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A Comparative Study of Efficacy of Fentanyl Versus Buprenorphine as an Adjuvant to Bupivacaine in Lower Abdominal Surgery

Yagna Munesh Gali[1], K. Laksmi Vasudha[2], A.S. Kameswara Rao[3], Anand Acharya[4]

[1,2]Post graduate student, [3,4]Professor, Konaseema Institute of Medical Science, Amalapuram, Andhra Pradesh 533201, India.

Abstract

Background: Pain poses a unique challenge to anesthesiologist. Continuous unrelieved pain activates the pituitary adrenal axis which can suppress the immune system resulting in postsurgical infection and poor wound healing. Opioids have been added as adjuvants to local anesthetics in spinal anesthesia to alleviate pain. Fentanyl is a phenylpiperidine derivative synthetic opioid agonist. As an analgesic fentanyl is 75-125 times more potent than morphine. Buprenorphine is an agonist antagonist derived from the opium alkaloid the baine. It is estimated that affinity of buprenorphine for mu receptors is 50 times greater than that of morphine. This study was carried out to evaluate the effects of Intrathecal Fentanyl with bupivacaine compared to intrathecal buprenorphine with bupivacaine on duration of post operative analgesia in lower abdominal surgeries. *Methods:* A double blinded randomised study was carried out with one hundred and thirty two patients of ASA grade I and II aged between 20 and 70 years undergoing lower abdominal and lower limb surgeries under spinal anaesthesia. The patients were given 3 ml of hyperbaric bupivacaine premixed with either 10 mcg Fentanyl (Group F), Buprenorphine 60 mcg (Group B) or 0.2 ml normal saline (Group S). Postoperatively VAS score for pain, time to first dose of analgesic required, total analgesic required and adverse effects with in 24 hours post operative period were noted. *Results:* Prolonged post operative analgesia was observed in Group BB (623.11 ± 98.86) compared to Group BF (536.56 ± 69.31) and BS (296.88 ± 36.32). Post operative rescue analgesic requirement was significantly less in group buprenorphine. *Conclusion:* Addition of Fentanyl and Buprenorphine as adjuvants to intrathecal 0.5% hyperbaric bupivacaine prolongs post operative analgesia. Intrathecal buprenorphine 60mcg as an adjunct to bupivacaine for subarachnoid block showed a longer duration of action and less postoperative rescue analgesic requirement in comparison to Intrathecal Fentanyl 10 mcg.

Keywords: Spinal anaesthesia; Buprenorphine; Fentanyl; Postoperative analgesia.

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Introduction

Pain has always been a major concern to mankind since the beginning of time and many efforts are made globally through many years to alleviate it. Appropriate management of pain is a major goal for healthcare professionals as it is one of the most important issues in the society

Corresponding Author: K. Laksmi Vasudha, Post Graduate Student, Dept of Anaesthesia, Konaseema Institute of Medical Science, Amalapuram, Andhra Pradesh 533201, India.

E-mail: anand_kims@yahoo.co.in

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Most individuals following a surgical intervention complain of pain consequently due to pain are unable to breathe and cough effectively. This instils fear, sense of helplessness, anxiety and depression. Therefore we anaesthesiologists have the prime ethical and moral responsibility to aid all patients in relieving pain in order to have a better post operative stay in the hospital and good outcome overall.

Multiple approaches are carried out to relieve the postoperative pain. Spinal anaesthesia with various adjuvants are given to prolong its duration of action.

Spinal anaesthesia with 0.5% hyperbaric bupivacaine is regularly administered these days for lower abdominal and lower limb surgeries. To prolong the duration of analgesia produced by local anaesthesia, many adjuvants have been added through the central neuraxial route. Intrathecal opioid administration provides effective postoperative analgesia following a variety of surgical procedures, but with a risk of respiratory depression**.**

Buprenorphine is a mixed agonist antagonist narcotic with high affinity at both m and κ opiate receptors. Buprenorphine produces no adverse reactions when given intrathecally and compatible with CSF. At low doses, buprenorphine produces adequate and increased duration of action with less side effects making it a suitable choice for intrathecal administration [1]. Fentanyl, in contrast is a phenylpiperidine derivative synthetic opioid agonist. As an analgesic fentanyl is 75-125 times more potent than morphine. Ithas no reported neural toxicity. When administered epidurally, fentanylhas been demonstrated to provide adequate postoperative analgesia after major abdominal surgery and caesarean section.

