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A PROSPECTIVE RANDOMIZED COMPARATIVE DOUBLE BLIND STUDY TO EVALUATE THE EFFICACY OF DEXMEDETOMIDINE TO BUPIVACAINE GIVEN INTRATHECALLY AS A ANAESTHETIC AGENTS

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ABSTRACT

Background: The regional anesthetic technique is the most preferred type of anesthesia in lower abdominal surgeries. The subarachnoid blockade is the commonly used technique for hysterectomy surgery as it is easy to perform, economical and also provides effective sensory and motor blockade. Despite the many advantages of spinal anesthetic, the relatively short duration of the local anesthetic, during prolonged surgery can be a problem. So various adjuvants have been investigated and tried with intrathecal bupivacaine in order to prolong the effects of spinal anesthetic.

Materials & Methods: The study done was a prospective, randomized double blind trial in 50 patients undergoing elective hysterectomy under subarachnoid blockade. The patients were randomly allocated in to 2 groups, Group A and Group B by picking random lots from a sealed bag and received the intrathecal drug as per the groups. Motor blockade and the level of sedation was assessed .

Results: The maximum level of sensory blockade of T4 was achieved in 9 patients in Group A compared to 15 patients in Group B. There was statistically Significant difference between the 2 groups in the maximum level of sensory blockade .The mean time taken for two segment regression of sensory block was 147.36 minutes in Group A. 201.52 minutes in Group B. There was statistically significant difference in 2 segment regression time when Group A is compared to Group B with the P Value < 0.001.

Conclusion: It was concluded that supplementation of 10 mcg of dexmedetomidine to 15mg of 0.5% heavy bupivacaine prolonged the duration of analgesia with stable hemodynamics and minimal sedation.

KEYWORDS :

INTRODUCTION

The regional anesthetic technique is the most preferred type of anesthesia in lower abdominal surgeries. The subarachnoid blockade is the commonly used technique for hysterectomy surgery as it is easy to perform, economical and also provides effective sensory and motor blockade. Despite the many advantages of spinal anesthetic, the relatively short duration of the local anesthetic, during prolonged surgery can be a problem. So various adjuvants have been investigated and tried with intracthecal bupivacaine in order to prolong the effects of spinal anesthetic.[1,2]

The search for an ideal adjuvant that produces long lasting analgesia with minimal effects on the cardiovascular and respiratory system continues till date. The advantage of addition of adjuvants to intrathecal local anesthetic is to decrease the dose of local anesthetic administered along with improved quality of analgesia. Various studies have been conducted to evaluate the efficacy of addition of dexmedetomidine to hyperbaric bupivacaine.[3,4]

The alpha 2 adrenergic agonist clonidine has been used widely as adjuvant in varying dose to potentiate the effects of local anesthetics. Dexmedetomidine is an alpha 2 agonist with high selectivity for alpha receptors. The binding affinity of dexmedetomidine compared with clonidine is 1:10. It has been used intrathecally in varying doses with different local anesthetic agents and proved to prolong the sensory and motor blockade. A number of animal studies conducted using intrathecal dexmedetomidine at a dose rang of 2.5 - 100 µg did not report any neurologic deficits with its use [5,6]However the optimal dose that prolongs analgesia with minimal side effects is not known and is in the investigative phase.

This study was designed to evaluate the efficacy of adding different doses of dexmedetomidine (5 mcg and 10 mcg) to 0.5% hyperbaric bupivacaine administered intrathecally in patients undergoing elective hysterectomy surgeries.

MATERIALS AND METHODS

This study was conducted at Madha medical college and research institute, Chennai between May 2018 - October 2018.The study done was a prospective, randomized double blind trial in 50 patients undergoing elective hysterectomy under subarachnoid blockade. The sample size was determined by power analysis based on the previous studies.

Patient undergoing elective hysterectomy surgery , aged 25 - 65 years, ASA I & II patients were included in the study. Patients with ASA III & IV, inflection at the site of regional blockade, Bleeding diathesis, Hypersensitivity to study drug, allergy to local anesthetics, neurological diseases, Spinal deformities were excluded in the study

After getting the ethics committee approval and informed consent, 50 patients undergoing elective hysterectomy with ASA I & II status were enrolled in the study. Preoperative assessment was done in all the patients and informed consent was obtained. All these patients were kept nil per oral for 8 hours prior to surgery. The patients were randomly allocated in to 2 groups, Group A and Group B by picking random lots from a sealed bag and received the intrathecal drug as per the groups.

GROUP A:3 ml of 0.5% hyperbaric Bupivacaine + 5 mcg of Dexmedetomidine.
GROUP B :3 ml of 0.5% hyperbaric Bupivacaine + 10 mcg of Dexmedetomidine.

After shifting the patient to operating room, routine monitors were connected which included electrocardiogram, pulseoximetry, noninvasive blood pressure and the baseline parameters were documented. An intravenous line was secured with 18 G cannula and Ringer lactate 10ml/ kg was given prior to spinal anesthesia. Oxygen 6 Lit Per minute was given through Hudson mask.

