ORIGINAL ARTICLE

A double blind, randomized, controlled study of the effect of addition of butorphanol to 0.25% bupivacaine for bilateral ilioinguinal nerve blocks in post-caesarean patients

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ABSTRACT

Background: Ilioinguinal nerve block (IIB) is highly effective in controlling postoperative pain following inguinal herniorrhaphy, orchidopexy and caesarean sections. Butorphanol has been claimed to increase the duration and quality of analgesia in various nerve blocks. This prospective, randomized, double blind study was designed to compare the effect of butorphanol when added to bupivacaine (0.25%) with plainbupivacaine (0.25%) in bilateral IIBs in post-caesarean patients.

Methods: This prospective, double blind, randomized, controlled study was conducted at University College of Medical Sciences / GTB Hospital, Delhi, which is a tertiary care healthcare centre, from March 2006 to December 2008. Sixty ASA 1 or 2 patients, scheduled for elective caesarean section via Pfannensteil incision under general anaesthesia , were selected for the study. The patients who had a known allergy to any of the drugs used; or had placenta previa, eclampsia or severe preeclampsia were excluded from the study. The patients were randomly divided into two groups of 30 each; Group A, to receive bilateral IIB with 0.25% bupivacaine (to a volume of 10 ml on each side), and Group B to receive bilateral IIB with 0.25% bupivacaine plus 1 mg butorphanol. The randomization was done using computer generated random number tables. All the patients completed the study.

After administering appropriate antacid prophylaxis, routine general anaesthetic technique was used with rapid sequence intubation. At delivery of baby, all patients received oxytocin infusion followed by inj. morphine (0.1 mg/kg) intravenously. Just after the last stitch, bilateral IIB was performed using the prefilled syringes with the block solution. Neuromuscular blockade was reversed and inj. diclofenac sodium (1.5 mg/kg i.m.) was selected as a rescue analgesic. Numeric pain scale (marked 0-10) and simple descriptive pain scoring were used for assessment of pain intensity at 1st, 2nd, 3rd and 4th hours postoperatively and then after 24 hours. The time to first rescue analgesic was noted and the study was terminated with that. The adverse effects, if any, were also noted.

Results: More than 86% of Group B and 70% of Group A complained of no pain in immediate 4 hours of postoperative period. In Group B, six patients felt no pain even after 4 hours of postoperative period. In Group A, all patients developed pain after 2 hours. Maximum analgesic effect was observed in Group B (18 hours).

Conclusion: Bilateral IIB with 0.25% bupivacaine and 2 mg of butorphanol is more effective and safe post-

operative analgesic technique in patients undergoing caesarean section.

Keywords: Bupivacaine; Butorphanol; Ilioinguinal block; Caesarean section; Postoperative analgesia

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INTRODUCTION

Postoperative pain management is influenced by multiple factors including sensitivity to pain, psychological factors, age and genetics[1,2]. Effective multimodal analgesia without sedation allows early mobilisation reducing the risk of thromboembolic events[3].

Although regional anaesthesia is now preferred for caesarean sections, general anaesthesia is still required in multiple situations, including surgeons and patient preference. Postoperative analgesia in this setting is usually provided by systemic opioids alone or in combination with non-steroidal anti-inflammatory drugs and paracetamol[4]. IIBs can be used for post caesarean analgesia but are not widely used. Bupivacaine is routinely used for this purpose in dilute solutions (0.125-0.25%), as it provides prolonged analgesia.

Butorphanol is a potent opioid analgesic with both agonist and antagonist effects. It acts directly on k (kappa) receptors and has a mixed agonist–antagonist effect on μ (mu) receptors. It has been shown to improve the analgesic duration of local analgesic solutions [5,6.]

This prospective, randomized, controlled, double blind study was conducted to compare the analgesic effects of bupivacaine plus butorphanol with bupivacaine alone in bilateral IIB, in post-caesarean section patients performed via pfannensteil incision under general anaesthesia.

