Scholars Journal of Applied Medical Sciences (SJAMS) **ISSN 2320-6691 (Online)**
Sch. J. App. Med. Sci., 2017; 5(11B):4405-4409 **ISSN 2347-954X (Print)**

(An International Publisher for Academic and Scientific Resources)
www.saspublishers.com DOI:10.36347/sjams.2017.v05i11.019

A Comparative Study of Intrathecal Bupivacaine with Nalbuphine and Bupivacaine with Fentanyl for Intra and Post-Operative Analgesia in Gynaecological Surgeries

Dr. Avinash Bapurao Pawar[1], Dr. Thorat PS [2], Dr. Rawat HS[3]
[1]Resident, [2]Associate Prof, [3]Prof and HOD
Department of Anaesthesia, Dr. Vitthalrao Vikhe Patil Medical College, Ahmednagar-414111

Original Research Article

***Corresponding author**
Dr. P.S. Thorat

Article History
Received: 01.11.2017
Accepted: 09.11.2017
Published: 30.11.2017

Abstract: Spinal anaesthesia is still the most commonly used technique for gynaecological surgeries as it is economical and easy to administer. Its main drawback is the short duration of action due to these different adjuncts have been used. The reason for mixing opioids and local anaesthetics is that this combination eliminates the pain by acting at two different locations, local anaesthetics acting at the nerve axon and the opioids at the receptor site in the spinal cord. A total 60 patients of ASA grade I and II in the age group of 40-60 years were randomly allocated with their consent in one of the two groups GROUP A: [n =30] received 0.5% hyperbaric Bupivacaine 15 mg with Nalbuphine 0.8 mg GROUP B: [n =30] received 0.5% hyperbaric Bupivacaine 15 mg with Fentanyl 25 mcg**.** The characteristics of onset of sensory and motor blockade, intraoperative hemodynamics, respiratory parameters and VAS score and side effects were recorded, tabulated and statistically analyzed**.** The onset of sensory block was more rapid with Fentanyl than Nalbuphine and this was statistically significant but the duration of post-operative analgesia(sensory and motor) and the effective analgesic time were more prolonged in Nalbuphine group than in Fentanyl group with no statistically significant difference. There was no significant difference found in various hemodynamic, vital parameters intra operatively or any side effects between the two groups. Addition of Nalbuphine to intrathecal Bupivacaine improved the quality of intraoperative and postoperative analgesia with minimal side effects.
Keywords: Bupivacaine, Fentanyl, Gynaecological surgeries, Intrathecal, Nalbuphine.

INTRODUCTION

Subarachnoid block with local anaesthetic is a commonly used regional anaesthetic technique for elective gynecological procedures as it is simple to perform with rapid onset of anaesthesia and complete muscle relaxation. Lower incidence of failed block, less drug doses and decreased incidence of aspiration pneumonitis are added advantages of spinal anaesthesia. When Bupivacaine is used alone, patients do experience pain during prolonged procedure due to their limited duration of action [1, 2]. Intrathecal opioids are synergistic with local anaesthetics and intensify the sensory block without increasing the sympathetic block. The reason for mixing opioids and local anaesthetics is that this combination will eliminate the pain by acting at two different locations, local anasthetics acting at the nerve axon and the opioids at the receptor site in the spinal cord. The combination of adjuvants to local anaesthetic are synergistic for producing the analgesia of prolonged duration without increasing the sympathetic or motor blockade, thus allow early ambulation of patients with reduction in their dosages. Nalbuphine is an agonist-antagonist opioid that is structurally related to oxymorphone and naloxone [3]. It acts as antagonist at μ-receptors and agonist at κ-receptors. Its affinity to k-opioid receptors results in analgesia, sedation, and cardiovascular stability with minimal respiratory depression. It was synthesized in an attempt to produce analgesia without the undesirable side effects of a μ agonist. Nalbuphine is widely studied as an adjuvant to local anaesthetics in central neuraxial techniques to improve the quality of perioperative analgesia as it provides reasonably potent analgesia for visceral nociception [4, 5]. Fentanyl, a lipophilic opioid, has rapid onset of action following intrathecal administration. It does not tend to migrate to the fourth ventricle in sufficient concentration to cause delayed respiratory depression when administered intrathecally[6].

