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INTRATHECAL LOW-DOSE LEVOBUPIVACAINE AND BUPIVACAINE COMBINED WITH FENTANYL IN A RANDOMIZED CONTROLLED STUDY FOR CAESAREAN SECTION IN I.Q CITY MEDICAL COLLEGE AND MULTISPECIALTY HOSPITAL, DURGAPUR, WEST BENGAL, INDIA.

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ABSTRACT

BACKGROUND: Intrathecal combination of local anaesthetic with opioids produces a synergistic effect without intensifying motor and sympathetic blockades. It also enables successful Anaesthesia with use of a low dose of local anaesthetic, which also results in more stable hemodynamics.

AIMS AND OBJECTIVE: To compare the onset and duration of action, levels of sensory and motor blocks and side-effects of equal doses of hyperbaric bupivacaine and levobupivacaine with Intrathecal fentanyl addition in spinal technique in elective cesarean cases.

METHODS AND MATERIAL: Seventy-two patients undergoing caesarean section with spinal Anaesthesia received low-dose 0.5% levobupivacaine (7 mg) plus fentanyl 25 µg (group A) or low-dose 0.5% bupivacaine (7 mg) plus fentanyl 25 µg (group B). The time to achieve sensory blockade of T6, the maximum spread of sensory blockade, time to S2 regression, sensorial blockade levels and motor blockade at the beginning and end of surgery were the parameters assessed. Hemodynamic parameters systolic and diastolic blood pressures, heart rate were recorded, as side-effects.

CONCLUSION: Intrathecal isobaric levobupivacaine-fentanyl combination is a good alternative to hyperbaric bupivacaine-fentanyl combination in cesarean surgery as it is less effective in motor block, it maintains hemodynamic stability at higher sensorial block levels.

KEYWORDS : Levobupivacaine, Bupivacaine, Fentanyl, Local Anaesthetic, Caesarean Section.

INTRODUCTION:

Spinal administration of local anesthetics is a preferred technique for cesarean section (CS) as it produces analgesia, anesthesia, and motor block. However, this effect depends upon the volume, concentration, and doses of the drug used.[1,2] 0.5% hyperbaric bupivacaine is more commonly used for spinal anesthesia for CS.[3] Although hyperbaric local anesthetic solutions have a remarkable record of safety, their use is not totally without risks.[4,5,6] To prevent unilateral or saddle blocks, patients should move from the lateral or sitting position rapidly and after mobilization of the patients, extension or early return of the block may be seen. Hyperbaric solutions may cause sudden cardiac arrest after spinal anesthesia because of the extension of the sympathetic block.[7,8] The use of truly isobaric solutions may prove less sensitive to position issues. Hyperbaric solutions may cause hypotension or bradycardia after mobilization; isobaric solutions are favored with respect to their less sensitive to position change properties [9]. Recently, levobupivacaine, the pure L (−) enantiomer of bupivacaine, is preferred during spinal anesthesia due to its lower cardiovascular side-effects and central nervous system toxicity.[10,11,12,13] The plain levobupivacaine has also been shown to be truly isobaric with respect to cerebrospinal fluid (CSF) of pregnant women.[14,15] Its use in this setting may offer special advantages because this property may translate to a more predictable spread. The addition of low doses of opioids to local anesthetics during spinal anesthesia for CS decreases the incidence of local anesthetic related side-effects, reduces the time of onset of the anesthetic effect, and increases the quality of intra- and post-operative analgesia by reducing the administered dose of the local anesthetic [16].

Fentanyl can be combined with local anesthetics for spinal anesthesia and when used in this way it prolongs the duration of action and spread of sensory block as well.[17] Fentanyl has been combined with bupivacaine for lower limb surgery and also for inguinal herniorrhaphy and CS.[17,18,19,20]

AIMS AND OBJECTIVE:

1. To compare the onset and duration of action, levels of sensory and motor blocks and side-effects of equal doses of hyperbaric bupivacaine and levobupivacaine with Intrathecal fentanyl addition in spinal technique in elective cesarean cases.
2. To compare the efficacy of low-dose local anesthetics used together with opioid to decrease side-effects associated with these local anesthetics.