METHODOLOGY

After obtaining approval from the institutional ethical committee, sixty ASA 1 or 2 patients,

undergoing elective caesarean section were selected for this double blind, prospective study, and randomization was done using computer generated random number tables. The study was conducted in University College of Medical Sciences / GTB Hospital Delhi, a tertiary care centre, from March 2006 to December 2008. Initially 80 patients were recruited at the patients' visits to preanesthesia clinic; and out of these 20 patients were excluded from the study. The patients who had history of allergy to any of the drugs used; or had placenta previa (4/20), moderate to severe preeclampsia (7/20), or who developed cord prolapse and/or fetal distress (3/20) in preoperative period and in whom the duration of surgery exceede > 1 .5 hours (6/20) were all excluded from the study.

Preoperatively, an informed consent, explaining the detailed procedure of the block, was obtained from all of the patients who were scheduled for caesarean section via Pfannensteil incision under general anaesthesia. Antacid prophylaxis was achieved with inj. ranitidine (1mg/kg), inj. metoclopramide (0.15 mg/kg) IV and 30 ml of 0.3M sodium citrate 15 minutes before the start of operation orally. All patients were then brought into the operation room and an 18 gauge intravenous cannula was inserted.

The routine monitoring included ECG, pulse rate, NIBP, oxygen saturation, temperature and neuromuscular monitoring using Datex S5®. All patients were preoxygenated with 100% oxygen for five minutes and rapid sequence induction with inj. thiopentone sodium (2.5%) 4 mg/kg was carried out. Cricoid pressure was applied by one of the assistants and relaxation for tracheal intubation was achieved with inj. suxamethonium (1.5 mg/kg). Appropriate sized endotracheal tube was inserted and anaesthesia was maintained with isoflurane ($\leq$0.5%) in 60% nitrous oxide and oxygen. Then inj. vecuronium bromide 0.1 mg/kg was administered with top – up doses as required. After delivery, all patients received infusion of oxytocin 20 units followed by inj. morphine (0.1 mg/kg) intravenously. Just after the last stitch, bilateral IIBs were performed with prefilled syringes containing one of the block solutions as follows:

Group A: 0.25% bupivacaine plus 1mg butorphanol (total volume of 10 ml each side)

Group B: 0.25% bupivacaine+ normal saline (0.9%) (total volume of 10 ml each side)

The anesthesiologist, who performed IIBs, did not know the type of solution and also the person who recorded the analgesic effects was blinded towards the solutions used.

Table 1: Demographic Profile (n=60)

Paramter	Group A (n=30)	Group B (n=30)
Age (in years) (Mean ± SD)	25.4±2	26.1±4
Weight (in kg) (Mean± SD)	56.3±4	57.3±3
Gravidity [N(%)] Primigravida Multigravida	3(10) 27(90)	5(16.6) 25(83.3)
Gestational age [N(%)] 30-37 weeks >37 weeks	7(23.3) 23(76.7)	9(30) 21(70)

The nerve blocks were performed under aseptic conditions, before full recovery of the patients, using a

Table 2: Intensity of pain for first 4 hours postoperatively as measured by Numeric Pain Scale (NPS). All values are given in N(%).

Time (hours) / NPS (cm)	0 hour		1 hour		2 hour		3 hour		4 hour	
	Group A (n=30)	Group B (n=30)	Group A (n=30)	Group B (n=30)	Group A (n=30)	Group B (n=30)	Group A (n=30)	Group B (n=30)	Group A (n=30)	Group B (n=30)
0	26(86.6)	21(70)	20(66.6)	16(53.3)	18*(60)	0	14*(46.6)	0	13*(43.3)	0
1-3	4(13.3)	9(30.0)	10(33.3)	14(46.6)	12(40)	22(73.3)	14(46.6)	12(40)	11*(36.6)	0
4-6	0	0	0	0	0	8*(26.6)	2(6.6)	18*(60)	6(20)	23*(76.6)
7-9	0	0	0	0	0	0	0	0	0	7*(23.3)
0	0	0	0	0	0	0	0	0	0	0