A study done was by Celleno D, Capogna G to compare two doses of intrathecal buprenorphine for postoperative analgesia in 45 women undergoing elective caesarean section under spinal anaesthesia concluded that patients receiving buprenorphine had a longer pain free interval [2].

Hence this study was undertaken in a randomized double blinded protocol to assess the effects of intrathecal fentanyl with bupivacaine compared to intrathecal buprenorphine with bupivacaine on duration of postoperative analgesia inlower abdominal and lower limb surgeries.

Materials and Methods

Study Design

- *Group BB* received 3 ml of 0.5% Bupivacaine (heavy) plus 60 mcg Buprenorphine intrathecally.
- *Group BF* received 3 ml of 0.5% Bupivacaine (heavy) plus 10 mcg of Fentany lintrathecally.
- *Group BS* received 3 ml of 0.5% Bupivacaine (heavy) plus 0.2 ml normal saline.

Inclusion Criteria

- Patients aged between 20-60 yrs of either sex posted for lower abdominal and lower limb surgeries under spinal anaesthesia.
- Weight of the patients between 40-80 kgs.
- Height of the patients between 150-170 cm.
- Patients belonging to ASA Status I & II.

Exclusion Criteria

1. Patients with neurological disorders, cardiorespiratory disease, bleeding disorders, gastrointestinal disorders and psychiatric illness.
2. Patients with history of allergy to opioids and local anaesthetic agents.
3. Patients with contraindications to spinal anaesthesia.
4. Pregnant breast feeding and menstruating women.
5. Morbidly obese patients.

Methodology

This study was conducted on one hundred and twenty patients undergoing lower abdominal and lower limb surgeries at Konaseema Insitute of medical sciences and research foundation between August 2017 to February 2018 after obtaining written informed consent.

During the pre anesthetic check up patients were educated about assessment of perioperative pain using the 10 cm visual analog scale (VAS) with 0 (zero) corresponding to no pain and 10 to the worst pain conceivable. Patients were divided into three Groups BB, BF and BS randomly by picking lots on the day of surgery.

To enable blinding a resident anaesthetist not involved in the study prepared the solutions for

spinal anaesthesia. After securing intravenous access with an 18G cannula, patients were preloaded with 10 ml/kg of Ringer Lactate over 10 min. Electrocardiogram, pulse oximetry, non invasive blood pressure monitors were connected and baseline values were noted. Under strict aseptic conditions, spinal anaesthesia given using a 25G Quincke's needle inserted at L3-4 or L4-5 with patient in sitting position. After freeflow of CSF the study solution was administered, following which patients were placed in supine position. Oxygen was supplemented at 4L/min through face mask. Vital parameters were monitored intraoperatively.

Time of onset of sensory blockade was tested by pin prickat the level of L1. Loss of sensation to pin prick test was noted on both sides and duration of sensory blockade was noted. The duration of sensory blockade (time for sensory regression) was taken from the time of injection of the drug to the time when the patient was able to complain pain in the S1 dermatome (i.e., the heel).

Hypotension (fall in SBP >20% from baseline), and bradycardia (HR<50/min) was treated with Intravenous bolus of Ephedrine 6 mg and Atropine 0.6 mg respectively.

Nausea, vomiting, shivering, pruritus and respiratory depression (RR<12 min) was recorded for 24 hrs postoperatively. Nausea and vomiting was treated with IV Ondensetron 4 mg.

After surgery, pain at rest was assessed using visual analogue scale (VAS) (0 for no pain and 10 for worst pain). VAS score was assessed every 4th hourly for a total of 24 hours. All the patients were instructedto request medication for pain if they wanted analgesia and not to wait for the next scheduled VAS score assessment. Pain was treated with Slow Intravenous tramadol 50 mg. During the first 24 hrs after surgery no other analgesics or sedatives were allowed.

The time to first analgesic dose, total amount of tramadol consumption and the occurrence any intraoperative or postoperative adverse events such as nausea, vomiting, pruritis, respiratory depression (RR<12 /min), postdural puncture headache or any other adverse events were documented. Results obtained were statistically analysed.

Results

One hundred and twenty patients were included and the results were as follows.

25% of patients in group BB had earlier onset of sensory analgesia when compared to 2% of patients in group BF and 5% in group BS. This observation was statistically significant when group BB was compared with group BF and BS (Table 1).

