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COMPARISON OF PREMIXED VS SUCCEDENT ADMINISTRATION OF MORPHINE AFTER HEAVY BUPIVACAINE IN SUBARACHNOID BLOCK FOR LSCS

Anaesthesiology

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ABSTRACT

Background: Pain is a major concern during and after surgical procedures, with inadequate pain management leading to significant complications, delayed recovery, and prolonged return to daily activities (1).The choice of anesthesia for lower segment cesarean section (LSCS) is regional anaesthesia.Regional anesthesia (RA) is preferred over general anesthesia (GA) due to its greater maternal safety and improved fetal outcomes (2). Neuraxial blockade with low-dose opioids, such as morphine, fentanyl, and sufentanil, is a well-established technique for intraoperative and postoperative analgesia in obstetric patients (3). **Aim And Objectives:** We aimed to assess SAB characteristics (Sensory and Motor Block), maternal Haemodynamics, Duration and amount of rescue of analgesia, and adverse effect. **Methodology:** Given the differences in baricity between intrathecal local anesthetics and opioids (hyperbaric 0.5% heavy bupivacaine and morphine), we conducted a single-blind, randomized controlled trial involving 104 full-term pregnant women undergoing elective or emergency LSCS under spinal anesthesia. The participants were randomly allocated into two groups: Group 1 (n = 52): Received IT hyperbaric bupivacaine (0.5%) 9 mg (1.8 mL) + morphine 200 mcg (0.2 mL) as a premixed solution in a single syringe. Group 2 (n = 52): Received IT hyperbaric bupivacaine (0.5%) 9 mg (1.8 mL), followed by morphine 200 mcg (0.2 mL) administered separately after bupivacaine. **Results:** The duration of postoperative analgesia was clinically prolonged in both groups, with greater duration observed in the premixed group. However, sensory and motor block characteristics were comparable between the two groups. Importantly, no major hemodynamic instability or significant adverse events were observed in either group. **Conclusion:** The administration of intrathecal morphine with 0.5% hyperbaric bupivacaine, whether premixed or given separately after local anesthetic, resulted in comparable SAB quality, maternal hemodynamic stability, and neonatal outcomes. Both techniques were effective in providing adequate intraoperative and postoperative analgesia, with no significant differences in safety profiles.

KEYWORDS

Lower segment cesarean section, separate intrathecal injection, morphine, hyperbaric bupivacaine, spinal anesthesia.

INTRODUCTION

Spinal anesthesia has been a standard practice for lower segment cesarean section (LSCS); however, ongoing research continues to explore methods to enhance intraoperative anesthesia quality and extend postoperative analgesia (4)(5). Opioids, such as morphine, exhibit a synergistic effect when combined with LA in the subarachnoid space (6)(7), effectively reducing visceral pain and thereby improving both sensory and motor blockade quality (8). This approach allows for a reduced LA dosage while ensuring hemodynamic stability during and after the procedure (4). Additionally, it significantly prolongs the duration of postoperative analgesia (9)(10).

In obstetric patients, incorporating opioids into neuraxial blockade is a well-established technique for labor pain relief during LSCS and postoperative analgesia as well as it provides substantial analgesic benefits with minimal risk to both the parturient and the fetus (4)(11).

We assessed SAB characteristics (Sensory and Motor Block), maternal Haemodynamics, Duration and amount of rescue analgesia and adverse effect.

MATERIALAND METHODS

Study Design And Setting

This single-blinded, randomized controlled trial was conducted in the Department of Anaesthesiology, Critical Care, and Pain Management at Himalayan Institute of Medical Sciences (HIMS), Swami Rama Nagar, Dehradun, following approval from the institutional ethics committee. The study was carried out over a period of 12 months. Written informed consent was obtained from all patients scheduled for both elective and emergency LSCS.

Inclusion Criteria

Patients meeting the following criteria were included in the study:

1. Full-term, non-laboring parturients with a singleton, uncomplicated pregnancy planned for elective or emergency LSCS.
2. Pregnant women classified under ASA grade I or II.

