International Journal of Clinical Trials
Sonya K et al. Int J Clin Trials. 2017 Feb;4(1):45-48
http://www.ijclinicaltrials.com
pISSN 2349-3240 | eISSN 2349-3259
DOI: http://dx.doi.org/10.18203/2349-3259.ijct20170308

Original Research Article

A prospective randomised double blind study of the comparison of two opioids- fentanyl and buprenorphine – as adjuvant to spinal bupivacaine in caesarean sections

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Received: 09 December 2016
Accepted: 14 January 2017

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ABSTRACT

Background: Opioids are first introduced as additives to spinal anaesthesia in 1979, with intrathecal morphine as forerunner. Neuraxial opioids when added to local anaesthetics prolong the duration of sensory block, improve quality of block and no unwanted sympathetic blockade leading to hypotension. This prospective randomized double blind study was undertaken to evaluate the duration of analgesia, sensory and motor blocking properties and side effects of two opioids – Fentanyl and Buprenorphine, when used as adjuvant to spinal Bupivacaine in caesarean section.
Methods: Sixty patients between the age group 18-35 years belonging to ASA I and II posted for elective LSCS were randomly divided into two groups. Each group consisting of 30 patients , received either 1.8 ml 0.5% Bupivacaine with 25 mcg Fentanyl (group F) or 1.8 ml 0.5% Bupivacaine with 75 mcg buprenorphine (Group B). The onset, maximum level and duration of sensory and motor blockade and hemodynamic parameters were monitored.
Results: Maximum height of sensory block was achieved faster in fentanyl group (i.e. 4.09±1.12 minutes compared to 4.56±1.21 minutes in buprenorphine group). Duration of analgesia was significantly prolonged in buprenorphine group. It was 317±54 minutes and 214±35 minutes respectively for buprenorphine and fentanyl groups.
Conclusions: The study thus concluded that although fentanyl produce faster sensory block, duration of analgesia is longer with buprenorphine, and both the drugs do not cause significant side effects.

Keywords: Spinal anesthesia, Adjuvants, Fentanyl, Buprenorphine

INTRODUCTION

Subarachnoid block is the most popular technique of anaesthesia for lower segment caesarean sections. Different local anesthetics are used for spinal anaesthesia, most popular being Lignocaine and bupivacaine. Intrathecal hyperbaric bupivacaine (0.5%) has become the most widely used drug as it provides intense motor and sensory blockade of long duration.[1]

Adjuvants are added to local anaesthetics for improving the quality of block and to increase the duration of analgesia, without causing significant adverse effects, Opioids are first introduced as additives to spinal anaesthesia in 1979, with intrathecal morphine as forerunner. Neuraxial opioids when added to local anaesthetics prolong the duration of sensory block, improve quality of block and no unwanted sympathetic blockade leading to hypotension.[2]

Fentanyl, a lipophilic opioid, has rapid onset of action following intrathecal administration with no respiratory depression. Buprenorphine is a mixed against – autogonist with high affinity at both mu and kappa opiate receptors. In our institution, both Fentanyl and Buprenorphine has been used as adjuvants for caesarean

section with spinal bupivacaine. So we decided to conduct a study to assess which opioid among the two is better with regard postoperative analgesia and haemodynamic stability.[3]

Hence a study was undertaken to compare the effectiveness of two opioids– fentanyl and buprenorphine as adjuvant to spinal bupivacaine for caesarean section.

METHODS

This study was undertaken in Jubilee Mission Hospital, Thrissur, during the period between December 2010 to December 2012. The study was undertaken after obtaining ethical committee clearance as well as informed consent from all the patients before the study.

Sixty patients belonging to ASA I and II, scheduled for elective lower segment caesarean section (LSCS) were included in the study. The study population was randomly divided into two groups with 30 patients in each group.[4,5]

- Group F (n=30) received 1.8 ml 0.5% hyperbaric Bupivacaine + 25 mcg Fentanyl
- Group B (n=30) received 1.8 ml 0.5% hyperbaric Bupivacaine + 75 mcg Buprenorphine.

