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Intrathecal 0.5% hyperbaric bupivacaine with varying doses (30 µg Vs 60 µg Vs 90 µg) of buprenorphine in lower abdominal and lower limb surgeries; hemodynamic changes

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Abstract

Bupivacaine hydrochloride is 2-piperidenecarboxamide-1-butyl-N-(2, 6 dimethyl phenyl) monochloride, a monohydrate is a white crystalline powder that is freely soluble in 95% ethanol, soluble in water, and slightly soluble in chloroform or acetone. Local anesthetics mainly work on the cell membrane of the axon. The considerable transient rise in sodium ion permeability that's also required for impulse transmission is inhibited. Depolarization in response to the stimulus is thereby blocked, and the resting membrane potential is preserved. 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. Hemodynamics during the operative period was similar in the 30 mcg group and 60 mcg, but for the 90 mcg group incidence of hypotension and respiratory depression was observed for a few cases.

Keywords: Intrathecal 0.5% hyperbaric bupivacaine, buprenorphine, hemodynamic changes

Introduction

In 19575, bupivacaine was found. The most critical pharmaceuticals required in a basic health system are included in the WHO Model List of Essential Medicines. Bupivacaine is a generic medication that is reasonably priced. Because of the qualities of an acceptable onset, long duration of action, profound conduction blockade, and significant separation of sensory and motor blocks, bupivacaine has probably had the most influence on the practice of regional anesthesia. It appeared first in 1963 [1].

Bupivacaine hydrochloride is 2-piperidenecarboxamide-1-butyl-N-(2,6dimethyl phenyl) monochloride, a monohydrate is a white crystalline powder that is freely soluble in 95% ethanol, soluble in water, and slightly soluble in chloroform or acetone [2].

Local anesthetics mainly work on the cell membrane of the axon. The considerable transient rise in sodium ion permeability that's also required for impulse transmission is inhibited. Depolarization in response to the stimulus is thereby blocked, and the resting membrane potential is preserved [3].

Bupivacaine works in nerve axons in the peripheral nervous system in a similar way to other

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local anesthetics. It also disrupts the function of all organ systems in impulse conduction or transmission. The CNS, the autonomic ganglia, the neuromuscular junction and all types of muscle fibers are all affected. It provides surgical anesthesia at large doses, but a sensory block (analgesia) with the less significant motor block at lower levels. Following absorption, bupivacaine may generate CNS stimulation followed by depression, and it operates primarily on the myocardium in the cardiovascular system, decreasing electrical excitability, conduction rate, the force of contraction and ultimately cardiac arrest.

Buprenorphine, produced from thebaine, is a semisynthetic mixed opiate agonist-antagonist. Because buprenorphine is a partial mu-receptor agonist with a physiological ceiling affect the risk of overdose, abuse liability, and toxicity may be lower than with complete opioid agonists. The FDA initially approved the immediate-release parenteral version of buprenorphine in 1981, and it is used to treat moderate to severe pain in patients who require daily, around-the-clock, long- term opioid medication [4].

It works as a partial agonist and antagonist at the opioid receptor. It works to relieve moderate to severe pain in the postoperative period, as well as cancer, renal colic, and myocardial infarction. It has a high lipid solubility (five times that of morphine) and a strong affinity for opioid receptors, which prevents cephalad distribution and delayed breathing depression. The antagonistic actions of this medication reflect its ability to displace opioid agonists from m receptors [5, 6].

Methodology

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 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.

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

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

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Group 1: received an intrathecal injection of 3 ml of 0.5% hyperbaric Bupivacaine with 30mcg 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, 2 and 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.

Results

Table 1: Heart Rate

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Heart rate – 0 min	92.0 ± 15.4	81.9 ± 18.3	73.3 ± 9.9	11.649	0.01
Heart rate – 5 mins	87.6 ± 16.1	75.4 ± 12.2	72.6 ± 10.0	11.239	0.12
Heart rate – 10 min	81.7 ± 17.8	80.4 ± 13.6	72.6 ± 8.0	3.778	0.27
Heart rate – 15 min	75.2 ± 15.5	80.4 ± 13.6	81.9 ± 16.4	1.597	0.20
Heart rate – 30 min	69.8 ± 11.5	71.1 ± 12.4	68.4 ± 9.9	0.428	0.65
Heart rate – 45 min	67.1 ± 10.5	75.9 ± 12.3	74.5 ± 14.1	4.3	0.26
Heart rate – 1 hour	66.1 ± 12.6	70.6 ± 11.3	75.7 ± 14.0	4.26	0.65

Heart rate at the given time interval between group 1, group 2, and group 3 shows P value >0.05 shows no statistical significance.

