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COMPARISON OF ANAESTHETIC PROPERTIES OF INTRATHECAL 0.75% ISOBARIC ROPIVACAINE OVER 1% ISOBARIC CHLOROPROCAINE FOR ELECTIVE CAESAREAN SECTION

Anesthesiology

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ABSTRACT

AIM - To compare the efficacy of intrathecal 0.75% isobaric ropivacaine with 1% isobaric chloroprocaine for elective caesarean section. **MATERIALS AND METHOD -** 60 full term parturients of American Society of Anaesthesiologists (ASA) grade II with weight < 80 kg and height between 145 cm to 165 cm, scheduled for Elective Caesarean Section under spinal anaesthesia were selected. All cases were divided into two groups: Group R:Patients receiving 22.5mg (3ml) of 0.75% Isobaric Ropivacaine and Group C:Patients receiving 40mg (4ml) of 1% Isobaric Chloroprocaine. Sensory and motor block characteristics were studied in both the groups. **RESULTS -** Patients who were administered intrathecal chloroprocaine showed a significantly earlier onset of sensory (4.67 ± 1.154 mins in group R and 1.40 ± 0.484 mins in group C) and motor (6.87 ± 1.33 mins in group R and 2.11 ± 1.071 mins in group C) blockade ($p<0.001$) compared to patients receiving ropivacaine. Time to reach maximum height and time to modified Bromage grade 3 was shorter in group C as compared to group R, $p < 0.0001$.Ropivacaine produced significantly longer duration of motor block (192.9 ± 15.4 mins) compared to Chloroprocaine (80.0 ± 13.30 mins). Duration of analgesia was also significantly longer in group R (244.30 ± 23.13 mins) than group C (67.21 ± 8.11mins), $p < 0.0001$. **CONCLUSION -** Isobaric chloroprocaine and ropivacaine doses used in the study produced adequate anaesthesia and analgesia for elective caesarean section without any serious side effects. Ropivacaine produces significantly longer duration of analgesia than Chloroprocaine but the onset of sensory and motor blockade are significantly faster with Chloroprocaine.

KEYWORDS

Chloroprocaine, Ropivacaine, Caesarean section, Spinal anaesthesia.

INTRODUCTION

Spinal anaesthesia is the optimal choice for elective caesarean section. The advantages of spinal anaesthesia include safe, economical, easy to perform and effective technique which provides rapid and reliable anaesthesia with muscle relaxation and good analgesic effect for patients undergoing elective caesarean section. However, they cause perioperative hypotension in most patients.

Traditionally bupivacaine, available in a commercial preparation as a racemic mixture (50:50) of its two enantiomers, levobupivacaine, S (−) isomer and dextrobupivacaine, R (+) isomer has been the drug of choice for the subarachnoid block in caesarean section. However, it's significantly long duration of action delays recovery of motor function and prolongs post-anaesthesia care unit stay. In addition, several studies have shown that bupivacaine produces higher neurological and cardiac toxicity compared to other local anaesthetics.1 The problems associated with the toxicity of racemic bupivacaine triggered the development of alternative suitable 'single enantiomeric' local anaesthetic agents with low cardiac and CNS toxicity.

Although Hyperbaric local anaesthetic solutions have a remarkable record of safety, their use is not totally without risk: high spinals have been described with hyperbaric bupivacaine. Their successful use requires rapid movement of the patient from the lateral or sitting position to prevent unilateral or saddle blocks, and conversely extension or return of the block may develop after mobilization. Extension of the sympathetic block by the same mechanism may play a role in sudden cardiac arrest after spinal anaesthesia with hyperbaric solution. Thus, the use of truly isobaric solutions may prove less sensitive to position issues.

This is very useful in a short procedure such as caesarean section where the hyperbaric local anaesthetic that has not fixed could migrate after early mobilization and cause hypotension or bradycardia.

