Original Article

Comparison of The Effects of The Intrathecal Dexmedetomidine Versus Clonidine As an Adjuvant to Hyperbaric Ropivacaine 0.75% for Infraumbilical Surgeries: A Prospective Randomised Study

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ABSTRACT

Introduction: Infraumbilical surgeries are most commomly done under spinal anesthesia. Many local anesthetic drugs and adjuvants have been used to prolong the effects of local anesthetics. The sample size calculation was done according to results of our pilot study and discussion with the institutional review board. The primary objective is to compare the sensory-motor characteristics of the two drugs and the secondary objective is to compare the duration of analgesia and assess perioperative hemodynamic stability and incidence of side effects during the study period.

Methods: The present prospective randomized study was conducted from April to October 2023. After written informed consent 180 patients posted for elective infraumbilical surgery were randomly divided into two groups of 90 patients each based on closed envelope method.Group RC: 3 ml of 0.75% hyperbaric Ropivacaine + 30 µg clonidine in 0.5 ml normal saline.Group RD: 3 ml of 0.75% hyperbaric Ropivacaine + 5 µg Dexmedetomidine in 0.5 ml normal saline.

Results: It was observed that the dexmedetomidine group had a faster sensory onset (4.5 ± 3.54 mins), faster motor onset(5 ± 3.54 mins) and longer duration of postoperative analgesia (310.11 ± 14.14 mins) as compared to the clonidine group (6.8 ± 1.41mins; 7.4 ± 2.83 mins; 240.22 ± 7.07mins respectively). The incidence of side effects such as nausea, vomiting, shivering, hypotension and bradycardia were also less in comparison to the clonidine group**.**

Conclusion: It was observed that dexmedetomidine offered a faster onset and prolonged duration of postoperative analgesia as compared to clonidine.

Key Words: Infraumbilical surgeries; intrathecal clonidine; intrathecal dexmedetomidine; intrathecal ropivacaine; postoperatiove analgesia.

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INTRODUCTION

Infraumbilical surgeries are mostly conducted under neuraxial anesthesia; spinal anesthesia being the most common. Spinal anesthesia offers with faster onset, adequate and effective sensory and motor blockade, adequate muscle relaxation and good postoperative analgesia. Over the years many local anesthetic drugs have been used for subarachnoid block like lignocaine, procaine, chlorprocaine, bupivacaine and ropivacaine. Various adjuvants are also combined with these drugs to prolong the effects of these local anesthetics along with providing better sensori-motor blockade. Some of these adjuvants are fentanyl, clonidine, dexmedetomidine, nalbuphine, magnesium sulphate etc. Ropivacaine is a pure S- enantiomer of parent chiral molecule propivacaine which belongs to the pipecoloxylidide group of local anesthestics[1,2]. It structurally resembles bupivacaine with similar anesthetics properties. It has reduced potential for cardiotoxicity and neurotoxicity with improved relative sensory and motor block profile[1]. Ropivacaine has low lipid solubility and blocks the nerve fibres which are involved in pain transmission to a greater degree than those involved in motor function, hence it has been extensively used.Addition of dextrose to ropivacaine is to increase the intrathecal cephalic spread, duration of block and speed of recovery[1,3].Spinal hyperbaric ropivacaine has a shorter duration of action, so to hasten the onset and prolong the analgesia intrathecal adjuvants are added to it.

Dexmedetomidine is an S- enantiomer of medetomidine with a highly selective α2 adrenergic receptor agonistic activity with a relatively high ratio of α2/α1 activity (1620:1) compared to clonidine (220:1)[1,4]. The analgesic action of intrathecal α2 adrenoceptor agonist is by depressing the release of C fibre transmitters and by hyperpolarization of postsynaptic dorsal horn neurons. Recent experimental studies indicate that dexmedetomidine

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produces a dose dependent increase in the duration of motor and sensory blocks regardless of the neuraxial route of administration(epidural, caudal, spinal) without any evidence of neurotoxicity in human volunteers[1,5].

Clonidine is a centrally acting partial α2 adrenergic receptor agonist with α2/α1 affinity ratio being 220:1. Clonidine provides dose dependent analgesia[6].The mechanism of action of clonidine is similar to that of dexmedetomidine. The efficacy and safety of clonidine when used intrathecally is well established[7].

Aim and objective: With this background the present study was conducted with the aim to evaluate and compare the anesthetic effects and analgesic efficacy of intrathecal dexmedetomidine versus clonidine as an adjuvant to hyperbaric ropivacaine in patients undergoing infraumbilical surgeries.

