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EFFECT OF INTRAVENOUS DEXMEDETOMIDINE ON CHARACTERISTICS OF SPINAL ANAESTHESIA WITH HYPERBARIC BUPIVACAINE: A PROSPECTIVE STUDY.

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Introduction:
Dexmedetomidine is a highly selective α2-agonist. α2-receptors are found in many sites throughout the body including central nervous system, spinal cord and peripheral tissues.[1]There is a hypothesis that by its actions on the substantia gelatinosa in the spinal cord and locus coeruleus in the brain, Dexmedetomidine can prolong spinal anaesthesia when given IV or intrathecally. Dexmedetomidine leads to sedation without respiratory depression[2] and causes decrease in stress response by lowering secretion of catecholamines. This can be of great value in perioperative period during which haemodynamic variations occur due to stress.[3]with the above background, the present study was aimed to evaluate the effects of IV dexmedetomidine on spinal anaesthesia with 0.5% of hyperbaric bupivacaine.

Subjects and Methods:
A randomized, prospective, double blind study of patients' undergoing elective lower abdominal surgeries was taken after institutional approval. Sample size of 60 was calculated by using OpenEpi software. We included patients of 18-65years of age, both sexes, ASA-I/II for the study and randomly divided into two groups of 30 each(Group-D (Dexmedetomidine) and Group-C (placebo)) by coin toss method. Pregnant women, patients' having deformity of spine or local infection, poorly controlled hypertension, hypovolemic shock, coagulation abnormality, severe liver and renal disease, pre-existing severe bradycardia, congestive heart failure were excluded. After pre-

anaesthestic checkup, patients were kept fasting from previous night. Procedure of spinal anaesthesia and the use of VAS scale were explained and informed written consent was obtained. Patients' baseline parameters were recorded and preloading was done with Inj. Ringer Lactate 15ml/kg 15minutes prior to induction. Group-D patients were recieved IV Dexmedetomidine 0.5µg/kg diluted to 10ml with Normal saline (NS) and infused over 10mins as Loading dose (LD). Group-C patients were received 10ml of NS infused over 10mins as LD. After that, with all aseptic and antiseptic precautions; spinal anaesthesia was performed in lateral position at L3–L4 space using 25G Quincke spinal needle with 15mg (3ml) of hyperbaric Bupivacaine. After spinal anaesthesia, Group-D patients were received maintenance infusion of Dexmedetomidine at the rate of 0.5µg/kg/h IV and Group-C patients were received NS at the same rate throughout surgery. Time for onset and duration of sensory and motor blockade, maximum level of sensory block, two segment regressions timeand duration of analgesia were observed. Sensory blockade was assessed by pin prick method, every 1min till first 5mins and then every 2mins till 10mins. Onset of sensory blockade (time interval from intrathecal injection to L1 level), time for maximum sensory level (intrathecal injection to T8 level), and time for two segment regressions (From T8 to T10) in mins were recorded. Motor blockade was assessed with Modified Bromage scale every 1min till first 5mins and then every 2mins till 10mins. Onset of motor block (time interval from intrathecal injection to Bromage1), complete motor block (time interval from intrathecal injection to Bromage3)and duration of motor block (time interval from Bromage3 to Bromage0) were recorded. Intra operatively HR, NIBP, SpO2 were recorded, every 2mins for the first 10mins, at 15mins and every 15mins till the end of surgery. Intra operative sedation was assessed every 15mins by using Modified Ramsay Sedation Scale. Side effects like hypotension, bradycardia, respiratory depression, nausea and vomiting were noted. Hypotension was treated with bolus dose of 6mg mephentermine IV. Bradycardia was treated with 0.6mg atropine IV. Incidence of respiratory depression defined as respiratory rate<9/min and SpO2<90% on room air was noted. Post operative pain had been assessed every 30mins by VAS scale and when VAS≥3, injection diclofenac sodium 1.5mg/kg IV was given as rescue analgesic.

Observation and Results:

Demographic data in terms of age, sex, height, weight, mean duration of surgery were comparable in both groups.

Table 1:-Sensory parameters in both study groups

Sensory Parameters (mins)	Group C		Group D		P value	Remarks
	Mean	SD	Mean	SD		
Onset of sensory block(L1 level)	2.22	0.61	1.80	0.40	0.002	S
Maximum level of sensory block (T8 level)	6.30	0.64	4.30	0.44	0.000	HS
Two segment regression(T8 to T10 level)	140.80	6.74	172.33	5.49	0.000	HS
Duration of sensory block (S1 level)	219.13	7.19	274.00	13.05	0.000	HS

As per the table-1, Mean time for onset of sensory block, time to reach maximum level of sensory block, time for two segment regressions and time for sensory regression to S1 segment were significant in Group-D compared to Group-C.

