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A COMPARISON OF INTRATHECAL DEXMEDETOMIDINE AND CLONIDINE AS ADJUVANT TO HYPERBARIC BUPIVACAINE FOR POSTOPERATIVE ANALGESIA IN ABDOMINAL HYSTERECTOMY.

Dr Rama Chatterji Professor,Department of Anaesthesiology, SMS Medical College, Jaipur.

Dr Chandra Shekhar Chatterji* Senior Professor,Department of Anaesthesiology, SMS Medical College, Jaipur. *Corresponding author

Dr Anupama Gupta Associate Professor,Department of Anaesthesiology, SMS Medical College, Jaipur.

Dr Lalit Kumar Kejriwal Ex PG Student,Department of Anaesthesiology, SMS Medical College, Jaipur.

ABSTRACT

Background & Aims: Various adjuvant are being used with intrathecal local anaesthetics for prolongation of duration of analgesia. Dexmedetomidine, the highly selective 2 adrenergic agonist is becoming popular as neuraxial adjuvant. We compared the duration of analgesia, block characteristics and adverse effects along with the hemodynamic changes, following intrathecal administration of dexmedetomidine or clonidine with hyperbaric 0.5% bupivacaine in patients undergoing abdominal hysterectomy under sub arachnoid block.

Material and methods: Seventy five patients of ASA grade I or II, ages between 25-60 years, were randomized and allocated into three groups using sealed envelope technique. Patients in group B received 15 mg hyperbaric 0.5% bupivacaine + normal saline intrathecally , in group BC received 15 mg hyperbaric 0.5% bupivacaine + 30 mcg clonidine+normal saline intrathecally and in group BD-received 15 mg hyperbaric 0.5% bupivacaine + 5 mcg dexemedetomidine +normal saline intrathecally.Total drug volume was kept constant 3.5 ml in all groups. Outcome measures include total duration of analgesia, onset and duration of sensory-motor block, hemodynamic changes and adverse effects, if any.

Results: There was no significant difference in patients demographic and duration of surgery. The total duration of analgesia was longest in group BD (271.0±23.4 min), it was significantly longer than group BC (229.4±28.0 min) and group B (155.1±12.8 min). The mean two segment sensory regression time was 222.4±18.73 min in group BD, 188.6±22.4 min in Group BC and 135.8±11. 6min in Group B. Time to onset of sensory block was comparable between three groups but motor block was early in Group BD and Group BC as compared to Group B. There was no significant difference in other variables like hemodynamic changes and adverse effects between the three groups.

Conclusions: Intrathecal dexmedetomidine is associated with prolonged duration of postoperative analgesia, motor and sensory block without causing any significant change in hemodynamic variables and adverse effects as compared to clonidine or lone bupivacaine.

KEYWORDS : α2, adrenoreceptor agonist, bupivacaine, clonidine, dexmedetomidine, subarachnoid block

INTRODUCTION

Subarachnoid blockade is the most commonly used regional anaesthetic technique for lower abdominal surgery. Intrathecal use of hyperbaric 0.5% bupivacaine often requires early analgesic intervention in the intraoperative and postoperative period. Various adjuvants such as opioids, alpha agonists, midazolam and ketamine are often used with local anesthetics to improve quality of anesthesia, prolong analgesic effects, and reduced required dose of local anesthetics.

For intrathecal alpha agonist, most of clinical studies are related to clonidine. Dexmedetomidine is a highly selective α2 agonist, is now emerging as preferable adjuvant to intrathecal local anaesthetics to provide longer duration of analgesia. Based on earlier human studies, it is hypothesized that intrathecal 5 µ g dexmedetomidine would produce more postoperative analgesic effect with hyperbaric bupivacaine in spinal anesthesia with minimal side effects [1],[2],[3],[4].

We conducted this prospective, randomized, double blind study to compare the effects of intrathecal clonidine and dexemedetomidine as an adjuvant to intrathecal bupivacaine with regards to characteristics of subarachnoid block, duration of postoperative analgesia, haemodynamic changes, and sedation score along side effects in patients undergoing abdominal hysterectomy.

MATERIAL AND METHODS

After obtaining approval from the Institutional Ethics Committee along with written informed consent, 75 patients aged between 25-60 yrs, belonging to American Society of Anesthesiology (ASA) class I and II and scheduled for abdominal hysterectomy with or without bilateral salpingoophrectomy under subarachnoid block, were enrolled in this prospective, randomized, controlled and double blind study. Patients with contraindication to regional anesthesia, history of significant coexisting diseases like ischemic heart disease, hypertension, impaired renal functions, rheumatoid arthritis, and severe liver disease where excluded from the study.

All patients were examined thoroughly including general physical examination and investigations a day prior to surgery in pre anaesthetic clinic, and were briefed about study protocols and visual analogue scale (VAS) .

Patients were randomized and allocated into three groups using sealed envelope technique. Both the patients and anaesthetist involved in performing SAB, intraoperative and postoperative monitoring was unaware of the group allocation. Patients in group B received 15 mg hyperbaric bupivacaine (0.5%) + normal saline intrathecally , in group BC received 15 mg hyperbaric bupivacaine (0.5%) + 30 mcg clonidine+normal saline and in group BD-received 15 mg hyperbaric bupivacaine (0.5%) + 5 mcg dexemedetomidine +normal saline. Total volume was kept constant 3.5 ml to maintain blinding.

