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Comparative study of incremental doses of buprenorphine as an adjuvant to 0.5% bupivacaine in lower abdominal and lower limb surgeries done under subarachnoid block

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Abstract

Spinal anesthesia can be performed with a wide range of local anesthetic drugs. using local anesthetics alone is associated with a relatively short duration of action.1 Postoperative pain control is a major problem with spinal anesthesia using local anesthetics alone, and thus early analgesic intervention is needed in the postoperative period. Bupivacaine is the local anesthetic most commonly used, although lidocaine, tetracaine, procaine, ropivacaine, levobupivacaine, and prilocaine may also be used. After institutional ethical committee approval, 90 patients aged between 18-60 years undergoing lower abdominal and lower limb surgeries were selected. A detailed history, complete physical examination, and investigations were done for all patients. Informed consent was taken. The study population was divided into 3 groups with 30 patients in each group. The study has demonstrated that increasing the dose of buprenorphine with 0.5% bupivacaine in spinal anesthesia significantly decreases the time of onset of sensory and motor block and prolongs the duration of sensory, motor blockade. The requirement of postoperative rescue analgesia is also decreased as the dose increased.

Keywords: Buprenorphine, bupivacaine, subarachnoid block

Introduction

Spinal anesthesia or sub-arachnoid block (SAB) is a form of regional anesthesia involving injection of a local anesthetic into the subarachnoid space, generally through spinal needle, usually 9 cm long (3.5 inches). The tip of the spinal needle has a point or small bevel. It is a safe, inexpensive, and commonly performed anesthetic technique for lower abdominal and lower limb surgeries. It is rapid in onset, provides good analgesia both intra-operatively and post-operatively [1].

The first spinal analgesia was administered in 1885 by James Leonard Corning (1855-1923), a neurologist in New York [2]. He was experimenting with cocaine on the spinal nerves of a dog when he accidentally pierced the dura mater. The first planned spinal anesthesia for surgery in man was administered by August Bier (1861-1949) on 16 August 1898, in Kiel, when he injected 3 ml of 0.5% cocaine solution into a 34-year-old patient in labor [3, 4].

Spinal anesthesia can be performed with a wide range of local anesthetic drugs. Using local

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anesthetics alone is associated with a relatively short duration of action.1 Postoperative pain control is a major problem with spinal anesthesia using local anesthetics alone, and thus early analgesic intervention is needed in the postoperative period. Bupivacaine is the local anesthetic most commonly used, although lidocaine, tetracaine, procaine, ropivacaine, levobupivacaine, and prilocaine may also be used. Various adjuvants such as morphine, Opioids like Buprenorphine, tramadol, fentanyl, sufentanil have been used to prolong the effect of spinal anesthesia [5].

Methodology

This study is designed to compare the effect of adding buprenorphine in varying incremental doses (30mcg.60mcg, 90mcg) to hyperbaric Bupivacaine in lower abdominal and lower limb surgeries.
After institutional ethical committee approval, 90 patients aged between 18-60 years undergoing lower abdominal and lower limb surgeries were selected. A detailed history, complete physical examination, and investigations were done for all patients. Informed consent was taken. The study population was divided into 3 groups with 30 patients in each group.

Inclusion criteria

1. ASA class I, II of both sexes.
2. Age between 18-60 years.
3. Informed consent of the patient.
4. BMI 18.5-24.9.

Exclusion criteria

1. ASA class III, IV patients.
2. Allergic reaction to local anesthesia.
3. Patients with coagulation disorders or on anticoagulant therapy.
4. Patient not willing to consent.
5. Local infection at the site of the proposed punctured the spinal block.

Materials

a) Inj. Hyperbaric Bupivacaine 0.5%.
b) Inj. Buprenorphine.
c) 23 G/25 G spinal (Quincke) needle.
d) Spinal tray.