The pure S (−) enantiomer of bupivacaine, i.e., ropivacaine was thus introduced into the clinical anesthesia practice. Nowadays Ropivacaine which blocks sensory nerve fibers more readily than motor fibers, is now gaining popularity due to its reduced cardiac toxicity and neurotoxicity with overdose. Recent studies with intrathecal Ropivacaine has demonstrated low cardiovascular and neurotoxic effects, good tolerability and efficacy with early ambulation and discharge with good quality of postoperative analgesia.[2]

Isobaric Chloroprocaine has recently gained interest as short acting spinal anesthetic. 1% Isobaric Chloroprocaine has a rapid onset of action producing excellent sensory and motor block and has a rapid hydrolysis in the blood stream by pseudocholinesterase and placental transfer is limited. Chloroprocaine can be used for low risk Cesarean section in healthy parturients. Motor recovery may be more predictable for Chloroprocaine and may be beneficial for breastfeeding initiation.[3]

Amide linked local anaesthetic agents such as lignocaine and bupivacaine can become trapped in their ionized forms on the fatal side of the placenta, so their net transfer across the placenta is increased. An ester linked local anaesthetic agent such as Chloroprocaine is rapidly metabolise d and placental transfer is limited. Chloroprocaine is the drug of choice for epidural analgesia and a decompensating foetus, because it does not participate in ion trapping. Placental transfer of Chloroprocaine is not influenced by foetal acidosis.

The in vitro half-life of chloroprocaine is 21 seconds for maternal and 43 seconds for fetal blood. In patients who are homozygous atypical for plasma cholinesterase, chloroprocaine typically exists for two minutes in circulation.

We selected the Ropivacaine dose based on the dose - response study by Khaw et al.4, 5 which estimated the 95% effective dose (ED95) of intrathecal Ropivacaine for caesarean section to be 26.8 mg (23.6 - 34.1mg) and that of Chloroprocaine based on studies of Maes et al3 who used 40mg of intrathecal chloroprocaine with sufentanyl for caesarean section.

AIMS AND OBJECTIVES

The aim of this study was to compare the intrathecal efficacy and safety of 0.75% Isobaric Ropivacaine with 1% Isobaric Chloroprocaine in Term Parturients for elective caesarean section with the following objectives:

1. To compare the onset and duration of Sensory and Motor blockade
2. To study the duration of Post-operative analgesia
3. To study the Hemodynamic effects
4. To study side effects and complications if any (intra-operative and post-operative period).

MATERIALS AND METHODS

This prospective randomised study was conducted at the JHALAWAR MEDICAL COLLEGE, JHALAWAR (RAJASTHAN). After approval of The Institutional Ethical Committee, written informed consent was taken from each patient. 60 full term parturients of American Society of Anaesthesiologists (ASA) grade II with weight < 80 kg and height between 145 cm to 165 cm, scheduled for Elective Caesarean Section under spinal anaesthesia, were included in this prospective randomized study.

All cases were divided into two groups:

Group R: Patients receiving 22.5mg (3ml) of 0.75% Isobaric Ropivacaine.

Group C: Patients receiving 40mg (4ml) of 1% Isobaric Chloroprocaine.

The primary outcome measure in present study was effect of motor and sensory blockade (VAS<3) in the Ropivacaine group as compared to Chloroprocaine group.

SELECTION OF PATIENTS:

INCLUSION CRITERIA:

- Patients aged 18-40 years.
- Height: 145 cms to 165 cms
- Weight: < 80 kgs.
- ASA grade II

EXCLUSION CRITERIA:

Parturients with

- Cardiac or neurologic disease, diabetes, pre-eclampsia or eclampsia,
- Hypersensitivity to study drugs,
- Bleeding or coagulation disorders,
- Decreased platelet counts,
- Local or systemic sepsis,
- Any obstetric complications or evidence of fetal compromise or suspected fetal abnormality,
- History of drug abuse and parturient refusal.

All patients were visited on the day prior to surgery and were explained about the anaesthetic technique and perioperative course. Each patient had a standard pre-anaesthetic check-up.

All patients underwent preoperative fasting for 8 hours and water deprivation for more than 4 hours.

The patients were placed in a supine position with a 15° left lateral tilt after entering the operating room.

Pre-anaesthetic check-up (PAC), NBM status, Consent – were checked. All vitals were monitored. They received premedication with ranitidine 50 mg and metoclopramide 10 mg intravenously (IV) and were preloaded with Ringer's lactate solution 10 – 15 ml/kg via 18-gauge cannula placed in a forearm vein before initiation of the subarachnoid block.