VAS scores at 4 hrs was significantly low in group BB (2.08 ± 0.56) when compared to group BF (3.49 ± 2.11) and group BS (6.63 ± 4.63). VAS score at 8, 12, 16, 20 and 24 hrs were comparable (Table 3).

The total duration of analgesia was significantly increased in group BB (623.11 ± 98.86 mins) when compared to group BF (536.56 ± 69.31 mins) and group BS (296.88 ± 36.32 mins) (Table 4).

The time to first rescue analgesic was longer in group BB (623.11 ± 98.86 mins) when compared to group BF (536.56 ± 69.31 mins) and group BS (296.88 ± 36.32 mins).

Also there was statistically significant time for sensory regression 318.79 ± 23.17 mins in group BB, 298.48 ± 18.63 minsfor group BF, 199.27 ± 21.54 mins for group BS.

Table 1: Onset of Sensory Block distribution in three groups of patients studied

Onset of Sensory Block	Group BB	Group BF	Group BS	Total
1-2	10 (25%)	2 (5%)	5 (12.5%)	17 (14.2%)
2-4	30 (75%)	38 (95%)	35 (87.5)	103 (85.8%)
4-6	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	40 (100%)	40 (100%)	40 (100%)	120 (100%)

p=0.002**, Significant, Fisher Exact test

Table 2: Total Dose of rescue analgesic distribution in three groups of patients studied.

Total Dose	Group BB	Group BF	Group BS	Total
<120	5 (12.5%)	2 (5%)	1 (2.5%)	8 (6.7%)
120-250	35 (87.5%)	38 (95%)	39 (97.5%)	112 (93.3%)
>250	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Total	40 (100%)	40 (100%)	40 (100%)	120 (100%)
Mean ± SD	158.66 ± 40.11	165.58 ± 31.21	178.90 ± 38.84	167.71 ± 38.34

p=0.051+, Significant, ANOVA test

Table 3: Comparison of VAS Score in three groups of patients studied

VAS Score	Group BB	Group BF	Group BS	Total	p value
4 hr	2.08 ± 0.56	3.49 ± 2.11	6.63 ± 8.02	4.06 ± 4.72	0.003**
8 hr	3.79 ± 2.01	3.28 ± 1.46	3.88 ± 1.34	3.65 ± 1.57	0.230
12 hr	4.54 ± 1.79	4.67 ± 1.78	4.96 ± 1.80	4.72 ± 1.76	0.185
16 hr	4.62 ± 1.88	4.39 ± 1.96	4.51 ± 2.24	4.50 ± 1.97	0.897
20 hr	4.49 ± 1.82	4.43 ± 1.89	5.06 ± 2.04	4.66 ± 1.93	0.601
24 hr	4.97 ± 1.84	5.63 ± 2.21	5.97 ± 1.97	5.52 ± 2.03	0.243

ANOVA test

Table 4: Comparison of analgesia time and sensory regression (duration of sensory blockade) time in three groups of patients studied

Variables	Group BB	Group BF	Group BS	Total	p value
Analgesia (min)	623.11 ± 98.86	536.56 ± 69.31	296.88 ± 36.32	485.51 ± 132.09	<0.001**
Sensory regression (min)	318.79 ± 23.17	298.48 ± 18.63	199.27 ± 21.54	272.18 ± 18.58	<0.001**

ANOVA test

Discussion

In our study we found that addition of intrathecal Buprenorphine to hyperbaric Bupivacaine produced similar intraoperative anaesthesia and considerably prolonged the post operative analgesia.

The total duration of sensory analgesia was significantly higher with buprenorphine group (623.11 ± 98.86 mins) when compared to Fentanyl group (536.56 ± 69.31 mins) and control group (296.88 ± 36.32 mins). Time for sensory regression was significantly prolonged in buprenorphine group (318.79 ± 23.17 mins) compared to fenatanyl (298.48 ± 18.63 mins) and control (199.27 ± 21.54 mins) respectively.

The prime objective of our study was to compare the post operative analgesic effects of intrathecal Fentanyl and intrathecal buprenorphine used as an adjunct to 0.5% bupivacaine. In our study, the VAS scores at 4 hours postoperatively was significantly lower in buprenorphine group and also the time to first rescue analgesic dose was significantly prolonged in buprenorphine (623.11 ± 98.86 mins) group when compared to Fentanyl (536.56 ± 69.31 mins) and control (296.88 ± 36.32 mins) group.

