Does Intravenous Low Dose Dexmedetomidine Supplementation has Beneficial Effects on Spinal Anaesthesia?

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ABSTRACT

Introduction: Dexmedetomidine has been reported to potentiate the effects of intrathecal local anaesthetics. This study was conducted to evaluate the effects of intravenous dexmedetomidine on spinal bupivacaine anesthesia.

Material and Methods: 80 female patients with ASA grade I/II aged 35-55 yrs. undergoing abdominal hysterectomy under spinal anaesthesia were randomized into two groups of 40 each. Before spinal anesthesia patients in group D received a loading dose of 0.5 µg /kg IV Dexmedetomidine over 10 min. by infusion pump followed by a maintainance dose of 0.5 µg/kg/hr till completion of the surgery, while patients in group C received the same calculated volume of normal saline. Time for onset of sensory and motor blockade, time to reach peak sensory level, time taken for two segment regression and maximum sensory level, Ramsay sedation score, duration of analgesia and haemodynamic parameters were recorded and statistically analyzed.

Results: Onset of sensory block in group D was 1.325 ± 0.474 min and 1.65 ± 0.483 min in group C. Time for two segment regression was 130.87 ± 11.76 min in group D and 105.38 ± 10.22 min in group C. Time for return of modified bromage score to 0 in group D was 216.25 ± 19.38 min and 161.75 ± 18.73 mn in group C. Total analgesia duration was 257.25 ± 15.18 min in group D and 195.63 ± 12.87 min in group C.

Conclusion; Intravenous Dexmedetomidine prolonged spinal bupivacaine sensory and motor blockade and provided satisfactory arousable sedation. It can cause transient, easily treatable bradycardia and hypotension.

Keywords: Intravenous, Dexmedetomidine Supplementation, Spinal Anaesthesia?

INTRODUCTION

Numerous trials of different techniques and drugs for postoperative pain control of abdominal surgeries has been conducted but none of them has ever emerged with overwhelming advantage. Popular and common anaesthetic technique used for abdominal hysterectomy is Spinal anaesthesia which is best to control intraoperative pain. Many drugs are used intrathecally like epinephrine, fentanyl, buprenorphine to prolong the duration of sensory block and achieve longer perioperative analgesia.[1] Clonidine and dextmedetomedine have been used intrathecally.[2] and also intravenously to prolong the duration of spinal anaesthesia using various local ansthetics.[3-6] apart from sedation and analgesia they also decrease the stress response to surgery and anesthesia. They produce sedation and anxiolysis by binding to presynaptic α 2 receptors in locus ceruleus.[7,8] Postsynaptic activation in CNS inhibits sympathetic activity thus decreasing heart rate and blood pressure. At the spinal cord stimulation of α 2 receptors at the substantia gelatonisa of the dorsal horn leads to inhibition of firing of the nociceptive neurones and inhibition of release of substance P contributing to their analgesic action. The most accepted mechanism of this action is by release of nitrous Oxide. Dextmedetomedine is more suitable adjuvant to spinal anesthesia compared to clonidine as it has more sedative and analgesic effect due to its more relative α 2 A receptor agonist activity.

Studies evaluating the efficacy of dexmedetomedine in prolonging the duration of subarachnoid block have used 1µg bolus followed by infusion.[9-12] We hypothesized that dextmedetomedine might have role in prolongation of SAB with 0.5% heavy bupivacaine if given small IV loading dose followed by infusion. Hence, present study was designed to evaluate the effects of intravenous dexmedetomedine 0.5µg/kg followed by its infusion, on the SAB block characteristics, its duration and level of sedation in patients undergoing open abdominal hysterectomy.

MATERIAL AND METHODS

After Institutional ethical committee approval, prospective, randomized, double blinded clinical comparative study was designed.

Sample Size: Based on previous study[15] the data on comparison of sensory and motor parameter was referred. The standardized effect size ranged between 0.2 to 0.6 for various paramete group, we. An average effect size of approximately 0.65 was used to determine the sample size. VAS ≥3 a power of 0.8 and significance level of 0.05, the estimated per group sample size was 39. We included 40 patients in each group for better validation of results.