* P<0.001-Significant

23G, short beveled needle. Following the technique described by Eriksson,[5] the needle was introduced perpendicular to the skin and gradually advanced until the first distinct loss of resistance 'pop' of the external oblique aponeurosis was felt, where 50% of calculated drug was deposited . The needle was further advanced until second 'pop' was felt, where the remaining 50% was injected assuming it to be the aponeuritic plane between the internal oblique and transverse abdominis. The neuromuscular blockade was reversed with inj. neostigmine and glycopyrrolate in combination. The intensity of pain was assessed with 11 point (0-10) Numeric Pain Scale (NPS) and Simple Descriptive Pain Intensity Scale (SDP)(no pain, mild pain, moderate pain, severe pain) at 1st, 2nd, 3rd and 4th hour postoperatively and then after 24 hours. Inj. diclofenac sodium (1.5 mg/kg intramuscularly) was administered as rescue analgesic when NPS was more than 5 and SDP was moderate or severe.

The time to first rescue analgesic dose injected in the patient was noted and the study was terminated at this point. The first rescue analgesic was injected by the resident on duty in high dependency unit, who was not aware of the groups allocated. The adverse effects, like pain, pruritus, nausea, vomiting, sedation and respiratory depression, were also noted.

The data were collected and analyzed using SPSS statistical software, version 10 (SPSS Inc., Chicago, IL). An acceptable alpha error was 0.05. The demographic data were analyzed using student's t-test and the intensity of pain was analyzed by ANOVA test. At 80% power (=0.05), it was calculated from previous literature that at least 29 patients in each group would be sufficient (with regard to pain relief) for this study. The power analysis was calculated according to the number of patients taken in similar past studies. Pain intensity assessed at 0, 1st, 2nd, 3rd and 4th hour was compared. The post-caesarean pain relief via IIB was a primary concern in this study.

RESULTS

The demographic profile with respect to age, weight, gravidity and gestational age was comparable between both groups (Table 1). Table 2 shows NPS scores for first four hours postoperatively. In the immediate postoperative period and at one hour, the number of pain free patients was statistically equal (26(86.6%) vs 21(70%) and 20(66.6%) vs 16(53.3%) in Groups A and B respectively. There was no pain (NPS=0) complained by majority of patients in Group B as compared to 18(60%) patients in Group A after 2 hours (p <0.001). After three hours, NPS was 4-6 in 2(6.6%) vs 18*(60%) patients in groups A and B respectively. Even after 4 hours only

Table 3: Intensity of pain for first 4 hours postoperatively measured on Simple Descriptive Pain score (SDP). All values are given as N(%).

Time (hours) / SDP	0 hour		1 hour		2 hour		3 hour		4 hour	
	Group A (n=30)	Group B (n=30)	Group A (n=30)	Group B (n=30)	Group A (n=30)	Group B (n=30)	Group A (n=30)	Group B (n=30)	Group A (n=30)	Group B (n=30)
Nil	26(86.6)	22(73.3)	22(73.3)	14(46.6)	19*(63.3)	0(0.0)	16*(53.3)	0(0.0)	14*(46.6)	0(0.0)
Mild	4(13.3)	8(26.6)	8(26.6)	16(53.3)	11(36.6)	20(66.6)	11(36.6)	16(53.3)	10*(33.3)	2(6.6)
Moderate	0	0	0	0	0	10*(33.3)	0	14*(46.6)	6(20)	19*(63.3)
Severe	0	0	0	0	0	0	0	0	0	9*(30)

* P<0.001-Significant.

6920%) patients had NPS 4-6 cm which is significantly less as compared to 23(76.6%) patients in Group B ($p<0.001$).

Table 3 shows the intensity of pain assessed by SDP. In postoperative period, 19(63.33%) patients of Group A had no pain at 2 hours whereas all patients in Group B had variable degree of pain; more than 50% patients of Group B had mild pain at 1hour. The frequency increased at 3