The primary objective is to compare the sensory-motor characteristics of the two drugs and the secondary objective is to compare the duration of analgesia and assess perioperative hemodynamic stability and incidence of side effects during the study period.

METHODS

The present prospective randomized study was conducted from April to October 2023. This study was approved by the institutional ethics committee and registered with Clinical trial registry of India (CTRI/2023/04/051732). After written informed consent 180 patients posted for elective infraumbilical surgery of either gender were randomly divided into two groups of 90 patients each based on closed envelope method. The two groups are-

- Group RC: 3 ml of 0.75% hyperbaric Ropivacaine + 30 µg clonidine in 0.5 ml normal saline. Total volume 3.5 ml intrathecally.
- Group RD: 3 ml of 0.75% hyperbaric Ropivacaine + 5 µg Dexmedetomidine in 0.5 ml normal saline. Total volume 3.5 ml intrathecally.

Inclusion criteria

- Patients who have given written informed cosent
- Patients posted for elective infraumbilical surgeries under spinal anesthesia
- ASA grade I and II
- Age – 18 to 60 years
- BMI < 30 kg/m^2

Exclusion criteria

- ASA grade III ad IV
- Patients with known psychiatric illness, chronic pain or any condition that precludes intrathecal anesthesia
- Patients with deformity of the spine
- Patients with skin infection at the site of anesthesia
- Patients with known sensitivity or allergy to the study drugs
- Patients on chrois anticoagulants or antiplatelet drugs or patients with coagulopathy.

In the operation theatre NBM status of the patient was confirmed ad the standard basic monitors (ECG, NIBP, SPO_2 and $ETCO_2$) are attached to the patient and the baseline parameters are recorded. Intravenous access was taken and patient was preloaded with ringer lactate 10 ml/kg body weight before the start of the procedure. Under all aseptic and antiseptic precautions and patient in the sitting position, spinal anesthesia was given in the L3-L4 subarachnoid space with 25 G spinal needle after confirming free flow of clear CSF. The drug injected was-

Group RC: 3 ml of 0.75% hyperbaric Ropivacaine + 30 µg clonidine in 0.5 ml normal saline. Total volume 3.5 ml intrathecally.

Group RD: 3 ml of 0.75% hyperbaric Ropivacaine + 5 µg Dexmedetomidine in 0.5 ml normal saline. Total volume 3.5 ml intrathecally.

Patient was made to lie in the supine position immediately after intrathecal injection.

Following parameters were observed-

- onset of sensory block- assessed by time (seconds) taken from injection of the drug to onset of sensory blockade to T10 level when checked with pin prick method
- onset of motor block- assessed by the time taken (in seconds) form injection of drug to onset of motor blockade (assessed by modified Bromage scale)
- time to highest sensory level- time taken (in seconds) to achieve the highest sensory level of T6 when checked with pin prick method every 1 minute.
- Time to modified Bromage scale 3- time taken to achieve the motor block of modified Bromage 3
- S2 segment regression- time taken (in minutes) for regression of the sensory effect to S2 level
- Time to modified Bromage 0- time taken (in minutes) to achieve full motor wearoff

Modified Bromage scale[8]

0: no motor block

1: inability to raise extended leg

2: inability to raise extended leg and move knee

3: complete motor block

Time to first rescue analgesic- the time at which the patient has the first complaint of pain and requires analgesic.

Intraoperative vitals (heart rate, blood pressure and oxygen saturation) were monitored at zero minute, at every 5 minutes till 30 mins, then half hrly till end of surgery. Intraoperative hypotension was defined as the fall in the systolic blood pressure of >20% of the baseline which was corrected with intravenous fluids or if required inj. Mephentermine 6 mg was given i.v., and bradycardia as heart rate < 50 bpm for which inj. Glycopyrrolate 0.2 mg i.v. or inj. Atropine 0.6 mg i.v. was given.

Postoperatively the vitals (heart rate, blood pressure, oxygen saturation and VAS score) were monitored immediately postop, then every 1 hourly till 6 hrs, then at 12 hrs and 24 hrs. adverse effects like nausea, vomiting, shivering, hypotension and bradycardia were also observed for both intra and postoperatively.

Statistical analysis- Data entry was done in Microsoft Excel. Continuous data were expressed as mean ± SD. For comparison of continuous variables across the two groups unpaired T test was used and for categorical variables Chi- square test was used. The *p value* was calculated online with the help of the site www.medcalc.org.

The *p value* < 0.05 was considered as statistically significant.