Eighty female patients, aged 35-55 yrs. ASA grade I/II, undergoing open abdominal hysterectomy were randomly divided into two groups of 40 in each group by a computer generated randomization table. Group D=Received single bolus iv dose of dexmedetomidine (0.5mcg/kg in 100 ml with NS over 10 min as a loading dose, before instituting SAB) as premedication. Group C=Received 100 ml normal saline over 10 minutes as pre-medication A study anaesthetist (Person A) prepared control and study group drugs, Person B did intraoperative and post operative monitoring i.e. heart rate, mean arterial pressure, sensory level, pain (VAS score), motor blockade (modified Bromage scale) and level of sedation (Ramsay Sedation Score). Person C administersed (intravenous

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and intrathecal) to the patients. Person A and C were constant throughout the study. Person B, C and the patient were unaware of the drug injected to enable double-blinding.

Exclusion criteria included Use of any opoids or sedative medications in the week prior to surgery, history of alcohol or drug abuse, contraindication for SAB, morbidly obese, patients on antihyperetensive therapy, with diabetes or renal dysfunction, with allergy to amide type of local anesthetics. All patients underwent a thorough preanaesthetic check up along with routine investigations like Haemogram, Urine examination, RBS, Chest X-Ray, ECG. If required additional investigations were carried out.

A written informed consent was taken. Patients were explained about plan of anaesthetic procedure, Visual analogue scale (VAS) was taught and how to express the degree of pain on the scale. On the day of surgery patients did not receive any premedication. After intravenous insertion of 18-G cannula in the operating room, before induction of SAB, all patients were preloaded with Ringer's lactate 10ml/kg. A single dose of dexmedetomidine 0.5µgkg^{-1} was administered i.v. in 100 ml normal saline over 10 min to group D. The same amount of saline was given to the patient in the group C. After SAB, supplemental dexmedetomidine infusion was continued in group D using infusion pump at the rate of 0.5mcg/kg/hr throughout the surgery. Same amount of normal saline was administered in control group in addition to routine requirement of IV fluid. Monitoring included three lead ECG in Std. lead II, Non invasive Blood pressure, Respiratory rate, Pulse oximetry for peripheral oxygen saturation (SpO2), Capnography for end-tidal carbon dioxide concentration (Et-CO2) were recorded. The base line Heart rate, Blood pressure, SpO_2, Respiratory rate, Et-CO2 was recorded at prior to premedication, after premedication, then after SAB, at every 1 minute interval for 5 minutes; then every 5 minutes interval for 25 minutes; then every 15 minutes interval till the procedure is completed and finally every 30 min in postoperative period. Under strict aseptic precautions, lumbar puncture was performed with 23 gauge Quincke needle at L3/4 or L2/3 interspace with patients in lateral position through midline approach with the bevel point tip upward. SAB was given with15mg of 0.5% hyperbaric bupivacaine injected after free flow of clear CSF. Patient was made to lie down supine immediately on the OT table without any tilt. Surgery was performed after confirmation of successful blockade with proper height of analgesia. All patients received oxygen at 2litres per min via a binasal prongs throughout the procedure. Arterial oxygen saturation was registered continuously by pulse oximetry. Fluid administration was continued intraoperatively with Ringer's lactate. After SAB, in addition to regular IV fluid supplementation, all the patients in Group D was received maintenance infusion of dexmedetomidine at rate of 0.5mcg/kg/hr and same rate of infusion of saline was administered in group C, throughout the duration of surgery, in same way.

Hypotension (MAP≤ 25% from baseline or systolic pressure < 90mm of Hg) was treated with Inj ephedrine 6 mg IV and bolous administration of 250 ml of ringer lactate over 10min were repeated if blood pressure remained low. Bradycardia (HR<25% from baseline or HR<50 beats/min) was treated with inj atropine 0.6 mg IV. Respiratory depression was defined as an EtCO2>50 mm Hg or RR <10 breaths min.$^{-1}$

