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INTRATHECAL ROPIVACAINE WITH DEXMEDETOMIDINE:COMPARISON OF HYPERBARIC AND ISOBARIC PREPRATIONS FOR SAFETY AND EFFICACY IN LOWER LIMB SURGERIES.

Anaesthesiology

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ABSTRACT

Spinal anaesthesia is popularly used for lower abdominal and lower limb surgeries because it provide good intraoperative conditions and early ambulation. Ropivacaine is a newer longer acting local anaesthetic structurally similar to bupivacaine with reduced cardiac and neurotoxicity . Our aim of study is to compare the Isobaric vs Hyperbaric preprations of Ropivacaine with Dexmedetomidine in terms of their efficacy, characteristics of block they produce, postoperative analgesia and safety.

Materials and Methods : It was Double blind study conducted on 60 patients, randomly divided into two groups each comprising (n=30) patients GpH- Hyperbaric Ropivacaine prepared by 0.75% 3ml (22.5mg) isobaric ropivacaine + 0.5ml of Dextrose 50% + 0.5ml of 15µg dexmedetomidine in 0.5 ml of normal saline=4ml

GpI – Isobaric Ropivacaine 0.75% 3ml(22.5mg) + 0.5ml of normal saline + 0.5ml of 15µg dexmedetomdine = 4ml, Both groups were compared in terms of Mean Onset time of sensory and motor block at T10 ,quality of anaesthesia, regression of sensory and motor block , duration of postoperative analgesia and incidence of any sideeffects such as hypotension, badycardia and respiratory depression.

OBSERVATIONS AND RESULTS: Mean onset time of sensory analgesia at T10 level in GP-H(6.4 ±3.53) vs (11.5 ±4.94 minutes)in GP-I($P<0.05$) and motor block grade-3 in GP-H

(7.5±2.82minutes) vs (15.6±1.41minutes) In GP- I,onset is faster in GP-H. The mean time to complete regression of sensory block was early in GP-H (238±2.82 min) vs (250±10.6 min) ($p<0.05$) . The mean time for complete motor regression was comparative (217.5±21.21 min) vs (225±21.21 min) ($p>0.05$) in both groups. The total duration of analgesia was prolonged in both groups Gp-H 506minutes vs 449minutes GP-I .

CONCLUSION:GP-I is comparable to GP-H in spinal anaesthesia for lower limb surgeries but GpH has faster onset, higher extent of spread, excellent quality and patient satisfactionfor operative procedures and prolonged postoperative analgesia.

KEYWORDS

Ropivacaine, Dexmedetomidine, Hyperbaric, spinal anaesthesia.

INTRODUCTION

Spinal anesthesia is an age-old technique popularly used for infraumbilical surgeries .It is easy to learn, has a definite end point of visualization of cerebrospinal fluid, provides optimal operative conditions , less intraoperative bloodloss ,excellent muscle relaxation , good post operative analgesia[1] , early ambulation , so early discharge can be given.Among local anaesthetics, risk of cardiotoxicity after inadvertent intravenous bupivacaine and transient radicular irritation after lignocaine spinal anesthesia prompted the search for alternative and ropivacaine could be promising in the settings[2].

Ropivacaine, a newer longer acting amide local anesthetic and first introduced into clinical practice in 1996 and has consistently demonstrated good tolerability and safety over bupivacaine because of reduced neurotoxic and cardiotoxic properties.[2]. Ropivacaine is a pure S-enatiomer, has low lipid solubility and blocks nerve fibres involved in pain transmission(A δ and C fibers) to greater extent than motor function (Aβ fibers)and widely used for epidural anaesthesia, peripheral nerve blocks and spinal anaesthesia in ambulatory surgeries.

Initial studies with the plain solution of ropivacaine showed unpredictable spread but later studies have proved that addition of dextrose provide reliable, faster onset and progression, higher extent of spread of drug ,good muscle relaxation for even caesarean section patients, early regression with minimal side effects.[3,4,5] Isobaric ropivacaine can be used in lower limb surgeries of short to intermediate duration[5]. Postopeerative pain is an issue with intrathecal ropivacaine, addition of adjuvants prolongs the duration of postoperative analgesia making it suitable for intermediate duration surgeries thus avoiding EA or GA. Commonly used neuraxial adjvants are opioids , α2 receptor agonists[6].