Inclusion criteria

Patient belonging to ASA I and II posted for elective LSCS and patients aged between 18 and 35 years

Exclusion criteria

Patient refusal, patient belonging to ASA 3, 4 and 5, patients having complication in pregnancy like GDM, pregnancy included hypertension, heart disease and patient having contraindication to spinal anaesthesia like raised intracranial pressure, bleeding coagulopathy, local infection

A routine pre aneasthetic examination was conducted on the evening before surgery to assess history, general conditions, airway and spine. The visual analogue scale (VAS) with end points labelled “no pain” and “worst possible pain’ will be shown to the patients and their use will be explained[(6).]

Patients were kept nil orally 10 pm onwards on the previous night and were given tab Ranitidine and Metaclopramide both at night and at 6 am on the day of surgery.

All the patients were preloaded with 500 ml ringer lactate solution 30 minutes prior to the procedure. Multi-parameter monitor was connected which records heart rate, non-invasive systolic, diastolic and mean arterial pressures, continuous ECG monitoring and oxygen saturation (SPO_2).

The study drugs were prepared and loaded in 2 ml syringes by anaesthesia technicians who are not involved in the study. The patients were placed in left lateral position and lumbar puncture was performed using 25 gauge quincke needle at either L2-L3 or L3-L4 level using midline approach.

Once free flow of CSF was obtained, the study drug was administered over 10-15 seconds. Patients were immediately turned supine with $15\text{-}20^0$ lateral tilt. HR, BP and SPO_2 were monitored at 0, 2 minutes, 5 minutes and then 10 minutes interval up to the end of surgery.

Assessment of sensory and motor blockage was done with patient in supine position. The onset time for the motor and sensory blocks and the maximum level of sensory and motor block were recorded.

Sensory blockade was assessed using a short bevel 22 gauge needle and was tested in mid clavicular line. Motor Blockade was assessed using modified Bromage Scale.

- 0-able to perform a full leg raise over the bed for 5 seconds
- 1-unable to perform the leg raise but can flex the leg of the knee joint
- 2-unable to flex the knee but can flex the angle
- 3-unable to flex the angle but can move the toes.
- 4-unable to move the toes

Measurement of BP, Heart rate, respiratory rate and oxygen saturation were obtained at 0, 2,5,10 minutes and then every 10 minutes.

Intra-operatively complications like fall in blood pressure, variation in heart rate were noted, treated and recorded. Hypotension is defined as >=20% decrease in systolic BP from baseline values.

They were treated with IV fluids and injection ephedrine 6 mg given in increments, bradycardia (heart rate <60 beats per minutes) was treated with injection atropine 0.6 mg IV. Respiratory depression was assessed as respiratory rate <10/minute. The condition of the neonate was assessed by APGAR score. In the postoperative period patients were assessed for analgesia using visual analogue scale. Patients were evaluated for duration of motor block, sensory regression and side effects like nausea, vomiting, pruritus and respiratory depression. Rescue analgesia was given as injection tramadol IV.

- Onset of sensory block: is the time from the completion of injection of drug till the patient does not feel pin prick T10 level.
- Time for maximum sensory block: is the time from completion of injection of drug to the maximum sensory blockage attained.

- Onset of motor blockade: time from the completion of injection of the drug till the patient develops modified Bromage scale grade 1 motor blockade.
- Time for maximum motor blockade: time from the completion of drug injection to the maximum motor blockade attained.
- Duration of Motor blockade: time from the injection of the drug till the patient attains complete motor recovery (Bromage 0)
- Duration of analgesia: time from injection of the drug till the patient complaints of pain (VAS score 7). The results of the study were statistically analyzed between the two groups.

Statistical analysis

Various statistical tests are used to compare the significant differences in two drugs. Komogrow-smirnow test is applied to find the indentity of distributions. Also Chi-square test is used to determine the rates of significance. Student's t-test was used to assess the significant differences on average in two medicines at 5% level of significance. Coefficient of variation is also mentioned to determine variability among the patients

RESULTS

Based on average and coefficient of variation (CV), there was no significant difference in the age group, height, weight and duration of surgery in both groups of patients. There was no significant difference between the groups regarding time for onset of sensory and motor blockage (P values 0.6441 and 0.6273 respectively). But, there was significant difference in time to reach maximum sensory level (P values 0.02).