The onset of sensory anaesthesia was tested with 23 G hytpodermic needle by pinprick. Sensory anaesthesia was defined as the loss of sharp sensation to pinprick bilaterally in the midclavicular line. Time taken for onset of sensory anaesthesia at L1 was recorded and tested for every minute till the peak level was achieved. Peak sensory level defined as the sensory level which remains same for three reading after every 1 min of interval. Peak sensory level and time to achieve peak sensory level was recorded. Two dermatomal regressions from the maximum level and regression to L1 level was noted. Sensory blockade was assessed every minute for first 10 minute thereafter every 15 min during surgery and every 30 min postoperatively. The time for total duration of analgesia (time from administration of SAB until the first request of rescue analgesia at VAS ≥ 3) was calculated. All duration was calculated considering the time of spinal injection as time 0. Motor blockade was determined using Modified Bromage scale.[13] Motor blockade was assessed every 2 min after SAB till complete motor block was achieved and every 30 min in PACU. The onset of motor blockade (Time taken for motor blockade to reach Modified Bromage Scale 3) and duration of motor blockade (Regression of motor blockade to Modified Bromage scale 0) was noted. Duration of analgesia was assessed by Visual Analogue Scale (VAS) postoperatively till request of first rescue analgesic. Total duration of analgesia was defined as time from administration of SAB to first request of rescue analgesia. Injection diclofenac 75mg intramuscular was used as rescue analgesic.

The level of sedation was evaluated both intra and post operatively every 15 min thought the study period using Ramsay sedation score[14] (RSS) as shown below till the patient was discharged from PACU. Grade1.Anxious or restless or both. Grade 2. Cooperative, orientated and tranquil. Grade 3. Responding to commands. Grad 4. Brisk response to stimulus. Grade5. Sluggish response to stimulus.Grade6. No response to stimulus

Adverse effect such as nausea, vomiting, shivering, hypotension, bradycardia were observed and treated accordingly.

STATISTICAL ANALYSIS

The anthropometric parameters like height, weight and BMI, sedation score, EtCo2 at each stage, mean of the vital parameters and time for motor bromage score 3 were compared between two groups using t-test for independent samples. The maximum sensory level between the groups was compared using Wilcoxon rank sum test. The proportion of patients in two groups with peak sensory levels for T6 and T8 was tested for statistical significance using Chi-square test. The analysis was performed using SPSS 20.0 (SPSS Inc.) software and the significance level was set at 5%. P value of < 0.05 was considered as significant.

RESULTS

The two groups were statistically similar to each other with respect to age, weight, height, BMI, duration of hysterectomy (Table-1). Onset of sensory blockade at L1 in group D was 1.325 ± 0.474 minutes while it was 1.65 ± 0.483minutes in group C. This difference was statistically significant (p -value 0.0033). There was no significant difference in onset of motor blockade, as it was 4.65± 0.948 min in group D and 4.70± 0.966 min in group C (p-value 0.815). Maximum sensory level

(Median) achieved was statistically higher in group D (6.75± 0.981) than in group C(7.55± 0.8458), p<0.0002. Time to two segment regression was longer in group D (130.87 11.76min.) than (105.38 10.22min) in group C,P<0.0001. Time for first rescue analgesic was longer in group D (257.25 ±15.18min) than (195.63 ±12.87min) in group C. Duration of motor block was prolonged in group D (216.25±19.38min) as compared to group C (161.75± 18.73min) p<0.0001 (table-3).

DISCUSSION

The results of our study indicate that intravenous dexmedetomidine premedication hastened the onset of sensory block, could be due to α-2 receptor activation induced inhibition of nociceptive impulse transmission, but motor block onset was not affected. Also there was prolongation of duration of analgesia and motor blockade. Sedation was also provided throughout the procedure without any haemodynamic instability or any side effects.

Dexmedetomidine administered intravenously produces analgesia by acting at both spinal and supraspinal levels. Primarily analgesic effect is due to inhibition of locus ceruleus at the brain stem. Additionally, its infusion may result in increased activation of α-2 receptors at spinal cord leading to inhibition of nociceptive impulse transmission via both pre and postsynaptic α-2 receptors.[16,17] We found statistically significant difference in the onset of sensory block i.e. 1.325 ± 0.474 min. in group D and 1.65 ± 0.483, p 0.0033,showing hastening effect Harsoor et al[15] observed hastening effect on sensory block onset but Reddy et al[18] and Chandrashekharappa k et al[19] found hastening of both the onsets of motor and sensory blocks. Gupta K, Tiwari V et al[20] did not observe hastening effect on motor and sensory block as iv dexmedetomidine supplementation was started 20 mins after SAB. The maximum sensory level (Median) achieved was more in group D (6.75 ± 0.981) than in control group (7.55 ± 0.8458) p< 0002.Al Mustafa et al,[3] Reddy V S et al,[18] Kaya F N et al,[21] also have reported higher level of sensory blockade of hyperbaric bupivacaine with intravenous dexmedetomidine supplementation.

