Original Research Paper

Volume-10 | Issue-2 | February - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Anaesthesiology

COMPARISON OF TWO DIFFERENT DOSES OF INTRATHECAL BUPRENORPHINE USING POSTOPERATIVE ANALGESIA FOR CESAREAN SECTION

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ABSTRACT

Background: Postoperative analgesia after caesarean section poses unique clinical challenges to anesthesiologist. Intrathecal buprenorphine is a promising drug for postoperative analgesia. The aim of this study was to compare the efficacy of two doses of buprenorphine (60 µg and 90 µg) as an adjuvant to hyperbaric bupivacaine for postoperative analgesia in caesarean section.

Materials and Methods: Prospective randomized double blind controlled study involving sixty parturients posted for elective caesarean section under subarachnoid block. Group B60 (n = 30) received 9mg of 0.5% hyperbaric bupivacaine with 60 µg buprenorphine, Group B90 (n=30) received 9mg of 0.5% hyperbaric bupivacaine with 90 µg buprenorphine. Following parameters were observed: onset and duration of sensory block, postoperative pain scores based on Verbal Numerical Rating Scale, rescue analgesic requirement, and maternal and neonatal side effects if any.

Results: Duration of postoperative analgesia was significantly prolonged in Groups B90 in comparison to Group B60. Rescue analgesic requirement and VNP score were significantly lower in the B90 group. No major side effects were observed.

Conclusion: Addition of buprenorphine to intrathecal bupivacaine prolonged the duration and quality of postoperative analgesia after caesarean section. Increasing the dose of buprenorphine from 60 µg to 90 µg provided longer duration of analgesia without major adverse effects.

KEYWORDS : buprenorphine, bupivacaine, subarachnoid block, caesarean section.

INTRODUCTION

Post-caesarean delivery pain relief is important. Good pain relief will improve mobility and can reduce the risk of thromboembolic disease, which is increased during pregnancy. Pain may also impair the mother's ability to optimally care for her infant in the immediate postpartum period and may adversely affect early interactions between mother and infant. Pain and anxiety may also reduce the ability of a mother to breast-feed effectively. It is necessary that pain relief be safe and effective, that it not interfere with the mother's ability to move around and care for her infant, and that it result in no adverse neonatal effects in breast-feeding women. The most commonly used modalities are systemic administration of opioids, either by intramuscular injection or IV by patient-controlled analgesia, and neuraxial injection of opioid as part of a regional anaesthetic for caesarean delivery.[1][2] Opioids, when compared to local anaesthetics, offers the advantage of providing good analgesia while allowing early ambulation of the patient by sparing sympathetic and motor nerves.[3]

Pain relief is of utmost importance in postoperative period and it is a matter of concern in parturient. Favorable results have been observed with buprenorphine as an analgesic.Buprenorphine is an agonist-antagonist opioid derived from the opium alkaloid thebaine. Its analgesic potency is great, with 0.3 mg IM being equivalent to 10 mg of morphine. It is estimated that the affinity of buprenorphine for mu receptors is 50 times greater than that of morphine, and subsequent slow dissociation from these receptors accounts for its prolonged duration of action.The high lipid solubility; high affinity for opioid receptors and prolonged duration of action makes Buprenorphine a suitable choice for intrathecal and peripheral nerve site administration.[4][5] Buprenorphine is effective in relieving moderate to severe pain such as that present in the postoperative period and that associated with cancer, renal colic, and myocardial infarction. Buprenorphine is high lipid solubility (five times that of morphine) and affinity for opioid receptors limits cephalad spread and the likelihood of delayed depression of ventilation. It is about 25 times more potent than morphine and has a low level of physical dependence.[6]

MATERIALS AND METHODS

The study protocol was approved by the Institutional Ethical Committee and informed written consent was obtained from parturient with or without the help of an interpreter and was certified by either the patient's signature or thumbprint. This is Prospective, randomized, double blind controlled study was done to compare the efficacy two different doses of intrathecal buprenorphine used as adjuvants to bupivacaine for postoperative analgesia for caesarean section.Sixty ASA physical status I and II parturients were posted for elective caesarean section between the age of 20 to30 years, with height of 150 to 180 cm and body weight 45 to 75 kg were selected for this study. Exclusion criteria were coexisting systemic illness, emergency surgery, history of allergy to LAs or opioids, patient refusal, fetal distress, or any contraindication to subarachnoid block. Those with failed or partial block were excluded from the study. A thorough preoperative assessment was done on the day before surgery to exclude any systemic illness and to select patients according to the criteria. Body weight, height, and vitals were recorded. Procedure was explained to the patient and verbal numerical pain scorewas discussed.