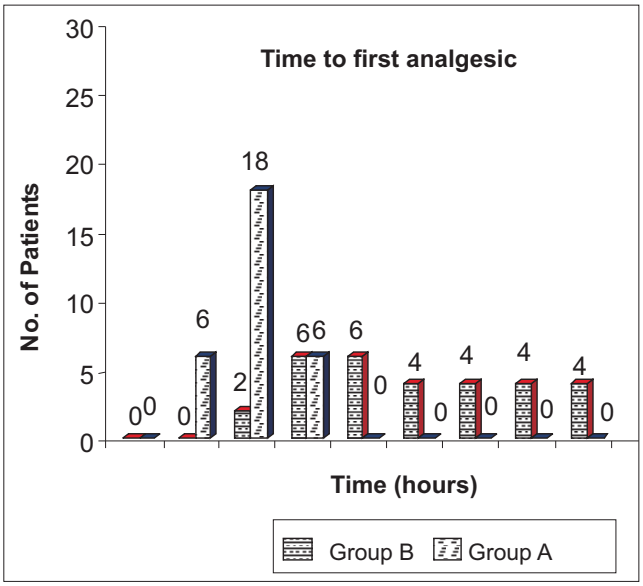

Figure 1: Time to First Rescue Analgesic (n=60)

hours, when 14*(46.6) patients in this group had moderate pain as compared to zero in Group A. At 4 hours postoperatively, 19*(63.3) patients had moderate pain and 9*(30) patients had severe pain as compared to 6(20) patients suffering from moderate pain in Group A. More than 96% patients had mild to moderate intensity of pain. In Group A majority of patients had nil to mild intensity of pain.

The time to first rescue analgesic is shown in Figure 1. It was observed that the duration of analgesia was up to 18 hours in Group A patients, where inj. butorphanol supplemented inj. Bupivacaine, as compared to none in Group B. In the later group, only 6(20%) patients had analgesia up to 6-8 hours ($p<0.001$) and a majority [18(60%)] had analgesia for $\leq$6 hours. No adverse effects or complications were observed in any patient of both groups.

DISCUSSION

Lower segment Caesarean section performed through a Pfannensteil incision is often associated with pain in the postoperative period. Bilateral blockade of ilioinguinal and ilio-hypogastric nerves at the level of anterior superior iliac spine produces analgesia covering the dermatome supplied by the first lumbar nerve in its distal distribution[7]. The Pfannensteil incision lies within this dermatome and it is possible, to provide analgesia of anterior abdominal wall following this incision using the technique described above. The NICE guidelines for caesarean sections suggests that wound infiltration and / or IIBs are viable alternatives to systemic analgesia[8].

Butorphanol is a morphinan-type synthetic opioid analgesic. It is most closely structurally related to levorphanol, and is available only as butorphanol tartrate in injectable form. It is a potent analgesic with both agonist and antagonist effects[9]. It acts on opioid receptors especially at k-opioid and mixed agonist – antagonist at μ (mu) opioid receptors[10]. Stimulation of these receptors on central nervous systemneurons causes an intracellular inhibition of adenylate cyclase, closing of influx membrane calcium channels, and opening of membrane potassium channels. This leads to hyperpolarization of the cell membrane potential and suppression of action potential transmission of ascending pain pathways.

There is increasing interest in peripheral nerve blocks because of potential benefits and concerns over interactions of systemic analgesics. In a recent survey of members of the American Society of Anesthesiologists and the American Society of Regional Anesthesia and Pain Medicine, nearly half of the respondents anticipated an increased use of peripheral nerve blocks in their practice [11].

Traditionally, nerve blocks have been performed with local analgesics. The search for a longer acting local analgesic lead to replacement of lignocaine, first with bupivacaine, and then ropivacaine. Bupivacaine has a narrow safety margin, and if large doses have to be used to block the larger motor nerves, the risk of toxicity is considerable[10]. Many researchers tried this drug with a variety of adjuvants in an effort to prolong its risk of toxicity and to prolong its duration of effective analgesia even further. Hence, sufentanil, clonidine, morphine, ketamine and tramadol, all have been tried[12-16].

Peripheral opioid receptors are known to be located primarily on end terminals of primary afferent neurons[17] and their expression is enhanced in the presence of inflammation[18]. But neither peripheral opioid receptors nor inflammation is typically located at the sites for plexus or peripheral nerve analgesia, this would seem to be an unlikely mechanism for adjunctive analgesia. In a systematic review, it was concluded that the benefit from the addition of opioid to single-injection peripheral nerve blocks was unsubstantiated[19]. However, in the majority of these studies, large doses of large-concentration local anesthetic were used for intraoperative anesthesia (e.g., 0.5% bupivacaine). In a recent study, it was observed that the addition of 100 μg of fentanyl to 40 mL 0.25% bupivacaine for axillary block provided a 45% increase in the duration of postoperative analgesia[20]. We used a similar dose of bupivacaine and a small dose of butorphanol for postoperative analgesia.

