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Original Research Article

Comparative study between intrathecal bupivacaine 0.5% heavy + fentanyl (0.5 microgram/Kg) versus intrathecal bupivacaine 0.5% heavy + buprenorphine (2 microgram/Kg) in lower abdominal and lower limb surgeries

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Abstract

Aim: To evaluate the efficacy of the combination of intrathecal bupivacaine 0.5% heavy + fentanyl (0.5 microgram/kg) versus intrathecal bupivacaine 0.5% heavy + buprenorphine (2 microgram/kg) in lower abdominal and lower limb surgeries.
Materials and Methods: A total of 80 patients who underwent lower abdominal and lower limb surgeries were taken up for the study. Patients were randomised into two groups each. Patients allotted with odd numbers were in GROUP F: Bupivacaine +Fentanyl group (n=40) and patients allotted with even numbers were in GROUP B: Bupivacaine + Buprenorphine group (n=40). Group F received 3ml, 0.5% hyperbaric bupivacaine + Fentanyl (0.5mcg/Kg), Group B received 3ml, 0.5% hyperbaric bupivacaine + Buprenorphine (2mcg/Kg).
Results: In the current study, onset of analgesia was significantly earlier due to the addition of buprenorphine. This may be attributed to high lipid solubility and highest affinity for opiate receptors of buprenorphine. Both the groups had the same mean time to achieve motor blockade. Both groups maintained hemodynamic stability which was statistically insignificant. The mean duration of effective analgesia in Group A and group B found significant statistically ($p<0.01$).
Conclusion: We observed that anaesthesia was superior when buprenorphine is mixed with bupivacaine (0.5%) as compared to bupivacaine with fentanyl. Addition of buprenorphine to bupivacaine 0.5% augments the sensory blockade of local anaesthetics without affecting the sympathetic activity. Thus, it is concluded that intrathecal buprenorphine is suitable drug for post-operative analgesia for caesarean section.

Keywords: Bupivacaine, sensory blockade, intrathecal buprenorphine

Introduction

Spinal anesthesia is the most commonly used technique for lower abdominal surgeries as it is very economical and easy to administer. However, postoperative pain control is a major problem because spinal anesthesia using only local anesthetics is associated with relatively short duration of action and thus early analgesic intervention is needed in the postoperative

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period. A number of adjuvants, such as clonidine and midazolam, and others have been studied to prolong the effect of spinal anesthesia [1, 2].
Neuraxial administration of opioids in conjunction with local anesthetics improves the quality of intraoperative analgesia and prolongs the duration of postoperative analgesia.
Hunt *et al*. reported that addition of fentanyl >6.25 μg to hyperbaric bupivacaine reduced intraoperative opioid requirement in patients undergoing cesarean delivery under spinal anesthesia [3]. Belzarena further demonstrated that low dose fentanyl 0.25 $\mu g.kg^{-1}$ intrathecally with bupivacaine 0.5% provided excellent surgical anesthesia with few side effects [4].
Buprenorphine and Fentanyl as adjuvants to intrathecal Bupivacaine has been less explored and evaluated in humans. This study may become helpful in reducing some of the general side effects and complications observed in bupivacaine, fentanyl and buprenorphine, and thus reducing the overall potential morbidity in patients. It may become an useful study clinically for many procedures under spinal anaesthesia like obstetric, gynaecological, orthopedic and urological surgeries.

Materials and Methods

The present prospective randomized comparative study was conducted in Patients between 18-65 years posted for lower limb and lower abdominal surgeries requiring spinal anaesthesia were included.

Study sample size

For estimating sample size, we referred to "Comparison of Intrathecal Fentanyl and Buprenorphine in Urological Surgery by Fauzia A. Khan, Gauhar A. Hamdani". The mean time for block to reach T10 level in bupivacaine with fentanyl group was found that 3.2 ± 2 minutes, while in bupivacaine with buprenorphine group it was found that 4.3±1 Minutes from the study [5]. Considering Z=1.96 is the critical value of the Normal distribution at α/2 (with confidence level of 95%, α is 0.05). Zβ =0.842 is the critical value of the Normal distribution at β (power of the test is 80%, β=0.20). σ2 =0.714 is the estimated population variance based on the previous study. d =0.593 minutes is the expected difference between the means. The minimum required sample per group was 33. Therefore, a minimum of 66 was required for the study. We obtained 40 patients per group, a total of 80 patients in this study.