Patients Under spinal anaesthesia were randomly assigned to two groups (Sixty) at term (ASA-II) scheduled for elective caesarean section and divided into two groups of thirty (30)each. The patients belonging to B60 group(2.1ml) received 9mg (1.8ml) bupivacaine (0.5%) with 60µg(0.2ml) Buprenorphine added with 0.1ml distilled water and B90 group(2.1ml) received 9mg (1.8ml) bupivacaine (0.5%) with 90µg (0.3ml) buprenorphine.All patients were kept nil by mouth for eight hours prior to surgery. The blood pressure, pulse rate ,respiratory rate and weight were noted before procedure. Intravenous line was secured with 18G cannula. Aspiration prophylaxis was done with oral ranitidine 150 mg on the night before surgery and in the morning along with metoclopramide 10 mg to both the groups. After preloading with 500ml of Ringer lactate infusion, patients were placed in sitting position and subarachnoid block was performed in the L3-L4 space using midline approach with 27G quincke spinal needle. As soon as free flow of C.S.F. was obtained, the solution was injected.Solutions were prepared by an anaesthesiologist, who was totally unaware of the nature of the study. Injections were made over 10 to 15 seconds. After withdrawing the needle, patient was turned supine with approximately 10 degree tilt head low with shoulder on pillow and left uterine displacement was done. Patients were supplemented with oxygen (5 L/min) via a facemask until delivery of baby.

After subarachnoid injection, blood pressure and pulserate were monitored immediately and subsequently at 2 minutes interval for first 10minutes and then every 10minutes for rest of the surgical procedure. Onset of cephalad spread of analgesia was determined as loss of sensation to pinprick. Intra operative hypotension was considered to be present whenever systolic blood pressure decreased to less than 90mm of Hg or <20% of the baseline whichever appeared first and treated with ephedrine. Bradycardia was to be treated with atropine I V 0.02 mg.kg-1if heart rate decreased to <60/min, any fall in respiratory rate less than ten per minute was noted. The attending pediatrician assessed the neonatal Apgar scores at 1 and 5 min of delivery of the baby.

Vital parameters such as pulse rate, mean arterial pressure, respiratory rate and SpO2 were monitored half hourly for first four hours and then hourly in postoperative period.Sensory block was tested by pinprick till level reached T4. The total duration of analgesia was calculated from onset of sensory block to end of analgesia i.e.; pain score of 5 or more on the Verbal Numerical Rating Scale (Table 1).[7]

Verbal numerical rating scale (Table 1)

Pain score	Degree of pain	Degree of analgesia
0	No pain	Profound Analgesia
2-4	Mild pain	Moderate Analgesia
5-7	Moderate pain	Mild Analgesia
8-10	Worst pain	No Analgesia

Rescue analgesia was with paracetamol 15 mg/kg given intravenously (IV). The number of rescue analgesic doses needed was noted. Patients with inadequate pain relief even after were given tramadol 1 mg/kg IM as additional analgesic. Patients were evaluated for efficacy of postoperative analgesia by analyzing the maximum pain score attained using verbal numerical pain score during the 24 h period. An effective analgesia time was the time taken between the injection of intrathecal drug and onset of worst pain. The number of rescue analgsic doses needed was noted. As bladder was catheterized, urinary retention was not looked into. Patients who had nausea or vomiting were treated with ondansetron 4 mg intravenous. Pruritus was treated with pheniramine maleate.

MEASUREMENTS

24-hour verbal numerical pain score, number of patients who requested rescue analgesics, frequency of requests for rescue analgesics per patient, and time interval before the first request for rescue analgesics were recorded. Frequency of pruritus and postoperative nausea and vomiting, sedation was also recorded.

STASTISTICALANALAYSIS

Statistical analysis was done with the help of computer using Epidemiological Information Package developed by Centre for Disease Control, Atlanta. Using this software range, frequencies, percentages, means, standard deviations, chi square and p' values were calculated. Kruskul Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's chi square test for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

OBSERVATION AND RESULTS

The two groups were compared in characteristics like demographic data and duration of surgery, duration of post operative analgesia, complications. Both groups were comparable with respect to age, weight, height, and duration of surgery as *P* was > 0.05 [Table 2]. The peak sensory level was comparable among the both groups [Table 3] B90 group significantly increase number of patients the peak sensory level greater than B60 groups. Onset of analgesia was comparable between Group B60 and Group B90 [Table 4]. There was no significant difference in the onset of analgesia in Group B90 when compared to Group B60.