After the ethical committee approval of our college, 90 ASA-I & ASA-II patients scheduled for lower abdominal and lower limb surgeries under spinal anesthesia were chosen for the study. A pre-anesthetic check-up was done one day before the surgery. Patients were evaluated for any systemic diseases and laboratory investigations were recorded. The procedure of SAB was explained to the patients and written consent was obtained. The preparation of patients included a period of overnight fasting. Patients were pre-medicated with Tab. Rantac 150 mg and Tab. Anxit 0.5mg H.S. In pre-operative assessment, patients were asked about any history of drug allergy, previous surgeries, or prolonged drug treatment. General, systemic examinations, airway assessment were performed and patients were asked to fast for a minimum of 6 hours before the operation. Patients also received Ranitidine 150

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mg orally the night before surgery and the following morning. All patients were clinically examined preoperatively when the whole procedure was explained. All patients underwent investigations to determine the following: hemoglobin concentration with Hematocrit, total and differential leukocyte count, erythrocyte sedimentation rate, platelet count, blood sugar, blood urea, creatinine, and coagulation profile.
A 12-lead electrocardiogram (ECG) and chest radiograph were also taken. On entering the patient into the operative room, standard intraoperative monitors were attached (ECG, SpO_2, NIBP) and baseline parameters were recorded using a multi-parameter monitor. Each subject is cannulated with an 18 G IV cannula and co-loading with ringer lactate at 15ml/kg/hour. The anesthetic procedure was standardized for all patients. The patient was in a seated position for a lumbar puncture at the L3 to L4 intervertebral space in median approach with a 23 G/25 G spinal (Quincke) needle using aseptic precautions.
Group 1: Received an intrathecal injection of 3 ml of 0.5% hyperbaric Bupivacaine with 30 mcg buprenorphine made into 0.5 ml with normal saline was taken with a syringe.
Group 2: Received an intrathecal injection of 3ml of 0.5% hyperbaric Bupivacaine with 60 mcg buprenorphine made into 0.5 ml with normal saline was taken with a syringe.
Group 3: Received an intrathecal injection of 3ml of 0.5% hyperbaric bupivacaine with 90 mcg buprenorphine made into 0.5 ml normal saline was taken with a syringe.

For blinding purposes, the final volume of the injected drug was kept constant at 3.5 ml for the 1,2and 3 groups and the solutions were prepared by junior doctors who are not related to this study. The intrathecal injection was given over 10 seconds. The patient was made to lie supine immediately after administering the drug Oxygen (6 L/min) was administered via a mask if the pulse oximeter reading was <90%. Any decrease in systolic blood pressure (SBP <100mmHg) or a drop >20% from baseline value was considered as hypotension and was treated with slow intravenous (iv) Mephentramine/ephedrine, which was repeated after 5 minutes if SBP was not corrected. Tachycardia was defined as an HR greater than 100 beats/minute and bradycardia when HR was less than 60 beats per minute.
The incidence of adverse effects like nausea, vomiting, respiratory depression, sedation, pruritus, bradycardia, and hypotension was recorded
Sensory testing was assessed by loss of pinprick sensation to 23G hypodermic needle and dermatomes levels were tested every two minutes until the highest level had stabilized Further testing was performed at 20min and after surgery was done postoperatively.
Motor blockade was assessed with the Bromage scale.
Bromage 0: Can move hip, knee, and ankle.
Bromage 1: Can move knee and ankle.
Bromage 2: Can move ankle.
Bromage 3: Unable to move hip, knee, and ankle. Bromage 3 is considered a motor blockade. Bromage 0 is considered as a motor reversal.

On achieving the highest sensory blockade level, surgery was allowed. The surgeon, patient, and the observing anaesthesiologist were blinded to the patient group. Data recorded are the time of onset of motor block, time of onset of sensory block, duration of motor block, duration of the sensory block, time of recovery of sensory block 2 segment regression from the peak level, incidence of adverse effects.