METHODOLOGY

After obtaining informed and written consent, minimum 60 patients undergoing, gynaecological surgeries, ASA risk I-II were selected for the study. Pre-anaesthetic check-up was done on the previous day of surgery. Routine and specific investigations were noted. All patients were informed in general terms regarding the procedure of study and their queries were answered. Patients were councelled about the advantages/disadvantages associated with different drugs and administered to them by their own choice. A sensitivity test was performed prior to drug administration. The patients were randomly allocated into 2 groups, each having 30 patients.

GROUP A: [n =30] received 0.5% hyperbaric Bupivacaine 15 mg with Nalbuphine 0.8 mg
GROUP B: [n =30] received 0.5% hyperbaric Bupivacaine 15 mg with Fentanyl 25 mcg

SELECTION OF CASES

Inclusion criteria

- Age of patient: Above 40-60 yrs.
- American society of anaesthesiologists (ASA) physical status I –II
- Patient undergoing elective gynaecological surgeries

Exclusion Criteria

- Patient refusal for the procedure.
- Allergic to amide local anaesthetic.
- All general contraindication for spinal anaesthesia.
- Extremes of height and weight.
- Emergency procedure.

Anaesthesia technique

All the patients were fasted overnight. Intradermal sensitivity test was performed on the volar surface of the forearm. A 1:100 dilution of Bupivacaine 0.25% was injected intradermally to produce an initial wheal of 2×2 mm. The intradermal skin tests were examined after 15 minutes. Patients with negative intradermal skin testing proceeded to be taken up for inclusion criteria list. Neither patient received any sedative or narcotic premedication before arrival in the operation theatre. All patients received inj. Ranitidine 50 mg i.v. 30 min. before surgery. Patients were taken to the O.T. and pulse rate, blood pressure, ECG, SpO2, respiratory rate, temperature were noted. Intravenous line was secured with 18 G intracath and patients were preloaded with Ringers lactate solution 10ml per kg over 20 minutes prior to surgery. A standard subarachnoid block was performed in L3-L4 Space in sitting position with 25 G spinal needle (Quincke's type) under all aseptic precautions. Drug was injected after checking of free flow of CSF and according to group selected. Immediately after completion of block, patients were placed in supine position until adequate sensory and motor blockade achieved for surgery.

Thereafter, all the patients were positioned accordingly and the surgery was started.

OBSERVATIONS MADE AS FOLLOWS

Onset and duration of sensory blockage, onset and duration of motor blockage, Systemic arterial pressure including the systolic, diastolic and mean arterial pressure, heart rate, SpO_2 and electrocardiography (ECG) were recorded.

Criteria of block

Onset of sensory block:

The sensory block was evaluated by pinprick method using 22-G hypodermic needle. Sensory block was assessed at 1 min intervals until block reaches T10, and then repeated every 2 minutes until the level stabilizes for four consecutive tests. This level was recorded as the peak sensory block level. Onset of adequate sensory block was defined as the achievement of a sensory block level of T10 dermatome or higher which is required to initiate the surgery. After the surgery, sensory block level was evaluated every 30 min in recovery room until its regression to L5 level.

Onset of motor block

Motor block was assessed by using the modified Bromage Scale. It was recorded every 5 minutes until the surgery was started. After surgery, total duration of motor blockage was noted.

Modified bromage scale

Grade-0: No block – full flexion of knee and feet.
Grade-I: Partial block - just able to flex knee but full flexion on feet.
Grade-II: Almost complete block – unable to flex knee but complete flexion of feet possible.
Grade-III: Complete block: Unable to flex knee and feet.

Peak level of sensory block

Time to peak level of sensory block was calculated from the time of drug injection intrathecally to the time at which the sensory blockade reaches the highest dermatome level and remains stable. Dermatomal levels was tested every 2 min from injection until the level stabilizes for four consecutive tests. Testing was then conducted every 10 minutes until 2 segment regression. Further testing was then performed at 20 minute intervals in the recovery room till reach pubic symphysis which corresponds to L5. Thus, total duration of sensory blockage was recorded.