Duration of postoperative analgesia was significantly longer in Group B90 (18 ±6 hours) when compared to Group B60 (12 ±4.5hours) [Table 4], [Figure 1].Rescue analgesic requirement was very less in Group B90 when compared to group B60. There was statistically significant difference in analgesic requirement between in this both groups. Five patients in Group B60 and Twelve patients in Group B90 did not require any analgesic during the study period. Maximum pain scores were significantly lower in Group B90 compared to Group B60 [Table]. Ninety three percent of patients in Group B90 compared to group B60 were seventy four percent had a maximum Verbal numerical rating pain scale is 0 to 4 only.

Apgar score of all babies was more than seven in the both groups. Incidence of sedation and PONV was significantly more in Group B90 when compared to Group B60. In Group B90 sedation and PONV were seen in 3% and 10 %, respectively [Figure 2]. None of the patients had sedation score more than 1. Pruritus was seen in one patient B60 group and three patients in Group B90. It was relieved by giving injection pheniramine maleate 1 ml intravenously. Naloxone was not needed. Respiratory rate was more than 12 per min in all patients in the study groups. None developed respiratory depression.

Table 2: Demographic data and duration of surgery

parameters	group **B60**	group **B90**	P VALUE	Significance
Age (years)	23.2±2.55	24.2±3.44	0.528	Not significance
Weight (kg)	56.88 ± 7.25	55.65 ±8.45	0.742	Not significance
Height (cm)	155.82 ±6.32	153.78 ±7.89	0.723	Not significance
Duration of surgery (min)	45.5 ± 15.55	46.5±14.55	0.546	Not significance

Mean±SD

Table 3: Peak sensory level

sensory level	Group **B60*n** (%)*	Group **B90*n** (%)*	P value	Significance
T4	16(53.8)	22(73.6)	0.001	significance
T5	10(33)	6(19.8)	0.001	significance
T6	4(13.2)	2(6.6)	0.001	significance

* Number of patients attaining the sensory level

Table 4: Sensory blockade

Sensory blockade	Group B60	Group B90	P value	Significance
Onset of analgesia (min)	2.5 ± 0.52	2.4 ± 0.45	0.76	Not significance
Duration of analgesia(hours)	12±4.5	18±6.0	0.001	significance
Mean number of rescue analgesic doses	1.45	0.70	0.001	significance

Mean±SD

Figure 1

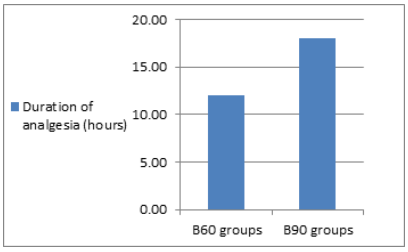

Table 5: Verbal numerical rating scale

Pain score	Group B60 *n** (%)	Group B90 *n** (%)	P value	Significance
0	10 (34)	23 (77)	0.001	Significance
2-4	12 (40)	5 (16)		
5-7	8 (26)	2 (7)		
8-10	0 (0)	0 (0)		

*Number of patients

Table 6: complications

Complications	Group **B60**		Group **B90**	
	NO	%	NO	%
PONV	1	3	3	10
SEDATION	0	0	1	3
PRURITUS	1	3	3	10
NIL	28	94	23	77
TOTAL	30	100	30	100
P value	0.05 significance			

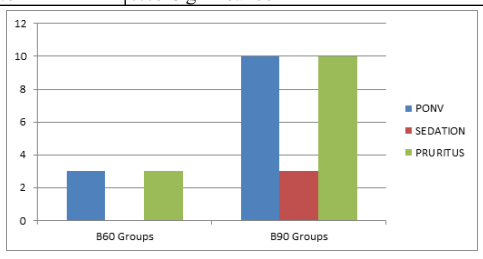

Figure2

DISCUSSION

Postoperative pain is one of the most prevalent forms of acute pain, and it is of major medical, economic, and social concern. It is defined as a complex physiologic reaction to tissue injury or visceral distension which is subjective and results in unpleasant, unwanted sensory, and emotional experience. Effective pain control is essential for the optimal care of surgical patients, as these patients suffer from considerable pain in the postoperative period. Therefore, it has been recognized as a prime concern for anesthesiologists.[8] Any method of postoperative analgesia must meet three basic criteria; it must be simple, safe, and clinically appropriate and evidence based. The majority of postoperative patients managed with parenteral or intramuscular opioid drugs are left with unrelieved pain. The

discovery of opioid receptors in the brain and spinal cord started a new era in the field of postoperative analgesia.[9] Jenkins et al,study for addition of opioid, like morphine, to intrathecal and/or epidurally administered local anesthetic provides an easy and effective means to maintain prolonged postoperative analgesia. [10]

