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Comparative effects of Dexmedetomidine and Buprenorphine as adjuvants to Bupivacaine in Spinal Anaesthesia

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Abstract

Background and Objectives: Addition of adjuvants to local anaesthetics during spinal anaesthesia to prolong the duration of analgesia has been practised for many years. While opioids are the most commonly employed adjuvants, α2 agonists like dexmedetomidine are becoming popular in this regard. We conducted a study to compare the efficacy of dexmedetomidine and buprenorphine as intrathecal adjuvants to 0.5% hyperbaric bupivacaine in terms of prolongation of sensory and motor blockade and duration of analgesia.

Materials and Methods: After obtaining institutional ethics committee approval, a prospective randomized controlled studywas conducted at Saveetha Medical College Hospital. 60 patients posted for lower abdominal surgeries under spinal anesthesia, were randomly divided into two groups of 30 patients in each group. Group D received 5 µg of dexmedetomidine with 3 ml (15mg) of hyperbaric 0.5% bupivacaine; total volume was 3.5ml. Group B received 60µg (0.2ml) of buprenorphine with 3 ml (15mg) of hyperbaric 0.5% bupivacaine; total volume was 3.5ml withthe addition of normal saline. The onset times of sensory and motor block, the time to two segment regression, the durations of sensory block, motor block and analgesia and side effects like sedation, hypotension, bradycardia, nausea and vomiting were recorded.

Results: The two groups were comparable with regard to age,sex, body mass index (BMI) distribution, maximum level of sensory block achieved and onset time of motor block.The duration of analgesia was significantly longer in Group D (349.33± 38.25* minutes in Group D vs 284±22.22* minutes in Group B, * mean± standard deviation). The onset of sensory block was quicker in Group D and the time to two segment regression, regression to S2 and duration of motor block were also significantly prolonged in Group D. The degree of sedation was significantly higher in Group D while other side effects like

bradycardia, hypotension, nausea and vomiting were not significantly different between the groups.

Conclusion: It can be concluded that 5µg of dexmedetomidine added to intrathecal 0.5% hyperbaric bupivacaine produces longer durations of sensory blockade, motor blockade and analgesia compared to 60 µg of buprenorphine in patients undergoing lower abdominal surgeries.

Keywords: Dexmedetomidine, Bupivacaine, Buprenorphine, Spinal Anaesthesia, Analgesia, Sensory Block, Motor Block.

1. INTRODUCTION

Sub arachnoid block with local anaesthetics is one of the most commonly performed techniques to provide anaesthesia for lower abdominal surgeries. Many adjuvants have been added to local anaesthetics to prolong the duration of sub arachnoid block in order to provide effective intraoperative and postoperative analgesia. These adjuvants include opioids like Morphine, Fentanyl and Sufentanil and non-opioids like Ketamine, Midazolam, Neostigmine and Clonidine[1]. Buprenorphine, a partial µ receptor agonist with low intrinsic activity, can also be used safely in subarachanoid block. It is compatible with CSF, lipophilic and has high molecular weight. This may prevent its rostral spread and thus respiratory depression[2].Buprenorphine has a high lipid solubility,strong affinity for opioid receptors anda longduration of action. These properties make it a good adjuvant to intrathecal local anaesthetics for managing postoperative pain.[3,4]
Dexmedetomidine, a highly selective α2-agonist, has also been studied as a neuraxial adjuvant. It offers effective prolongation of postoperative analgesia, stable haemodynamic conditions and sedation with minimal side effects.[5,6]

We conducted a study to compare the effects of dexmedetomidine and buprenorphine on sensory blockade, motor blockade and duration of analgesia, when used as adjuvants to 0.5% hyperbaric bupivacaine for lower abdominal surgeries under subarachnoid block.