Results

Table 1: Time of onset of sensory block

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Time of onset of sensory block	3.2 ± 0.9	2.7 ± 0.7	2.4 ± 0.6	9.573	0.001

Group 1 containing 30 subjects shows time of onset of sensory level from the time of injection with mean of 3.2 min and SD of 0.9, Group 2 containing 30 subjects shows time of onset of sensory level from the time of injection with mean of 2.7 min and SD of 0.7, Group 3 containing 30 subjects shows time of onset of sensory level from the time of injection with mean of 2.4 mins and SD of 0.6 three groups are compared with f value of 9.575 and the P value of <0.001 which is statistically significant. The onset time of sensory block was less with 90 mcg group when compared with 30 mcg and 60 mcg groups.

Table 2: Time of onset of motor block

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Time of onset of motor block	5.7 ± 1.0	5.0 ± 1.2	4.1 ± 0.3	19.674	0.001

Group 1 containing 30 subjects shows time of onset of the motor block from the time of injection with a mean of 5.7 min and SD of 1.0 and Group 2 containing 30 subjects shows time of onset of the motor block from the time of injection with mean of 5.0 min and SD of 1.2, Group 3 containing 30 subjects shows time of onset of the motor block from the time of injection with mean of 4.1 min and SD of 0.3 three groups are compared with f value 19.6 and the P value is <0.000 which is statistically significant.

Table 3: Duration of sensory block

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Duration of sensory block	346.1 ± 51.9	545.2 ± 45.7	832.8 ± 61.6	618.963	0.000, Sig

Group 1 containing 30 subjects shows duration of the sensory block from time of injection with a mean of 346.1 min and SD of 51.9 and Group 2 containing 30 subjects shows duration of the sensory block from time of injection with mean of 545.2 min and SD of 45.7 and Group 3 containing 30 subjects shows sensory block from time of injection with mean of 832.8 min and SD of 61.6. Three groups are compared with f value 618.96 and the P value of 0.000 which is statistically significant so as the dose of the drug increasing the duration of the sensory block also increases.

Table 4: Duration of motor block

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Duration of motor block	203.8 ± 31.3	258.5 ± 41.1	289.7 ± 71.4	19.138	0.001, Sig

Group 1 containing 30 subjects shows duration of the motor block from the time of injection with a mean of 203.8 min with SD of 31.3 and Group 2 containing 30 subjects shows duration of the motor block from the time of injection with mean of 258.5 and SD of 41.1 and Group 3 containing 30 subjects shows duration of the motor block from the time of injection with mean of 289.7 with SD of 71.4 Three groups are compared with F value of 19.3 and the P value of <0.001 which is statistically significant. Duration was prolonged in 90 mcg group.

Table 5: Time of 2 segment regression from the peak level of sensory block

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Time of 2 segment regression from the peak level of sensory block	258.7 ± 52.6	276.5 ± 41.1	382.7 ± 74.1	95.282	0.000, Sig

Group 1 contained 30 subjects shows time of recovery from sensory blockade from the time of injection with a mean of 258.7 min with an SD of 52.6. Group 2 contained 30 subjects shows time of recovery of sensory blockade from the time of injection with a mean of 258.7

with an SD of 52.6. Group 3 contained 30 subjects shows time of recovery from sensory blockade from the time of injection with a mean of 382.7 min with SD of 74.1. Three groups were compared with f value 94.28 and the P-value of <0.00 which is statistically significant.

Table 6: Time of first complaint of pain

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Time of the first complaint of pain	469.3 ± 67.8	690.1 ± 52.8	916.7 ± 56.9	277.7	0.001, Sig

Group 1 contained 30 subjects shows time taken for the first complaint of pain from the time of injection with a mean of 469 min and SD of 67.8.
Group 2 contained 30 subjects shows time taken for the first complaint of pain from the time of injection with a mean of 690 min and SD of 52.8.
Group 3 contained 30 subjects shows time taken for the first complaint of pain from the time of injection with a mean of 916 min and SD of 56.9.
Three groups are compared with F value of 277.7 and the P value is <0.001 which is statistically significant. As dose increases time for the first complaint of pain also increases gradually.

