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STUDY OF EFFECT OF INTRAVENOUS DEXMEDETOMIDINE FOR PROLONGATION OF SPINAL ANAESTHESIA WITH HYPERBARIC BUPIVACAINE – RANDOMIZED DOUBLE BLIND STUDY

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ABSTRACT **Background:** Dexmedetomidine, a specific alpha 2 adrenoreceptor agonist decreases the stress response, can prolong the duration of spinal anaesthesia by its antinociceptive action. **Aim:** To evaluate the effect of IV dexmedetomidine 1 mcg/kg bolus followed by 0.5 mcg/kg/hour infusion for prolongation of spinal anaesthesia with hyperbaric bupivacaine. **Method:** A Prospective, randomized, double Blind, comparative study was carried out in 60 patients divided in two groups of 30 each. Dexmedetomidine group or Group B received IV Dexmedetomidine 1 mcg/kg bolus followed by 0.5 mcg/kg/hour infusion for 60 minutes. Control group or Group A was given normal saline in similar fashion. Visual analogue pain score (VAS), Ramsay Sedation Score (RSS), Modified Bromage scale, Vital parameters were recorded at 1, 5, 10, 15, 30, 45, 60 minutes & every 15 min thereafter for up to 2 hours and hourly till 6 hours postoperatively. **Result:** The duration of the sensory and motor blockade was significantly prolonged in group B patients who received intravenous dexmedetomidine. Significant difference in Modified Bromage Scale was observed in immediate postoperative period, 1 hour and 3 hours of postoperative period. There was significant prolongation of motor block in group B than group A. VAS score was less in Group B patients as compared to group A. During intraoperative period RSS was higher in group B than in control group A. It was highest at 60 minutes, and decreased from 75 minutes till immediate postoperative period, 1 hour and 3 hours of postoperatively. **Conclusion:** IV Dexmedetomidine 1 mcg/kg bolus followed by infusion of 0.5 mcg/kg/hour significantly prolonged the duration of sensory and motor blockade and postoperative analgesia for first 6 hours with minimal hemodynamic side effects and without deep level of sedation.

KEYWORDS : Intravenous Dexmedetomidine, Spinal Anaesthesia, Hyperbaric Bupivacaine.

INTRODUCTION

Spinal anaesthesia (SA) is the technique of regional anaesthesia used for the surgeries of lower limb and lower abdomen.[1] Though the operating site is anaesthetized and the patient does not feel pain, they remain awake during the whole surgery resulting in mental stress. Sedation during neuraxial block alleviates the anxiety and mental stress.[2] Alpha 2-adrenergic receptor (α2-AR) agonists produces sedation, analgesia, anxiolysis, perioperative sympatholysis, reduced anaesthetic demand with preservation of respiratory function.

Clonidine, a first generation alpha 2 agonist, prolongs spinal anaesthesia whether administered by intravenous or intrathecal route.[3] Dexmedetomidine a more specific alpha 2 adrenoreceptor agonist, has all the properties of an ideal analgesic. Food and Drug Administration (FDA) has approved the use of dexmedetomidine in 1999 for short-term sedation and analgesia in the ICU.[4] Intravenous dexmedetomidine by its antinociceptive action at substantia gelatinosa (spinal action) and locus coeruleus area (supra spinal action), can prolong duration of spinal anesthesia.[5] Studies have proved that dexmedetomidine when given intravenously or intrathecally prolongs the duration of spinal anesthesia.[6,7] Decrease in stress response, heart rate and blood pressure can be beneficial in the perioperative period.

MATERIALS AND METHODS

A prospective, randomized, double blind, comparative study was carried out at tertiary care center after approval by Institutional ethics committee.

Total 60 subjects were randomly divided using computer generated randomization list & sealed envelope technique into 2 groups with 30 patients in each group with allocation ratio 1:1. Informed written consent was taken in vernacular language as per declaration of Helsinki. The participants were free to withdraw anytime during the conduct of study. Patients of American Society of Anaesthesiologists grade 1 and 2, age 20-55 years, weighing 40-70 Kg, both sexes undergoing elective surgery under SA were included. Patient's refusal to participate in the study, allergy to study drugs, ASA grade 3 or more, emergency surgeries, patient with gross spinal abnormality or any contraindication to spinal anaesthesia were excluded. IV access was obtained on the forearm with 18G cannula and preloading with lactated ringer solution 10ml/kg was started. Monitoring including non-invasive blood pressure, ECG and pulse oximeter was done. Under all aseptic precautions, SA was given with hyperbaric 0.5% bupivacaine 15mg using 23G Quincke's spinal needle. Oxygen supplementation at 6 liters/minute via face mask was given. Following spinal anaesthesia, Group A or Placebo group received IV Normal Saline 100 ml over 10 minutes as bolus & infusion of 100ml NS over 60 minutes. Group B or Dexmedetomidine group received IV dexmedetomidine 1mcg/kg over 10 minutes in 100 ml NS as bolus followed by 0.5 mcg/kg/hr infusion in 100ml NS over 60 minutes. Maintenance fluid & blood products were given according to patient's hemodynamic parameters & blood loss.