For recovery of block, time to 2 dermatome regressions and time to complete motor recoveries were recorded. The duration of effective analgesia was taken as the time from the completion of spinal injection to the time of administration of the first rescue analgesic. Patients with VAS score ≥3 received diclofenac 75 mg intramuscularly for rescue analgesia. The VAS score of >3 constituted the end point of the study. The following complications were noted

1-Hypotension**, 2**-Hypoxia**, 3**-Bradycardia**, 4**-Nausea/ vomiting, 5-Restlessness**, 6**-Shivering**, 7**-Urinary retention**, 8**-Pruritus**, 9**-Surgical complications

Hemodynamic changes

Hemodynamic parameters, sensory and motor blockage were assessed by anaesthesiologist at 0, 5,10,15,30,45,60,90 and 120 min following block. Thereafter observation were continued at 30 minutes intervals until the motor block regresses completely as defined by modified Bromage score. Postoperatively the parameters were recorded at 30 min intervals until the patient meets the criteria for discharge. IV fluids were administered according to requirement. Criteria for hypotension was considered as BP below 30% of pre-induction value and bradycardia was considered if fall in heart rate was greater than 20% of pre-induction value. Hypotension was treated with intravenous fluids and Inj. Mephentermine, if necessary. Bradycardia was treated by Inj. Atropine defined as HR < 60/min. The duration of spinal anaesthesia was calculated from the time of spinal injection to the time taken for two level sensory regressions from the peak block height. Time of sensory regression to below L5 level and time to complete motor

STATISTICAL ANALYSIS

Results were expressed as means ± standard deviation of the means (SD) or number (%). Comparison between different parameters in the two studied groups was performed using unpaired t test. Comparison between categorical data was performed using Chi square test. The data were considered significant if p value was equal to or less than 0.05 and highly significant if p value < 0.01. Statistical analysis was performed with the aid of the SPSS computer program (version 12windows).

RESULT

The present study compared the clinical efficiency of intrathecal Fentanyl and Nalbuphine as adjuvant to intrathecal 0.5% hyperbaric Bupivacaine in 60 patients, scheduled for elective gynaecological surgery under Sub arachnoid block. There was no protocol deviation and all patients successfully completed the study protocol and were cooperative with subsequent assessment. Hence, all patients were included for data analysis. Surgical procedures were performed uneventfully and there were no surgical or anaesthetic complications. Patients of both groups were statistically comparable regarding mean age, weight, height, gender, ASA physical status, and surgical characteristics [Table 1].

Table-1: Demographic profile

CHARACTERISTICS	NALBUPHINE N=30	FENTANYL N=30	P VALUE
AGE(yr)	56±2.8	54.9±4.2	NS
ASA GRADE I & II	12/18	10/20	NS
Wight(kg)	60.45±9.22	61.24±9.1	NS
Height(cm)	158.8±6.12	157.43±4.7	NS
Duration of surgery (min)	109.68±23.74	108.89±26.22	NS

Data were expressed as means± standard deviation NS=p>0.05 =not significant.

There was no statistically significant difference among the two groups as regards

Age, ASA grade, weight, height, and duration of surgery. As regards the onset of motor block, there was no statistically significant difference between group A and group B. The onset of sensory block was more rapid with Fentanyl than Nalbuphine and this was statistically significant. The duration of post-operative analgesia and the effective analgesic time were more prolonged in Nalbuphine group than in Fentanyl group but with statistically significant difference. There was no significant difference found in various hemodynamic or vital parameters intra operatively between the two groups.

As regards the side effects, they were less in nalbuphine group than the fentanyl group with no statistically significant difference.

Table-2: Sensory and motor block characteristics

CHARACTERISTICS	NALBUPHINE N=30	FENTANYL N=30	P VALUE
Time of onset of sensory block(min)	2.92± 0.85	2.15± 0.7	<0.001
Time of onset of motor block(min)	8.63±2.43	7.97±3.29	0.37
Duration of sensory block(min)	205.14± 5.4	164.5± 5.7	<0.001
Duration of motor block(min)	183.26±29.63	141.63±8.05	<0.003
Time to administer first rescue analgesia(min)	280.62± 13.95	208.84± 10.7	<0.001

Data are expressed as means± standard deviation.
NS=p> 0.05=not significant.
p<0.01 =highly significant

Table-3: **Adverse effects**

CHARACTERISTICS	NALBUPHINE N=30	FENTANYL N=30	P VALUE
Hypotension	6 (20%	8 (26.7%)	0.542 (NS)
Nausea and vomiting	1 (3.3%)	3 (10%)	0.301 (NS
Pruritus	0	1 (3.3%)	0.313 (NS)
Shivering	0	1 (3.3%)	0.313 (NS)

