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Original Article

Intrathecal Butorphanol: An Effective Option for Post Operative Pain Relief in Caesarean Patients

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Abstract
Introduction: *A pain free post-operative period is a boon to mother for caring the neonate .Spinal anesthesia is most preferred technique for caesarean section. Spinal opiates as adjuvants potentiate effect of local anesthetics and give prolonged postoperative analgesia.*
We evaluated the effect of addition of 25 mcg of injection butorphanol to hyperbaric injection bupivacaine 0.5% on hemodynamic changes neonatal outcome and post-operative analgesia in patients undergoing elective lower segment caesarean section (LSCS).
Methodology: *After obtaining ethical committee clearance and patient consent a double blinded prospective RCT was conducted between July2016- Feb2017. 60 ASA grade-I and II patients were divided into two equal groups. Group A(n=30) patients received injection hyperbaric bupivacaine 0.5%1.8 ml + injection butorphanol 25 mcg in 0.5 ml normal saline (NS) and Group B (n=30) received injection hyperbaric bupivacaine 0.5%1.8 ml + 0.5ml NS making total volume 2.3 ml by intrathecal route .*
The principle outcome measures were onset, duration of sensory and motor block, hemodynamics, apgar scores and duration of postoperative analgesia. Study groups were analysed using chi-square test. P-Value by SPSS software.
Results: *Duration of analgesia was significantly better in group A (264.16 min vs 141.36min) Hemodynamics and Apgar scores showed no statistical significance in both groups.*
Conclusion: *Intrathecal butorphanol gives longer duration of post-operative analgesia without compromising neonatal scores and maternal hemodynamics.*
Keywords: *Bupivacaine, Butorphanol, Caesarean, Spinal.*

Introduction

A pain free postoperative period is the most desired requirement for any women post delivery. Spinal anesthesia is the most desired and popular form of regional anesthesia for both elective and emergency caesarean section[1]. But one limitation with spinal anesthesia is its relatively short duration of postoperative analgesia. To counter this many adjuvants to local anesthetics have been tried. Intrathecally administered local anesthetics

and opioids have been shown to have a synergistic analgesic effect[2,3]. Opioids with μ-receptor agonists like fentanyl, buprenorphine, etc. have been tried extensively for this purpose. However, side effects due to μ-receptor stimulation like respiratory depression, pruritus, urinary retention and abuse liability remain a concern. Intrathecal opioids enhance the sensory block induced by local anesthetics without causing systemic side effects[4]. This makes it necessary for the search of an opioid which can prolong the duration of analgesia but without μ-receptor related side effects like nausea and pruritis Butorphanol has been shown to antagonize pruritus and nausea produced by morphine (μ-agonist) while prolonging the duration of analgesia [5] .Two recent randomized controlled trials have also found intrathecal butorphanol to significantly prolong the duration of postoperative analgesia[6,7] . With this background, we have decided to compare the effects of intrathecal bupivacaine alone and in combination with butorphanol. Butorphanol acts as partial agonist and antagonist at μ opioid receptor. It also exhibits competitive antagonist and partial agonist activity at k opioid receptor.

Materials and Methods

The study was conducted after taking ethical committee approval and written informed patient consent in a medical college hospital during July 2016 to Feb 2017. A double-blinded randomized, prospective control study was carried out on 60 American Society of Anaesthesiologist (ASA) grade-I and II patients, aged 18-40 years posted for elective LSCS under subarachnoid block. Patients requiring emergency LSCS, prematurity, preeclampsia, multiple gestation, contraindication to spinal anaesthesia, allergic to drugs were excluded from study. Patients were divided into two equal groups by computer table. Group A (n=30) patients received injection hyperbaric bupivacaine 0.5%1.8 ml + injection butorphanol 25 mcg in 0.5 ml normal saline (NS) 1 mg/ml preservative-free injection butorphanol diluted up to 20 ml by normal saline) making total volume 2.3 ml. GroupB (n=30) received injection hyperbaric bupivacaine 0.5%1.8 ml + 0.5ml NS making total volume 2.3 ml by intrathecal route.