The time for first rescue analgesic was significantly prolonged, in group D it was 257.25 ± 15.18,in group C, 195.63 ± 12.87 (p< 0.0001)Complete regression of motor blockade was prolonged in group D (216.25 ± 19.38min vs 161.75 ± 18.73 min in group C, P< 0.0001). The effect of clonidine on motor blockade is concentration dependant,[22] as Kaya et al[21] did not observe any effect on motor blockade duration with single dose of 0.5µg/kg Dexmedetomidine, there might be same explanation of this phenomenon with dexmedetomidine also. In spite of use of 0.5µg/kg initial loading dose, motor blockade was prolonged in our study may be due to continuous infusion of dexmedetomidine. Al-Mustafa et al[3] also observed prolongation of both sensory and motor blockade with intravenous supplementation of dexmedetomidine.

Intravenous administration of dexmedetomidine should not be done in less than 10 min. duration as rapid administration might produce hypertension and reflex bradycardia[23] due to peripheral α2B adrenoreceptor stimulation of vascular smooth muscle that can be attenuated by slow infusion over 10 or more minutes. To evaluate various doses of IV dexmedetomidine (0.25, 0.5,1 µg/kg) on ischemic pain in healthy volunteers moderate analgesia with ceiling effect at 0.5µg/kg[24] was observed. Keeping this in mind we chose dose of 0.5µg/kg given over 10 min.

Dexmedetomidine induced sleep qualitatively resembles normal easily arousable sleep[25] Patients remains cooperative and it is dose dependant, even low doses might be cause sufficient sedation[26] thus eliminating the need for additional sedatives thus providing better conditions for surgeon and patient. In our study intraoperatively the sedation scores were higher in group D than in control group continued for 30 min postoperatively as the dexmedetomidine infusion was discontinued postoperatively. Swati Bisht et al[27] observed Similar results. Al Mustafa et al[3] observed scores in range of 2-5 could be due to more loading dose (1µg/kg). There was no respiratory depression in any patients. Respiratory rate, SpO_2 and Et-CO2 remained within normal limits.

Side effects of the dexmedetomidine like dizziness, bradycardia, hypotension, pruritus, nausea, vomiting were studied (table-9). The incidence of bradycardia was 10% in group D and 2.5% in group C and that of hypotension was 5% in group D and 2.5% in group C (Table 4-8). Both were found to be more in group D could be due to decreased sympathetic outflow and circulating levels of catecholamines due to dexmedetomidine.[3] Incidence of bradycardia and hypotension was unremarkable, transient and easily treatable with atropine and ephedrine respectively as we used low dose infusion at slower rate.

Our study was done on healthy female patients and we administered a fixed slow dexmedetomidine infusion with adequate hydration. Hence different studies are required to investigate the efficacy of dexmedetomidine in geriatric and medically compromised patients also. Moreover, we studied the action of dexmedetomidine on only one local anaesthetic i.e hyperbaric bupivacaine hence study with more than one local anaesthetic for SAB so as to have more comparative data are also required to be done.

CONCLUSION

Our study has demonstrated that intravenous supplementation of loading dose of dexmedetomidine 0.5µgm/kg followed by infusion of 0.5µgm/kg/hour hastened the onset and prolonged the duration of sensory block of spinal anaesthesia. The motor block was also prolonged. It also provided sufficient sedation without respiratory depression and transient easily treatable hypotension and bradycardia. Hence, intravenous low dose dexmedetomidine supplementation, appears to be beneficial during spinal anesthesia provided the anesthesiologist is alert of development of bradycardia and hypotension.

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