After taking strict aseptic precautions, the subarachnoid block was performed in sitting or right lateral position with a 25-gauge Quincke type spinal needle.

The subarachnoid block was given by midline approach at L3-L4 / L4-L5 / L5-S1 interspace and study drug was given over 30 seconds based on the group.

Immediately after intrathecal injection, patients were placed in supine position.

The sensory and motor block was assessed after the intrathecal injection at 1 and 2 minutes and then subsequently at 2 minutes intervals until surgical anaesthesia is achieved.

The segmental level of sensory block to pin prick was evaluated bilaterally along the midclavicular line by using a short bevelled 27-gauge sterile needle.

The motor block of both legs was assessed using the modified Bromage6 scale (0 = full movement, 1= unable to raise extended leg, 2= unable to flex knee, 3= no movement).

The induction of anaesthesia was considered when at least the T10 dermatome was anesthetized.

The Hemodynamic parameters that were monitored included: maternal heart rate by electrocardiogram (ECG), non-invasive blood pressure and oxygen saturation (SpO2). The values were recorded before the induction, every 2 minutes during the first 10 minutes after subarachnoid block, then every 5 minutes during the first hour and then every 10 minutes until the patient was transferred to the recovery room. Oxygen was administered at a rate of 3 - 5 L/min via Hudson face mask.

A significant change in the heart rate or blood pressure is defined as a value greater than 20% change from baseline values. Hypotension was treated with intravenous boluses of mephentermine 6 mg and Ringer's lactate solution, and bradycardia with IV atropine. Nausea and vomiting was treated with IV ondansetron.

The condition of neonate was evaluated by APGAR scores at 1, 5 and 10 minutes after delivery.

The time to achieve sensory block at T10 level, the maximum cephalad spread of the sensory block, the time to achieve the motor block and the total duration of analgesia were recorded intraoperatively.

Postoperatively, the blocks were assessed at 15 minutes intervals until regression or complete recovery of motor function has occurred.

All patients were evaluated for possible adverse effects due to hemodynamic changes and for headache, nausea, vomiting and transient neurologic deficits.

Sensory block assessment was done using Hollmen Scale, Motor block assessment was done using Modified Bromage Scale and Straight Leg Raising Test while Visual Analogue Scale and Verbal Pain Scores were used to assess level of analgesia and analgesia efficacy extending to the post operative period.

OBSERVATIONS AND RESULTS

The populations in both the groups were comparable demographically and there was no statistically significant difference between the groups (Table 1).

Table 1: Patient Characteristics

Variables:	Group R: (30)	Group C: (30)	P value:
Age (years)	24.9 ± 3.82	25.1± 3.97	0.8431
Weight (kgs)	59.8 ± 7.48	56.4 ± 6.41	0.0637
Height (cms)	155.2 ± 4.85	156.7 ± 3.74	0.0516
Gestation (weeks)	38.2 ± 0.35	38.1 ± 0.21	0.1849
Duration of Surgery (mins)	42.1 ± 7.34	44.8 ± 9.30	0.2170

Block characteristics are shown in table 2.

Table 2: Spinal Anaesthesia Characteristics

BLOCK CHARACTERISTICS:	R:	C:	P Value:
Sensory Block:			
Onset of sensory block (min)	2.13 ± 0.86	0.44 ± 0.015	0.0001
Time to reach T10 (min)	4.67 ± 1.154	1.40 ± 0.484	0.0001
Median max. level of sensory block (range)	T6 (T5-T8)	T5 (T4-T6)	
Time to reach max. sensory block (min)	7.23 ± 1.478	3.84 ± 2.006	0.0001
Regression of sensory block to T12 (min)	192.60 ± 11.27	58.63 ± 8.13	0.0001

Motor Block:			
Onset of motor block to Bromage 3 (min)	6.87 ± 1.33	2.11 ± 1.071	0.0001
Total duration of motor block (min)	192.90 ± 15.37	80.0 ± 13.30	0.0001
Analgesia:			
Duration of analgesia (min)	244.30 ± 23.13	67.21 ± 8.11	0.0001