Exclusion Criteria

Patients Were Excluded From The Study If They Met Any Of The Following Criteria:

1. Multiple pregnancies or complicated pregnancies.
2. Pregnancy associated with bleeding disorders.
3. Presence of spinal deformity or other contraindications to spinal anesthesia.
4. Cases with acute fetal distress, intrauterine fetal death, or known fetal anomalies.
5. Pregnant women diagnosed with severe pregnancy-induced hypertension (PIH).
6. Parturients classified under ASA grade III or IV.
7. Presence of systemic diseases such as renal, cardiac, or hepatic disorders.
8. Known drug allergies.
9. Refusal to provide informed consent.

Sample Size Calculation

Sample size estimation was based on prior correlated studies. Power analysis determined that a minimum of 52 patients per group was required to achieve 80% power at a significance level of 0.05 to detect a statistically significant difference between the two groups.

Randomization And Group Allocation

The parturients were randomly assigned into two groups (n = 52 per group):

- Group 1 (n = 52): Received premixed IT 0.5% hyperbaric bupivacaine (9 mg, 1.8 mL) + morphine (200 mcg, 0.2 mL).
- Group 2 (n = 52): Received IT hyperbaric bupivacaine (0.5%) 9 mg (1.8 mL) followed by separate syringe administration of morphine (200 mcg, 0.2 mL) via a 27G Quincke's needle.

Preoperative Preparation

Parturients scheduled for elective LSCS were kept nil per os (NPO) for 8 hours, whereas emergency cases were taken up regardless of their fasting status. Informed consent was obtained from all patients before the procedure.

Intravenous Access and Premedication

Intravenous (IV) access was secured using two wide-bore cannulas

(16G or 18G) either in the ward for elective cases or in the emergency department for emergency procedures. Premedication included:

- Injection Ranitidine (50 mg IV)
- Injection Metoclopramide (10 mg IV)

Both medications were administered 30 minutes before surgery.

Drugs Used

To avoid variability, both drugs were sourced from the same manufacturer. The following formulations were used:

- **Hyperbaric Bupivacaine (0.5%):** 20 mg (HEAVY ANAWIN ampoule, Neon Laboratories).
- **Preservative-free Morphine:** 10 mg (MORPHITROY ampoule).

Intraoperative Monitoring And Anesthetic Technique

In the operating room, standard multiparameter monitors (Drager Vista 120) were attached. Baseline recordings included:

- Oxygen saturation (SpO_2)
- Systolic blood pressure (SBP)
- Diastolic blood pressure (DBP)
- Mean arterial blood pressure (MABP)
- Heart rate (HR)

Preloading was performed with 20 mL/kg of Ringer's lactate solution IV, administered 15–20 minutes before spinal anesthesia. Foley's catheterization was completed before the administration of subarachnoid block (SAB).

Under strict aseptic precautions, following hospital infection control protocols, the patient's back was cleaned and draped. With the patient in the sitting position, a local anesthetic (2% lignocaine) was administered at the selected L3-L4 intervertebral space. A 27G Quincke's needle was inserted, and after confirming cerebrospinal fluid (CSF) flow, the anesthetic drug was administered.