A detailed pre-anesthetic checkup was done for all patients undergoing LSCS surgery. All patients were kept fasting overnight prior to the day of operation. Pre-operatively all vital parameters were monitored (pulse rate, blood pressure (BP), oxygen saturation (spO2), electrocardiogram (ECG)). Sedatives and hypnotics inclusive of opioids were avoided in pre-medication as well as intra-operatively. Large bore I.V. access secured. All patients were pre-medicated with Inj Ranitidine and Inj. Metaclopramide slow intravenously 20 min prior to the procedure. All patients were preloaded with ringer lactate solution 10 ml per kg body weight over 20 min. Vital parameters were noted before and after pre-loading. NIBP (noninvasive blood pressure), pulse rate, spO2, respiratory rate .

Subarachnoid block was performed with 25G Quincke needle at L3-L4 inter space, and anesthetic solution injected at a rate of 1 mL per.10 sec. After block procedure patients were placed in the supine position and a wedge was used to displace the uterus to the left. Oxygen supplementation was provided with the aid of a nasal prongs or face mask. Hydration was maintained with Ringer's lactate (10 mL/kg/hr).

The following parameters were studied:

- Onset of sensory block – time elapsed between the end of anesthetic solution injection into the subarachnoid space (assessed every minute) and loss of pain sensitivity to pinprick at T10;
- maximum level of sensory block – evaluated 20 minutes after anesthetic solution injection;
- maximum degree of motor block – evaluated 20 minutes after anesthetic solution injection, according to the modified Brom age scale
  - 0 = free movement of lower limbs
  - 1 = ability to bend knees and move feet
  - 2 = ability to flex feet only

- ❖ 3 = complete immobility of lower limbs.
- ➢ Duration of motor block – time elapsed between the end of solution injection into the subarachnoid space and free movement of lower limbs.
- ➢ Duration of analgesia – time elapsed between the end of solution injection into the subarachnoid space and spontaneous complaint of pain (NVAS ≥ 3) reported by the patient in the post anesthesia recovery.;
- ➢ Intraoperative discomfort – pain complaint (NVS ≥ 3) requiring supplementation via epidural catheter
- ➢ Maternal respiratory and cardiovascular parameters: Systolic blood pressure (SBP– mm Hg), heart rate (HR; bpm), respiratory rate (rpm), and oxygen saturation (SpO2;%) were evaluated at the following times: before blockade (M0), immediately after blockade (M1),every five minutes during procedure (M2), at the end of procedure (M3)
- ➢ Level of consciousness in perioperative period according to the scale (Braz et al.)
- ❖ 1 = awake [anxious, agitated],
- ❖ 2 = awake[calm],
- ❖ 3 = drowsy
- ❖ 4 = sleeping [awaken to verbal stimuli]
- ➢ Intraoperative maternal side effects- nausea, vomiting, pruritus, respiratory depression (SpO2 ≤ 90% and respiratory rate less than 10 bpm);
- ➢ Neonatal repercussions: Apgar score in the first and fifth minutes.

Statistical Analysis

Continuous data results were summarized as Mean and standard deviation while categorical data were expressed as percentage (%). The outcome measures (pulse rate, systolic BP, diastolic BP, SpO2, sedation score and VAS score) of both the groups over the periods (time) were compared by analysis of variance (ANOVA). The categorical variables were compared by chi-square ($\chi 2$) test. A result value of $p<0.05$ was considered statistically significant. All analyses were performed on SPSS version 21 by statistician from department of community medicine.

Results

There were no significant differences in patient's age, weight, height, and ASA status. Thus both groups were comparable with respect to their demographic profile (Table-1).

The onset time (in seconds) of sensory and motor block were delayed in butorphanol group when compared to plain bupivacaine group (22.467±2.2397 vs 26.857±3.4098 and 50.33 ±2.783 vs 46.23 ±3.971 respectively).The time to 2-segment regression was also seen to be prolonged in the study group (133.70 ±4.527 min vs 125.00 ±2.652 min).Time to rescue analgesia was more in the study group (264.162 ±13.9010 vs 141.367 ±3.5475 min respectively). (Table-2) and Figure-1. The Pain scores assessed as Visual Analog Score (VAS) were found to be more in plain bupivacaine group (2.6 vs 1.4) when compared to butorphanol group.(Figure-2) Which were shown to be statistically significant.

Apgar score in neonates of both groups at 1, 5, and 10 min was compared showing no clinical or statistically significant difference (Table-2).