Table 2:- Motor parameters in both study groups

Motor Parameters	Group C		Group D		P value	Remarks
	Mean	SD	Mean	SD		
Onset of motor block (Bromage 1)	2.88	0.19	2.00	0.00	0.000	HS
Partial motor block (Bromage 2)	3.74	0.40	2.23	0.48	0.000	HS
Complete motor block (Bromage 3)	6.07	1.01	3.68	0.44	0.000	HS
Duration of motor block (Bromage 3 to 0)	190.67	6.16	224.13	9.72	0.000	HS

As per the table-2,mean time for onset of motor block, time for partial motor block, time for complete motor block and duration of motor block were significant in Group-D compared to Group-C.

After injecting study drug, the mean HR in Group-C was 86.97±5.3bpm and Group D was 76.30±4.24 bpm. The difference was highly significant (p<0.001). After SAB the mean HR in Group-C was 87.37±5.39 bpm and Group D was75.93±4.07 bpm. The difference in HR was highly significant in both group (p<0.001). At 10min the mean HR in Group-C was 85.80±5.08bpm and Group-D was 68.87±3.88bpm. The difference in HR was highly significant in both group (p<0.001). Group-D has maintained lower heart rate as compared to Group-C throughout the surgery which was found to be statistically significant. After injecting drug, the mean MAP in Group-C was 95.03±7.24mmHg and Group-D was 90.47± 8.06mmHg which was significant in both group (p<0.05). After SAB, the mean MAP in Group-C was 94.63±7.18 mm of Hg and Group-D was 90.33±8.08 mmHg which was significant in both groups (p<0.05). At 10min the mean MAP in Group-C was 90.73±7.28mmHg and Group-D was 84.67±7.92mmHg which was significant in both group (p<0.05). Group-D has maintained lower MAP as compared to Group-C throughout the surgery. This was found to be statistically significant (p<0.05). Mean respiratory rate in Group-C was 14.8±1.3 per minute while in Group-D was 15.00±0.9 per minute which was statistically insignificant (p>0.05). Mean SpO2 in Group-C was 99±0.5% while in Group-D was 99±0.7% which was statistically insignificant (p>0.05).

In both groups, baseline sedation was comparable. Throughout the surgery, sedation score in Group-D was highly significant than Group-C(p<0.001). In our study, in control group one patient developed hypotension and in Group-D two patients developed hypotension which was treated with fluid and inj. Mephentermine 6mg IV. In our study, in Group-D three patients developed bradycardia which was treated with inj. Atropine 0.6mg IV.

Discussion

Spinal anaesthesia is a widely used regional anaesthetic technique for lower abdominal surgeries. Spinal anaesthesia produces intense sensory, motor and sympathetic blockade with significantly lesser dosage of local anaesthetics.[4, 5] Adjuvants like buprenorphine, tramadol, fentanyl, α2 agonists can be used to overcome limited duration of spinal anaesthesia.[6, 7, 8]α2 agonists produces sedation, analgesia, anxiolysis, perioperative sympatholysis, cardiovascular stabilizing effects, reduced anaesthetic requirements and preservation of respiratory function.[9] These α2 receptors are found in many sites in CNS, spinal cord and peripheral tissues. α2 receptors are present in highest densities in the locus coeruleus in the brain. Dexmedetomidine is a highly selective α2 agonist.[1, 2, 3] the hypnotic, sedative effects and anti-nociceptive action of dexmedetomidine is due to the action on the locus coeruleus.[10, 11, 12]it prolongs the duration of spinal anaesthesia due to the action on substantia gelatinosa. Dexmedetomidine causes a decrease in HR and BP by lowering secretion of catecholamines which is beneficial in the perioperative period during which haemodynamic variationoccurs due to stress.[13] We had done our study in 60 ASA I & II patients who underwent lower abdominal surgeries under spinal anaesthesia. Patients of Group-D were received IV Dexmedetomidine 0.5µg/kg diluted to 10ml NS infused over 10mins as LD followed by maintenance infusion at the rate of 0.5µg/kg/h after SAB throughout the surgery and patients of Group-C were received NS as same manner. Our study is comparable with Harsoor S.S.[14] regarding dose and delivery method of the study drug. Mean age in Group-C was 46.77±10.68years while the mean age in Group-D was 46.27±11.36years. Mean height of patients in Group-C was 163.03±8.35cm, while in Group-D was 163.00±8.08cm. Mean weight of patients in Group-C was 69.30±10.58kg while mean in Group-D was 73.47±9.67kg. Both Group-C and Group-D had male preponderance as compared to females. These differences were found to be statistically non-significant. In our study, both groups were comparable in demographic data. In the study done by Harsoor S.S.[14], mean age, height, weight and malefemale ratio were comparable in both study groups. In the study done by Sekar E.B, Vijayaraghavan U.[16], Fazil K., Philip S.[18]and Santpur M.U.,

