for two segment regression would indicate prolonged duration of SAB.

We hypothesized that a low-dose bolus of 0.5 mcg/kg over 10 min followed by two different maintenance doses 0.25 and 0.5 mcg/kg/h might help us to arrive at the dose needed to prolong SAB while ensuring adequate sedation, which is the primary aim of this study. We also studied its effect on hemodynamics and side effects.

**Material and Methods**

After institutional ethics committee approval, the study was conducted over a period from December 2013 to December 2015. A written, informed consent was taken from patients posted for lower abdominal, infra umbilical and lower limb surgeries under spinal anesthesia prior to enrolment in this prospective, randomized, comparative, double-blinded study. Patients with known allergy to local anesthetics, baseline heart rate less than 50, patients on beta blockers or with conduction blocks were excluded from the study. Consecutive patients who were part of the study, were randomized based on computer generated random numbers (www.randomizer.org) into two groups, group A and group B, and blinded to the dose of dexmedetomidine administered to them.

Baseline monitoring included electrocardiogram (ECG), heart rate (HR), respiratory rate (RR), non-invasive blood pressure (NIBP), mean arterial pressure (MAP) and oxygen saturation (SpO₂). All patients were preloaded with Ringer lactate at 10 ml/kg intravenously (IV) through an 18 G cannula. Supplemental oxygen was administered via nasal prongs at 2 l/min.

Patients in both the groups were administered injection (inj) dexmedetomidine 0.5 mcg/kg in normal saline in 20-ml syringe (5 mcg/ml) through infusion pump over 10 min IV. At the end of this bolus infusion, SAB was given using 3 ml of 0.5% heavy bupivacaine via 25 gauge Quincke’s needle with the patient in the left lateral position. After SAB, patients in group A received dexmedetomidine 0.25 mcg/kg/h while patients in group B received dexmedetomidine 0.5 mcg/kg/h, throughout the duration of surgery. The anesthetist conducting the case was given preloaded syringes of dexmedetomidine, and told the rate of infusion in ml/h to be administered and was unaware of the concentration of dexmedetomidine in the syringe. Sensory block was assessed by loss of pin prick while motor block was determined using Modified Bromage Scale. Onset of sensory block was defined as loss of pin prick sensation at T10 dermatome. Level of sensory and motor block, HR, NIBP, RR and SpO₂ were taken at baseline, at the start of bolus infusion, at the end of bolus infusion, at SAB, and then every 1 min for the first 15 min followed by every 5 min till 1 h, and every 15 min till the completion of surgery. Sedation was evaluated using Ramsay Sedation Score (RSS) at 15 min intervals. Target RSS score was 3 or 4, a score of 1 or 2 was considered as inadequate while 5 or 6 was considered as excess sedation. In case of inadequate sedation infusion of dexmedetomidine would be increased by 1 ml/h every 10 min till RSS of 3 was achieved. Similarly in case of excess sedation, the infusion would be reduced till RSS of 3 was achieved. Dexmedetomidine infusion was stopped at the end of surgery. Monitoring of all parameters was continued in the recovery room till Modified Bromage Scale 2 and a Visual analogue scale (VAS) >3 for pain was attained. The assessment of the sensory and motor block, sedation, hemodynamics and side effects was done by an independent anesthetist who was unaware of the drug as well as concentration of dexmedetomidine, and hence, double blinding was ensured.

Bradycardia (HR <50 beats/min) was treated with inj atropine 0.6 mg IV. Hypotension (reduction in MAP by 25% from baseline) was treated with inj ephedrine 6 mg IV. Patients who had persistent bradycardia or hypotension despite treatment were excluded from the study. Time for two segment regression was noted. Duration of motor block was considered from onset of Modified Bromage Scale 3 till regression to Modified Bromage Scale 2. Post-operatively, pain was assessed using VAS (0: no pain; 1, 2, 3: mild pain; 4, 5, 6: moderate pain; 7, 8, 9, 10: worst pain imaginable). Total duration of analgesia was defined as time from administration of SAB until the first complaint of pain (VAS ≥3), after which inj. paracetamol 1 gm IV was given as analgesic.