Table 7: Adverse effects

Side effects	Group 1 n (%)	Group 2 n (%)	Group 3 n (%)
No complications	29 (96.7)	24 (80.0)	7 (23.3)
Hypotension	0	0	8 (26.7)
Itching	0	1 (3.3)	5 (16.7)
Nausea and vomiting	0	2 (6.7)	4 (13.3)
Shivering	1 (3.3)	3 (10.0)	0
Respiratory depression	0	0	6 (20.0)
Total	30 (100)	30 (100)	30 (100)

$\chi 2$ value=52.25df=10, P value, sig=0.000**,**

Adverse effects at the given time interval between group 1, 2 and 3 with a P value is <0.00 shows there is statistical significance. Group one containing 30 subjects shows 96% no complications observed group 2 containing 30 subjects shows 80% no complications, while group 3 containing 30 subjects shows 23% no complications while 8 subjects observed with hypotension (23.3%), 5 subjects with itching (26.7%), 4 subjects with nausea and vomiting (13.3%), 6 subjects with respiratory depression (20%).

Discussion

Spinal anesthesia is the most preferred regional anesthetic technique, and it is economical and easy to perform with thorough knowledge of the anatomy and physiology of the spinal cord and vertebrae.it gives rapid onset of anesthesia and analgesia and complete motor activity will be blocked with this technique.
The main aim of neuraxial anesthesia is to give adequate local anesthetic intrathecally and provide sensory and motor blockade to the lower limb and lower abdominal surgeries. Hyperbaric 0.5% bupivacaine was used most commonly as an intrathecal local anesthetic
Spinal anesthesia with bupivacaine is a well-known procedure for lower abdominal and lower limb surgeries. If proper pain relief is provided, ambulation of the patient in the postoperative period is faster providing faster recovery of the patient [6].
To prolong the duration of the neuraxial blockade and to shorten the onset time various adjuvants has been used like opioids such as buprenorphine, fentanyl, nalbuphine, α2 agonist like clonidine, dexmedetomidine, NMDA antagonists, magnesium, etc. postoperative