RESULTS

Table 1: Demographic Parameters (Age, Height, Weight, Duration of Surgery)

PARAMETERS	Group RC (n=90)	Group RD (n=90)
Age(years)	41.94±6.36	40.23±6.36
Height (cms)	162.70 ±14.14	163.91 ±3.54
Weight (kgs)	67.20 ±8.49	69.22 ± 5.54
Duration of surgery (min)	109.22 ±7.07	107.11 ±14.14

Both The Groups Were Comparable in Terms of Patient Characteristics Like Age, Height and Weight. The Duration of Surgery in Both The Groups Was Statistically Insignificant.

Table 2: Sensorimotor Characteristics

Parameter (mean ± SD)	Group RC (n=90)	Group RD (n=90)	*P value*	Inference
Onset of sensory blockade (min)	6.8 ± 1.41	4.5 ± 3.54	<0.001	HS
Time to highest sensory level(min)	11.9 ± 0.71	10.8 ± 0.35	<0.001	HS
Onset of motor blockade(min)	7.4 ± 2.83	5 ± 3.54	<0.001	HS
Time to highest motor level (Bromage grade 3) (min)	12.4 ± 0.57	11.2 ± 0.49	<0.001	HS
Time for motor grade to 0 (min)	210.56 ± 14.14	260.44 ± 7.07	<0.001	HS
Time to S2 segment regression(min)	140.72 ± 0.35	168.83 ± 14.14	<0.001	HS
Time of first analgesic request(min)	240.22 ± 7.07	310.11 ± 14.14	<0.001	HS

Shows The Comparison of The Sensory and Motor Characteristics of The Spinal Anesthesia Between The Two Groups.

Table 3: Heart Rate

HR mean ± SD	Group RC (n=90)	Group RC (n=90)	*P value*	Inference
Baseline	83.68 ± 4.45	82.4 ± 5.39	0.084	NS
0 min	82.32 ± 4.54	81.92 ± 5.28	0.586	NS
5 min	81.16 ± 4.07	79.98 ± 4.85	0.078	NS
10 min	80.56 ± 3.91	80.14 ± 4.95	0.524	NS
15 min	79.56 ± 3.71	78.78 ± 4.59	0.211	NS
20 min	78.32 ± 3.90	77.72 ± 4.76	0.356	NS
25 min	77.44 ± 4.32	76.22 ± 4.50	0.065	NS
30 min	77.34 ± 3.87	76.72 ± 4.32	0.311	NS
60 min	78.25 ± 3.68	77.1 ± 4.55	0.063	NS
90 min	78.72 ± 4.30	77.61 ± 5.69	0.141	NS
120 min	79.42 ± 3.32	78.76 ± 5.82	0.351	NS
150 min	80.72 ± 3.21	79.46 ± 6.48	0.100	NS
180 min	81.82 ± 3.36	81.16 ± 5.67	0.343	NS

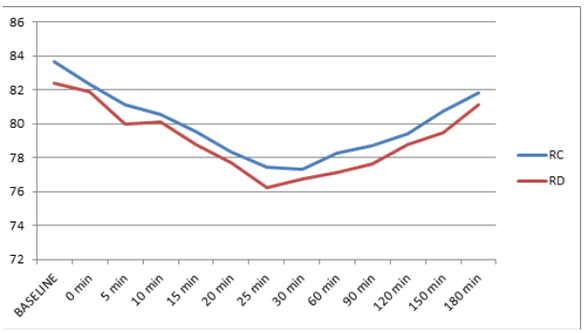

Fig. 1: The Above Table Shows The Trend of The Changes in The heart Rate in Both The Groups During The Course of The Surgery. Although There Was A Decrease in The Heart Rate in Both The Groups During 20 min to 30 mins, It Was Statistically Not Significant.

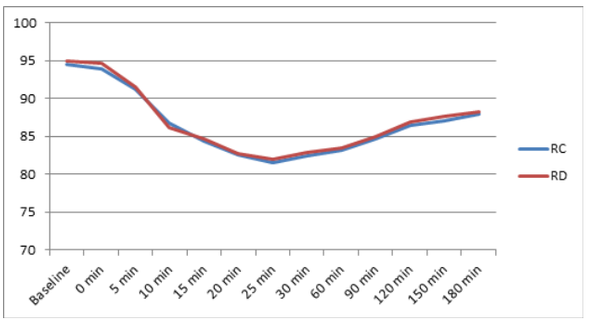

Fig. 2: The table 4 shows the trend of the changes in the mean arterial pressure during the course of surgery. Although there was a decrease in the mean arterial pressure in both the groups during 15 min to 30 mins, it was statistically not significant.