Keeping the power at 80% and confidence interval at 95% to detect at least a difference of 10% in the onset as well as prolongation of the subarachnoid block in both groups, the minimum sample size required was 78 patients; 95 patients were assessed for eligibility, of which 12 patients were excluded as per the exclusion criteria; 83 patients were enrolled in the study of which 2 were excluded due to inadequate spinal while 1 patient needed general anesthesia due to prolonged surgery.
Finally, a total of 80 patients were studied. Data collection and entry were done in Microsoft Excel while data analysis was done with the help of SPSS Software version 19.

Quantitative data were expressed as Mean ± Standard Deviation (SD). Comparison among study group was done with the help of Unpaired ‘t’ test, and Mann Whitney U test. Qualitative data were expressed as frequency and percentage while association among study group was assessed with the help of Chi-square test. *P* value less than 0.05 was taken as significant.

Results

Demographic data between groups A and B was comparable [Table 1].

Onset of sensory block in group A and group B was similar (*P* = 0.558). Onset of motor block in group A was at 4.6 ± 0.9 min and at 4.3 ± 0.9 min in group B (*P* = 0.13). Time for two segment regression was 139.7 ± 29.7 min in group A and 152.3 ± 18.7 min in group B and was statistically significant (*P* < 0.05). Duration of motor block was also statistically significant as 235.6 ± 12.4 min in group A and 245.3 ± 9.3 min in group B (*P* < 0.05). Thus there was a significant prolongation in duration of motor block as well as time for two segment regression in group B [Table 2]. Total duration of analgesia was comparable in both the groups at 259.3 ± 92.4 min in group A and 273.8 ± 52.3 min in group B (*P* = 0.39).

Mean baseline HR was comparable in both groups while there was a significant reduction in HR compared to baseline in both the groups [Figure 1]. Similarly, there was a significant reduction in MAP in both the groups when compared to the baseline [Figure 2].

Discussion

In this study, the effect of IV dexmedetomidine bolus followed by two different maintenance doses on spinal anesthesia, intra operative sedation and hemodynamics

| Table 1: Demographic data |
|---------------------------|
| Parameters               | Group A | Group B | *P*  |
| Sex M:F                  | 20:20   | 13:27   | 0.112|
| ASA I/II                 | 27/13   | 32/8    | 0.4  |
| Mean age (years)         | 43.7±12.3 | 45.1±12.1 | 0.6 |
| Weight (kg)              | 67.9±12.6 | 64.7±11.4 | 0.23|

| Table 2: Comparison of study parameters |
|-----------------------------------------|
| Parameters                              | Group A | Group B | *P*  |
| Onset of sensory block (min)            | 2.1±0.3 | 2.1±0.3 | 0.558|
| Onset of motor block (min)              | 4.6±0.9 | 4.3±0.9 | 0.13 |
| Duration of motor block (min)           | 235.6±12.4 | 245.3±9.3 | 0.000*|
| Time for two segment regression (min)   | 139.7±29.7 | 152.3±18.7 | 0.026*|
| Total duration of analgesia (min)       | 259.3±92.4 | 273.8±52.3 | 0.39 |
| RSS                                     | 3±1     | 3.5±0.5 | -    |

*Statistically significant

| Table 3: Comparison of side effects |
|------------------------------------|
| Side effects | Group A | Group B | *P*  |
| Hypotension     | 8       | 10      | 0.813|
| Bradycardia    | 3       | 3       | -    |

Figure 1: Comparison of HR showing a significant reduction as compared with baseline in both the groups

Figure 2: Comparison of MAP showing a significant reduction as compared with baseline in both the groups
were determined. We observed that group B patients had a significantly longer duration of motor and sensory block compared to group A patients. Both the doses caused a significant reduction of HR and mean blood pressure from baseline within the groups. Patients in both the groups had adequate and comparable sedation (RSS 3) compared to the baseline (RSS 2).