Hemodynamic effects were found to be more in the injection butorphanol group as compared with the control group, particularly in the early stages of observation, as estimated by

a fall in systolic and diastolic blood pressures (Table-3). None of the patients in either group had any significant respiratory depression (fall in spO2<95% and increase in respiratory rate>20/min) needing intervention, at any time interval. Four patients had hypotension in the injection butorphanol group as compared with two patients in the control group. Two patients had bradycardia in the injection butorphanol group as compared with two patients in the control group. None of the patients in any group showed signs of other side effects such as nausea, vomiting, and shivering, or respiratory depression.

Table-1: Demographic Data

	GROUP A(n=30)	GROUP B(n=30)	P-Value
Age(Yrs)	25.43±1.851	26.67±3.457	0.092
Weight(Kgs)	59.300±5.2899	59.000±5.1729	0.825
Height(Cms)	154.50±2.764	153.20±3.969	0.147
Duration of surgery(mins)	52.73±5.930	49.63±6.322	0.055

Table-2: Block Characteristics

	GROUP A(n=30)	GROUP B(n=30)	p-value
Onset of sensory block(sec)	26.857±3.4098	22.467±2.2397	<0.01
Onset of motor block(sec)	50.33±2.783	46.23±3.971	<0.01
Time of peak sensory block(min)	4.263±0.4335	4.313±0.2360	0.582
Time of peak motor block(min)	4.393±0.1893	4.907±0.3676	<0.01
Time to 2 segment regression(min)	133.70±4.527	125.00±2.652	<0.01
Sensory regression to S1(min)	180.7±33.682	163.7±31.357	<0.01
Time to rescue analgesia(min)	264.162±13.9010	141.367±3.5475	<0.01
Apgar scores	8.60±0.498	9.00±0.000	0.07

Table-3: Hemodynamic Changes

	GROUP A(n=30)	GROUP B(n=30)
Systolic Blood Pressure(mm/Hg)	114.67±6.557	116.10±4.046
Diastolic Blood Pressure(mm/Hg)	61.30±4.942	69.60±4.875
Heart rate(bpm)	78.50±4.732	75.47±4.416

Figure-1: Duration of Analgesia

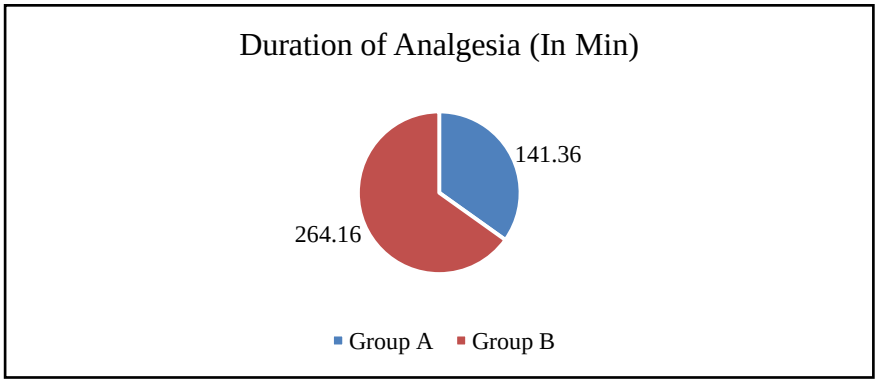
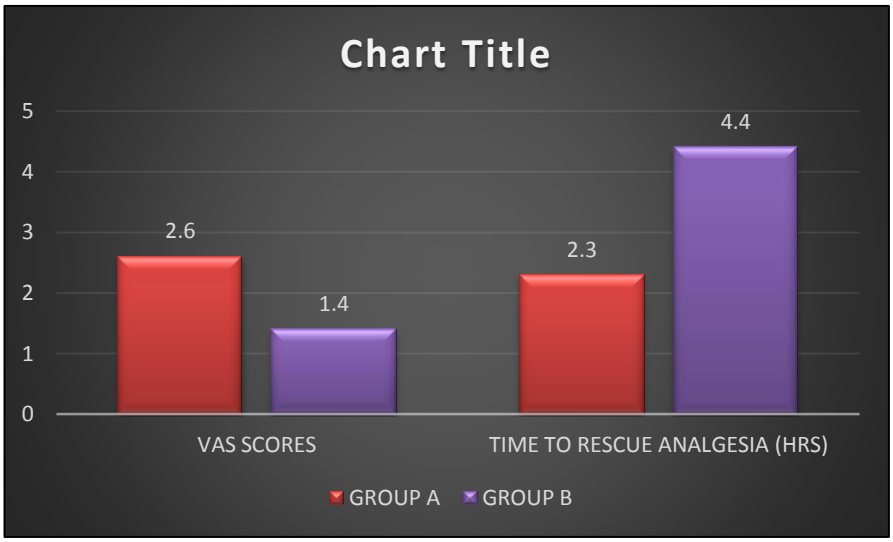