The participant and investigator were blinded to the drug administered. The onset of sensory block was tested by pin prick method. The duration of sensory blockade was taken as time from onset to time to return of pinprick sensation to S1 [heel] dermatomal area. The duration of motor block was taken from the time of injection to complete regression of motor block [ability to lift the extended leg]. Vital parameters, Ramsay Sedation Score (1-Patient anxious, agitated or restless, 2-Patient cooperative, oriented, accepting ventilation, 3-Patient responds only to commands, 4-Asleep, but with brisk response to light glabellar tap or loud auditory stimulus, 5-Asleep, sluggish response to light glabellar tap or loud auditory stimulus but does not respond to painful stimulus, 6-Asleep, no response), Modified Bromage scale (score 0 – Able to move hip, knee, ankle, 1- Unable to move hip, but is able to move knee and ankle 2- Unable to move hip and knee but is able to move the ankle, 3- Unable to move hip, knee and ankle), ECG changes were recorded at 1, 5, 10, 15, 30, 45 minutes & every 15 minutes thereafter for up to 2 hours and hourly till 6 hours

postoperatively. Postoperative pain was recorded using 10 cm Visual Analogue Pain Scale. Duration of postoperative analgesia was measured from the time of spinal anaesthesia to the time when pain score becomes more than or equal to 4.

Intravenous infusion of Paracetamol 1 gram was given as analgesic to those patients who complained of pain (VAS>4).

Patients were observed intraoperatively and postoperatively for any side effects like nausea, vomiting, pruritis, arrhythmias, bradycardia, hypotension, respiratory depression, sedation, dizziness, etc.

Sample size was calculated from mean and standard deviation of reference study with power 80 %, difference in mean arterial pressure 20% of baseline value considered to be significant.

$$n = 2 \times \left(\frac{Z_{1-\alpha/2} + Z_{1-\beta}}{ES}\right)^2$$

Z = Standard score, α = Type 1 error, β = Type 2 error, ES = effect size.

STATISTICALANALYSIS

Data was entered in Microsoft Excel and analyzed using SPSS version 24.0. Mean and SD was calculated for quantitative variables and proportions were calculated for categorical variables. Unpaired t-test or Chi-square test was applied to check significance between two groups. P- Value of <0.05 will be considered statistically significant.

RESULTS

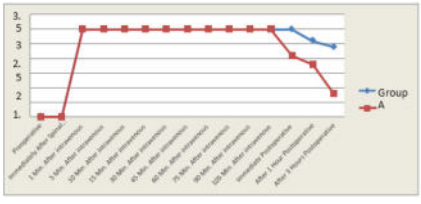
The demographic data like age, gender & ASA grade of participants was comparable between the two groups (p >0.05) (Table 1).

Table 1: Distribution of patients according to Age, Gender & ASA status

Group	Group A Mean±SD or n (%)	Group B Mean±SD or n (%)	P-value
Age	39.27±10.31	39.47±9.61	0.921
Gender Male Female	 14 (46.7%) 16 (53.3%)	 14 (46.7%) 16 (53.3%)	1.00
ASA status Grade I Grade II	 19 (63.3%) 11 (36.7%)	 16 (53.3%) 14 (46.7%)	0.621

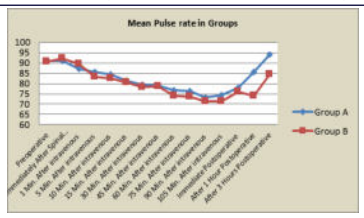
The duration of the sensory and motor blockade was significantly prolonged in group B patients who received intravenous dexmedetomidine. Modified Bromage Scale of group A and B was comparable at preoperative, immediately after spinal anaesthesia & during intra operative period. There was significant prolongation of motor block in group B than group A with statistically significant difference in Modified Bromage Scale during immediate postoperative period, 1 hour and 3 hours of postoperative period (Graph 1).

Graph 1: Comparison of Modified Bromage Scale in study groups

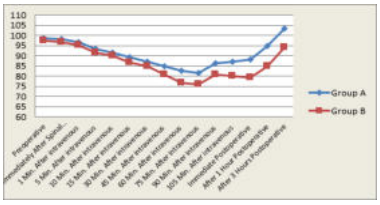


Baseline parameters like PR, SpO2, RR, SBP, DBP and MAP were comparable in both the groups. There was no statistically significant difference observed at preoperative stage, immediately after spinal anaesthesia, during intra operative up to 105 minutes and immediate postoperative period. But there was statistically significant difference in mean pulse rate & mean arterial pressure of group A and B were observed after 1 hour and 3 hours of postoperative period (Graph 2 & 3).

Graph 2: Comparison of Pulse rate in the study groups



Graph 3: Comparison of Mean Arterial Pressure in study groups



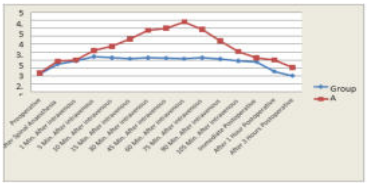
There was no statistically significant difference in mean respiratory rate & SpO2 of group A and B were observed during study period. VAS score was comparable preoperatively, immediately after spinal anaesthesia & immediate postoperative period. During postoperative period, group B patients showed significantly less VAS score as compared to group A (P<0.05) (Table-2).