The following emergency drugs injection Ephedrine 6 mg / cc and inj Atropine 0.6 mg / cc were kept before the subarachnoid blockade. The drug solution was prepared by the anesthesia resident who was not a part of the study. The other anaesthesiologist who was blinded to the loaded drug performed the block and monitored the physiological data and the details of the blockade. Under aseptic precautions, the spinal block was given for all patients in L3 L4 space in the lateral position using 25G Quincke spinal needle. The drug was deposited in the space after ensuring free flow of cerebrospinal fluid from the needle. Then the patients were placed in supine position. The time of intrathecal injection was considered as zero and the following parameters were observed.

Motor blockade was assessed using the BROMAGE SCALE. The level of sedation was assessed based on **RAMSAY SEDATION SCALE.** The sedation sore was assessed intra operatively for every 15 minutes till the end of the surgery and in the recovery room.[7,8]

Heart rate, pulseoximetry, repiratory rate was monitored continuously

and blood pressure was recorded every 5 minutes in the intra operative period. The monitored physiological data were documented every 15 minutes. The sedation score was assessed every 15 minutes intra operatively and in the recovery room for 2 hours. If the sedation score was more than 2 then it was considered to be deep sedation and the monitoring was continued in the PACU for extended period till the sedation score was two.

Hypotension was defined as fall in systolic BP more than 30% from the baseline. This was manages with inj Ephedrine 6 mg increments. Bradycardia was defined as heart rate < 45 per minute and this was managed with injection Atropine 0.01 mg/kg IV.

Respiratory depression was defined as RR<10/mtor SPO2<93% that was managed with supplemental oxygen and ventilation if needed. Pain was assessed using VAS scale at the end of surgery by the PACU nurse and the ward staff who were not aware of the study drug. The duration of effective analgesia was defined as the time interval between onset of spinal blockade and the time to reach VAS>=3.When the pain score was equal or more than 3 it was intervened with inj Tramadol 50 mg slow IV.>=3.The time taken for the first analgesic request was noted in both the groups.

OBSERVATION AND RESULTS:

50 patients were enrolled in the study. The data collected was analyzed using the SPSS software and the results are expressed as men, standard deviation and percentage. All the continuous data were represented by man with standard deviation and it was analyzed by Independent t-test. Categorical data was analyzed by using Chi – Square. All the analysis was done by using SPSS 14.0 Version, and a p value less than 0.05 was considered as significant.

The two groups were comparable with respect the age. There was no statistically significant difference in age between the 2 groups. The mean age in Group A was 53.48 and 50.12 in Group B. There was no statistically significant difference in the weight between the 2 groups.

The mean duration of surgery was 1.416 in Group A, 1.402 in Group B. The two Groups were comparable with respect to the duration of the surgery. There was no statistically significant difference among the 2 groups in the duration of surgery.

The mean time taken for the onset of sensory blockade to level T 10 was 3.32 minutes in Group A and 3.16 minutes in Group B. There was no statistically significant difference among the 2 groups in the onset of sensory blockade to level T 10.

ONSET OF GRADE 3 MOTOR BLOCKADE

The mean time taken to achieve grade 3 motor blockade on modified Bromage scale was 5.04 min in group A and 4.60 min in group B. There was statistically significant difference in the time of onset of grade 3 motor blockade when group A was compared to group B with the P value of 0.036.

Onset of Motor Blockade (min)				
	N	Mean	Std Deviation	P Value
Group A	25	5.04	0.841	0.036
Group B	25	4.60	0.577	

The maximum level of sensory blockade of T4 was achieved in 9 patients in Group A compared to 15 patients in Group B. There was statistically Significant difference between the 2 groups in the maximum level of sensory blockade (P Value 0.035).The maximum level of blockade to reach level T4 was 60% in Group B and 36% in Group A. The maximum level of blockade to reach level T6 was 56% in Group B and 32% in Group B.

TWO SEGMENT REGRESSION TIME

The mean time taken for two segment regression of sensory block was 147.36 minutes in Group A. 201.52 minutes in Group B. There was statistically significant difference in 2 segment regression time when Group A is compared to Group B with the P Value < 0.001.

Two segment regression time (mins)				
	N	**Mean**	**Std Deviation**	**P Value**
Group A	25	147.36	30.252	<0.001
Group B	25	201.52	48.433	

The mean duration of analgesia was 226.32 minutes in Group A and 255.12 minutes in Group B. The duration of analgesia was longer for patients in Group B when compared to Group A that was statistically significant with the P value 0.003.The heart rate, systolic blood pressure and diastolic blood pressure at various time intervals in the intra operative period were compared between 2 groups. There was no statistically significant difference between the 2 groups at any time in the intra operative period. One Patient in Group B had bradycardia immediately after spinal block and this was managed with inj. Atropine 0.6 mg IV. One patient in group A and four patients in group B had hypotension and this was managed with inj. Ephedrine 6 mg IV once. Sedation – None of the patients in Group A and Group B had a sedation score than two in the intra operative period.