Table 2: Respiratory effect

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Si
Respiratory rate - 0 min	19.5 ± 3.2	20.1 ± 3.3	21.3 ± 3.1	2.267	0.11
Respiratory rate - 5 mins	18.3 ± 3.8	18.3 ± 3.8	21.0 ± 4.1	4.847	0.11
Respiratory rate - 10 mins	17.5 ± 3.3	18.5 ± 3.5	17.5 ± 3.3	0.925	0.40
Respiratory rate - 15 mins	17.5 ± 2.9	18.4 ± 2.7	17.6 ± 3.0	0.976	0.38
Respiratory rate - 30 mins	16.8 ± 2.6	18.7 ± 3.2	16.8 ± 2.6	4.689	0.21
Respiratory rate - 45 mins	17.0 ± 2.8	18.7 ± 3.3	16.8 ± 2.6	2.068	0.13

The respiratory rate at the given time interval between group 1, group 2, and group 3 with a P value >0.005 shows no statistical significance.

Table 3: Systolic blood pressure

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Systolic blood pressure - 0 min	132.7 ± 10.4	113.8 ± 13.4	111.2 ± 10.5	30.97	0.10
Systolic blood pressure - 5 mins	121.9 ± 15.4	113.2 ± 15.4	110.4 ± 10.0	5.671	0.05
Systolic blood pressure - 10 mins	114.0 ± 14.0	126.8 ± 17.1	110.2 ± 11.8	10.77	0.26
Systolic blood pressure - 15 mins	111.3 ± 12.1	126.1 ± 17.3	107.3 ± 10.1	15.97	0.01
Systolic blood pressure - 30 mins	109.1 ± 10.4	112.7 ± 11.4	109.7 ± 9.0	1.062	0.35
Systolic blood pressure - 45 mins	107.0 ± 11.0	108.7 ± 10.8	109.8 ± 11.6	0.504	0.60
Systolic blood pressure - 1 hour	107.4 ± 9.8	109.8 ± 13.1	110.6 ± 9.8	0.681	0.50

Systolic blood pressure at a given time interval between group 1, group 2, and group 3 with a P value >0.005 shows no statistical significance.

Table 4: Diastolic blood pressure

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
Diastolic blood pressure - 0 min	80.4 ± 13.6	76.8 ± 12.1	79.5 ± 10.3	0.70	0.49
Diastolic blood pressure - 5 mins	76.8 ± 12.1	78.8 ± 10.9	78.7 ± 11.8	0.44	0.66
Diastolic blood pressure - 10 mins	64.8 ± 8.8	85.4 ± 15.2	77.8 ± 11.4	2.47	0.70
Diastolic blood pressure - 15mins	63.9 ± 7.6	85.2 ± 13.8	74.0 ± 8.9	0.38	0.74
Diastolic blood pressure - 30 mins	64.8 ± 8.2	78.5 ± 10.2	78.7 ± 8.4	0.67	0.54
Diastolic blood pressure - 45 mins	64.0 ± 8.1	77.9 ± 9.7	77.8 ± 9.2	0.50	0.68
Diastolic blood pressure - 1 hour	63.5 ± 6.8	78.3 ± 11.9	75.3 ± 12.9	0.52	0.98

Diastolic blood pressure at a given time interval between group 1, group 2, and group 3 with a P value >0.05 shows no statistical significance.

Table 5: Comparision of spo2

Mean ± SD	Group 1	Group 2	Group 3	F value	P value, Sig
SPO2 - 0 min	99.9 ± 0.4	99.9 ± 0.4	99.1 ± 1.4	9.55	0.000, Sig
SPO2 - 5 mins	99.9 ± 0.5	99.9 ± 0.5	99.6 ± 0.9	1.542	0.22, NS
SPO2 - 10 mins	99.9 ± 0.5	99.9 ± 0.5	99.9 ± 0.5	0.000	1.000, NS
SPO2 - 15 mins	99.7 ± 0.8	99.7 ± 0.8	99.7 ± 0.8	0.000	1.000, NS
SPO2 - 30 mins	99.7 ± 0.9	99.7 ± 0.9	99.7 ± 0.9	0.000	1.000, NS
SPO2 - 45 mins	99.7 ± 0.7	99.7 ± 0.7	99.7 ± 0.7	0.000	1.000, NS
SPO2 - 1 hour	100.0 ± 0.2	100.0 ± 0.2	100.0 ± 0.2	0.000	1.000, NS

Spo2 at 1 hour duration time interval with P value is <0.05 shows with statistical significance with fall of spo2 from 100% to 99.2% in group 3 the fall is not statistically significant

Discussion

Buprenorphine is a lipid-soluble drug due to rapid absorption into the spinal venous plexus there is minimal increase in spinal fluid concentration thus minimal risk of respiratory depression associated with rostral spread is seen so undergo close surveillance and monitoring for adequacy of breathing.