After confirming fasting status, patients were shifted in operation theater. Multipara monitors for electrocardiogram (ECG), pulse oximetry, and noninvasive blood pressure was attached and baseline parameters were recorded. Intravenous (IV) access was secured and preloading was done with ringer lactate solution 10 ml/kg prior to performing sub arachnoid block.

With all aseptic precautions, SAB was performed at the L3–4 inter space with 25G spinal needle in the lateral decubitus position. The drug solution was injected over 30 seconds and the patient was

immediately placed in the supine position with 15 degree head down tilt immediately after SAB to achieve level of block T5-6.

The onset and duration of sensory block, highest level of sensory block, time to reach the highest dermatomal level of sensory block, motor block onset, time to complete motor block recovery, were recorded.

The onset of sensory block was assessed by using pin prick bilaterally at mid clavicular line, initially every 2 minutes up to 15 minutes and then every 15 minutes. Onset of sensory block was defined as the time between injection of intrathecal local anesthetic and the time taken to attain absence of pain at the T6 dermatome. The duration of sensory block was defined as the time of regression of two segments in the maximum block height, evaluated by pinprick.

The motor block was assessed using modified Bromage score: (Bromage 0, the patient is 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 is unable to move hip and knee, but is able to move the ankle; and Bromage 3, the patient is unable to move the hip, knee, and ankle). Time for motor block onset was defined as modified Bromage score of 3. Complete motor block recovery was assumed when modified Bromage score was 0.

The duration of analgesia was taken as the time from intrathecal injection and appearance of pain requiring rescue analgesia. All durations were calculated considering the time of spinal injection as time zero.

Monitoring of heart rate, mean blood pressure and SpO2 were done at 1,5,10,15,30,60 and 120 minutes. Hypotension was defined as a decrease in systolic blood pressure (SBP) by 20% from baseline and was treated with IV boluses of 6 mg mephentermine or crystalloid fluids. Bradycardia was defined as Heart rate (HR) less than 50 beats/min, and was managed using 0.6 mg of IV atropine sulfate.

The incidence of hypotension, bradycardia, pruritus, nausea, vomiting, shievering, respiratory depression and sedation were recorded and treated accordingly. Degree of sedation was assessed using 4 point sedation scale. (Grade 0 = patient is awake and fully alert; 1 = patient is awake but drowsy; 2= patient is somnolent but easily arousable; 3 = patient somnolent and difficult to arouse; 4=patient is unresponsive to verbal and tactile stimulation).

VAS score was recorded at 2hrs and any patient showing VAS more than or equal to 3 was administered a supplemental dose of inj. diclofenac 75mg.

Statistical analysis

Quantitative data were represented as means ± standard deviation (SD); numbers and percentages were used for qualitative data. Statistical analysis was done for comparing observed data by using Student's t-test and analysis of variance (ANOVA). P value < 0.05 was considered statistically significant.

RESULTS

In the present study, a total of 75 patients were randomized and allocated into three groups. All patients completed trial .All three groups were comparable in terms of age, weight, ASA physical status, duration of surgery and baseline hemodynamic parameters. [Table1] Characteristics of sensory and motor are shown in [Table 2]

Table 1. Patient Demographics

Variables	Group B (mean±SD)	Group BC (mean±SD)	Group BD (mean±SD)	P value
Number of Patients	(n=25)	(n=25)	(n=25)	
ASA I/II	22/3	23/2	22/3	>0.05(NS)
Age in Yrs	40.3±6.3	42.6±5.7	44.6±7.53	>0.05(NS)
Weight in Kgs	54.4±6.7	55.2±3.9	55.7±3.67	>0.05(NS)
Surgical time in min.	65.4±10.8	61.4±8.4	63.28±8.83	>0.05(NS)

Table 2: Sensory and Motor Blockade Characteristics

	Group B (mean±SD)	Group BC (mean±SD)	Group BD (mean±SD)	P Value		
Number of patients	(n=25)	(n=25)	(n=25)	B vs BC	B vs BD	BCvs BD
Onset of Sensory block(min)	9.6±1.2	8.5±1.9	8.4±1.78	0.0132	0.0059	0.8784
Onset of Motor block(min)	12.4±1.4	10.8±1.1	9.96±1.06	0.0001	0.0000	0.0053
Time for 2 segment sensory regression (min)	135.8±11.6	188.6±22.4	222.4±18.73	0.0000	0.0000	0.0000
Duration of Motor block(min)	135.4±10.3	191.3±21.8	217.0±19.2	0.0000	0.0000	0.0001
Total duration of Analgesia(min)	155.1±12.8	229.4±28.0	271.0±23.4	0.0000	0.0000	0.0000
VAS score(2 hrs0	10.64±6.74	0.67±2.54	0.69±2.58	0.0001	0.0001	1.000
VAS score at first rescue analgesic	28.5±7.2	20.6±5.1	20.6±5.07			
Sedation score	1	1	1			

