Original Article

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Comparison of Premixed with Sequential Administration of Intrathecal Morphine and Hyperbaric Bupivacaine for Lower Segment Caesarean Section

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Abstract

Background: Adequate pain relief is considered as a basic human right .In obstetrics patients, using low dose opioids (Morphine, Fentanyl, sufentanil) in neuraxial blockade is effective method for anaesthesia and postoperative analgesia in LSCS and nearly no danger to parturient or unborn. **Subjects and Methods:** Keeping in mind the difference in the baricties of commonly used hyperbaric bupivacaine and morphine, we conducted a single blind randomized controlled trial on 156 full term parturient scheduled for elective and emergency LSCS under SAB and on the technique of intrathecal administration of drug parturients were divided into 3 groups. GROUP 1 (n=52) - Hyperbaric bupivacaine (0.5%) 9mg (1.8ml) + morphine 200mcg (0.2ml) as a mixture GROUP 2 (n=52)-Hyperbaric bupivacaine (0.5%) 9mg (1.8ml) + Morphine 200mcg (0.2ml) administered after bupivacaine GROUP 3 (n=52)-Hyperbaric bupivacaine (0.5%) 9mg (1.8ml) + Morphine 200mcg (0.2ml) administered before bupivacaine. We observed for block characteristics, maternal hemodynamics and neonatal outcome. **Results:** In our study, duration of analgesia was clinically prolonged in all the groups. The block characteristics were comparable between the groups.These beneficial effects were not accompanied by any major hemodynamic instability or adverse effects and no untoward effect on the newborn. **Conclusion:** Premixed and sequential administration of IT morphine with hyperbaric bupivacaine were comparable in terms of quality of subarachnoid block maternal hemodynamic and neonatal outcome.

Keywords: Lower segment cesarean section, Sequential intrathecal injection, Morphine, Hyperbaric bupivacaine, Spinal anesthesia.

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Introduction

Spinal anaesthesia has long been used for LSCS, but there has always been an area of interest to search for method to provide better quality of interaoprative anaesthesia and prolongation of postoperative analgesia.[1] Opioids (e.g.morphine) have synergistic effect with local anesthetic when given intrathecally[2,3] by reducing visceral pain, thereby improving the the block quality,[4] while also causing reduction of LA dosages and maintaining stable hemodynamic parameters.[1] It enhances postoperatively analgesia period.[5,6]

Routine practice of mixing opioid to local anaesthetic is although easy but may alter the baricity and hence effecting spread in CSF .We planned this study with the hypothesis that simply depositing Local anaesthetic and opioid using separate syringes may reduce these changes and influence spread.we compared the effect of premixed (Hyperbaric bupivacaine and Morphine) and sequential administration of additive (Morphine) before and after hyperbaric bupivacaine on block characterstics and maternal and fetal outcome.

Subjects and Methods

This single-blinded randomized controlled study was conducted in the Department of Anaesthesiology intensive Care and Pain Management Himalayan Institute medical science Swami Rama Nagar, Dehradun after approval from ethics committee over a period of 12 month. Patient selection was done after taking written informed consent from them.

156 healthy, full term, non laboring parturient, ASA I or ASA II with singleton, uncomplicated pregnancy planned for both elective and emergency LSCS under SAB were involved in the study. Parturients with complicated pregnancies like Multiple pregnancy, Pregnancy with bleeding disorders, spinal deformity, any other contraindication to spinal anesthesia block, Pregnancy with acute fetal distress, Intrauterine deaths or known fetal anomaly, Severe PIH (Pregnancy Induced Hypertension), systemic diseases like (renal, cardiac, or liver), those with an

allergy to the drug or patients who provided refusal against regional anesthesia administration were excluded.

Parturient posted for elective LSCS were kept fasted orally for 8-10hrs and emergency cases were taken up irrespective of fasting status. Intravenous access was established with a wide bore cannula (16G or 18G) either in the ward for elective cases or in the emergency department for the emergency cases. All the parturient were premeditated with injection Ranitidine 50mg and injection Metaclopramide 10mg given intravenously 30 minutes prior to surgery.

For our study the two drugs used, were kept same throughout then study period to avoid manufacturer's difference. Hyperbaric bupivacaine was used HEAVY ANAWIN (Neon laboratories) and morphine (MORPHITROY) was used.