MATERIAL AND METHOD:

Study has been done on 72 women of age, 18–42 years of American Society of Anesthesiologists (ASA) physical status I–II who required elective CS at gestation >36 weeks for delivery of a singleton baby at term. The study period is from April 2019 to August 2019 in I.Q City Medical College and Multispecialty hospital, Durgapur, west Bengal. The **exclusion criteria** were patients who would not accept spinal Anaesthesia and those with abnormal coagulation profiles, known hypersensitivity to amide local anaesthetic and/or opioids, skin infections; cardiac disease, hypertension, diabetes mellitus. All patients were premedicated with intravenous (i.v.) 40 mg of pantoprazole slowly and 10 mg of metoclopramide 2 h before surgery. Thirty minutes before the induction of spinal Anaesthesia, we started the intravenous infusion of 10 ml.kg–1 of crystalloid solution (Ringer lactate solution) to provide volume preload. Patients were randomized into two groups via a sealed-envelope method. A wedge was placed under the right hip of the women during the spinal Anaesthesia procedure. In both groups, spinal anesthesia was performed by one anesthesiologist using the same technique with the patient in the lateral position using a midline approach at L3 –L4 or L4 –L5 with a 25-G Quincke needle. After free flow of CSF was observed, patients in the levobupivacaine group (group L) received 7 mg (1.2 ml) 0.5% levobupivacaine + 25 µg fentanyl (0.5 ml), and the bupivacaine group (group B) received 7 mg 0.5% bupivacaine (1.2 ml) + 25 µg fentanyl (0.5 ml) at an injection interval of ≈30 s. Patients were moved to the supine lateral tilt position immediately after administration of the spinal blockade. The anesthesiologist who performed spinal Anaesthesia was blinded to the study groups. The study solutions used in the present study were prepared by another anesthesiologist and used at room temperature (23°C). All patients underwent non-invasive monitoring of systolic blood pressure (SBP) and diastolic blood pressure (DBP), measurement of blood oxygen saturation (SpO2) using pulse oximetry, and electrocardiography for heart rate (HR) with a Monitor. An observer recorded these parameters before spinal Anaesthesia, every 1 min for 15 min after spinal Anaesthesia, every 3 min thereafter for 30 min, and every 5 min until the end of surgery. Supplementary oxygen (2ml/min) was given to all patients via nasal cannula. Blockade characteristics were assessed by testing for sensory and motor blockade. Sensory blockade was monitored with the pin-prick test at 1-min intervals for the first 5 min, then every 2 min for 20 min, until the end of surgery. Surgery was allowed if the upper dermatome to the level of the loss of discrimination to a pin-prick was at least T6. The time to achieve sensory blockade of T6, maximum spread of sensory blockade, and time to S2 regression (as well as sensorial blockade levels at the beginning and end of surgery) were recorded. Motor blockade was assessed based on a modified Bromage scale (0 = no paralysis, able to flex hips/knees/ankles; 1 = able to move knees, unable to raise extended legs; 2 = able to flex ankles, unable to flex knees; 3 = unable to move any part of the lower limbs) at 1-min intervals for the first 5 min, then every 2 min for 20 min, until the end of surgery. Bromage scores at the beginning and end of surgery were noted. Perioperative maternal hypotension (SBP <20% of baseline or 90 mmHg) or episodes of bradycardia (heart rate < 50 beats/min) were recorded and treated with boluses of fluid, or 5 mg ephedrine or 0.5 mg atropine given via the intravenous route. Any other side-effects (e.g. respiratory depression, nausea, vomiting and pruritus) were recorded.

STATISTICALANALYSIS:

Data were analyzed using SPPS 20.0 software. Results were expressed as mean ± standard deviation (SD). Continuous variables analyzed with student t-test, while the chi-square test was used to compare discrete variables. p<0.005 were considered significant, and exact values are given when < 0.001.

RESULT:

There were no significant differences with regard to mean values of age, weight and gestational age among women as well as the duration of surgery in the two groups (Table 1). Values of SBP, DBP and heart rates were comparable and almost stable during surgery in both groups (Table 2).

Table: 1 Patients' demographics and duration of surgery in Levo bupivacaine and Bupivacaine groups.

Variables	Group A	Group B
Age (years)	29.05 ± 6.3	28.62 ± 5.66
Weight (kilograms)	76.45 ± 10	78.65 ± 13.52
Gestational age (months)	37.3 ± 1.06	37.66 ± 0.82
Duration of surgery (minutes)	45.55 ± 11.12	48.60 ± 8.90

Data are expressed as Mean ± Standard Deviation (SD), Group A: Group Levobupivacaine, Group B: Group Bupivacaine.

Table-2: Sensorial block characteristics' of Levobupivacaine and Bupivacaine groups.

Variables	Group A	Group B
Time to achieve sensory block of T6 (minutes)	8.32 ± 1.23	7.7 ± 1.05
Max spread of sensory block *	T5 (T4-T6)	T4 (T4-T6)
Time to S2 regression (minutes)	69.04 ± 4.60	66.68 ± 5.47

Data are expressed as Mean ± Standard Deviation (SD), *: median (range), Group A: Group Levobupivacaine, Group B: Group Bupivacaine.

Table-3: Sensorial block level and motor block degree of Levobupivacaine and bupivacaine groups.