We have performed the following study to compare the isobaric and hyperbaric solutions of ropivacaine with adjuvant dexmedetomidine in terms of their efficacy, characteristics of the block they produce and safety.

METHODS &MATERIALS

- After acquiring the institutional ethical committee clearance, we performed our study at Government Medical College, Surat in the period of April 2015 to September 2015. It was a prospective randomized double blind study conducted on 60 patients undergoing selective lower limb surgeries. The randomization was done by computer generated random numbers into two groups.

- **Inclusion criteria:** ASA class 1&2, between the age group 18-50 yrs and having height 145-180cm undergoing lower limb surgeries.
- **Exclusion criteria**

a) patient's refusal for taking part in the study
b) presence of co-morbid conditions
c) any condition in which spinal anaesthesia is contraindicated eg. Patients with coagulation disorders, local site infections, spinal column anomalies etc.
d) h/o allergy to drug

- After Preanaesthetic check –up , written and informed consent was taken from patient and relatives.
- In the operating room,18G intravenous canula was taken and started preloading with inj. Ringer lactate 10ml/kg.Patients were premedicated with Inj.Glycopyrrolate 0.2mg iv and Inj. Midazolam 1 mg iv.
- Non invasive blood pressure, ECG leads and pulse oxymeter were applied and baseline pulse rate, blood pressure, RR and SPO2 were recorded.
- Under strict aseptic precautions spinal anesthesia was given in L3-L4 space with 23/25Gauge quincke's spinal needle in sitting position. Patient were randomly divided into 2 groups ,each comprising 30 patients and received the following drugs intrathecally. Study drug was prepared under aseptic conditions by one doctor who was not involved in further study. The Anaesthetist involved in further assessment and patient were blind to which group patient belongs.
- **In Group H :** Hyperbaric Ropivacaine was prepared by taking 0.75% Isobaric Ropivacaine (3ml) and inj Dextrose 50% and (0.5ml) and Dexmedetomidine 15µgm in (0.5 ml) normal saline to make it 4ml (5.525%ropivacaine and 62.5% dextrose/ml). 0.5 ml of dextrose solution was taken from a sterile new ampoule of 10ml of 50% dextrose .
- **In Group I:** Isobaric Ropivacaine was prepared by taking 3ml of 0.75% of Plain Ropivacaine and 15µg dexmedetomidine in 0.5ml

normal saline and 0.5ml normal saline to make it 4ml (5.525% isobaric ropivacaine). Immediately after injection patient was turned supine and time for intrathecal injection was taken as 0 time.

- The sensory blockade was assessed by loss of pin prick sensation with 23G hypodermic needle to no sensations(Gromley and Hill ; normal sensation-0, blunted-1, no sensation-2).Motor block was assessed by modified Bromage scale (0-able to raise whole limb at hip, 1-able to flex knee but unable to raise hip, 2 able to flex ankle but unable to flex knee, 3-no movment of lower limb) . Sensory and motor assessment done every 2 minutes for 10 min., then every 5 minutes till 30 minutes & then every 15 minutes until the end of surgery.
- Onset and duration of sensory and motor block , time to develop sensory block at T10 and at T6 dermatome , highest sensory level achieved , maximum motor block , time to 2 segment regression of sensory block from maximum block and time to complete sensory and motor regression and total duration of analgesia was noted.
- **All Patients monitored for** ECG and SPO2 continuously.
- Pulse rate, systolic and diastolic blood pressure, SpO2 recorded every 2 minutes for 10 minutes and every 5 minutes till 30 min and every 15 min thereafter till completion of surgery.

Onset of sensory block was taken as time from intrathecal injection to loss of pin prick sensation at T10 and onset of motor block was time taken to achieve Bromage score of 3.Time from intrathecal injection to regression to L1 level was taken as total duration of sensory block and Bromage score to grade 1 as total duration of motor block.

- To know the quality of anaesthesia, Patients were asked for feeling of sensation and pain during the lower limb surgery and graded as following groups:

Excellent- no supplementary sedative or analgesic required
Good- only sedative required
Fair- both sedative and analgesic required
Poor- general anaesthesia and tracheal intubation required.

In case of discomfort iv midazolam (1mg) was given and if patient is feeling pain, iv fentanyl (1µg/kg) was given and repeated if necessary.

Also If adequate level for surgery was not achieved , patient was excluded from study.