Table 2: Comparison of mean Visual Analogue Pain Score in study groups

Visual Analogue Scale	Group A Mean (SD)	Group B Mean (SD)	P-value
Preoperative	6.80 (1.71)	6.38 (1.40)	0.926
Immediately After S.A.	6.27 (1.80)	6.40 (1.52)	0.734
Immediate Postoperative	0.33 (0.61)	0.00 (0.00)	-
After 1 Hour Postoperative	4.67 (0.80)	0.07 (0.25)	0.0001
After 3 Hours Postoperative	6.00 (0.64)	1.33 (1.37)	0.0001

Ramsay Sedation Score was comparable at preoperative stage (Graph-4). During intraoperative period, it was significantly higher in group B than in group A, highest at 60 minutes and decreased from 75 minutes till immediate postoperative period, 1 hour and 3 hours postoperative.

Graph 4: Comparison of Ramsay Sedation Score in study groups



No significant side effects were observed in either group.

DISCUSSION

Spinal anaesthesia for infraumbilical surgeries is advantageous in terms of low cost, easy to administer, less risk of aspiration in full stomach patients. Regional anaesthesia allows early return of gastrointestinal functions, decreased stress response. But the disadvantage of spinal anaesthesia is its limited duration of action. Usually, spinal anaesthesia with hyperbaric bupivacaine intrathecally lasts for 2 to 2.5 hours. Various adjuvants are added to hyperbaric bupivacaine to prolong the anaesthetic effects. They act perineurally or at different sites in the spinal cord to exert their antinociceptive action and prolong anaesthesia and decrease pain in the post operative period, but they are yet to be approved for intrathecal use. Hence, we selected intravenous route in our study.

Dexmedetomidine is a more suitable adjuvant to spinal anaesthesia as it has more sedative and analgesic effects due to its more selective alpha2 adrenergic receptor agonist activity. Dexmedetomidine is found to prolong action of SA by both intrathecal & intravenous route. Dinesh et al., had demonstrated that the total duration of sensory blockade was significantly prolonged in the dexmedetomidine group (269.8 ± 20.7 min) whereas it was 169 minutes in the control group (169.2 ± 12.1 min).[8] Similar results were seen in our study.

Al Mustafa et al., had demonstrated that the total duration of sensory blockade was significantly prolonged in the dexmedetomidine group (261.5 ± 34.8 min) as compared to control group (165.2±31.5 min) ($p < 0.05$).[9] Dexmedetomidine group had higher level of sensory block than the control group in our study, similar to the results of Kaya et al. The Modified Bromage score remain same in both the groups due to the effect of spinal anaesthesia. But in immediate postoperative period, the mean score was higher in dexmedetomidine group at 1 and 3 hours.

The mean arterial pressure was significantly lower in dexmedetomidine group as compared to control group but within physiological limits.This has proved the fact that dexmedetomidine has got a definite role in hypotensive anaesthesia. Previous studies have shown that the hypotensive effect of dexmedetomidine persists in the intraoperative as well as in the postoperative period.[10,11] Eliceck et al., reported significant decrease in mean arterial pressure (MAP) after 20, 25, and 30 min after dexmedetomidine infusion as compared to control group.[12] Contrary to above studies and the present study, Al Mustafa et al [9] and Tekin et al [13] reported no significant difference in mean arterial pressures in dexmedetomidine and control groups.

The mean VAS was comparable in both groups due to effect of Spinal Anaesthesia, while the score was still zero for dexmedetomidine group in the immediate postoperative period. After 1st and after 3 hours in postoperative period, dexmedetomidine group showed significantly less VAS score with added advantage of extended postoperative analgesia. Similar results were found by Rapolu et al & Ahmed et al that there was statistically significant difference in VAS pain score upto 24 hours after surgery. [14,15]

Ramsay sedation score was significantly higher in dexmedetomidine group as compared to control group from 15 minutes till 90 minutes intraoperatively. Throughout the intraoperative period, all patients had good sedation score (R3- R2) who received dexmedetomidine compared to the control group. Dexmedetomidine causes arousable sedation. Kaya et al., explained about the benefits of dexmedetomidine over midazolam.[7]

Thus, intravenous dexmedetomidine prolonged the sensory and motor blockade significantly with minimal hemodynamic side effects.[16]

CONCLUSION

Intravenous dexmedetomidine 1 microgram/kg bolus followed by at 0.5 microgram/kg/hr infusion for 60 minutes given after spinal anaesthesia for patients undergoing infraumbilical and lower limb surgeries significantly prolong the duration of sensory and motor blockade as compared to control group.

Dexmedetomidine provides excellent sedation during surgery and sedation scores reach normal within 15 mins after stopping the drug. Dexmedetomidine is effective in providing significant postoperative analgesia in first 6 hours. All these effects were achieved without causing deep level of sedation and with minimal hemodynamic side effects.

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