IV dexmedetomidine produces analgesic effects at both spinal and supraspinal levels primarily from inhibition of locus ceruleus at the brain stem and may cause inhibition of nociceptive impulse transmission by increased activation of alpha-2 receptors at the spinal cord.[11] In our study, we noted prolongation in the duration of motor block and time for 2 segment regression with a dose of dexmedetomidine which was similar to Harsoor et al.[5] Our results are similar to the study done by Kumari et al., although the bolus of dexmedetomidine used by them was higher at 1 mcg/kg followed by infusion of 0.6 mcg/kg/h.[12] Additionally, both the above mentioned studies observed faster onset of sensorimotor block and prolonged duration of analgesia. We too observed a faster onset of sensory block and prolonged duration of analgesia although it was not statistically significant. This could be explained by their study design which compared dexmedetomidine to saline in contrast to ours where two different doses of dexmedetomidine were compared.[5,12] Abdallah et al. in their meta-analysis of seven high-quality trials found that IV dexmedetomidine prolonged the duration of sensory block by 34%, motor block by 17%, and time to first analgesic request by 53% associated with 3.7-fold increase in transient reversible bradycardia without respiratory depression.[13] In our study, group A patients achieved a maximum mean sensory level of T8, whereas group B patients achieved a maximum mean sensory level of T6 which was comparable. Harsoor et al. in their study achieved a maximum sensory level of T10 in dexmedetomidine group and T8 in the control group with both groups being comparable.[5] The higher sensory level achieved in our study could be explained by the fact that we had administered 3 ml of 0.5% heavy bupivacaine as against 2.5 ml of 0.5% heavy bupivacaine in their study.

In our study, there was a statistically significant reduction of HR as well as MAP in the intra operative period with respect to the baseline which was comparable in both the groups. Song et al., compared 3 different infusion doses of dexmedetomidine 0.25, 0.5 and 0.75 mcg/kg/h after bolus of 1 mcg/kg and found a decrease in HR, 20 min after dexmedetomidine infusion which was comparable between the groups but with a significant decrease as compared to baseline.[6] Similar results were observed in our study where we found a significant reduction in HR compared to baseline in both the groups, 15 min after infusion of dexmedetomidine. The lowest value of HR was 58.3 in group A and 59.3 in group B at approximately 2 hours post SAB. Harsoor et al. too observed a statistically significant decrease in HR in dexmedetomidine group for 15-90 min.[3] Our findings are in concurrence to Song et al., where they found a dose dependent significant hypotensive response to dexmedetomidine as compared to baseline.[6] The 0.75 mcg/kg/h group in their study had a lower MAP compared to 0.5 and 0.25 mcg/kg/h which is explained by the higher dose of dexmedetomidine. In our study we found a reduction in MAP from baseline which is similar to the findings of Harsoor et al. in their dexmedetomidine group. Kumari et al. also found similar reduction in intra operative HR as well MAP.[12] In our study, interventions were required for bradycardia as well as hypotension in both the groups and were comparable, although the infusion did not have to be stopped at any point of time. Kumari et al. found significant patients had bradycardia in the dexmedetomidine group though this can probably be due to the 1 mcg/kg bolus of dexmedetomidine which is more than the bolus used in our study.[12] Ok et al. found similar incidence of side effects and they too did not need intervention for hypotension whereas bradycardia needed treatment.[14] The lowest MAP at which hypotension was treated was 50 mmHg in their study while it was higher in our study. This possibly explains why no intervention was needed for hypotension by them.

The sedation caused by dexmedetomidine sufficed during the intra operative period. Ramsay Sedation Score (RSS) in both groups of patients in our study was comparable. Similarly, Harsoor et al. had adequately sedated patients in their study whereas Kumari et al. had patients with excessive sedation as the bolus used was of a higher strength.[5,12] Song et al. in their study compared sedation with three different doses of dexmedetomidine and concluded that the appropriate dose was a bolus of 1 mcg/kg followed by an infusion of 0.25 mcg/kg/h.[6] Ok et al. too concluded that in surgeries of duration up to 90 min, a bolus of 1 mcg/kg/10 min followed by maintenance of 0.2 mcg/kg/h would produce adequate sedation.[14]

Our study was limited by our usage of RSS while BIS would have allowed continuous monitoring of sedation without awakening the patient. A fixed dose of 3 ml 0.5% hyperbaric bupivacaine was used without accounting for variations in height and weight of patients, which might be a confounding factor.
Conclusion

We conclude that low-dose bolus of 0.5 mcg/kg of IV dexmedetomidine followed by maintenance infusion of 0.5 mcg/kg/h is more effective than a bolus of 0.5 mcg/kg followed by maintenance infusion of 0.25 mcg/kg/h for increasing the duration of motor block and time for two segment regression of SAB. Both these doses render stable intra operative hemodynamics while ensuring an adequate depth of sedation.

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Conflicts of interest
There are no conflicts of interest.

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