- Post-operatively ,Patients vitals were monitored in the recovery room. Sensory and motor block assessment done every 15 minutes for 1hr, 30 min. interval for next 2hr and at hourly intervals until complete regression of sensory block at S2 level and motor Bromage scale 1.
- Total Duration of analgesia was recorded by time from injection of subarachnoid block to the first analgesic request.
- All patients were monitored for occurrence of side effects like

1) Hypotension defined as systolic blood pressure <20% of baseline or systolic BP < 80 mmHg) managed with bolus iv fluids(inj. RL) and inj. ephedrine 6mg IV in increments.
2) Bradycardia if pulse rate <50 / min managed with Inj. Atropine0.01 mg/kg intravenously .
3) Nausea, vomiting
4) Respiratory depression managed with O2 supplementation 5l/min with Hudson mask if Spo2<92%
5) Sedation
Patients were asked about the level of satisfaction at the end of surgery.

OBSERVATION AND RESULTS

Statistical Analysis

Data were analyzed using computer statistical software system SPSS® version 17 (statistical packages for the social sciences, chicago, IL). All data are presented as mean (SD) except where specified . The unpaired 't' test was used for intergroup comparison. Probability values <0.05 were considered significant.

DEMOGRAPHIC DATA

The patients in both group are comparable with respect to age, sex ,height , type of surgery (femur, tibia, patella and knee arthroscopies) and duration of surgery.

ASSESSMENT OF SENSORY AND MOTOR BLOCK ONSET, PROGRESSION AND REGRESSION TIME: Table 1

ONSET, PROGRESSION AND REGRESSION TIME: it shows that both sensory and motor onset is delayed in patients in GP-I but regression time is prolonged in GP-I. Total duration of analgesia is much prolonged in GP-H.

	GROUP-H n=30 MEAN	±SD	GROUP-I n=30 MEAN	±SD	P VALUE
AGE	36.4	13.43	36.03	7.07	>0.05
TIME TO ACHIEVE T10 LEVEL (MIN)	6.4	±3.53	11.5	±4.94	<0.05
TIME TO ACHIEVE T6 LEVEL (MIN)	11.54	±7.07	19.58	±7.07	<0.05
TIME TO ACHIEVE HIGHEST LEVEL (MIN)	12.83	±7.07	19.2	±7.07	<0.05
2 SEGMENT REGRESSION TIME(MIN)	109.5	±21.21	127.5	±10.6	<0.05
COMPLETE SENSORY REGRESSION TIME (MIN)	238	±2.82	250	±10.6	<0.05
TIME OF ONSET OF MAXIMUM MOTOR BLOCK (MIN)	7.5	±2.82	15.16	±1.41	<0.05
COMPLETE MOTOR BLOCK REGRESSION TIME (MIN)	217.5	±21.21	225	±21.21	>0.05
DURATION OF ANALGESIA(MIN)	506.5	84.85	449	21.21	<0.05

Onset and progression time of sensory and motor block was faster in GP-H as compared to GP-I, statistically significant($p<0.05$)

Time of regression of sensory block at L1 was prolonged in GroupI, statistically significant($p<0.05$). The mean time for complete motor regression (Modified Bromage grade 0) was prolonged in Group I, not statistically significant ($p>0.05$).

The total duration of analgesia in GpH and GpI (506.5 ± 84.85 min) vs. (449 ± 21.21 min), is longer in GroupH, statistically significant ($p<0.05$).

TABLE 2 Highest Level Achieved Less number of patients in Gp I achieved >T10 sensory level and grade 3 motor block (p<0.05)

	GROUP H (n=30)	GROUP I(n=30)	P value
≥ T6 SENSORY LEVEL	24 (80%)	17 (56.6%)	<0.05
≥ T10 SENSORY LEVEL	30 (100%)	28 (90%)	<0.05
GRADE 3 MOTOR BLOCK	30 (100%)	25 (83.33%)	<0.05

Chi square test was applied for statistical analysis for difference in both groups for highest sensory level achieved.

T10 level of sensory block was achieved in 30 (100%) patients in Group H and 28(90%) of patients in Group I.

In group I, two patients failed to achieve T10 level(T12 and L1) , but as we conducted study in lower limb surgery cases, it was possible to perform surgery with these levels of anaesthesia, so we also included them in this study.

All the 30 patients (100%) in group H achieved grade 3 motor block, 25 (83%) patients in groupI achieved grade 3 motor block. Among the rest 5 patients in groupI, 3 patients achieved grade 2 block and 2patients achieved grade1 motor block.