DISCUSSION

Regional anaesthetic techniques of spinal anaesthesia offer many advantages over General anaesthesia including reduced stress response to surgery with postoperative analgesia[7]. Since spinal anaesthesia provided postoperative analgesia for a short time, many intrathecal adjuvants to local anaesthetic have been addressed to augment the clinical efficiency and duration of analgesia[8]. Several intrathecal adjuvants have been used to improve the quality as well as prolong the duration of postoperative analgesia, of which opioids have been the gold standard agents[9]. Local anaesthetics such as Bupivacaine act mainly by blockade of voltage gated Na+ channels in the axonal membrane and presynaptic inhibition of calcium channels. Both Fentanyl and Nalbuphine exert their action by opening K+ channels and reducing the Ca++ influx, resulting in inhibition of transmitter release. A combination of these effects may explain the observed synergism between Bupivacaine and Fentanyl/Nalbuphine. The synergism is characterized by enhanced somatic analgesia without an effect on the degree of level of local anaesthetic induced sympathetic or motor blockade. Opioid analgesics activate opioid receptors located on the primary afferent neurons, resulting in the activation of pain modulating systems. Their activation may either directly decrease neurotransmission or inhibit the release of excitatory neurotransmitters. Opioid receptors are classified as mu, delta, and kappa receptors. Opioid agonist acts on µ receptors and are principally responsible for supraspinal and spinal analgesia along with sedation, nausea, vomiting, pruritus, and respiratory depression. Opioid, an agonist–antagonist, act principally on kappa receptors. Site of action in the spinal cord is substantia gelatinosa. Analgesia with neuraxial opioids is dose-related and specific for visceral rather than somatic Pain .Opioids selectively decreases nociceptive input from A delta and C fibers without affecting dorsal root axons or somatosensory-evoked potentials [10].In our study we compared Nalbuphine with Fentanyl in spinal anaesthesia. The first study with intrathecal Nalbuphine in obstetric patients was conducted by Culebras *et al*., in which they injected 200 µg, 800 µg, and 1600 µg mixed with hyperbaric 0.5% Bupivacaine versus morphine 200 µg with Bupivacaine in cesarean patients and concluded that 0.8 mg of Nalbuphine produced analgesic duration comparable with 1.6 mg of Nalbuphine without producing maternal or newborn respiratory depression. Overall, the duration of analgesia was significantly prolonged with 200 mg of intrathecal morphine in their study.16 Itching and postoperative nausea and vomiting were significantly greater with morphine in this study [11]. Mukherjee *et al*. studied the duration of analgesia with different dosages of intrathecal Nalbuphine (0.2, 0.4, and 0.8 mg) to find out the optimum dose of intrathecal Nalbuphine which could prolong the postoperative analgesia without increasing the side effects. Their study concluded that effective analgesia was increased with increase in the doses of Nalbuphine as adjuvant to 0.5% hyperbaric Bupivacaine without any side effects. Hence, in our study we used 0.8 mg Nalbuphine as a adjuvant in spinal anaesthesia. As regards the neurotoxicity of intrathecal Nalbuphine, it has been used in modern practice for more than 10 years without

any reports of neurotoxicity [12]. Intrathecal Fentanyl is used commonly with heavy Bupivacaine 0.5% for spinal and epidural anaesthesia by many researchers [13–16]. Kang *et al*. [16] combined it with heavy Bupivacaine during cesarean section to provide adequate depth of anaesthesia. The duration of complete analgesia was longer in (Bupivacaine and Fentanyl) group 146 ±47 min versus Bupivacaine alone 104 ± 44 min. Obara *et al*. evaluated the effects of intrathecal Fentanyl added to hyperbaric Bupivacaine for cesarean section and concluded that addition of intrathecal Fentanyl to hyperbaric Bupivacaine improved the quality without side effects[17]. In our study we compared Nalbuphine 0.8 mg and Fentanyl 25 mcg with 0.5% hyperbaric Bupivacaine 15 mg and found that the duration of post-operative analgesia and the effective analgesic time were more prolonged in Nalbuphine group than in Fentanyl group but the onset of sensory block was more rapid with Fentanyl with no statistical significance and also there was no statistically significant difference among the two groups as regards Age, ASA grade, weight, height, duration of surgery and various hemodynamic or vital parameters intra operatively between the two groups. As regards the side effects, in our study we observed that they were less in Nalbuphine group than the Fentanyl group with no statistically significant difference

CONCLUSION

In our study we conclude that both Nalbuphine and Fentanyl in combination with hyperbaric Bupivacaine (15mg) is efficacious and hemodynamically stable in patients undergoing gynaecological surgeries. However, Nalbuphine has comparatively prolonged post-operative analgesia and effective analgesia time and lesser side effects is a better adjuvant than Fentanyl for intrathecal injections of Bupivacaine 0.5% (H) in gynaecological surgeries undergoing spinal anaesthesia.