Inclusion criteria

- ASA physical status class I and II.
- Age between 18-65 years of either sex (Males and Females).

Exclusion criteria

- Emergency surgery.
- Deformities of the spine.
- Hypersensitivity to any of the drugs.
- Contraindications to spinal anaesthesia, patient refusal, bleeding diathesis.

Methodology

- Patients were screened and explained about the procedure. An Informed consent was

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obtained (Appendix II). Patients were then included and a Study proforma was taken. 80 ASA I and II patients scheduled for Lower limb and Lower abdominal surgeries under spinal anaesthesia were chosen for the study.

- Preanesthetic check-up was done one day prior to the surgery. Patients were evaluated for any systemic diseases and laboratory investigations recorded. The procedure of SAB was explained to the patients and an informed written consent is obtained. The patients were educated about the use of visual analogue scale.
- Preparation of patients includes period of overnight fasting.
- Patients were premedicated with Tab. Rantac 150mg and Tab. Alprazolam 0.5mg H.S.

Preparation of operating theatre

- Boyle‘s anaesthesia machine was checked. Appropriate size endotracheal tubes, working laryngoscope with medium and large size blades, stylet and working suction apparatus were kept ready before the procedure.
- Emergency drug tray consisting of atropine, adrenaline, mephentermine, ephedrine and dopamine was kept ready.

Randomization and Blinding

- The study was designed as a prospective randomized, double blind study. Patients were allocated to two equal groups of 40 each using a computer-generated random number list. Patients allotted with odd numbers were in GROUP F: Bupivacaine +Fentanyl group (n=40) and patients allotted with even numbers were in GROUP B: Bupivacaine + Buprenorphine group (n=40). Group F received 3ml, 0.5% hyperbaric bupivacaine + Fentanyl (0.5mcg/Kg), Group B received 3ml, 0.5% hyperbaric bupivacaine + Buprenorphine (2mcg/Kg).
- Intraoperatively Pulse rate, non-invasive Blood pressure, Electro cardiogram, SpO2 were recorded every 2 minutes for the first 10 minutes, every 10 minutes for the next 50 minutes and every 15 minutes till the end of surgery.
- Time of onset of sensory block was noted using pin prick method, time of onset of motor block was noted.
- The allocation sequence was generated by other anaesthesiologist. To avoid bias, the drugs were prepared by the same anaesthesiologist who is not involved in administering the injections and in further evaluation of the patients. The block was given by me who is unaware of the contents of the drugs and was blinded to treatment group. All observations were carried out by a single investigator who was also blinded to the treatment group.

Procedure

- Patients were shifted to Operating table and baseline vitals were recorded. IV access was obtained on the forearm with No. 18G IV cannula and all patients were preloaded with 15ml/Kg, Ringer‘s Lactate, 15 mins before the surgery.
- Patients were randomly allocated into groups.
- Under strict asepsis, using 25G Quincke-Babcock spinal needle, lumbar puncture was performed at L3-L4 space.
- Group F received 3ml, 0.5% hyperbaric bupivacaine + Fentanyl (0.5mcg/Kg), Group B received 3ml, 0.5% hyperbaric bupivacaine + Buprenorphine (2mcg/Kg).
- Intraoperatively Pulse rate, non invasive Blood pressure, Electro cardiogram, SpO2 were recorded every 2 minutes for the first 10 minutes, every 10 minutes for the next 50 minutes and every 15 minutes till the end of surgery.

- Time of onset of sensory block was noted using pin prick method, time of onset of motor block was noted.

Study Outcomes and Definitions

1. Motor block was assessed with Modified Bromage scale:

Bromage 0: The patient is able to move the hip, knee and ankle.
Bromage 1: The patient is unable to move the hip but is able to move the knee and ankle.
Bromage 2: The patient is unable to move the hip and knee but able to move the ankle.
Bromage 3: The patient is unable to move the hip, knee and ankle.