Intraoperative Management

i. After subarachnoid block, parturients were placed in a supine position with a 15°–20° left tilt.
ii. Oxygen (5 L/min) via a simple face mask was administered throughout surgery and discontinued postoperatively unless clinically indicated.
iii. IV fluid therapy was maintained with Ringer's lactate at 10 mL/kg/hr.
iv. An anesthesiologist, blinded to group allocation, assessed the spinal block and other physiological parameters. HR, SBP, DBP, and SpO_2 were recorded every 2 minutes for the first 20 minutes, followed by 5-minute intervals until 75 minutes.
v. Onset of sensory block was evaluated subjectively by the patient's perception of warmth, heaviness, or tingling, and objectively by Visual Analog Scale (VAS) ≤5 to pinprick at the calf region. Surgery commenced once the T6 dermatome level was achieved.
vi. Demographic data (age, weight, height), and duration of surgery were recorded.
vii. Hypotension (SBP ≤100/60 mmHg) was managed with IV crystalloids (200 mL) and IV ephedrine (5–10 mg).
viii. Bradycardia (HR <50 bpm) was treated with IV atropine (20 mcg/kg). Any other intraoperative adverse events were noted and managed accordingly.
ix. Sensory and motor block characteristics were documented, including onset time, time to reach T6 level, and regression to T10.
x. Motor blockade was assessed using the Modified Bromage Scale:

Bromage Score	Motor Function
1	Complete block (no movement in feet or knee)
2	Almost complete block (able to move feet only)
3	Partial block (able to move knee)
4	Detectable hip weakness (able to flex knee fully)
5	No detectable hip weakness (while supine)
6	Able to perform partial knee bend

Motor block onset was defined as the time taken to reach Bromage score of 6, and the total motor block duration was recorded until complete recovery (17).

xi. Newborn APGAR scores were assessed at 1, 5, and 10 minutes by a pediatrician (12).
xii. Spinal anesthesia-related intraoperative and postoperative complications such as hypotension, bradycardia, nausea, vomiting, pruritus, sedation, and respiratory depression were recorded.
xiii. Total postoperative analgesia duration was defined as the time from SAB to the first request for rescue analgesia.
xiv. Postoperative pain was assessed using VAS scores: (13)

VAS Score	Pain Intensity
0	No pain
1–3	Mild pain
4–6	Moderate pain
7–10	Severe pain

Rescue analgesia was provided in the form of IV paracetamol (1 g).

xv. Any postoperative complications including bradycardia, hypotension, postoperative nausea and vomiting (PONV), prolonged sedation, and other adverse effects were documented and managed accordingly. On postoperative day one, parturients were assessed for post-dural puncture headache (PDPH), backache, or neurological deficits.

Study Outcomes

The primary objective of this study was to evaluate block characteristics (onset and duration of sensory and motor blockade, highest sensory level attained), hemodynamic stability, and neonatal outcomes.

Statistical Analysis

Statistical analysis was done using Microsoft Excel and version 22 of SPSS. Continuous variables are noted as mean ± SD and categorical variables are presented as percentages and numbers. Normally distributed continuous variables were compared using ANOVA. If the F value was significant and variance was homogenous, for individual group differences Tukey multiple comparison test was used otherwise, Tamhane's T2 test was used. The chi-square test was applied for categorical variables analysis.

Flow Diagram Showing Premixed Vs Separate Syringes Assessment Of Pregnant Female Enrolled In The Study

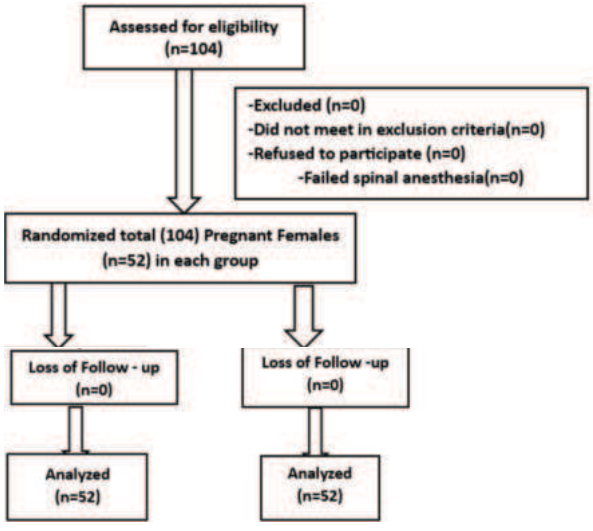

Fig.1. CONSORT-flow chart of Parturients 104 pregnant female underwent screening for eligibility,none of the parturient were excluded .Therefore for total of 104 parturient, randomization was done into study groups after we received consent from those patient (52 parturient in each group), and the study was completed

RESULTS

Table 1 compares the demographic parameters, including mean age, height, and weight between the group,this differences were statistically non-significant ($p > 0.05$), indicating homogeneity between the groups.