Onset of anaesthesia to T10 was 4.67 ± 1.154 mins in group R and 1.40 ± 0.484 mins in group C ($p < 0.0001$). The median (range) maximum height achieved in terms of dermatomes in group R was T6 (T5–T8) while in group C was T5 (T4-T6). The time to reach maximum height was longer in group R (7.23 ± 1.478 mins) as compared to group C (3.84 ± 2.006 mins) with a $p < 0.0001$. The time to modified Bromage 3 (MB-3) grade was 6.87 ± 1.33 mins in group R and 2.11 ± 1.071 mins in group C with $p < 0.0001$.

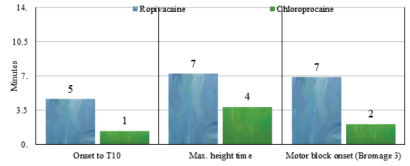

Table 3: Intra-operative and Post-operative Monitoring

Time:	PR /min	B.P /mmHg	Hollmen's scale	BMB score	VAS	Analgesi
	R: C:	R: C:	R: C:	R: C:	R: C:	R: C:
PAE	90.64 88.65	128.9/74.4 126.4/78.2	0 0	0 0	0 0	- -
0min	92.84 91.38	120.5/69.3 122.5/74.6	0 0	0 0	0 0	- -
3min	93.46 90.59	121.8/69.1 123.3/72.7	2.03. 2.56	0 3	0 0	+ +
5min	94.25 93.92	119.3/66.5 118.9/66.8	2.9 3	2.16 3	0 0	+ +
10min	86.56 88.35	118.6/67.8 119.6/65.2	2.93 3	2.8 3	0 0	+ +
15min	82.55 85.85	117.8/66.3 117.5/67.6	2.93 3	2.86 3	0 0	+ +
30min	78.25 76.56	115.3/62.5 114.6/63.7	2.96 3	3 3	0 0	+ +
45min	76.87 75.51	112.9/64.4 114.2/63.1	3 3	3 3	0 0	+ +
60min	75.55 78.42	117.6/65.5 116.6/66.5	3 0.83	3 2.23	0 0	+ +
90min	80.29 76.79	115.4/67.2 120.5/69.5	3 0	3 0	0 5.4	+ -
120min	78.85 79.36	118.1/66.8 117.5/68.5	2.13 0	2.23 0	1.5. 6.7	+ -
180min	76.92 79.87	121.3/66.6 119.9/69.2	1.39 0	1.19 0	2.5 6.8	+ -
240min	75.66 76.73	119.5/70.3 120.3/72.2	0.83 0	0.67 0	5.4 6.8	+ -
300min	70.52 74.24	124.8/69.5 122.6/71.1	0 0	0 0	6.6 7.1	- -

The MAP decreased significantly in both the groups compared to baseline/preoperative values ($p < 0.05$) but overall incidence of hypotension was not significantly different. Furthermore, it was transient (5 - 10 mins) in chloroprocaine group as compared to ropivacaine group (25 – 30 mins).

There were no significant difference between the two groups with respect to PR and SpO2 ($p > 0.05$).

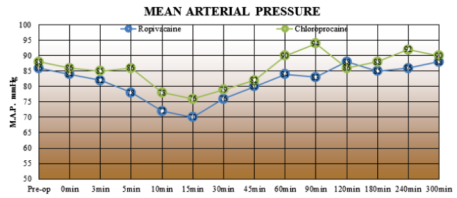

Figure 3: Mean Arterial Pressure variation with time

Hypotension was the most common side effect seen in both the groups, however, total amount of mephentermine used was significantly not different ($p > 0.05$). Shivering was seen in intra-op period in 5 patients of Group R and 2 patients of Group C. Bradycardia occurred during intra-op period in 3 patients of Group R and 1 patient of Group C. None of the patients in the Group C exhibited any histamine release related or allergic adverse effects which are expected as chloroprocaine belongs to ester group of local anesthetics.