2. MATERIAL AND METHODS

After getting approval from the institutional ethical committee, a prospective randomized controlled study was conducted at Saveetha Medical CollegeHospital.Sixty patients of ASA I and ASA II physical status, in the age group of 18-60 years of either sex,who were posted for lower abdominal surgeries under subarachnoid block, were included in the study. Informed consent was obtained from all these patients. Pregnant women, patients with cardiac disease and contraindication to regional anesthesialike bleeding disorder and receiving anti-coagulanttherapy were excluded from the study. The enrolled patients were randomly allocated to two groups of 30 patients in each group using computer generated random numbers.

Group D received 5 µg of dexmedetomidine (0.5 ml) with 15mg (3 ml) of hyperbaric 0.5% bupivacaine; the total volume was 3.5ml.
Group B received 60 µg (0.2ml) of buprenorphine with 15mg(3 ml) of hyperbaric 0.5% bupivacaine; the total volume was adjusted to 3.5ml with the addition of normal saline.

All patients received premedication with oral diazepam 5 mg the night before and on the day of surgery. In the operating room (OR),standard monitors- electrocardiogram (ECG), non-invasive blood pressure (NIBP) and pulse oximetry (SpO_2) were connected to the patients. An 18-gaugeintravenous cannula was placed for the administration of fluids and drugs. Under aseptic conditions, spinal anaesthesia was administered in the L3-4 interspace with the patients in sitting position in both the groups using the drug combinations as described above. The drug was injected over 10-15 seconds following the free flow of CSF. All measurements were recorded from the point of completion of subarachnoid injection. Following the subarachnoid block, the patients were made to lie in a supine position. Sensory block was assessed by loss of pin prick sensation using a blunt 23 gauge needle every minute till the stabilization of the highest level of block as confirmed by consecutive tests. The onset time and duration of sensory block were recorded. The time interval between the injection of intrathecal anaesthetic and the absence of pain at the T10 dermatome assessed by pinprick was taken as the onset time of sensory block. The time interval between the onset of sensory block to regression of sensory block to S2 segment was taken as the duration of sensory block.Surgery was allowed to proceed after attainment of T10 level blockade. Testing was then repeated every 10 minutes until two segment regression of the block was observed. Further testing was carried out at 20-minute intervals until the recovery of S1 dermatome. The highest level of sensory block, the time to reach the highest dermatomal level of sensory block and the time taken for two segment regression from the highest level of block achieved were also recorded.

Motor block was assessed by modified Bromage scale (MBS).
Bromage 0- the patientis able to move the hip, knee and ankle
Bromage 1- the patient is unable to move the hip, but is able to move the knee and ankle
Bromage 2- the patient isunable to move the hip and knee, but is able to move the ankle
Bromage 3- the patient is unable tomove the hip, knee and ankle.

The time taken to reach Bromage score 3 was noted as the onset time of motor block. The time interval between the onset of motor block and regression to Bromage 0was recorded as the duration of motor block.

The haemodynamic parameters- heart rate, systolic, diastolic and mean arterial pressures and SpO_2 were recorded every 5 minutes from the shifting of the patients to OR to the completion of surgery. Hypotension (fall in systolic blood pressure to 90 mmHg or fall by 30% of baseline) was treated with Inj Ephedrine 6mg boluses while bradycardia (heart rate< 50/minute) was treated with Inj. Atropine 0.6 mg.
The degree of pain was assessed using visual analogue scale (VAS) with scores from 0 to 10 (0- no pain; 10- most severe pain) postoperatively every hour. When a VASscore > 4 was

reached, Inj. Diclofenac 75mg was given intramuscularly as rescue analgesic. The time interval between the onset of sensory block and rescue analgesic administration was noted as the duration of analgesia.Sedation was assessed by modified Ramsay sedation scale after shifting the patients to OR, after 10 minutes of administration of spinal anaesthesiaand then postoperatively.

Ramsay Sedation Scale:

1. Anxious, agitated
2. Co-operative, oriented and tranquil
3. Responding to commands
4. Brisk response to glabellar tap
5. Sluggish response to glabellar tap
6. No response

Patients were also monitored for side effects like nausea and vomiting postoperatively.