The scientific literature has been enriched with reports of

effective peripheral opioid analgesia,[21-25] and work on the development of novel selectively peripherally acting opioid agonists with more favourable safety and efficacy profiles.[26-28] Some researchers have used butorphanol in combination with mepivacaine for continuous infusion for upper limb surgery and postoperative analgesia with good favourable results5,6.We conducted this study to compare the analgesic efficacy of butorphanol plus bupivacaine (0.25%) with bupivacaine (0.25%) alone, when administered through bilateral IIB.

Thirteen patients who were given bupivacaine plus butorphanol complained of no pain for initial four hours postoperatively, whereas, in 70% of Group B patients, analgesia did not last for more than 2 hours. This result was similar to the results reported by Bunting and Mc Conchie[29]. In their study, Bunting and Mc Conchie emphasized pain relief with bupivacaine via IIB and showed decrease in pain scores from 4-24 hours postoperatively. In our study, 4 patients in Group A had pain relief for more than 10 hours, e.g. 18 hours. Postoperatively, initial four hours always remain significant and pain relief is essential and the bearable pain relief (NPS $\leq$5 cm) was observed in 28 patients of Group A till first 4 hours (Figure 1). The decrease in NPS scores and requirement of rescue analgesic further proves the efficacy of technique.

Opioids have been administered on patient demand, or by patient–controlled analgesia (PCA), which has the advantage of less fluctuations in plasma opioid concentration. Even with PCA administration, several studies have shown a great variability of postoperative pain control and individual analgesic requirement[4]. When opioids are administered after caesarean section, the mother is exposed to a high dose of opioids that may be detrimental for breastfed newborn. Continuous monitoring and vigilance are essential with PCA as a death has been reported due to side effects and programming errors[30].

Whilst opioids are the mainstay for relief of severe pain, they are far from perfect analgesics as they have many significant adverse effects.[31] The common opioid side-effects of respiratory depression, sedation, depression of gastrointestinal motility, nausea and vomiting, and the potential risk of abuse reflect the striking and generalized role endogenous opioids play in general human physiology.[32]

The majority of opioid-related side-effects are associated with their central nervous system actions, that decrease patients' satisfaction and acceptability towards this technique. IIB is relatively a simple and easy technique and if butorphanol supplemented with local anaesthetic is administered, it provides excellent analgesia and for long duration (more than 10 hours). It was observed that in more than 53% patients, it showed excellent results. Without butorphanol, the patients needed rescue analgesic earlier. This might be due to slow absorption of butorphanol from the site or its action on local pain receptors. Another hypothesis may be its synergistic effect on bupivacaine. The time to first rescue analgesic was 8-10 hours in majority of patients in Group A, whereas 80% of patients in Group B required rescue analgesic as early as 2 hours postoperatively. No complication or any discomfort was observed in any patient .The analgesia can be inadequate if the skin incision extends beyond the dermatome supplied by the concerned nerve.

The IIB is simple, safe regional anaesthetic technique and easier to perform. The permitted maximum dose of local analgesic agent should not be exceeded, asepsis must be maintained and intravascular injection should be avoided.

It was a small study, and we used bupivacaine in a concentration of 0.25% in both of the groups. It proved beyond any doubt that the addition of butorphanol prolonged the effect of bupivacaine. It is perhaps, advisable that a separate study is undertaken to compare 0.25% bupivacaine with 0.125% or even 0.0625% bupivacaine plus butorphanol, or with butorphanol alone.

CONCLUSION

It is concluded that bilateral IIBs, performed with 0.25% bupivacaine plus butorphanol, after caesarean sections under general anaesthesia via Pfannensteil incision is a safe and effective technique and it provides prolonged postoperative analgesia when compared to IIBs performed with 0.25% bupivacaine alone.

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