Table 4: Mean Blood Pressure

MBP mean ± SD	Group RC (n=90)	Group RD (n=90)	*P value*	Inference
Baseline	94.5 ± 3.4	95.0 ± 3.9	0.360	NS
0 min	94.0 ± 3.2	94.7 ± 3.9	0.189	NS
5 min	91.2 ± 2.4	91.6 ± 3.8	0.399	NS
10 min	86.8 ± 3.2	86.2 ± 2.5	0.162	NS
15 min	84.4 ± 2.6	84.7 ± 3.1	0.482	NS
20 min	82.6 ± 2.8	82.8 ± 3.2	0.656	NS
25 min	81.6 ± 2.6	82 ± 3.5	0.385	NS
30 min	82.5 ± 3.5	82.9 ± 2.7	0.391	NS
60 min	83.2 ± 1.9	83.5 ± 2.3	0.341	NS
90 min	84.7 ± 1.9	85 ± 2.0	0.303	NS
120 min	86.5 ± 2.5	86.9 ± 1.7	0.211	NS
150 min	87.1 ± 2.3	87.6 ± 1.3	0.074	NS
180 min	87.9 ± 1.7	88.3 ± 1.5	0.095	NS

Table 5: Adverse Effects

ADVERSE EFFECT	Group RC (n=90)	Group RD (n=90)
Nausea	6	4
Vomiting	2	1
Shivering	6	4
Bradycardia	2	0
Hypotension	4	3

The Above Table Shows The Incidence of Adverse Effects in The Two Groups. It Was Slightly More in The RC Group as Compared To The RD Group.

DISCUSSION

Intrathecal anesthesia is considered to be the gold standard technique to provide complete and dynamic anesthesia in patients undergoing lower abdominal or lower limb surgeries. To improve the efficacy of spinal anesthesia adjuvants are used which prolong the duration of analgesia which decreases the postoperative pain and thus enhancing early mobilization and recovery.

Ropivacaine is a pure S- enantiomer of parent chiral molecule propivacaine which belongs to the pipecoloxylidide group of local anesthestics.[1,2] By the addition of the propyl group to the piperidine nitrogen atom compared to the butyl group in bupivacaine, ropivacaine structurally resembles the bupivacaine with similar anesthetics properties. It has reduced potential for cardiotoxicity and neurotoxicity with improved relative sensory and motor block profile[1].

Dexmedetomidine is an S- enantiomer of medetomidine with a highly selective α2 adrenergic receptor agonistic activity with a relatively high ratio of α2/α1 activity (1620:1) compared to clonidine (220:1)[1,4]. The analgesic action of intrathecal α2 adrenoceptor agonist is by depressing the release of C fibre transmitters and by hyperpolarization of postsynaptic dorsal horn neurons.

Clonidine provides dose dependent analgesia[6]. The mechanism of action of clonidine is similar to that of dexmedetomidine by attaching to the intrathecal α2 adrenoceptors.

I Drug and dosage

In the present study we have taken 3 ml of 0.75% ropivacaine in both the groups. In one group we have added 30 µg clonidine (in 0.5 ml normal saline) to it and in the other group we have added 5 µg dexmedetomidine (in 0.5 ml normal saline) to it. The total volume taken in both the groups was 3.5 ml.

Fettes *et al* [9] provided evidence that 15 mg hyperbaric ropivacaine produces reliable spinal anesthesia for a variety of short duration surgical procedures.

Bi *et al* [10] in their study observed that addition of 3 µg or 5 µg dexmedetomidine to hyperbaric ropivacaine for spinal anesthesia in parturients hastened the onset of sensory and motor block, improved muscle relaxation and enhanced postoperative analgesia.

Sulekha Saxena *et al* [11] in their study had observed that addition of 5 µg dexmedetomidine to ropivacaine was safe and it prolonged duration of spinal block while maintaining hemodynamic stability and producing minimal side effects.

De Kock *et al* [12] had concluded that small doses of clonidine (15 and 45 µg) given as spinal adjuvant significantly improved the quality of the spinal block.

Kallapur B *et al* [8] in their study also compared 5 µg dexmedetomidine versus clonidine 30µg given intrathecally as adjuvants to isobaric ropivacaine.

II Patient characteristics

In the present study the average duration of surgery was comparable in both the groups. The patient characteristics like age, weight and height were also comparable in the two groups.

Kujur *et al*[13] carried out a similar study by adding dexmedetomidine and clonidine to isobaric ropivicane given intrathecally and in their study also the average duration of surgery were comparable in the two groups.