Rapid drug clearance from subarachnoid space has been reported for fentanyl and sufentanil [3]. HenceIt is possible that the analgesic effects of Fentanyl has regressed sooner. Buprenorphine, due to its high lipid solubility, high affinity for opioids and prolonged duration of action is a suitable choice for intrathecal administration.

The total dose of rescue analgesic (tramadol) requirement during first 24 hours after surgery was high in control group (213.37 ± 41.15 mg) compared to buprenorphine (166.45 ± 44.21 mg) and Fentanyl (179.57 ± 34.43 mg) group. The observations were statistically significant.

The second objective of our study was to study the adverse effects during the first 24 hours following its administration. In the present study, five (12.5%) patients in buprenorphine and three (7.5%) patients in control group developed post operative shivering where asnone of the patients in Fentanyl group developed shivering. This finding was statistically significant. A study conducted by Techanivate A etalconcluded that addition of 20 mcg fentanyl in 2.2 ml of 0.5% hyperbaric bupivacaine with 0.2 ml of morphine 0.2 mg intrathecally can reduce the incidence and severity of intraoperative and postoperative shivering after spinal anesthesia for patients who were receiving cesarean section [4].

Four patients in Fentanyl group and one patient in buprenorphine group had post operative nausea / vomiting. This may be because nausea and vomiting depends on other major factors like dose, time and mode of administration, pain intensity, type of surgery and anaesthesia and history of motion sickness [5].

None of the patients reported other adverse effects like pruritis, postdural puncture headache, respiratory depression and neurological complications.

With spinal opioids, the major advantage is absence of sympathetic blockade and postural hypotension, allowing patients to ambulate

earlier. The intrathecal route is technically easier to perform and a single injection produces pain relief of sufficient duration.

In our study intrathecal buprenorphine provided prolonged post operative analgesia without any significant increase in side effects. The quality of surgical anaesthesia and post operative analgesia were commendable. A study done by S.M. Rabiee et al. showed similar results where Intrathecal Buprenorphine given to patients undergoing caesarean section prolonged the duration of analgesia [6]. J C Mishra et al. also observed that a single dose of 150 µg of Buprenorphine added to interthecal bupivacaine provides analgesia for a significant length of time [7]. Thomas et al. assessed the efficacy of buprenorphine as post operative analgesic using the Magill's classification [8]. The longer duration of action for buprenorphine is due to its high affinity for narcotic receptors [9]. Even intrathecal fentanyl prolonged duration of analgesia in our study which corroborates with study done by Kaushik Rao Seetharam et al. who concluded that addition of fentanyl to ropivacaine significantly prolongs the duration of postoperative analgesia [10]. Besides our study is also supported by Yegin et al. who witnessed that addition of 25 µg to hyperbaric ropivacaine for spinal anesthesia in patients undergoing Transurethral resection of Prostate significantly improved the quality and duration of analgesia [11].

We conclude that intrathecal buprenorphine is a suitable drug for post operative analgesia when compared to intrathecal Fentanyl. A similar result was seen in a prospective double blind study conducted by Arvinder Pal Singh et al. in which ninety ASA 1 and 2 patients between 18 and 60 years of age undergoing lower limb surgery. They concluded that addition of buprenorphine and fentanyl as adjuvants to intrathecal 0.75% ropivacaine prolongs post operative pain relief without causing any increase in duration of motor blockade, but buprenorphine is better as compared to fentanyl in prolonging the duration of sensory block and achieving a better outcome in terms of pain relief [12].

Hence, we suggest intrathecal buprenorphine as a better adjunct for post operative analgesia.

Conclusion

- Addition of adjuvants i.e. intrathecal fentanyl or buprenorphine to hyperbaric bupivacaine produced comparable intraoperative hemodynamic changes.
- Prolonged post operativeanalgesic effect was observed when intrathecal buprenorphine was added as an adjunct to 0.5% bupivacaine when compared to intrathecal fentanyl or normal saline as an adjunct. Total dose of rescue analgesic requirement was low in buprenorphine group and highest in saline group.
- Addition of both opioids buprenorphine and fentanyl, produced minimal intraoperative and postoperative side effects.
- Fentanyl produced a significantly reduced incidence of post operative shivering when compared to buprenorphine.

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