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Original Research Article

A prospective randomised double-blind study of comparison of efficacy and safety of dexmedetomidine and clonidine as adjuvants to intrathecal isobaric ropivacaine 0.75% in lower limb surgeries

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ABSTRACT

Background: Studies comparing the efficacy of dexmedetomidine and clonidine as adjuvants to ropivacaine 0.75% in spinal anesthesia are few. The objective was to study the safety and efficacy of dexmedetomidine in comparison to clonidine as an adjuvant to ropivacaine in subarachnoid block.
Methods: Patients were randomly allotted into 3 groups. Group R (n=30) patients received 3 ml of 0.75% isobaric ropivacaine +0.5ml of 0.9% normal saline to a total volume of 3.5ml. Group RD (n=30) patients received 3ml of 0.75% isobaric ropivacaine +5µg of dexmedetomidine +0.9% normal saline to a total volume of 3.5ml. Group RC (n=30) patients received 3ml of 0.75% isobaric ropivacaine +30µg of clonidine +0.9% normal saline to a total volume of 3.5ml. The patients and the investigator were blinded for the study.
Results: Time to reach T10 level of sensory block in group R was 7.6±1.3 min, group RC was 7.8±1.4 min and in group RD it was 7.9±1.4 min which was statistically not significant with p value 0.66. Time to reach motor onset to Bromage scale 4 was 9.8±1.4 min in group R, 10±1.4 min in group RC, 10.5±1.5 min in group RD which was statistically not significant with p value 0.24. Time to reach maximum sensory block in group R was 10.7±1.4 min, 10.6±1.1 min in group RC, 11±1.7 min in group RD which was statistically insignificant with p value 0.51.
Conclusions: Intrathecal dexmedetomidine had superior anaesthetic effects with respect to duration of sensory blockade, motor blockade and duration of analgesia compared to intrathecal clonidine.

Keywords: Clonidine, Dexmedetomidine, Effect, Patients, Surgeries

INTRODUCTION

Neuraxial blockade has a wide range of clinical applications which includes various surgical procedures, labour analgesia, acute postoperative pain management, and chronic pain relief. Single-injection spinal anesthesia with local anesthetics is most commonly used for surgeries of the lower abdomen, pelvic organs, lower limbs and for cesarean deliveries.[1]

Bupivacaine is being extensively used and produces an adequate sensory and motor blockade. However, it has its own disadvantages and side effects like hypotension, bradycardia.[2-4] These adverse effects have prompted a

search for drugs with lesser toxicity. As a safe option to bupivacaine, drugs like levobupivacaine and ropivacaine were developed. They have equal efficacy to bupivacaine. At the same time, they have lesser side effects compared to bupivacaine.[5,6] Ropivacaine was found to have less cardio toxicity and neurotoxicity as compared to bupivacaine.[7] Unlike bupivacaine which is racemic mixture of S and R enantiomer, ropivacaine is a pure S (-) enantiomer of propivacaine. It is less lipophilic than bupivacaine hence less cardio toxic and neurotoxic.[8] Another advantage of ropivacaine is faster recovery from motor block.[9,10]

However, ropivacaine when used alone for spinal anesthesia cannot provide prolonged postoperative analgesia. Hence, to overcome this drawback several adjuvants such as morphine, fentanyl, midazolam, ketamine, neostigmine etc., have been tried along with ropivacaine. However, they have been associated with several side effects such as nausea and vomiting, sedation, respiratory depression etc.[10]

Drugs like clonidine and dexmedetomidine are alpha 2 receptor agonists. They exhibit the antinociceptive action. When given intrathecally they relieve not only somatic pain but also visceral pain.[10] They produce spinal analgesia by interacting with the alpha-2 adrenergic receptors present in the spinal cord. Dexmedetomidine is presently the drug of choice. It contains medetomidine's dextrogyre enantiomer. It produces analgesic effect when given to the patient by intrathecal route. It also enhances the effects of the local anesthetic agents. Similar action is produced by clonidine when it is given intrathecally.[11,12]

Thus, use of these alpha 2 receptor agonists can reduce the dose requirement of local anesthetic agents such as ropivacaine and bupivacaine and hence also reduce the adverse effects of these agents. Dexmedetomidine has been considered as having more effective action than clonidine as the selectivity ratio of alpha 2 receptors is 8 times more in dexmedetomidine compared to clonidine.[12] Studies comparing the efficacy of dexmedetomidine and clonidine as adjuvants to local anesthetic agents in spinal anesthesia are few. Hence, present study was undertaken to compare the efficacy of dexmedetomidine and clonidine in patients undergoing surgeries of lower limb and lower abdomen under spinal anesthesia.