In the operating room all essential multipara monitor (Drager vista 120) were attached. Baseline percentage of oxygen saturation of hemoglobin (SPO2), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MABP) and heart rate (HR) were noted. Pre-loading was done with 20ml/kg ringer's solution intravenously (I.V), 15-20 minutes before giving the spinal block. Foley's catheterization was done before administration of subarachnoid block (SAB). After thorough hand washing and wearing personal protective equipment's, patient's back was cleaned and draped under all aseptic precautions as per the hospital infection control protocol. With patient in sitting position, a local block with 2% lignocaine was given at the selected intervertebral space L3-L4. A 26G Quincke's needle was inserted and after confirmation of CSF flow, the anesthetic drug was administered.

The parturients were randamised into three groups and each group has 52 patients. The Group 1 (n =52) received intrathecal hyperbaric bupivacaine (0.5%) 9mg (1.8m1) + morphine 200 mcg (0.2ml) as a mixture ,GROUP 2 (n =52) received intrathecal hyperbaric bupivacaine (0.5%) 9mg (1.8m1) + Morphine 200mcg (0.2m1) administered after hyperbaric bupivacaine and GROUP 3 (n =52) received intrathecal hyperbaric bupivacaine (0.5%) 9mg (1.8m1) + Morphine 200mcg (0.2m1) administered before hyperbaric bupivacaine by using seperate syringe via G26 Quincke's needle.

After the spinal block was given, the parturient were laid supine position with 15°-20° left tilt. Oxygen (5L/min) by simple facemask was administered throughout the surgery and was discontinued post-operatively (unless otherwise indicated as per patient requirement). Fluid therapy was continued with ringer's solution 10ml/kg/hr. Anesthesiologist, who was not knowing the group allocation, assessed the spinal block and other physiological parameters. Heart rate, SBP, DBP, SpO_2 were monitored at every 2 minutes (min) for the first 20min and then every 5 min subsequently till 75 min. Onset of sensory block was noted which was evaluated by the patient providing information regarding feeling of warmth, limb heaviness, or sense of tingling and objectively established by reduced Visual Analogue Scale (VAS) scores of 5 and less to pinprick at level of calf. After the T6 level reached, the surgery began after intimation to surgeon for the initiation of procedure. Demographic data, such as age, weight (kg), height (cm), and the duration of the operation were recorded. After onset of hypotension (NIBP ≤ 100/60), anesthetist was allowed managing the patient by giving IV crystalloids (200ml) fluids and (IV) ephedrine (5–10 mg) . Bradycardia (HR <50 beats/minute) Injection Atropine 20 mcg/kg iv. was administered for the same & other intraoperative adverse events were noted and managed accordingly.

The duration of onset of sensory block, time to maximal sensory block height at (T6) the dermatomal level and regression time to T10 were recorded. Assessment of Motor blockade was done by the Bromage scale , in which 0- indicated that patient, is able to lift an extended leg, 1- not able to lift the extended leg , 2- not able to flex, the knee joint and 3- inability in flexing the ankle joint . Onset of motor block was defined as time to attain Bromage scale 3 from subarachnoid block administration. While total duration of motor blockade was defined as the onset of motor block to complete recovery was recorded.[7] Newborn's APGAR scores were recorded by a pediatrician at 1, 5, 10 minutes.[8] The spinal anesthesia-related intraoperative and postoperative complications, such as hypotension, bradycardia, nausea vomiting, pruritis, sedation and respiratory depression was noted and recorded. The total time of postoperative analgesia was recorded as the time interval between the SAB and the first intimation by the patient for rescue analgesia. By Visual analogue scale (VAS) score, assessed the degree of postoperative pain. VAS scores described the postoperative pain intensity as having no pain (0 to 4 mm), having mild pain (5 to 44 mm),having moderate pain (45 to 74 mm), and having severe pain (75 to100 mm) (9). Rescue analgesia was given in form of 1 gram of paracetamol (IV) was given for analgesia. Postoperatively any incidence of bradycardia, hypotension PONV, prolonged sedation reported by the allocated postoperative care unit staff was managed accordingly. On the first post-operative day, parturient were also evaluated for post dural puncture headache, backache and examined for any neurological deficit.

Aim of our study was to determine block chracterstics (sensory block onset time, motor blockade onset time, highest level of sensory blockade, motor blockde duration interval), hemodynamic status and neonatal outcome.

Sample Size

The previous correlated studies were taken into account to calculate the sample size. Power analysis recommended that sample size of 52 patients each group were required to attain a power of 80% and a level significance of 0.05 to be able to identify a difference between the groups.