III Hemodynamic characteristics

In the present study the changes in the heart rate and mean arterial pressures were comparable in both the groups and were not statistically significant.

Kujur S *et al*[13] in their study also compared ropivacaine, ropivacaine + clonidine and ropivacaine + dexmedetomidine. They also found there was no significant difference in the pulse rate and systolic and diastolic pressures between the three groups.

Bi *et al*[10] in their study compared the different doses of dexmedetomidine as an adjuvant to ropivcaine and they also found no significant differences in the hemodynamics in the three groups.

IV Sensorimotor characteristics

- In the present study the time for sensory onset was 6.8 ± 1.41 min for clonidine group which is consistent with the results of study conducted by **Kallapur** *et al*[8] in which the time for sensory onset was 7.8 min and also with Kujur S *et al* [13] where the time was 6.15 min.
- In this study the sensory onset time for dexmedetomidine group was 4.5 ± 3.54 mins which is similar to the study conducted by **Alhuwalia** *et al*[14] (3.5 mins) and also Gupta *et al* [15] (4.8 min)
- **Kallapur** *et al*[8] and **Bathari** *et al*[16] in their studies had showed that the time to highest sensory level for clonidine group was 10.6 mins and 10.4 mins respectively which is similar to the findings of present study (11.9 ± 0.71min)
- Similarly for dexmedetomidine group **Gupta** *et al*[15] in their study had shown the time to highest sensory level to be 11.7 mins which is similar to the present study i.e. 10.8 ± 0.35 min.
- In the present study the time for motor onset and the time to achieve the highest motor level were found to be faster in dexmedetomidine group (5 ± 3.54 mins & 11.2 ± 0.49 mins & respectively) than in the clonidine group (7.4 ± 2.83 mins & 12.4 ± 0.57 mins respectively).
- **Kujur S** *et al*[13] also concluded in their study that the motor onset was faster in dexmedetomidine group (2.7 ± 54.62) as compared to the clonidine group(7.4 ± 46.63).
- In this study the time to achieve motor bromage grade 0 i.e the duration of motor block was 210.56 ± 14.14 mins in the RC group while it was 260.44 ± 7.07 mins in the RD group. These results are consistent with the results of the study conducted by **Kallapur** *et al*[8] where these variables were 217.4 ± 8.6 mins and 280 ± 10.6 mins respectively.
- The time taken for S2 segment regression was longer in the dexmedetomidine group (168.83 ± 14.14 mins) as compared to the clonidine group (140.72 ± 0.35 mins).
- **Kallapur** *et al*[8] in their study found that the time for the first rescue analgesic was 231.7 ± 8.3 mins in the RC group whereas it was 298.9 ± 10.3 mins in the RD group. The present study also concluded similar results (240.22 ± 7.07 mins for clonidine group and 310.11 ± 14.14 mins for dexmedetomidine group).

V Adverse effects

In the present study the adverse events like nausea, vomiting , shivering, bradycardia and hypotension were observed more in the clonidine group as compared to the dexmedetomidine group.

Hypotension (MAP< 20% of preoperative value) was seen in 4 % patients in the clonidine group and 3 % patients in the dexmedetomidine group and was treated with doses of inj. Mephentermin i.v.

Bradycardia was seen in 2 patients in the clonidine group and in none in the dexnedetomidine group and was treated with inj. Atropine 0.6 mg i.v.

Nausea and vomiting were also seen more in the clonidine group (6% and 2%) as compared to the dexmedetomidine group (4% and 1%).

Shivering was also seen marginally more in the clonidine group(6%) than the dexmedetomidine group (4%).

Lakshmi Priya *et al*[17] in their study had observed hypotension in 15 % patients in the clonidine group.

Shashikala T.K. *et al*[1] in their study compared the intrathecal adjuvants fentanyl and dexmedetomidine with hyperbaric ropivacaine. they had also observed hypotension in 33% patients and bradycardia in 23 % patients in the dexmedetomidine group. Shivering was also observed in 3 patients of the dexmedetomidine group.

CONCLUSION

In this study we concluded that both clonidine and dexmedetomidine when added to intrathecal hyperbaric ropivacaine are safe and provide satisfactory spinal block, excellent postoperative analgesia with minimal hemodynamic instability and side effects. However it was observed that between the two drugs, dexmedetomidine offered a faster sensory and motor block onset and prolonged duration of postoperative analgesia as compared to clonidine.

CONFLICT OF INTERESTS

There are no conflicts of interest.

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