METHODS

This was prospective randomized double-blind study with sample size for 90 patients undergoing surgeries of lower limb and lower abdomen conducted at Department of Anesthesia, KIMS hospital, Hubli, India from January 2015 to January 2017.

Grouping randomly allotted patients into 3 groups. Group R (n=30): patients received 3ml of 0.75% isobaric ropivacaine+0.5ml of 0.9% normal saline to a total volume of 3.5ml. Group RD (n=30): patients received 3ml of 0.75% isobaric ropivacaine+5µg of dexmedetomidine+0.9% normal saline to a total volume of 3.5ml.

Group RC (n=30): patients received 3ml of 0.75% isobaric ropivacaine+30 µg of clonidine+0.9% normal saline to a total volume of 3.5ml. The patients and the investigator were blinded for the study.

Patients of age 18-60 years with ASA 1 and 2, giving informed written consent and scheduled to undergo elective lower abdominal and limb surgeries under spinal anaesthesia were included.

Patients with ASA 3 and 4, extremes of ages <18 and >60 years of age, contraindications to regional anaesthesia like patients in hypotension, uncooperative patients, coagulation defects and local site infections, significant coexisting diseases such as neurologic, cardiopulmonary, psychiatric disease, seizures, pregnant women/parturient, antiarrhythmics/beta blockers/anticoagulants, history of allergy to dexmedetomidine, clonidine or ropivacaine were excluded.

The study solution was prepared at the time of surgery by anesthetist who is aware of the content of the study solutions but not involved in data collection. The investigator as well as patients was blinded to the contents of the study solutions.

In the operation theatre, nil per oral status was confirmed. Intraoperative monitoring included electrocardiogram, pulse oximetry, noninvasive blood pressure and EtCO2. Once monitors are connected baseline parameters including blood pressure, pulse rate, spo2, respiratory rate was recorded.

Intravenous access was obtained and the patients were preloaded with ringer lactate solution 10ml/kg body weight before performing spinal anaesthesia. A tray containing emergency drugs, equipments necessary for resuscitation and general anaesthesia were kept ready.

With aseptic precautions, under local anaesthesia with 2% lignocaine lumbar puncture was performed with, midline approach with the patient in sitting position using 24-26-gauge lumbar puncture needle in the L3-L4 intervertebral space.

The subarachnoid placement of the needle was confirmed by free flow of clear CSF. The 3.5ml of solution prepared (3ml of 0.75% isobaric ropivacaine+0.5ml of 0.9% normal saline to a total volume of 3.5ml or 3ml of 0.75% isobaric ropivacaine+5µg of dexmedetomidine+0.9% normal saline to a total volume of 3.5ml or 3ml of 0.75% isobaric ropivacaine+30µg of clonidine+0.9% normal saline to a total volume of 3.5ml) was injected into subarachnoid space and patient was made to lie supine immediately. Oxygen 5litre/min through face mask was administered. The parameters were observed and

recorded. Standard monitoring was recorded in the form of pulse rate, oxygen saturation, ECG, Non-Invasive arterial Blood Pressure (NIBP), respiratory rate monitoring, mean arterial pressure. If hypotension occurred (defined as fall in systolic blood pressure more than 20% of the baseline or <90mmHg systolic BP in presence of symptoms like nausea, vomiting and dizziness) Inj. Mephenteramine 6mg I.V. was administered. If patient developed bradycardia (defined as heart rate <50bpm), Inj. Atropine 0.6mg I.V. was administered.

Following parameters were observed: time of onset of sensory blockade i.e. time in minutes to achieve loss of pinprick sensation to 23G hypodermic needle at T10 dermatomal level tested every minute, time to achieve maximum dermatomal level of sensory blockade i.e., time in minutes for loss of pinprick sensation to 23G hypodermic needle tested every 2 minutes until the highest level had stabilized for four consecutive tests, time for 2 segment regression from highest sensory level i.e. the time (in minutes) taken for the level to regress to two lower sensory dermatomal levels, duration of spinal anesthesia defined as time from intrathecal drug administration to the first complaint of pai, duration of effective analgesia defined as time of intrathecal administration to the time of first analgesic request and motor blockade which was tested every 30 seconds till modified Bromage score 3 was achieved and every 15 minutes later. Modified Bromage scale was defined as 0: no motor block, 1: inability to raise extended leg, 2: inability to raise extended leg and move knee, 3: complete block of motor limb and sedation: measured by Ramsay Sedation Score and the patient was considered sedated if the score was ≥4.