Common side effects following buprenorphine administration may include sedation, nausea and/or vomiting, dizziness, and headache. Respiratory depression may occur and may not be responsive to treatment with naloxone; however, as a mu-opioid partial agonist with a demonstrated ceiling on respiratory depression, buprenorphine may have a better safety profile compared to full mu agonists.

The intrathecal route has advantages of greater technical ease and a single injection producing pain relief of sufficient duration is always beneficial. Since the first clinical use of intrathecal opioids was by Wang *et al.* [7]

Postural hypotension and exaggerated sympathetic blockade are absent with the use of opioids which allows the parturient to ambulate early and the mother can breastfeed the child effectively. During pregnancy risk of thromboembolic disease is increased, as good pain relief postoperatively provided by intrathecal buprenorphine improves mobility thereby reducing the chances of the thromboembolic phenomenon.

Buprenorphine increases sensory block without affecting motor block and hemodynamic alterations.

Capogna *et al*. duration of analgesia is dose-dependent, and buprenorphine increased the

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duration of analgesia [8] Haribabur *et al*. concluded that the Addition of buprenorphine to the local anesthetic will improve the patient's compliance, prolonged postoperative analgesia is useful for the patient. Hence, this technique is useful for patients undergoing LSCS [9].

Fauzia A Khan *et al*. studied buprenorphine 30 mcg with hyperbaric bupivacaine 0.75% in spinal anesthesia observed normal hemodynamic parameters like blood pressure remained baseline and duration of sensory block is prolonged but there is associated increased incidence of nausea and vomiting in elderly patients [10].

Sandhya Gujar *et al*. concluded that old methods of providing analgesia with intrathecal buprenorphine have more advantages as analgesia provided is more than 12 hours which is very important in the postoperative period, and it is without risk of respiratory depression. Definite prolongation of both sensory and motor blockade of spinal anesthesia in clonidine and morphine groups. So that prolonged surgeries like orthopedics can be accomplished without the difficulties of epidural anesthesia [11].

Intrathecal adjuvants buprenorphine and clonidine, even in low doses, have been shown to provide effective post-operative analgesia with a lesser requirement of systemic analgesics in the postoperative period. A low dose of buprenorphine has better efficacy in terms of longer analgesic effect and decreased requirement of supplemental analgesics than a low dose of clonidine.

Intrathecal Buprenorphine 60µg gives adequate analgesia up to 818.9 ± 135min mins to which is significantly longer than that of intrathecal clonidine i.e. ± 41.9 min. Quality of analgesia was acceptable to patients in both groups though VAS assessment was better in the Buprenorphine group.

The use of opioids in elderly patients with impaired hepatic and renal function: Functional impairment of excretory organs is common in the elderly, especially with respect to renal function. For all opioids except buprenorphine, the half-life of the active drug and metabolites is increased in the elderly and in patients with renal dysfunction. It is, therefore, recommended that except for buprenorphine doses be reduced, a longer time interval be used between doses, and creatinine clearance be monitored. Thus, buprenorphine appears to be the top-line choice for opioid treatment in the elderly.

Buprenorphine is the only opioid demonstrating a ceiling for respiratory depression when used without other CNS depressants.

Although intrathecally administered combinations of 0.5 percent isobaric levobupivacaine (3 mL)–fentanyl (10 mcg) and 0.5 percent isobaric levobupivacaine (3 mL)-buprenorphine (60 mcg) have a good safety profile, the levobupivacaine–buprenorphine combination is superior in terms of prolonging sensory block and longer duration of postoperative analgesia As a result, in long- term procedures, a combination of levobupivacaine and buprenorphine may be preferable.

If buprenorphine (60 g) or dexmedetomidine (5 g) is added to intrathecal bupivacaine for TURP in senior male patients, the intraoperative and postoperative profiles are comparable, with an increase in the interval between the first and second analgesic doses

Addition of 60µg buprenorphine to hyperbaric Bupivacaine for spinal anaesthesia is a good alternative compared to 25µg Fentanyl. It provides longer duration of both sensory and motor blockade, good quality of both Intraoperative and postoperative analgesia. It had minimal side effects and better hemodynamic stability [12].

Conclusion

Hemodynamics during the operative period was similar in the 30 mcg group and 60 mcg, but for the 90 mcg group incidence of hypotension and respiratory depression was observed for a few cases.

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