Variables	Group A	Group B
Sensorial block level at the beginning of the surgery (T4/ T4-T6/T6)	13(38.7)/1(2.7)/21 (58.2)	20 (55.4)/ 3(8.2)/13 (36.0)
Sensorial block level at the end of the surgery (T4/ T4-T6/T6)	5 (12.8)/ 7 (21.2)/22 (62.8)	10 (26.8)/ 6(15.7)/17 (46.2)
Bromage scores at the beginning of the surgery	0-0/33 (90.7) / 3 (8.2)	0-0/ 25 71.2 / 10 26.7*
Bromage scores at the beginning of the surgery	0-17 (46.2) / 18 (51.7) /0	0-9(24)/21 (57.3)/6 (16.6)*

Data are expressed as number of patients (n) - %, *: p<0.05 compared with group A, Group A: Group Levobupivacaine, Group B: Group Bupivacaine.

CONCLUSION:

In spinal Anaesthesia for caesarean section, using low-dose levobupivacaine in combination with fentanyl elicits effective sensorial blockade and less motor blockade with similar hemodynamic and neonatal effects than usage of low-dose bupivacaine in combination with fentanyl.

DISCUSSION:

In this present study, low-dose levobupivacaine and low-dose bupivacaine combined with fentanyl produced a similar quality of sensorial blockade as well as maternal hemodynamic and neonatal effects in CS under spinal Anaesthesia. Combination of fentanyl with low-dose levobupivacaine induced less motor blockade than low-dose bupivacaine when administered via the Intrathecal route. The efficacy of neuraxial local anaesthetic is enhanced by the addition of Intrathecal opioids. Such combinations are usually associated with improved Anaesthesia and analgesia. It also allows the use of very low doses of local anaesthetic, which contributes to more stable hemodynamics [13-15]. In the study by Parpaglioni et al [16], the addition of fentanyl via the Intrathecal route reduced the minimum local anaesthetic dose (MLAD) of spinal levobupivacaine and ropivacaine. It did not affect their potency ratio significantly, and resulted in enhanced spinal Anaesthesia. Intrathecal fentanyl added to low-dose local anaesthetic produces a synergistic effect without increasing sympathetic blockade or delaying discharge from hospital [17]. Lee et al study [18] was published as the first study on the Intrathecal use of 0.5% levobupivacaine with fentanyl. Significant differences were not observed between the two groups with respect to hemodynamic changes and the quality of sensory and motor blockades. In a recent study by Cuvas et al [19], addition of fentanyl 15 µg (0.3 ml) to 0.5% levobupivacaine (2.2 ml) produced a shorter duration of motor blockade than pure 0.5% levobupivacaine (2.5 ml solution) in spinal Anaesthesia, whereas both regimens were effective for transurethral resections. Akcaboy et al [20] and Erbay et al [21] compared the effectiveness of low doses of 0.5% levobupivacaine and 0.5% bupivacaine (5 mg and 7.5 mg, respectively) when combined with fentanyl (25 µg). These regimens were shown to be effective in spinal Anaesthesia for transurethral resection of the prostate (TURP) if used in higher doses. In both studies, levobupivacaine plus fentanyl resulted in effective sensorial blockade with less motor blockade than bupivacaine plus fentanyl. Studies have demonstrated the effect of a combination of local anaesthetic and opioid for regional Anaesthesia in CS [22-25]. Different results with regard to the characteristics of sensorial blockade between levobupivacaine and bupivacaine have been observed. However, most of these studies have concluded that there was less motor blockade with levobupivacaine than with bupivacaine. They compared fixed doses of Intrathecal hypertonic 0.5% levobupivacaine (10 mg) and 0.5% bupivacaine (10 mg) combined with Intrathecal fentanyl (10 and 20 µg), or sufentanil (5 µg) in terms of the characteristics of sensory and motor blockade in parturient undergoing elective CS with spinal Anaesthesia. In that study, levobupivacaine produced a significantly shorter and less pronounced motor blockade than racemic bupivacaine regardless of the type and dose of opioid added. In the present study, we preferred to use 7 mg of 0.5% levobupivacaine and 0.5% bupivacaine as a low dose in combination with 25 µg fentanyl for spinal Anaesthesia for patients undergoing CS. Levobupivacaine produced adequate and comparable sensorial blockade with bupivacaine but induced less motor blockade than bupivacaine, a result consistent with previous studies. In the present study, decreases in SBP and DBP as well as changes in heart rate were in acceptable ranges. Erdil et al [26] noted, in spinal Anaesthesia, better hemodynamic stability associated with low-dose levobupivacaine plus fentanyl compared with that seen with low-dose bupivacaine plus fentanyl.

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