Postoperatively patients were shifted to recovery unit. Here the vitals were recorded and they were monitored for occurrence of any side effects. Time for rescue analgesia was recorded. Time required to reach Bromage 0 score was also recorded.

SPSS v.23 was used. Statistical tests like Kruskal Wallis test, one-way ANOVA was used. If it was found that the p value was less than 0.05, it indicated the statistical significance.

RESULTS

That all the three groups R, RC and RD are comparable regarding mean values of age, weight and height (P>0.05) Duration of surgery was 86.8±7.5 min in group R, 89±27.8 min in group RC, 87±27.6 min in group RD which was statistically insignificant with P value 0.92 (Table 1).

Time to reach T10 level in group R was 7.6±1.3 min, group RC was 7.8±1.4 min and in group in RD was 7.9±1.4 min which was statistically not significant with p value 0.66. Time to reach motor onset to Bromage scale 3 was 9.8±1.4 min in group R, 10±1.4 in group RC, 10.5±1.5 in group RD which was statistically not significant with p value 0.24. Time to reach maximum sensory block in group R was 10.7±1.4 min, 10.6±1.1 min in group RC, 11±1.7 min in group RD which was statistically insignificant with p value 0.51 (Table 2).

Time for 2 segment regression in min was 77.3 (1.6) in group R, 87.4 (1.6) in group RC and 105.9 (3.2) in group RD. This difference was statistically significant with p value <0.001. Hence, the sensory block action started receding earlier in R group compared to RC and RD groups. Time for sensory regression to S2 dermatome was 134.6±8.5 min in group R, 226.3±8.5 min in group RC and 289.2±10.6 min in RD which was statistically significant with P value <0.001. Time for motor regression (minutes) was 125.8 (8.3) min in group R, 217.4 (8.6) in group RC and 280 (10.6) in group RD. This difference was statistically significant with p value <0.001. Patients in group R asked for rescue analgesia earlier i.e. 137.2 (8.3) min as compared to patients in group RC and RD (231.7 (8.3) and 298.9 (10.3) min respectively). This difference was statistically significant with p value <0.001. Hence duration of analgesia was significantly prolonged in group RC and RD (Table 3).

All three groups were comparable in gender and ASA physical status distributions, which was statistically insignificant. None of the patients had side effects in group R. Side effects were seen in group RC and RD.

Table 1: Comparison of age, height, weight and duration of surgery among the study groups (R, RC and RD groups).

Study variable	Group, values in mean (SD)			F value, df	P value[#]
	R	RC	RD		
General characteristics					
Age in years	42 (13.6)	41.6 (12)	37.2 (10.6)	1.40, 2	0.25
Height in cm	163.9 (6.8)	163.4 (5.1)	162.2 (5.2)	0.63, 2	0.53
Weight in kg	58.7 (6.6)	59.4 (6.2)	60.7 (6.4)	0.71, 2	0.49
Duration of surgery in min	86.8 (7.5)	89 (27.8)	87 (27.6)	10.4, 2	0.92

Table 2: Comparison of intraoperative variables among three groups (Group R, RC, and RD).

Study variable	Group, values in mean (SD)			F value, df	P value#
	R	RC	RD		
Intra operative features					
Sensory onset at T10 in min	7.6 (1.3)	7.8 (1.4)	7.9 (1.4)	0.41, 2	0.66
Motor onset (min)	9.8 (1.4)	10 (1.4)	10.5 (1.5)	1.45, 2	0.24
Time to maximum sensory block (min)	10.7 (1.4)	10.6 (1.1)	11 (1.7)	0.67,2	0.51

Table 3: Comparison of post-operative variables among the three groups (Group R, RC and RD).

Study variable	Group, values in mean (SD)			F value, df	P value#
	R	RC	RD		
Postoperative features					
Time for 2 segment regression in min	77.3 (1.6)	87.4 (1.6)	105.9 (3.2)	1138, 2	<0.001*
Time for sensory regression in min	134.6 (8.5)	226.3 (8.5)	289.2 (10.6)	2010, 2	<0.001*
Time for motor regression (minutes)	125.8 (8.3)	217.4 (8.6)	280 (10.6)	2006, 2	<0.001*
Time of rescue analgesia (minutes)	137.2 (8.3)	231.7 (8.3)	298.9 (10.3)	2298, 2	<0.001*
Number of doses of analgesia given in 24 hours (Inj. Diclofenac 75mg)	2.5 (0.5)	2 (0.1)	1.4 (0.4)	52.8, 2	<0.001*

Table 4: Comparison of gender, ASA, drugs requirement and side effects among the three groups (Group R, RC and RD).