Statistical Analysis

The data were expressed as mean and standard deviation and analyzed using SPSS 20 software. The parametric data were analyzed using unpaired t test while the non parametric data (sex distribution, side effects) were analyzed using Chi square test. P value < 0.05 was considered to be statistically significant.

3. RESULTS

The two groups were comparable with regard to age, sex, body mass index (BMI)and duration of surgery (Table 1).The onset of sensory block was significantly quicker in Group D compared to Group B (109. 83±12.42seconds in Group D compared to 139. 67± 12.79 seconds in Group B, Table 2). There was also a significant difference between the groups with respect to two segment regression, with Group D requiring a longer time compared to Group B. The durations of motor block and analgesia were also significantly longer in Group D. The degree of sedation was significantly higher in Group D compared to Group B.There were no statistically significant differences between the groups in the maximum level of sensory block achieved (median level of block was T6) or onset time of motor block (Table 2). The incidence of adverse effects like hypotension, bradycardia, nausea and vomiting were also similar in both the groups (Table 3).

Table 1
Demographic data

Parameters		Group D	Group B	P value
Age (years)		44.77±13.54*	44.7±13.61*	0.985
Sex (M: F)		21:9	20:10	0.781
BMI		22.47±2.14*	22.28± 1.98*	0.728
Type of Surgery	Inguinal hernia repair	16	14	0.606

	Total abdominal hysterectomy	14	16	
Duration of surgery (minutes)		103.83±28.78*	98.33±23.53*	0.421

* Mean ± SD., M: F- Male: Female

Table 2
Sensory and Motor block

Parameters		**Group D**	**Group B**	**P value**
Onset time of sensory block (T10) (seconds)		109. 83±12.421	139. 67± 12.794	<0.001
Onset time of motor block (seconds)		174± 61.87	178.83± 14.42	0.678
Maximum level of Sensory block T4:T6: T8:T10		6:19:7:0*	5:17:5:1*	0.674
Time to reach maximum sensory block (minutes)		4.27± 0.87	4.60 ±0.86	0.140
Mean time to two segment regression (minutes)		149± 12.55	136 ± 14.1	<0.001
Mean time to regression to S1 (minutes)		323± 42.762	252.33± 21.605	<0.001
Duration of motor block (minutes)		328.83 ± 39.01	258.33± 25.51	<0.001
Duration of analgesia (minutes)		349.33 ± 38.25	284 ± 22.22	<0.001
Degree of sedation	Sedation score <3	8	28	<0.001
	Sedation score >3	22	2	

* Number of patients with the corresponding sensory block level

Table 3

Side effects	**GroupD (n=30)**	**Group B(n=30)**	**P value**
Bradycardia	5	2	0.228
Hypotension	3	2	0.688
Nausea	0	2	0.150
Vomiting	0	2	0.150

4. DISCUSSION

Buprenorphine has both spinal and supra spinal components of analgesia[7,8]. It has a high affinity for spinal opioid receptors. It has been used intrathecally in various doses ranging from 30 µgto 150 µg[9]. Addition of 60 µgof buprenorphine to bupivacaine produced a rapid onset of sensory block and prolonged the duration of analgesia significantly compared to control group in studies conducted by Ravindran[9] et al and Dixit [10]. Intrathecal dexmedetomidine has been used in dosages ranging from 3 µg to 15µg[5, 11,12].In studies conducted by Gupta R[5]et al and Al Ghanem [13]et al, the authors found that 5 mcg of dexmedetomidine is an effective intrathecal adjuvant to local anaesthetics in terms of prolongation of analgesia with minimal side effects.