Group B-Bupivacaine; Group BC- Bupivacaine + Clonidine; Group BD- Bupivacaine + Dexmedetomidine; SD-Standard deviation

Table 3: Adverse effects

Adverse effects	Group B	Group BC	Group BD
Hypotension	2(8%)	4(16%)	4(16%)
Bradycardia	1(4%)	2(8%)	3(12%)
Respiratory depression	0(0%)	0(0%)	0(0%)
Shivering	0(0%)	4(16%)	2(8%)
Nausea, Vomiting	0(0%)	0(0%)	1(4%)
Pruritus	0(0%)	0(0%)	0(0%)
Headache	0(0%)	0(0%)	0(0%)

All the patients in three groups remained hemodynamically stable during the intraoperative and postoperative period; the mean values of heart rate and mean arterial pressure were comparable between all three groups.There were no significant differences were observed regarding the incidences of adverse effects such as nausea, vomiting, pruritus, headache, hypotension, bradycardia and sedation.

DISCUSSION

In this study, we observed that supplementation of intrathecal bupivacaine with 5mcg dexmedetomidine significantly prolonged both sensory and motor block compared with intrathecal clonidine 30 mcg. Quality of analgesia significantly improved with use of dexmedetomidine as an adjuvant when compared to the group clonidine or bupivacaine.

The mechanism by which intrathecal α2-adrenoceptor agonists prolong motor and sensory blockade of local anesthetics is not well understood. The prolongation of effects might result from synergism between the local anesthetic and the α2-adrenoceptor agonist. Local anesthetics act by blocking sodium channels. Intrathecal α2-adrenoceptor agonists produce analgesia by binding and depressing the release of pre-synaptic C-fiber neurotransmitters and also by hyperpolarisation of post-synaptic dorsal horn neurons.[5],[6] This anti nociceptive effect may explain the prolongation of the sensory block while prolongation of motor

block may be due to the binding of α2-adrenoceptor agonists to motor neurons in the dorsal horn.[7]

Dexmedetomidine is eight times more specific and highly selective α_2 adrenoreceptor agonists compared to clonidine, thereby making it a useful and safe adjunct in diverse clinical applications. [8],[9] In our study, the intrathecal dose of dexmedetomidine selected was based on previous human studies wherein no neurotoxic effects have been observed.[1],[2],[3]

Time of onset of sensory block was significantly shorter in group BC and group BD as compared to group B, similar findings were observed in various other studies. [3], [10], [11], [12] While group BD and group BC were comparable. Onset of motor block was also earlier in group BD and group BC in comparison to group B, similar to other studies[3],[10],[11],[12]. Onset time of motor block found to be significantly shorter in group BD as compared to group BC, this is in contrast to study conducted by Kanazi et al[1] in which they found no significant difference between group BD and groupBC,reason for this may be attributed to higher dose dexmedetomidine (5 mcg) in our study as compared to Kanazi et al[1], they had used lower doses (3 mcg).

In our study sensory regression up to T10 segment was significantly longer in group BD and BC as compared to group B,while it was comparable between groups BD and BC. Our results are in accordance with other studies. [3],[4],[10],[13]Duration of motor block was found to be longest in group BD, followed by Group BC and group B. These findings are similar to Kanazi et al[1] and Al Ghanem et al[2] as they found that dexmedetomidine and clonidine added bupivacaine produced a similar prolongation in the duration of the motor and sensory block, with preservation of hemodynamic stability. Al-Mustafa et al [3]and Hala et al[15] observed dose dependent prolongation of motor and sensory blockade with reduced analgesic requirement with increasing dosages of intrathecal dexmedetomidine.

Duration of analgesia and time to first rescue analgesic was significantly longer in group BD as compared to group BC and group B. Patients in group BC had prolonged duration of analgesia as compared to group B, these results are supported by various other studies. [1],[3],[11],[12],[13],[14]We observed significantly lower VAS scores and delayed requirement of rescue analgesic with use of dexemedetomidine (5mcg) when compared to clonidine (30 mcg) or bupivacaine alone. Thus the analgesic efficacy of dexemedetomidine as an adjuvant to intrathecal bupivacaine is superior to clonidine.

The most significant side effects reported about the use of intrathecal α_2 adrenoreceptor agonists are bradycardia and hypotension. [16]In our study ,addition of dexemedetomidine or clonidine to intrathecal bupivacaine did not cause significant decrease in blood pressure and heart rate. Intrathecal local anaesthetics block the sympathetic outflow and reduce the blood pressure, addition of low dose alpha2 agonist does not further affect the near maximal sympatholysis. There was no significant difference was reported in incidence of shivering, nausea and vomiting. No incidence of headache, pruritus and respiratory depression was reported.

Intrathecally administered alpha2 agonists have a dose dependent sedative effects, but no sedation was observed in any of study group, small doses of adjuvant may be responsible for it.

CONCLUSION

We conclude that dexmedetomidine as an adjuvant to intrathecal bupivacaine is superior alternative to clonidine as it provides prolonged duration of postoperative analgesia without causing hemodynamic instability and any other side effects.

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