Study variable	Group, values in mean (SD)			X2 value, df	P value#
	R	RC	RD		
Gender					
Male	15 (53.6)	14 (46.7)	17 (56.7)	0.62, 2	0.73
Female	13 (46.4)	16 (53.3)	13 (43.3)		
ASA					
I	21 (75)	24 (80)	24 (80)	0.28, 2	0.86
II	7 (25)	6 (20)	6 (20)		
Drugs required					
Inj. Mephentermine	0	5 (16.7)	3 (10)	4.91, 2	0.08
Inj. Atropine	0	3 (10)	0	6.0, 2	0.05*
Side effects					
Bradycardia	0	3 (10)	0	6.0, 2	0.05*
Hypotension	0	5 (16.7)	3 (10)	4.91, 2	0.08
Nausea and vomiting	0	1 (3.3)	0	1.95, 2	0.37

#- P value was based on Chi-square (X2) test. *Statistically significant (p<0.05), df-degrees of freedom.

In group RC, 3 patients had bradycardia that required Inj. Atropine, 5 patients had hypotension episodes that required Inj. Mephentermine and 1 patient had nausea. In group RD, 3 patients had hypotension episodes that required Inj. Mephentermine (Table 4).

DISCUSSION

Author attempted to compare the efficacy of Dexmedetomidine and clonidine as adjuvants to intrathecal Ropivacaine. It was found that dexmedetomidine in the dose of 5µg compared to clonidine in the dose of 30µg given intrathecally was able to give more duration of sensory as well as motor block and this was found to be statistically significant. Patients receiving Dexmedetomidine as adjuvant had more prolonged analgesia as compared to the patients in the other two groups.

In the present study, the average surgery duration for patients in the three groups was comparable. Kujur S et al, carried out a similar study.[13] They added clonidine and dexmedetomidine as an adjuvant to ropivacaine which was given intrathecally. They studied this effect in patients who underwent surgeries of the lower limb in the orthopedics department. They also gave similar results in terms of average duration of surgery for the patients. Suthar O et al, also carried out similar study where they added Clonidine and Dexmedetomidine as an adjuvant to ropivacaine which was given intrathecally.[14] They studied

this effect in patients who underwent surgeries of the lower limb. They also stated that the average surgery duration for patients in the three groups was comparable. Author found that in terms of loss of pinprick sensation at T10, patients in the three groups were comparable.

Chaudhary AK et al, observed that this time was 5.25+1.21 min in the ropivacaine+clonidine group while it was 4.60±1.04 min in the plain ropivacaine group.[15] This difference was statistically not significant. In the study conducted by Suthar O et al, this time duration was 6±1.28 min in the bupivacaine group while it was 6.00±1.258 min in the clonidine group and in the dexmedetomidine group it was 6.32±1.474 min.[14] This difference was statistically not significant. Author observed that in terms of peak sensory block level achieved, patients in the three groups were comparable.

Parmar NK et al, carried out a study among patients undergoing vaginal hysterectomy.[16] They added dexmedetomidine as an adjuvant to intrathecal ropivacaine. They also noted that in terms of peak sensory block level achieved, patients in the two groups were comparable. Oztin C et al, carried out a study among women undergoing caesarean section.[11] They added clonidine as an adjuvant to intrathecal ropivacaine. They also noted that the difference in terms of achieving sensory block in two groups was not found to be statistically significant. The time required from giving the intrathecal drug to the achievement of motor block level 4 is called the onset of motor block. Author observed that this time was 9.8±1.4 min in group R while in the group RC it was 10±1.4 min and in the group RD, it was 10.5±1.5. These differences were not found to be statistically significant by the author. Parmar NK et al, observed that in the group R time was 5.46±0.91 min, in the group D it was 5.54±0.85 min and the p value for difference was 0.60.[16] The time taken in the present study was longer compared to the study by Parmar NK et al.[16]

CONCLUSION

Author concluded that dexmedetomidine when added as adjuvant to intrathecal ropivacaine 0.75% was superior to clonidine in terms of duration of sensory blockade, motor blockade and duration of analgesia. Intrathecal dexmedetomidine in a dose of 5mcg, with intrathecal ropivacaine, causes significant prolongation in the duration of analgesia with lesser incidence of side effects.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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