Kahalekar G.M.[15] demographic data in both the groups were comparable. Our study was comparable with all above study regarding demographic data.
In our study, mean time for onset of sensory block in Group-C was 2.22±0.61mins & in Group-D was 1.80±0.40mins which was statistically highly significant. Mean time to reach maximum level of sensory block in Group-C was 6.30±0.64mins and in Group-D was 4.30±0.44mins which was statistically significant. Mean time for two segment regression in Group-C was 140.80±6.74mins and in Group-D was 172.33±5.49mins which was statistically highly significant. Mean time for sensory regression to S1 segment in Group-C was 219.13±7.19mins and in Group D was 274.00±13.05mins which was statistically significant. In the study done by Harsoor S.S.[14], Onset of sensory block was significantly faster in Group-D (66±44.14sec) compared to Group-C (129.6±102.4 sec). Two-segment regression was prolonged in Group-D which was 142.5±2.32 and in Group-C was 93±1.8, which was statistically significant. In the study done by Sekar E., Vijayaraghavan U.[16], time taken for sensory regression to L1 in Group-C was 191.11±17.64min and 278.89±14.53min in Group-D, showing a highly significant difference. Our study was comparable with the study of Harsoor S.S.[14]; Santpur M.U., Kahalekar G.M.[15], Sekar E., Vijayaraghavan U.[15] regarding sensory parameters.
In our study mean time for onset of motor block in Group-C was 2.88±0.19mins and in Group-D was 2.00±0.00mins which was statistically significant. Mean time for complete motor block in Group-C was 6.07±1.01mins and in Group-D was 3.68±0.44mins which was statistically highly significant. Mean time for duration of motor block in Group-C was 190.67±6.16mins and in Group-D was 224.13±9.72mins which was statistically highly significant. In the study done by Harsoor S.S.[14], mean time for onset of motor block in Group-C was 4.20±2.08mins and in Group-D was 3.76±2.02mins which was statistically significant. There was a significant prolongation in duration of motor block in our study, which was comparable with the study done by Harsoor S.S.[14], Dinesh C.N., Sai Tej N.A.[16], Bhirud P., Chellam S.[19] regarding motor parameters.
Duration of analgesia in Group-C was 210.23±21.42mins and in Group-D was 321.40±14.19mins which was statistically highly significant. In the study done by Harsoor S.S.[14], mean time for total duration of analgesia in Group-C was 138.36±21.62mins and in Group-D was 222.80±123.40mins which was statistically highly significant. In the study done by Santpur M.U. and Kahalekar G.M.[15], mean time for total duration of analgesia in Group2 was 150.20±5.7mins and in Group1 was 219.70±2.55mins which was highly significant. Our study was comparable with the study done by Harsoor S.S.[14]; Santpur M.U., Kahalekar G.M.[15]; Sekar E., Vijayaraghavan U.[16] regarding duration of analgesia. IV Dexmedetomidine has been shown to produce analgesic effects by acting at both spinal and supraspinal levels. The analgesic effect primarily results from the inhibition of locus coeruleus at the brain stem and at the spinal cord resulting in inhibition of nociceptive impulse transmission. The effect seems to be mediated through both presynaptic and the post-synaptic α2 receptors. Faster onset of the sensory block may be due to α2 receptor activation induced inhibition of nociceptive impulse transmission. Dexmedetomidine infusion used as a LD followed by an infusion has been found to prolong the duration of analgesia and motor blockade.