2. Modified Ramsay Sedation Scale (MRSS) was used for intraoperative sedation.

1 = Agitated, restless.
2 = Cooperative, tranquil.
3 = Responds to verbal commands while sleeping.
4 = Brisk response to glabellar tap or loud noise while sleeping.
5 = Sluggish response to glabellar tap or loud noise while sleeping.
6 = No response to glabellar tap or loud noise while sleeping.

3. Following parameters were recorded.

- Hypotension (> 20% fall of base line blood pressure) was treated with bolus dose of 6mg ephedrine intravenous.
- Bradycardia (pulse rate < 50bpm), was treated with intravenous Atropine 0.6mg.
- Incidence of respiratory depression defined as respiratory rate less than 9/min and SpO_2 less than 90% on room air, was noted.
- Side effects if any were noted.
- Postoperatively regression of the sensory block and the motor blockade to reach modified Bromage was noted.

4. Pain was assessed using VISUAL ANALOGUE SCALE advocated by Revilland Robinson in 1976. It is linear scale, consists of 10cm line anchored at one end.

Visual analogue scale

By a label such as-No pain and other end by-Worst pain imaginable. Patient simply marks the line to indicate the pain intensity. Supplemental analgesia was given for visual analogue score of more than 6. Time of supplemental analgesia was noted. Visual analogue scale was used to assess post-operative pain. 0 = no pain, 10 = severe pain.

Statistical methods

All the patient information was recorded on each patient's study proforma, and data collected as study outcomes measures was compiled in a data spreadsheet in Excel and was kept confidential. Study data was analysed, to provide descriptive statistics on patient demographics, including age and gender for the two study groups Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Student t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Chi-square/Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups. P value less than 0.05 was considered as significant. Data entered in Ms. Excel and Analyzed

by using SPSS 19.0v.

Results

Table 1: Demographic details

Variables	Group F	Group B	P Value
Age (Years)	43.98±11.746	37.23±11.358	0.011
Sex			
Male	20	20	1.000
Female	20	20	
Height (cm)	153.98±5.332	154.03±6.078	0.969
Weight (Kg)	59.38±8.851	57.82±8.911	0.439
ASA Grade			
I	21	22	0.823
II	19	18	
Total	40	40	

Table 2: Onset and duration of sensory & motor blockade

Time of Onset of Sensory Block (Min)	Mean	Std. deviation	P Value
Group F	3.52	0.656	0.017
Group B	3.19	0.524	
Duration of Sensory Blockade (Min)			
Group F	183.63	7095	<0.001
Group B	229.3	33.79	
Onset of Motor Block (Min)			
Group F	4.08	0.624	<0.001
Group B	3.36	0.379	
Duration of Motor Blockade (Min)			
Group F	158.68	9.068	<0.001
Group B	207.9	32.187	

Table 3: Comparison of MRSS and VAS between the groups

MRSS	Group F	Group B	P Value
30 Mins	2.05 ± .221	2.15 ± .362	0.002
60 Mins	2 ± 0	3.13 ± .607	<0.001
90 Mins	2.20 ± 0.405	3.48 ± 0.506	<0.001
120 Mins	2.15 ± 0.362	2.13 ± 0.335	0.749
150 Mins	2.05 ± 0.221	2.05 ± 0.221	1
180 Mins	2.08 ± 0.267	2.08 ± 0.267	1
VAS			
6 Hrs	3.55 ± 0.504	1.55 ± 0.815	<0.001
12 Hrs	5.78 ± 0.920	4.33 ± 0.526	<0.001
18 Hrs	7.25 ± 0.899	5.48 ± 0.506	<0.001
24 Hrs	7.20 ± 1.043	5 ± 0.961	<0.001

Table 4: Distribution of side effects

Side Effects	Group F	Group B	P Value
Bradycardia	2 (40%)	3 (60%)	0.286
Hypertension	7 (77.78%)	2 (22.22%)	0.228
Hypertension + Bradycardia	1 (25%)	3 (75%)	0.111
Hypertension + Nausea	2 (66.67%)	1 (33.33%)	0.842
Nausea	2 (50%)	2 (50%)	1

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Discussion

Pain is a more terrible lord of mankind than death itself". Pain is a complicated subjective experience, which is challenging to measure in a reproducible way [6]. Operative pain is more extreme after surgery which thereafter gradually tapers over the next 24 hours [7]. Existence of pain has been a led to the discovery of both newer drugs and procedures of pain relief.