REFFERENCES

1. Rudra A, Halder R, Sen A, Kundu S. Efficacy of low dose propofol for control of emetic episodes during cesarean delivery with spinal anaesthesia. Indian J Anaesth 2004;48:31–4.
2. Bogra J, Arora N, Srivastava P. Synergistic effect of intrathecal Fentanyl and Bupivacaine in spinal anaesthesia for cesarean section. BMC Anaesthesiol 2005;5:5.
3. DeSouza EB, Schmidt WK, Kuhar MJ. Nalbuphine: An autoradiographic opioid receptor binding profi le in the central nervous system of an agonist/antagonist analgesic. J Pharmacol Exp Ther 1988;244:391-402.
4. Yaksh T, Birbach DJ. Intrathecal Nalbuphine after caesarean delivery: Are we ready? Anaesthesia and analgesia. 2000;91(3):505-8.
5. Fournier R, Van Gessel E, Macksay M, Gamulin Z. Onset and offset of intrathecal morphine versus Nalbuphine for postoperative pain relief after total hip replacement. Acta Anaesthesiol Scand. 2000;44(8):940-5.
6. Etches RC, Sandler AN, Daley MD. Respiratory depression and spinal opioids. Can J. Anaesth 1989; 36; 165-85.
7. Courtney MA, Bader AM, Hartwell B, Hauch M, Grennan MJ, Datta S. Perioperative analgesia with subarachnoid sufentanil administration. Reg Anaesth 1992;17:274–8.
8. Butterworth J. Physiology of spinal anaesthesia: what are the implications for management? Reg Anaesth Pain Med 1998;23:370-3.
9. Hindle A. Intrathecal ropioids in the management of acute postoperative pain. Contin Educ Anaesth Crit Care Pain 2008;8:81-5.
10. Hindle A. Intrathecal opioids in the management of acute postoperative pain. Continuing education in anaesthesia, critical care and pain. Br J Anaesth 2008;8:81-5.
11. Culebras X, Gaggero G, Zatloukal J, Kern C, Marti RA. Advantages of intrathecal Nalbuphine, combined with intrathecal morphine, after cesarean delivery: An evaluation of post-operative analgesia and adverse effects. Anaesth Analg 2000;91:601-5.
12. Mukherjee A, Pal A, Agrawal J, Mehrotra A, Dawar N. Intrathecal Nalbuphine as an adjuvant to subarachnoid block: What is the most effective dose? Anaesth Essays Res 2011;5:171-5.
13. Bano F, Sabbar S, Zafar S, Rafeeq N, Iqbal MN, Haider S, Aftab S, Sultan ST. Intrathecal fentanyl as adjunct to hyperbaric bupivacaine in spinal anesthesia for caesarean section. Journal of the College of Physicians and Surgeons--Pakistan: JCPSP. 2006 Feb;16(2):87-90.
14. Biswas BN, Rudra A, Bose BK, Nath S, Chakrabarty S, Bhattacharjee S. Intrathecal Fentanyl with hyperbaric Bupivacaine improves analgesia during cesarean delivery and in early post-operative period. Indian J Anaesth 2002;46(6):469–72.
15. Choi DH, Ahn HJ, Kim MH. Bupivacaine sparing effect of Fentanyl in spinal anaesthesia for cesarean delivery. Reg Anaesth Pain Med 2000;25:240–5.
16. Kang FC, Tsai YC, Chang PJ, Chen TY. Subarachnoid Fentanyl with dilute small dose Bupivacaine for cesarean section. Acta Anaesthesiol Sin 1998;36(4):207–14.
17. Obara M, Sawamura S, Satoh Y, Chinzei M, Sekiyama H, Tamai H, Yamamoto H, Hanaoka K. The effect of intrathecal fentanyl added to hyperbaric bupivacaine for caesarean section. Masui. The Japanese journal of anesthesiology. 2003 Apr;52(4):378-82.