The mean duration of postoperative analgesia was 12 hours for B60 µg group and 18 hours for B90 µg group. There was significantly prolonged analgesia in both study groups when compared to control group. The mean duration of analgesia was highly significant in B90 µg groups compared to B60 groups. A similar study was conducted by Ravindran et al, in cesarean section with 90 patients in three groups. The mean duration of analgesia12 hours was highly significant in 60 µg group compared to both the other groups.[11] Another study conducted by dixit et al conducted in 60 patients divided into two groups In the control group, he used 1.7 ml of 0.5% hyperbaric bupivacaine and in the study group, bupivacaine with 60 µg buprenorphine.[12] The 60 µg buprenorphine group had a mean duration of analgesia of 8.2 hours.

In our study intrathecal buprenorphine in postceasarean analgesia to reduce the rescue analgesic dose and increse the pain free interval. Five patients in Group B60 and Twelve patients in Group B90 did not require any analgesic during the study period.

Celleno et al; study results was Forty-five women undergoing elective caesarean section under spinal anaesthesia were randomly divided into three groups. Group A (controls, n = 15) received hyperbaric bupivacaine; Groups B and C received the same but with the addition of 0.03 mg or 0.045 mg buprenorphine, respectively. Patients receiving buprenorphine had a longer pain-free interval than the controls (P less than 0.01). Within the buprenorphine groups, patients receiving the higher dose had a longer effect (420 min s.d. 24) than those receiving the lower dose (173 min s.d. 31) (P less than 0.01) without any increase in side-effects.[13] Jenkins JG et al; addition of opioid, like morphine, to intrathecal and or epidurally administered local anesthetic provides an easy and effective means to maintain prolonged postoperative analgesia. Neuraxial techniques may be used for post caesarean delivery pain relief even in women having general anesthesia, if they so desire, once they are awake.[14]

In our study intratheacal buprenorphine does not cause any respiratory depression and less opioids related complications like pruritus, sedation,nausea and vomiting. Carvalho et al, Neuraxial opioids have contributed significantly to improved labor and post caesarean delivery analgesia. In the obstetric population, epidural and intrathecal opioids are associated with a very low risk of clinically significant respiratory depression. [15] Wolff J et al, study results was the only serious side effects were recorded in the morphine group, with two patients complaining of pruritus and five of urinary retention.[16] Ackerman WE et al, the incidence of Nausea and Vomiting was 20% in GP I which was slightly higher than the other groups. Pruritus is one of the commonest side effects of neuraxial opiods. It is more likely to occur in obstetric patients due to the interaction of estrogen with opioid receptors. This studies show the incidence of pruritus after epidural administration of 50 mcg fentanyl was 47% and with 300 mcg Buprenorphine, 10%. [17] In our observation, pruritus of a mild nature occurred in both groups but was slightly higher with B90 than B60 groups.

LIMITATIONS OF THE STUDY

In our study, we chose a maximum dose of 90 µg of buprenorphine though higher doses might have resulted in further prolongation of analgesia. However, higher doses have been reported to cause more adverse effects which were undesirable in this particular study population. We also did not study the effect of adding buprenorphine on hemodynamic variables and characteristics of motor block during intra operative period. This is accountable as we preferred to concentrate on postoperative analgesia. Neonatal effects were assessed using Apgar score though umbilical cord blood gas analysis would have been less subjective.

CONCLUSION

Addition of buprenorphine to intrathecal bupivacaine prolonged the duration of analgesia in Group B90 was 18 ±6 hours and Group B60 was 12 ±4.5 hours after caesarean section. Duration of postoperative analgesia was significantly longer an increasing the dose of buprenorphine from 60 µg to 90 µg provided longer duration of analgesia without major adverse effects. Buprenorphine did not have any adverse outcome on the baby as assessed by Apgar score. Intrathecal buprenorphine to bupivacaine is a safe, easy, and effective method of postoperative analgesia after cesarean section.

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