Table 1: Demographic Characteristics

	Group 1	Group 2	p value
	Mean ± SD	Mean ± SD	
Age	26.54 ± 3.41	26.92 ± 4.01	0.116
Height(cm)	158.12 ± 3.12	157.45 ± 3.561	0.085
Weight(kgs)	67.04 ± 13.08	64.88 ± 10.11	0.221

(n=52)number of patients in each group, Data are represented as mean ± S.D standard deviation, **statistically insignificant (P>0.05).

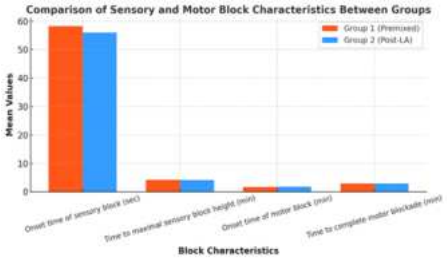

Figure 2 shows the comparison of Sensory and Motor Block Characteristics between groups

The bar diagram compares sensory and motor block characteristics between Group 1 and Group 2 . Group 1 demonstrates slightly shorter times for onset and completion of sensory and motor blocks compared to Group 2.

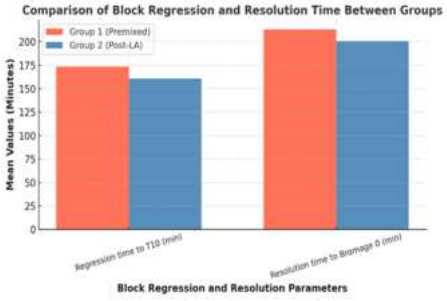

Figure 3 Shows The Comparison Of Block Regression And Resolution Time Between Groups

This bar diagram compares block regression and resolution times between Group 1 and Group 2. Group 1 shows a slightly shorter regression time to T10 and resolution time to Bromage 0 compared to Group 2, indicating minor variations in block duration between the groups.

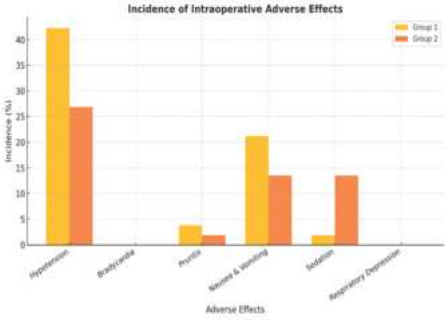

Figure 4 Shows The Incidence Of Intraoperative Adverse Effects

The bar graph compares the incidence of intraoperative adverse effects between Group 1 and Group 2. Hypotension is more common in both groups, with a higher incidence in Group 1, while other adverse effects like bradycardia, nausea, vomiting, sedation, and respiratory depression are relatively less frequent and vary slightly between groups.

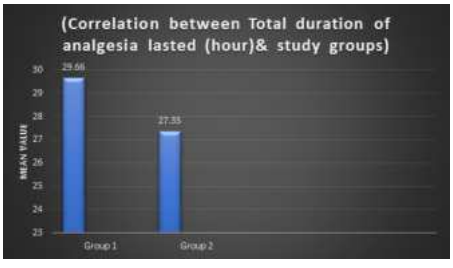

Figure 5 Shows The Comparison Of Total Duration Of Analgesia

The bar diagram shows total duration of analgesia is maximum in Group1 (29.66 hours) as compared to Group2. However, this difference was statistically nonsignificant, but the clinical duration of analgesia was higher in the premixed group.