HEMODYNEMIC PARAMETERS

MEAN PULSE RATE : Table 3

It shows variations in heart rate at various time intervals.

Time	Group H n=30		Group I n=30		P VALUE
	MEAN	±SD	MEAN	±SD	>0.05
Baseline	84.86	±2.82	84.8	±8.48	>0.05
2Min	90.23	±0.7	90.6	±5.65	>0.05
4Min	91.66	±2.82	90.3	±9.89	>0.05
6Min	89.56	±2.82	90.5	±12.72	<0.05
8Min	87.4	±2.82	91.03	±8.48	<0.05
10Min	85.20	±0.7	91.16	±8.48	<0.05
15Min	82.03	±11.31	88.93	±12.72	>0.05
20Min	79.90	±5.65	84.73	±15.55	<0.05
25Min	77.00	±2.82	83.73	±15.55	>0.05
30Min	76.43	±2.82	81.33	±15.55	>0.05
45Min	73.46	±1.41	77.83	±12.72	<0.05
60Min	71.16	±1.41	77	±11.31	<0.05
75Min	70.63	±2.82	74.76	±1.41	<0.05
90Min	71.76	±1.41	74.4	±5.65	<0.05
End of Surgery	73.86	±3.53	76.9	±1.41	<0.05

Initially, 8min. onwards, the pulse rate was less in groupH as compared to groupI.(except at 20, 30 and 45 min).

Two patients in groupH had bradycardia (PR < 50/ min).No patient in group I had bradycardia.

MEAN SYSTOLIC AND DIASTOLIC BLOOD PRESSURE : Table 4

MEAN DIASTOLIC BLOOD PRESSURE

It shows variations in diastolic blood pressue at various time intervals.

TIME	Group H n =30		Group I n =30		
	MEAN	±SD	MEAN	±SD	P VALUE
Baseline	79	±7.07	75.93	±7.07	>0.05
2Min	80.36	±7.07	77.3	±14.14	<0.05
4Min	77.1	±9.89	75.83	±14.14	>0.05
6Min	75.03	±9.89	75.86	±15.15	>0.05
8Min	74.33	±9.89	76.16	±14.14	>0.05
10Min	73.3	±7.07	74.4	±14.14	>0.05
15Min	73.2	±7.07	73.63	±8.48	>0.05
20Min	71.73	±2.82	73.83	±7.07	>0.05
25Min	69.93	±5.65	73.93	±7.07	<0.05
30Min	70	±2.82	72.66	±8.48	>0.05
45Min	69.96	±8.48	70.1	±9.89	>0.05
60Min	68.63	±11.31	70.2	±7.07	>0.05
75Min	68.93	±4.24	70.06	±1.41	>0.05
90Min	68.93	±0.7	69.6	±1.41	<0.05
End of Surgery	69.9	±7.07	70.23	±1.41	>0.05

MEAN SYSTOLIC BLOOD PRESSURE

It shows variations in systolic blood pressure at various time intervals.

The systolic and diastolic blood pressure were comparable in both groups.

5 patients in groupH and 4 patients in groupI had hypotension.

QUALITY OF ANAESTHESIA: Table 5

Less number of patients has excellent quality of anaesthesia in GpI

QUALITY OF ANAESTHESIA	GROUP H (n=30)	GROUP I (n=30)	P value
EXCELLENT	30	24	<0.05
GOOD	0	6	
FAIR	0	0	
POOR	0	0	

All the patients in group H achieved excellent anaesthesia.

In group I, 6 patients had good anaesthesia with some sensation at the surgical site and supplemented with inj.Midazolam1mg iv but incremental doses were not required.

No patient in any group had poor anaesthesia and needed conversion to general anaesthesia.

SIDE EFFECTS :

5 patients in group H and 4 patients in group I had hypotension (systolic blood pressure < 80 mm Hg), which was easily treated with intravenous fluids and Ephedrine.

2 patients in group H had bradycardia (PR<50/min), which was treated with intravenous Atropine.

No patient in this study showed any other side effects like excessive sedation, respiratory depression, nausea-vomiting, shivering , transient neurological symptoms or post dural puncture headache.