DISCUSSION

The use of intrathecal adjuvant along with local anesthetics to prolong the duration and quality of subarachnoid block has been widely popular and is being investigated with multiple drugs to find the ideal adjuvant. But most of the studies done with alpha 2 agonists are with clonidine in varying doses. There are few studies with use of intrathecal dexmedetomidine and the ideal dose of the study we evaluated the efficacy of adding 5 mcg and 10 mcg of dexmedetomidine with hyperbaric 0.5% bupivacaine (15 mg) in patients coming for hysterectomy surgeries.

Mustafa et al,[13] reported decrease in the onset time of sensory blockade to T 10 level, with use of 10 mcg of dexmedetomidine compared to that of 5 mcg added to 0.5% isobaric bupivacaine.

Shukla et al,[14] found the onset time of sensory blockade to T10 level decreased with 10 mcg of dexmedetomidine added to 15mg of 0.5% bupivacaine compared to the control group with saline and the other group that received 50 mg of Magnesium as an adjuvant with 0.5% bupivacaine.

In our study, the onset of sensory blockade to T 10 level was similar in both the groups. But the maximum level of sensory block was higher in the group that received 10 mcg of dexmedetomidine probably due to the synergistic effects with local anesthetics.

One study [15]intrathecal small dose of dexmedetomidine (3 μg) used in combination with bupivacaine (12 mg) for spinal anaesthesia to produce a shorter onset of motor blockade to grade 3. Mustafa et al., found similar decrease in the onset time for grade 3 motor block which was also dose dependent (5 mcg, 10 mcg) for dexmedetomidine. We found similar results in our study where the time of onset for grade 3 motor block was significantly less in the group that received l0 mcg of dexmedetomidine.

In our study, intrathecal administration of dexmedetomidine 10mcg as an adjunct to hyperbaric bupivacaine resulted in significant increase in the two segment regression time, thereby prolonging the duration of spinal anesthesia compared to 5 mcg of dexmedetomidine. The duration of analgesia was also increased as the time of first request for rescue analgesic was significantly prolonged in group B when compared to group when compared to group A. This was comparable with the other studies done by Mustafa et al dexmedetomidine in varying doses as an adjuvant to different local anesthetics produced prolonged period of analgesia.

The local anesthetic acts by blocking the sodium channels, whereas the alpha 2 adrenoceptor agonist act by binding to pre – synaptic C –fibers and post – synaptic dorsal horn neurons. These antinocieptive effects explain the prolongation of the sensory block when added spinal anesthesia. The binding of α2 adreno receptor agonist to the motor neurons in the spinal cord result in prolongation of motor blockade after sub arachnoid placement with local anesthetics.

In our study there was no significant decrease in blood pressure and heart rate between both the groups that correlates with the study done by Mustafa et al where the same dose of dexmedetomidine(5& 10 mcg) was given intrathecally with bupivacaine for urological procedures. The sympathetic block is near – maximal with the dose of local anesthetic used for spinal anesthesia. So the addition of alpha 2 agonist to a high dose of local anesthetic did not affect the near – maximal sympatholysis. In addition the degree of sympathetic blockade with alpha 2 agonist is dependent on the lipophilicity of the drug, the site of neuraxial administration, and the dose of the drug. These factors could have contributed to the absence of adverse hemodynamic events in our study.

Intrathecal alpha 2 agonists have a dose dependent sedative effect. There was no incidence of Ramsay sedation score more than 2 in our study with use of 5 mcg and 10mcg of dexmedetomidine. The highest dose of intrathecal dexmedetomidine is 15 mcg in human studies which has been reported by Eid et al. They observed sedation score that was significantly higher with 15 mcg. The dose of dexmedetomidine selected in our study was lower that explains the lack of sedative effects between the study groups.

Our study shows that the supplementation of 10 mcg of dexmedetomidine with 15 mg of 0.5% heavy bupivacaine produced a decreased onset of motor blockade and a longer duration of analgesia when compared to that of 5 mcg of dexmedetomidine there was no hemodynamic effects noted between both the groups.

CONCLUSION

In our study the addition of dexmedetomidine 10 mcg to 3ml of 0.5% hyperbaric bupivacaine in hysterectomy surgeries resulted in Higher level of sensory blockade. Prolongation of 2 segment regression time ,Shorter onset time for grade 3 motor blockade, Increase in the duration of sensory blockade when compared to 5 mcg of dexmedetomidine. The onset of sensory blockade to T 10, hemodynamics and sedation were similar in both the groups. We conclude that, supplementation of 10 mcg of dexmedetomidine to 15mg of 0.5% heavy bupivacaine prolonged the duration of analgesia with stable hemodynamics and minimal sedation.

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