The concomitant use of buprenorphine or fentanyl along with the local anesthetics puts the patient in an established state of analgesia by the time the spinal anesthetic wears off. The present study was conducted in 80 patients posted for various lower abdominal and limb surgeries to compare the onset of sensory and motor block, sensory and motor characteristics of the block, duration of postoperative analgesia, and hemodynamic effects of both the drugs. These timings were statistically significant showing that addition of Fentanyl (25 μg) to 15 mg of bupivacaine (BF) hastened the onset of sensory block considerably followed by the addition of buprenorphine to bupivacaine (BB), whereas only Bupivacaine with NS (BN) took maximum time for the onset of sensory block.

In the present study, the buprenorphine group had significant early onset of analgesia. This is by virtue of high lipid solubility and highest affinity for opiate receptors of buprenorphine [8, 9]. The findings in our study also correlates with the study done by Singh H *et al.* [10] concluded that addition of intrathecal fentanyl 25μg to hyperbaric bupivacaine did not hasten the onset of sensory block.

Studies conducted by Khanna *et al.* using different doses of Fentanyl intrathecally found no significant difference in the onset of sensory blockade [11]. Techanivate *et al.* in their study used 25 μg fentanyl with 3 mL 0.5% hyperbaric Bupivacaine and concluded that the onset of sensory block was early compared with control group (3 mL 0.5% hyperbaric bupivacaine) and the time taken to reach maximum level was also less in the fentanyl group [12]. Singh H *et al.* in their study added 25 μg Fentanyl to 13.5 mg hyperbaric bupivacaine 0.75% and found that intrathecal fentanyl did not change the onset of sensory or motor block, or prolong the duration of bupivacaine-induced motor spinal block [10].

	Hamdani *et al.* [5]	Dr. Sittaramane *et al.* [13]	Present study
Year	2006	2017	2017-2018
Sample Size	60	50	80
Drugs Compared	2 ml 0.75% Bupivacaine (H), Fentanyl 10mcg with 2 ml 0.75% Bupivacaine (H), Buprenorphine 30mcg with 2 ml 0.75% Bupivacaine(H)	1.5 ml 0.5% bupivacaine(H) with 25m Fentanyl, 1.5 ml 0.5% bupivacaine(H) with 60mcg buprenorphine and 0.3 ml Normal saline	c3gml 0.5% bupivacaine(H) with 0.5mcg/kg Fentanyl, 3 ml 0.5% bupivacaine (H) with 2 mcg/kg Buprenorphine
Time of Onset of Sensory Block	Faster with fentanyl	Faster with Buprenorphine	Faster with Buprenorphine
Duration of Sensory Block	Longer with Buprenorphine	Longer with Buprenorphine	Longer with Buprenorphine
Time of Onset of Motor Block	Faster with fentanyl	Not much significant	Faster with Buprenorphine
Duration of Motor Block	Longer with Buprenorphine	Not much significant	Longer with Buprenorphine
Duration of Post-Op Analgesia	Longer with Buprenorphine	Longer with Buprenorphine	Longer with Buprenorphine
Side Effects	More PONV in buprenorphine gro	uMp ore with Fentanyl group	More with Fentanyl group
Outcomes	Buprenorphine has good post-op analgesia but with side-effects in elderly	Buprenorphine has good post-op analgesia, Fair sensory block with less side-effects	Buprenorphine has better sensory and motor characteristics, good post-op analgesia with less side- effe

Limitations

This study sample was small which included only 80 patients. The sample size could be increased for better outcome and accurate results. The duration of study was 1 year which could be increased for accurate results. The study population included only ASA Grade I and II and age between 18 to 65 years. It does not include emergency surgery, ASA III to VI, hypersensitivity to drugs and any contraindications to spinal anaesthesia which may not give appropriate results.

Conclusion

The present study findings reveled that there was no significant hemodynamic changes in either of the groups. Anaesthesia was superior when buprenorphine is mixed with bupivacaine (0.5%) as compared to bupivacaine with fentanyl. Addition of buprenorphine to bupivacaine 0.5% enhances the sensory blockade of local anaesthetics without affecting the sympathetic activity. Thus it is concluded that intrathecal buprenorphine is suitable drug for post-operative analgesia.

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