DISCUSSION

In this study differences in onset, progression and regression of sensory and motor block are attributed to difference in baricities of both the solution.[12]. Hyperbaric solution spreads under the influence of gravity, so patients position is accepted as the main determinant of the spread of the drug. When we turned the patient supine after giving spinal anaesthesia , drug tends to spread along the curvature of lumbar spine in supine position[4,5]so has an equal distribution of the drug and increases height of block. Isobaric ropivacaine produces unpredic table and variable height of block, therefore patients felt some discomfort during the surgery. The drug remain near the site of injection, producing more extensive and long lasting block in those lumbar and sacral segments, making the drug less useful for surgery[9]. The spread of isobaric ropivacaine is depandent upon the current produced by injection and simple diffusion.[10] Hyperbaric ropivacaine has faster complete sensory and motor regression time but not clinically significant and total duration of postoperative analgesia was prolonged in both groups, addition of dexmedetomidine has prolonged the duration of intraoperative and postoperative analgesia.

Intrathecal dexmedetomidine lower than 10mcg dose blocks smaller C & A δ fibers involved in pain transmission. In higher doses it also blocks large Aβ fibers which are responsible for motor transmission. It acts by depressing release of excitatory nociceptive transmitters (glutamate and substance P) and hyperpolarization of the postsynaptic dorsal horn neurons. It also inhibits the release of excitatory neurotransmitters in spinal motor neurons and thus prolongs both sensory and motor block.[1]

Kim S Khaw et al[11] compared hyperbaric and isobaric ropivacaine 25mg in cesarean delivery in 2002 reported that in isobaric group 25% patients did not achieved adequate block at 30min and required conversion to epidural anaesthesia. Onset time 5.6 (3.6) min. to T7 and 16.8(4.7) to highest level in Hyperbaric group and 11.4(6.8)to T7 and 20.1(11.1) to highest level is comparable to our studies.

H. Kallio et al[6] in2004,compared hyperbaric and plain ropivacaine 15mg in lower limb surgeries has concluded all patients in Group HYP achieved T10 level of analgesia but 64% in PL. In Group HYP Sensory block (5 min vs 10 min T10 level) and motor block (10 min vs 20 min to) were faster in onset and also faster recovery of block .

J. B. Whiteside et al[4] in 2001 in lower abdominal, perineal and lower limb surgeries had concluded that hyperbaric ropivacaine relative to CSF can produce predictable and reliable spinal anaesthesia of intermediate duration.

P.D.W. fettes et al[8]in 2004 concluded that addition glucose10mg/ml or 50mg/ml to ropivacaine 5mg/ml increases the speed of onset , block reliability, duration of useful block, and also fast recovery in ambulatory surgeries. Plain solutions are less reliable for surgery above dermatomal level of L1..

Rajni Gupta et al[10] concluded that hyperbaric ropivacaine (18mg) has predictable and good quality of sensory and motor block , early mobilization for day –case surgery. In Isobaric ropivacaine, patients required supplementation with analgesics and sedatives because inadequate motor block.

Rajni Gupta et al[6] 2011conducted a study of 5µg dexmedetomidine as on intrathecal adjuvant with 22.5 mg plain ropivacaine undergoing lower limb surgeries reported that Duration of effective analgesia (time to requirement of first analgesic)was significantly prolonged in

dexmedetomidine group (478.4±20.9min) as compared to plain ropivacaine (241.67±21.67) with minimal side-effects.

Sapna Joshi et al(1) in 2015 did a study of 15µg dexmedetomidine as an adjuvant with15mg hyperbaric bupivacaine in 40 patients undergoing elective lower abdominal or lower limb surgeries also has significant prolongation of motor and sensory block and it is beneficial in surgeries of long duration percluding the need for an epidural and general anaesthesia.

Limitations of our study is that 15 µg dexmedetomidine as adjuvant to 22.5mg intrathecal ropivacaine prolonged the anaesthetic effect of ropivacaine. So we could not study the suitability of ropivacaine for ambulatory surgeries.

Conclusion :

In spinal anaesthesia, Hyperbaric Ropivacaine (22.5mg) with dexmedetomidine has more success rate, faster onset, higher cephalic spread of sensory block and complete motor block with excellent quality of anaesthesia but Isobaric Ropivcaine(22.5mg) with dexmedetomidine can be used for lower limb surgeries. Addition of 15µg dexmedetomidine as adjuvant has prolonged the duration of intraoperative sensory and motor block and duration of postoperative analgesia .

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