Table 2: Comparison Of Rescue Analgesia

Rest to analgesia used	Group 1	Group 2	p-value
	Group 1	Group 2	
	Frequency (%)	Frequency (%)	
No	43 (82.7%)	41 (78.8%)	0.147
Yes	9 (17.3%)	11 (21.2%)	
Total	52 (100%)	52 (100%)	

Table 2 shows the requirement of rescue analgesia was slightly lower in Group 1 (17.3%) compared to Group 2 (21.2%). However, this difference was not statistically significant (p = 0.147), indicating that both methods provided comparable postoperative analgesic efficacy.

DISCUSSION

Spinal anesthesia is the preferred technique for LSCS.The addition of adjuvants to intrathecal LA aims to extend its duration of action while providing effective postoperative analgesia (14).

The onset time of motor block and Bromage 1 in our study correlates with the observations of Hussien R.M. et al., who found no statistically significant difference (p = 0.35) in motor block onset between rapid and normal sequential administration of intrathecal fentanyl with hyperbaric bupivacaine. They concluded that rapid sequential administration of fentanyl increased somatic analgesia without affecting the degree or level of motor block produced by LA (15).

The regression time to T10 in our study was not significantly different between the two groups, aligning with previous findings by Hussien R.M. et al. and Desai S. et al. (8)(15). Similarly, resolution time to Bromage 6 was comparable and statistically insignificant (p > 0.05), further correlating with the studies of Desai S. et al. and Hussien R.M. et al., who found no significant difference in motor block regression between premixed and sequential groups (8)(15).

Regarding postoperative analgesia, clinically, the premixed group experienced longer analgesia than the separate syringes group, but the difference was not statistically significant. However, Hussien R.M. et al. concluded that rapid sequential intrathecal fentanyl administration prolonged postoperative analgesia (15). Additionally, Ummenhofer W.C. et al. found that intrathecally administered morphine provides prolonged and effective analgesia due to its hydrophilic nature, slower systemic absorption, cephalad CSF spread, and delayed clearance from opioid receptors (16).

Hemodynamic parameters (SBP, DBP, MABP) remained statistically comparable between the two groups when compared to baseline values. Similar findings were reported by Hussien R.M. et al. (15).

Analysis of neonatal outcomes, based on APGAR scores at 1, 5, and 10 minutes, showed no statistically significant difference (p > 0.05) between the groups. These findings are consistent with the studies of Atalay C. et al. and Biswas B.N. et al.(18)(19).

CONCLUSION

The premixed and separate administration of intrathecal (IT) morphine with hyperbaric bupivacaine demonstrated comparable efficacy in terms of SAB quality, maternal hemodynamic stability, and neonatal outcomes. When IT morphine was administered either separately after hyperbaric bupivacaine or as a premixed solution, it provided an equally prolonged duration of postoperative analgesia, both at rest and during activity, lasting up to 24 hours. Clinically, the premixed group exhibited a prolonged postoperative analgesic effect, facilitating early ambulation, quicker return to routine activities, and a reduced risk of postoperative deep vein thrombosis (DVT) and related complications. Additionally, it led to lower postoperative rescue analgesic requirements, thereby minimizing potential adverse effects on both the mother and the neonate.

Strengths

Our study's strengths include its randomized controlled design, ensuring robust comparative analysis between premixed and separate administration of intrathecal morphine with hyperbaric bupivacaine. The study comprehensively evaluated subarachnoid block characteristics, maternal hemodynamic stability, postoperative

analgesia duration, and neonatal outcomes, providing clinically relevant insights. The inclusion of both elective and emergency LSCS cases enhances generalizability, while standardized drug preparation minimizes variability. Additionally, the study's detailed assessment of postoperative recovery, early ambulation, and reduced analgesic requirements underscores its clinical significance in improving maternal postoperative outcomes and neonatal safety.

Limitations

Our study had few limitations. We did not take into consideration the temperature of the drugs and the baricity of the drugs used.

Conflict Of Interest: None.
Funding: None.
Ethical Approval: Obtained.
Consent: Written Consent Secured.

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