Baseline HR in both group were comparable. After injecting study drug, the mean HR in group C was 86.97± 5.3bpm and group D was 76.30±4.24bpm. The diffrence in HR was highly significant. After SAB the mean HR in group-C was 87.37±5.39bpm and group-D was75.93±4.07bpm. The diffrence in HR was highly significant in both groups. Group-D has maintained lower HR as compared to Group-C throughout the surgery which was found to be statistically significant. In the study done by Harsoor S.S.[14], there was a clinically and statistically significant decrease in HR in Group-D from 15mins following SAB. In the study done by Sekar E., Vijayaraghavan U.[16], baseline HR was similar in both groups. In Group-D, HR showed significant decreasebetween both the groups from 15mins. Our study was comparable with the study of Harsoor S.S.[14], Santpur M.U., Kahalekar G.M.[15] and Sekar E., Vijayaraghavan U.[16] regarding HR changes.

In our study, baseline MAP in both groups was comparable. After injecting drug, the mean MAP in group C was 95.03±7.24mmHg and group-D was 90.47±8.06mmHg which was significant in both groups. After SAB, the mean MAP in group-C was 94.63±7.18mmHg and group-D was 90.33±8.08mmHg which was significant in both groups. Group-D has maintained lower MAP as compared to Group-C throughout the surgery. This was found to be statistically significant. In the study done by Harsoor S.S.[14], baseline MAP was comparable between the groups. Intra-operatively, there was a clinically and statistically significant decrease in MAP in Group-D following SAB. In the study done by Dinesh C.N., Sai Tej N.A.[17], D'souza O., Kapoor N.[20] Systolic, diastolic and mean arterial pressures were relatively lower in group-D compared to group-C. Our study was comparable with the study done by Harsoor S.S.[14], Dinesh C.N., Sai Tej N.A.[17], D'souza O., Kapoor N.[20]on regarding MAP. Dexmedetomidine stimulates α2 inhibitory neurons in the medullary vasomotor center resulting in a decrease sympathetic nervous system outflow. It is manifested as peripheral vasodilatation; decrease systemic BP, HR and CO. In our study, mean respiratory rate in Group C was 14.8±1.3 per minute while in Group D was 15.00±0.9 per minute which was statistically insignificant. Mean SpO2 in Group C was 99±0.5% while in Group D was 99±0.7% which was statistically insignificant. In the study done by Harsoor S.S.[14], respiratory rate was lower in patients receiving dexmedetomidine but oxygen saturation was maintained equally well in both groups.
In our study, throughout the surgery, sedation score in Group-D was highly significant than Group-C. In the study done by Santpur M., Kahalekar G.M.[15], sedation score was higher in Group-1 (Dexmedetomidine) as compared to Group-2 (Control). In the study done by Sekar E., Vijayaraghavan U.[16], intraoperative Ramsay Sedation score was significantly higher in the dexmedetomidine group. The hypnotic and sedative effects of α2 adrenergic agonist are due to the action on the locus coeruleus. Dexmedetomidine has all the properties of an ideal sedative, which leads to sedation without respiratory depression.

In our study, in control group one patient developed hypotension and in Group-D two patients developed hypotension which was treated with fluid and inj. Mephentermine 6 mg IV. In our study, in Group-D three patients developed bradycardia which was treated with inj. Atropine 0.6mg IV. In the study done by Santpur M.U., Kahalekar G.M.[15], bradycardia was observed in 7patients, hypotension in 2patients and nausea in 1 patient in dexmedetomidine group, whereas in control group2(6.66%) patients had bradycardia, 3(10%) patients had hypotension. In the study done by Harsoor S.S.[14], bradycardia was observed in 4patients, hypotension in 2patients in dexmedetomidine group, whereas in control group, 1 patient had hypotension. In the study done by Sekar E., Vijayaraghavan U.[16], 50% of patients showed bradycardia in group-D, out of which only 10% of patients had HR≤50/min which was transient and was treated with inj glycopyrrolate. It has been noted that bradycardia is a prominent side effect, with incidence varying from 30% to 40% sometimes requiring treatment with atropine.

Conclusions:

IV Dexmedetomidine fasten the onset of sensory block, time to reach T8 level, increases time for two segment regression and increases duration of sensory blockade. It also fastens the onset of motor blockade, decreases time for complete motor blockade and increases total duration of motor blockade. It increases duration of analgesia so it delays time for giving 1st rescue analgesic dose post-operatively. It also decreases the heart rate and blood pressure with arousable sedation without respiratory depression throughout the surgery.

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