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 percentage 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 comparision test was used otherwise, Tamhane's T2 test was used. Chi square test was applied for categorical variables analysis.

Flow diagram showing Sequential assessment of parturient enrolled in study

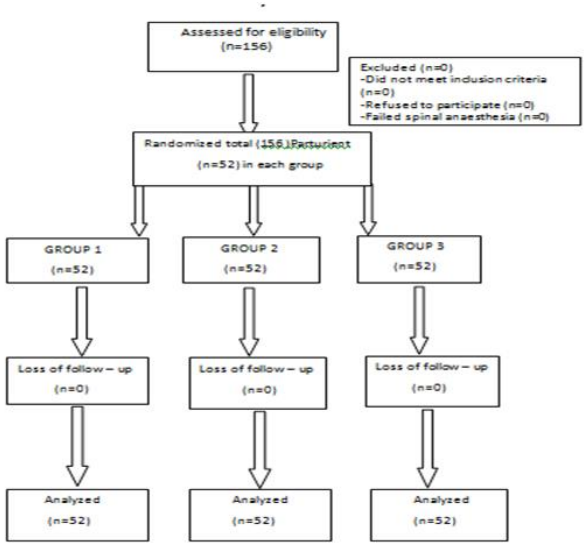


Figure 1: Consort

Flow chart of Parturients.156 parturient underwent screening for eligibility, none of the parturient were excluded .Therefore for total of 156 parturient, randomization was done into study groups after we received consent from those patient (each group have 52 parturient), and the study was completed.

Results

Table 1: Demographic Profiles

	Group 1	Group 2	Group 3	p value*
	Mean ± SD n=52	Mean ± SD n=52	Mean ± SD n=52	
Age	26.54 ± 3.41	26.92 ± 4.01	28.06 ± 4.11	0.116
Height(cm)	158.12 ± 3.12	157.45 ± 3.561	159 ± 3.94	0.085
Weight(kgs)	67.04 ± 13.08	64.88 ± 10.11	68.67 ± 9.91	0.221

ANOVA*

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

Demographic data such as age,height,weight ,ASA status and duration of surgery were comparable between the groups [Table-1].

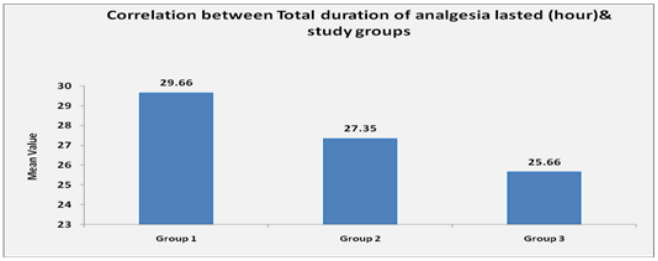
No statistical significant difference was observed in the onset of sensory block, time to maximal sensory block height and time to complete motor blockade between the groups (P > 0.05).Regression time to sensory block T10 was found statistically significant between the groups (P=0.002).

On intergroup comparisons the regression time to T10 among the groups was significantly higher in Group3 compared to Group2 (p = 0.002).Group1 was comparable to Group2 and Group3 and statistically insignificant.

Table 2: Comparison of Block Characteristics

Block characterstic	Group 1	Group 2	Group 3	p value
	Mean ± SD	Mean ± SD	Mean ± SD	
Onset time of sensory block(sec)	58.29 ± 27.95	56.02 ± 16.68	56.06 ± 18.11	0.827
Time to maximal sensory block height(min)	4.22 ± 1.49	4.13 ± 1.15	4.05 ± 1.20	0.808
Time to complete motor blockade(min)	2.94 ± 0.57	2.92 ± 0.6	2.8 ± 0.67	0.443
Regression time to T10(min)	173.44 ± 30.77	160.88 ± 39.1	185.58 ± 33.53	0.002

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



Graph 1: Comparison of Total Duration of Analgesia

The bar diagram show total duration of analgesia is maximum in Group1 (29.66hour) and minimum in Group3 was (25.66hour). However this difference was statistically nonsignificant.

Intraoperative hypotension, bradycardia, pruritis, sedation, respiratory depression, were statistically nonsignificant. Nausea and vomiting was more in Group2 as compared to Group1 and Gruop3. On comparing incidence among the groups statistically nonsignificant difference was observed between premixed and sequential group.

Postoperative hypotension was more in Group2 as compared to Group1. Between the groups statistically significant difference was obsereved (p=0.026). However on comparing among the groups, no statistical significant difference was observed.