Figure-2: Comparision of VAS Scores and rescue analgesia duration in both groups



Discussion

Spinal anesthesia is the most preferred technique for both elective and emergency lower segment caesarean section. Neuraxial blockade with local anesthetic agents reduces the pain and surgical stress response by preventing the central sensitization to pain. This technique has the advantage of avoiding the depressant effect of general anesthetic drugs on the fetus and also limits the difficult intubation but with side effects of limited duration of action, systemic toxicity and hemodynamic instability which threatens the effective and safe use of spinal anesthesia. Different anesthetic techniques are employed to lower the incidence of the hemodynamic complications by using either the low dose of local anesthetic agents or addition of adjuvants to local anesthetic. Although low dose bupivacaine reduces the cardiovascular effects but it is not enough to provide an adequate level of sensory blockade. If an analgesic drug like opioid or α 2 agonist is added to hyperbaric bupivacaine, it would reduce the required dose of bupivacaine and will also ensure the adequate surgical analgesia, as they exert their action independently via different mechanisms. The intrathecal adjuvants are synergistic with local anesthetic agents to intensify the sensory block without increasing the level of sympathetic block.

As previously described, the use of low dose bupivacaine (7.5 to 10 mg) has been proved insufficient to promote adequate perioperative analgesia, with pain incidence about 71%, a problem that can be minimized by adding adjuvants to local anesthetics[8].Combination of clonidine and opioids (morphine, fentanyl, sufentanil) with local anesthetics has been a very common practice because it improves the quality of intraoperative analgesia and prolongs postoperative analgesia in addition to allowing the use of smaller doses of local anesthetics, with reduced risk of maternal hypotension and harm to the fetus [9,10]. Morphine contributes little to the quality of surgical analgesia due to its pharmacodynamic characteristics, such as slow onset of action and prolonged duration. The isolated use of hyperbaric bupivacaine in the subarachnoid space requires higher doses (12-15 mg) to prevent visceral pain, nausea, and vomiting resulting from peritoneal traction occurring in this type of procedure[11]. However, the major factor triggering the incidence of hypotension associated with spinal anesthesia (50% to 85%) in cesarean section is the local anesthetic dosage, along with other factors such as oxytocin infusion and those involved in cephalad spread of local anesthetics in cerebrospinal fluid[12].

The combination of local anaesthetic and adjuvants effectively inhibit multiple areas of neuronal excitability to provide a dose sparing effects of local anaesthetics. Bupivacaine acts mainly by blockade of voltage-gated Na+ channels in the axonal membranes and presynaptic inhibition of calcium channels. Butorphanol exert its action by opening the K+ channels and reducing the Ca ++ influx, resulting in inhibition of transmitter release to enhance the analgesia and sedation without detrimental hemodynamic effects. Intrathecal butorphanol potentiates bupivacaine-induced sensory block and reduces the analgesic requirement in the early post-operative period without prolonging motor block recovery time[13].Few studies[14]observed that laparoscopic surgery patients when randomized to either low-dose hypobaric lidocaine (25 mg) with 25 mg intrathecal fentanyl (lipophilic opioid similar to butorphanol) or plain hyperbaric lidocaine (75 mg) had less need for intravenous propofol supplementation for intrathecal fentanyl, concluding that the same prolongs sensory two-segment regression time which support the findings in our study. Gunion *et al* reported that opiate analgesics provide effective pain relief and are widely used for control of mild-to-severe pain[14].

Our finding that the duration of analgesia in the butorphanolgroup was significantly prolonged compared with the control group has the potential to limit the requirement of postoperative

analgesics. Similarly one study found intrathecal pentazocine produced sufficient analgesia and motor block without any significant hemodynamic instability in 60 patients undergoing various surgical procedures below the umbilicus[15].

Thus our study supports the finding that Neuraxial administration of opioids in conjunction with local anesthetics improves the quality of intra-operative analgesia and prolongs the duration of post-operative analgesia without causing significant side effects.

Conclusion

We conclude from our study that intrathecal butorphanol potentiates bupivacaine-induced sensory spinal block and reduces the analgesic requirement in the early post-operative period without prolonging motor block recovery time and without any maternal and neonatal repercussions.

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