Table 4: Adverse Effects

	R: (n=30)	Percentage:	C: (n=30)	Percentage:	P value:
Hypotension	6	20%	5	16.67%	0.7386
Bradycardia	3	10%	1	3.34%	0.30062
Headache	1	3.34%	1	3.34%	1.0000
Backache	1	3.34%	1	3.34%	1.0000
Nausea	2	6.67%	2	6.67%	1.0000
Vomiting	2	6.67%	1	3.34%	0.5536
Shivering	5	16.67%	2	6.67%	0.2276

DISCUSSION

In our study isobaric chloroprocaine showed significantly faster onset of sensory and motor block but with decreased duration of analgesia compared to ropivacaine.

Not many studies are available where chloroprocaine has been used in parturients for elective cesarean section. Previous authors have used different doses (40 mg) of chloroprocaine with or without fentanyl.3,7 Maes S et al.3 used 40 mg chloroprocaine with and without fentanyl and compared it to bupivacaine in patients for elective cesarean section. Most of the other authors have also taken the median effective dosage of chloroprocaine for sub-arachnoid block as 40 mg and have regarded lesser dosages insufficient for spinal anaesthesia. Taking into consideration the previous studies, MLAC and potency ratio we have used chloroprocaine 40 mg (10 mg /ml) to compare ropivacaine 22.5 mg (7.5 mg /ml), so as to achieve adequate sensory and motor block for elective caesarean sections.

Taking into account the maximum block height, chloroprocaine achieved higher sensory block levels as compared to ropivacaine and also took significantly lesser time than ropivacaine to attain that level. In the present study, chloroprocaine also achieved sensory level of T10 significantly faster than ropivacaine consistent with the past researches. The variations in the finding of these studies could be due to sample size, demographic profile, methodology, drug dose and baricity. Vaghadia et al.7 did their study on patients undergoing TURP under spinal anaesthesia while Casati A Fanelli G et al.8 did their study on outpatients undergoing knee arthroscopy.

When it comes to sensory block onset time, it can be very well concluded in coherence with all other studies that chloroprocaine definitely has a significantly quicker onset time as compared to ropivacine or any other local anaesthetic for that matter. This was also seen in our study but the onset time was quickest in our study compared to all other studies available. This may be due to the fact that our study was conducted on parturients and rest most of the studies with chloroprocaine have been done on non-parturients.

In the present study, ropivacaine achieved the median dermatomal height of T6 but chloroprocaine achieved a median dematomal height of T5 and took significantly lesser time to achieve maximum block level than ropivacaine. Maes et al.3 achieved a median dermatomal level of T7-T8 while Vaghadia et al.7 achieved a maximum level of T7 when fentanyl was used as an adjuvant but only till T9 when plain chloroprocaine was used.

In our study, sensory (T12) and motor regression of chloroprocaine was comparatively faster than ropivacaine. Various authors in the past obtained similar results with chloroprocaine showing faster sensory and motor recovery and same can be reciprocated by the data obtained in our study.

No significant differences in patient characteristics and baseline hemodynamic parameters were observed between the two groups.

Decrease in MAP and PR are two most frequently encountered complications of neuraxial blocks. In our study, it was observed that fall in BP was transient in chloroprocaine group but sustained in

ropivacaine group. In spite of this, there was no significant difference in the overall incidence of hypotension and these were promptly treated without any serious consequences. Further, the total mephentermine dose required in both the groups was comparable ($p > 0.05$).

An important limitation of our study was that we did not measure the specific gravity of either of the drug. Maintenance of temperature could be a problem in tropical countries which could have influenced the overall results.

CONCLUSION

We, therefore, conclude that isobaric chloroprocaine and ropivacaine doses used in the study produced adequate anaesthesia and analgesia for elective caesarean section without any serious side effects. Ropivacaine produces significantly longer duration of analgesia than Chloroprocaine but the onset of sensory and motor blockade are significantly faster with Chloroprocaine.

Efficacy, lack of toxicity and suitable hemodynamic profile makes chloroprocaine a suitable agent for day-care procedures with low threshold for hypotension and also providing early ambulation and more predictable motor block resolution which may be beneficial for breast feeding initiation, while ropivacaine can be a suitable agent for elective caesarean section especially in patients with variable hemodynamic profile with good post-operative analgesia.

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