Table 1: Mean and SD of time for max sensory level I minutes.

Time for max sensory level (minutes)	Fentanyl	Buprenorphine
Mean	4'09"	4'56"
SD	1'12"	1'21"
CV	28.81	27.11

Table 2: Mean and SD of analgesia minutes.

Duration of analgesia (minutes)	Fentanyl	Buprenorphine
Mean	214	317
SD	35	55
CV	16.40	17.27

There was significant difference in duration of analgesia between the groups (P value 0.000005) Buprenorphine Group had prolonged duration of sensory block compared to fentanyl group as given in Table 2.

There was no statistically significant difference between the groups when time for maximum motor block and duration of motor block were assessed. (P value 0.0558 and 0.2239 respectively)

Average heart rate, systolic BP, Diastolic BP, Mean arteries and pressures were comparable in both the groups. Also, no other statistically significant side effects were noted in any of the group of patients.

DISCUSSION

Subarachnoid block is the most popular technique for both elective and emergency LSCS as it provides intense motor and sensory blockade, at the same time preserving consciousness and open airway[7]. However, it has limited duration of action and causes heamodynamic instability.[8]

Several adjuvants have been tried along with local anesthetics to prolong the duration of spinal anaesthesia, at the same time maintaining haemodynamic stability. Alpha 2 agonists, opioids, ketamine, midazolam are few of those drugs tried. Opioids are most popular among them.

We have selected 2 opioids belonging to different groups. Both are lipophilic drugs and while fentanyl is a pure agonist, Buprenorphin is partial agonist and widely used.[9] Both drugs are easily available and though this study, we tried to analyse the advantage and disadvantage of one drug over the other.

Both groups of patients had comparable age, height, weight and duration of surgery. Though the onset of sensory block was comparable in both groups, time to reach maximum height of sensory block was shorter in fentanyl group, whereas Buprenorphine took longer time to achieve maximum height of sensory block.

Our study also showed that duration of analgesic is longer with buprenorphine group. It is 317±54 minutes for B group compared to 214±35 minutes in F group. This is highly significant statistically with a P value of 0.000005. Our findings are consistent with studies of Capogna et al.[10] Wang et al suggested that duration of analgesia is dose dependent.[11] The longer duration of action of buprenorphine is due to its high affinity for opioid receptors and high lipid solubility. Fentanyl also prolonged the duration of postoperative analgesia, comparable to the result obtained by Sergio et al and Bruce et al, but duration is less compared to buprenorphine.[12,13]

Onset motor block and duration of motor block was comparable in both groups. This result was consistent with the findings of Biswas et al.[14]

There was no significant difference in heart rate between the two groups at various time intervals. None of the patients in either group had bradycardia. There was no

statistically significant difference in SBP, DBP and MBP monitored at various time intervals between the two 2 groups, however both the groups had significant hypotension within the first 10 minutes.[15] But the magnitude of BP fall and use of ephedrine is similar in both the groups. These results are comparable to the findings of Khan et al, Dixit et al, Shaik et al.[16-18]

There was no change in neonatal APGAR scores among the groups, which were similar with the observations made by Hunt et al and Shendi et al.[19,20]

In our study, we found that Buprenorphine produced prolonged analgesia without increase in the incidence of side effects, when compared to fentanyl.

CONCLUSION

From our study, it can be concluded that there is no significant difference in the onset of sensory and motor blockade between Buprenorphine and Fentanyl when used as adjuvants to spinal bupivacaine. But duration of analgesia is significantly prolonged in Buprenorphine group, though time for achieving highest sensory block is shorter for Fentanyl group. Haemodynamic variables, side effects and neonatal outcome are comparable in both the groups.

ACKNOWLEDGEMENTS

The Dr. Davies CV, Professor, Department of Anaesthesiology, Jubilee Mission Medical College Thrissur, Kerala, India for providing constant encouragement and support during the study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Sonya K, Davies CV. A prospective randomised double blind study of the comparison of two opioids- fentanyl and buprenorphine – as adjuvant to spinal bupivacaine in caesarean sections. Int J Clin Trials 2017;4(1):45-8.