Therefore,we decided to compare the analgesic efficacy of 60 µg of buprenorphine and 5µg of dexmedetomidine added as adjuvants to 0.5% hyperbaric bupivacaine for spinal anaesthesia.In our study, we found that the duration of analgesia was significantly prolonged in Group D (349.33± 38.25minutes in Group D vs 284±22.22 minutes in Group B, P <0.001). Our observations were similar to the findings reported by Gupta M[14] et al who also found that the duration of analgesia was significantly longer in dexmedetomidine group compared to buprenorphine group (493.56±385.95 in Group D vs289.66±64.94 in Group B). The authors had used similar dosages of buprenorphine (60 µg) and dexmedetomidine (5 µg) as in our study. However they observed a higher margin of increase in the duration of analgesia compared to our study.

The onset of sensory block was quicker in Group Dand the time to two segment regression, regression to S2, duration of motor block and duration of analgesia were significantly prolonged in Group D in our study.There was no significant difference in the onset of motor block or peak sensory level achieved between the groups. These findings were again similar to the observations recorded by Gupta M[14] et al in their study.

In a study conducted by Gupta R[15] et al, the authors reported that the patients who received intrathecaldexmedetomidine (5µg) experienced prolonged motor and sensory block, better haemodynamic stability and reduced demand for rescue analgesics in 24 hours as compared to those who received fentanyl (25µg). Here the authors had used a total volume of 3 ml intrathecally in each group while we used 3.5 ml. There was no difference in the onset time of motor block and maximum level of sensory block achieved between the dexmedetomidine and fentanyl groups. These findings were similar to what we observed in our study. In another study, Gupta R[11] et al, also found that there was prolongation of motor and sensory block with the addition of 5µg dexmedetomidine to 0.75% isobaric ropivacaine compared to 0.75%ropivacaine alone.

The mechanism of action by which intrathecal α2 agonists prolong motor and sensory block of local anaestheticsis not well known. They act by binding to pre-synaptic C-fibres and post-synaptic dorsal horn neurons. Theanalgesic effect could be due to depression of release of C-fibre transmitters and hyperpolarisation of post-synaptic dorsal horn neurons[16]. This antinociceptive effect could lead to prolonged sensory block when α2 agonists are added to

spinal anaesthetic agents. The prolongation of the motor block by α2 agonists could be due to their binding to motor neurons in the dorsal horn[17, 18].

The heart rates and mean arterial pressures recorded in both the groups were comparable. Bradycardia was seen in 5 patients in Group D and 2 patients in Group B. It responded to treatment with Atropine. Hypotension requiring treatment with Ephedrine was seen in 3 and 2 patients in Group D and B respectively. These differences were not statistically significant. Similar findings were reported by Gupta M [14]et al in their study where they noted that6 patients (4 in Group B and 2 in Group D) had bradycardia, which required treatment with Atropine.However, Ravindran[9] et al and Dixit[10]did not observe any bradycardia with intrathecal buprenorphine in their studies. Dexmedetomidinecauses bradycardia but the effect is more pronounced when it is given intravenously at a higher dose [19].

The sedation scores were significantly higher in Group D. Similar observations were recorded byGupta M[14] et al and Gupta R[15] et al.The sedative effect of dexmedetomidine is due to its action on α2-adrenergic receptors in locus ceruleus[20,21]. Following intrathecal administration of dexmedetomidine, sedation could be due to its systemic absorption and vascular redistribution to higher centres or cephalad migration in CSF[16].

Nausea and vomiting were reported by 2 patients in Group B while there were no such complaints in Group D. The differences were not statistically significant. These observations were similar to those recorded by Sapkal[22] et al, who compared clonidine 60μg with buprenorphine 60μg and reported thatthe incidence of nausea and vomiting was higher in buprenorphine group compared to clonidine group.

Limitations

We did not have a control group to compare the effects of the two drugs separately. We also did not assess the incidence of side effects like pruritus and shivering in this study.

5. CONCLUSION

It can be concluded that 5 μgof dexmedetomidine added to 0.5% hyperbaric bupivacaine in subarachnoid block prolongs the intraoperative sensory and motor blockade and the duration of postoperative analgesia more effectively compared to 60 μg of buprenorphine.

Conflict of Interest- None declared

Source of Funding- None

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