Postoperative bradycardia, nausea and vomiting, pruritis, prolonged sedation were statistically nonsignificant between the groups (p>0.05).None of the parturient experienced PDPH and neurologyical deficit in any group.

In all the groups outcome of neonate was analyzed, which came out similar in all the groups, in terms of APGAR scores. Statistically nosignificant difference was obsereved between the groups.

Discussion

Spinal anaesthesia is a preferred technique for emergency or elective LSCS and enabling early detection of complications. For extending duration of action the IT LA dosage need to be increased. However, it can contribute to significant hemodynamic instability especially in pregnant patients .The mixing of adjuvants to LA interathecally aims to extend LA duration of action and provides post operative analgesia.[10]

In our reports that sensory blockade onset was comparable between difference groups. Keera A.A.et al. observed mean

level of maximal sensory block was nonsignificantly higher in sequential group.[11]

We observed mean values of maximum sensory block height was T6 in all the three groups. Cesur M et. al. suggested loss of pin prick sensation at T6 sufficient for continuation of surgery.[12]

The onset time of motor block and Bromage3 were correlated with Hussien RM.et al. who discussed that, there was no significant difference on the onset of motor block between rapid and normal sequential administration of intrathecal fentanyl with hyperbaric bupivacaine (p=0.35). When fentanyl was injected in a rapid sequential manner, resulted in increased somatic analgesia with no effect on degree or level of motor block, induced by LA.[13]

In our study regression time to sensory block T10 was found statistically significant between the groups (p=.002), but on comparison between premixed and sequential group no statistically significant difference was seen. Hussien RM et.al.and Desai S et al. also reported similar result.[4][13]

Resolution time to motor block (Bromage 0) was comparable to each other, and it was statistically insignificant (p>0.005). Our study correlated with Desai S. et al. and Hussien RM. et al. study who found no difference in regression time to bromage 0 between premixed and sequential groups.[4][13]

We observed that in our study, clinically maximum analgesia lasted in premixed group after the surgery followed by sequential groups but statistically it was nonsignificant. However Hussien RM et al. concluded that sequential injection of IT fentanyl when given rapidly, it prolongs postoperative analgesia.[13] Ummenhofer WC.et al. found that morphine injected intrathecally results in adequate and long lasting analgesia due to its hydrophilicity, decreased systemic absorption, cephalad spread in cerebrospinal fluid and slow rate of clearance from the opioid receptors.[14]

Hemodynamic parameters (SBP, DBP, MABP) showed no statistically significant difference in all the three groups when compared with base line. Similarly Keera AA.et al. and Hussien RM.et al. found no difference in blood pressure measurements when compared from baseline when heavy bupivacaine was given along with fentanyl in sequential and premixed groups.[11][13]

Intraoperative incidence of hypotension, bradycardia, pruritis, sedation, respiratory depression and additional analgesic requirement are comparable in each group.

The incidence of intra-operative nausea and vomiting was statistically significant among the group (p=0.021) , but on comparison between premixed and sequential group no statistically significant difference was seen. Hussien RM et.al.and Desai S et al. also reported similar result.[4][13]

Peritoneal traction and exteriorization of the uterus during a cesarean section and predominant vagal effect can lead to nausea and vomiting by triggering the vomiting center.[15]

Postoperative hypotension was statistically significant (p=0.026). However on comparing incidence among the groups, no statistical significant was observed (p>0.05). Kyokong O. et al. first described late hypotension, but mechanism of late hypotension is unidentified.[16]

According to keera AA.et al. who described late hypotension mechanism, some patients have moderately weak compensatory mechanism in the upper half of the body which is exhausted after more than 30 min.[11]

Statistical analysis of the APGAR score at 1min, 5min, 10 min was statistically insignificant (P>0.005) among the groups . Our study correlated with Atalay C. et al and Biswas BN. et al. who observed no significant differences in APGAR SCORE among the groups.[17][18]

Limitations

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

Conclusion

Premixed and sequential administration of IT morphine with hyperbaric bupivacaine were comparable in terms of quality of subarachnoid block maternal hemodynamic and neonatal outcome.

IT morphine when given sequentially and as a mixture with hyperbaric bupivacaine for spinal anaesthesia provides comparable analgesia to mother at rest and during activities up to 24hours. It also clinically prolong the duration of postop analgesia.So that parturient may have early ambulation and return to routine activity, which reduces chances of post op DVT. It also reduced post op analgesic requirements with no serious adverse effect on neonates.

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