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analgesic requirement also reduced by the addition of adjuvants to local anesthetics.
Adjuvants are medications that work synergistically with local anesthetics to help enhance the duration and quality of analgesia in regional techniques. regional anesthesia has become more prevalent as evidence continues to show efficacy and enhancement of patient care, increased patient satisfaction, and improved patient safety practitioners in the perioperative setting need to not only be familiar with regional techniques but also the medications used for them. Regional adjuvants can improve patient safety, increase patient satisfaction and enhance clinical efficacy. Future studies and best practice techniques can facilitate standardization of regional anesthesia adjuvant dosing Based on its physicochemical and pharmacological profile, buprenorphine, a partial mu-opioid agonist that has been in clinical use for over 25 years, has been determined to be receptive to novel formulation technologies [7].
Parenteral, sublingual, and transdermal forms of buprenorphine are available. Buprenorphine's physiological and subjective effects, including euphoria, reach a plateau at greater doses, unlike complete mu-opioid agonists. This ceiling may reduce the opportunity for abuse and provide a larger safety margin.
Buprenorphine has been used for the treatment of acute and chronic pain, as a supplement to anesthesia, and behavioral and psychiatric disorders including treatment for opioid addiction. Prolonged use of buprenorphine can result in physical dependence. However, withdrawal symptoms appear to be mild to moderate in intensity compared with those of full mu agonists. Overdoses have primarily involved buprenorphine taken in combination with another central nervous system depressants [8].
Buprenorphine partial agonist, when added to bupivacaine, is known to increase the duration of analgesia at least 12-15 hours and it was not associated with any significant fall in bp or pulse rate. It may help in decreasing time to recovery and discharge can be achieved easily by administration of intrathecal buprenorphine and helps in increasing duration of anesthesia for prolonged surgeries.
Using buprenorphine as an adjuvant provides excellent selective spinal analgesia as it is a highly lipophilic known risk of respiratory depression associated with morphine is much less with buprenorphine because it is a partial agonist.
Postoperative pain continues to be inadequate and not effectively managed because of fear of opioids causing respiratory depression and or addiction. Even though opioids are a mainstay in postoperative pain management. Different drugs are used for postoperative pain relief but when opioids are used excellent pain relief was observed.
The addition of buprenorphine along with bupivacaine provides the significant duration of sensory and motor blockade and prolonged the duration. There is little data addressing the usage of this drug as an adjuvant for regional anesthesia.
The study has demonstrated that increasing the dose of buprenorphine with 0.5% bupivacaine in spinal anesthesia significantly decreases the time of onset of sensory and motor block and prolongs the duration of sensory, motor blockade. The requirement of postoperative rescue analgesia is also decreased as the dose increased [9].
Thomas W *et al.* in their study showed that there is a statistical difference in the onset of analgesia and that the addition of buprenorphine hastens the onset of action of bupivacaine.
Also assessed was the efficacy of buprenorphine as postoperative analgesia using Magill's classification. The high affinity of buprenorphine for narcotic receptors produces a longer duration of action [10].
Capogna *et al.* duration of analgesia is dose-dependent, and buprenorphine increased the duration of analgesia in our study [11].
Dubey R *et al.* in their study conclude that buprenorphine is superior for postoperative analgesia as compared to the control group. Hence low dose intrathecal buprenorphine offers convenient, simple, inexpensive, effective, and safe means of excellent postoperative analgesia [12].

Aravind paul Singh *et al.* concluded their study by Addition of buprenorphine and fentanyl as adjuvants to intrathecal 0.75% ropivacaine prolongs postoperative pain relief without causing any increase in the duration of the 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 [13].

Ravindran *et al.* studied varying doses of intrathecal buprenorphine as an adjuvant to hyperbaric bupivacaine and also compared postoperative analgesia between two groups has concluded that the addition of buprenorphine 40 mcg and 60 mcg to intrathecal bupivacaine prolonged the duration and quality of postoperative analgesia without adverse effects after cesarian section [14].

Meena Padmaja Gandhi *et al.* did a comparative study of intrathecal buprenorphine and fentanyl along with 0.5% hyperbaric bupivacaine for postoperative analgesia in fewer patients under spinal anesthesia, by adding Buprenorphine 60mcg to 1.6 ml of 0.5% Hyperbaric Bupivacaine has a comparable clinical onset of sensory and motor blockade, time for two-segment regression, total duration of the motor blockade but longer effective analgesia time when compared to Fentanyl 20 microgram added to 1.6 ml of 0.5% Hyperbaric Bupivacaine in patients undergoing LSCS under spinal anesthesia [15].

The onset of analgesia was significantly earlier due to the addition of buprenorphine mainly due to high lipid solubility and highest affinity for opiate receptors the major side effects of buprenorphine seen were drowsiness, though sedation can be considered desirable in the postoperative period. Though drowsy, all patients were easy arousable [16].

Conclusion

- The addition of buprenorphine as an adjuvant to 0.5% bupivacaine provided the prolonged duration of sensory and motor blockade when compared to 30 mcg group to 60 mcg and 90 mcg group got faster onset of action and duration.
- The time of onset of the blockade was almost similar for the 30 mcg and 60 mcg group but somewhat faster with the 90 mcg group.
- Hence it was concluded that the addition of incremental doses of buprenorphine to hyperbaric 0.5% bupivacaine for neuraxial anesthesia in the lower abdomen and lower limb surgeries prolonged the blockade and also prolonged the post-operative analgesia and the requirement of analgesics was reduced as dose increases but meticulous monitoring is required as dose increases.

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