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Comparison of Efficacy of Buprenorphine Adjuvant to Bupivacaine and Plain Bupivacaine in Spinal Anaesthesia for Lower Abdominal and Lower Limb Surgeries

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ABSTRACT

Background: Regional block induced by bupivacaine causes limited postoperative analgesia and adverse effects. Opioids as an adjuvant to bupivacaine can overcome this limitation. Buprenorphine, a potent lipophilic agonist-antagonist of opioid receptors has a long duration of action making it apt as an adjuvant for postoperative analgesia. The study attempted to assess intrathecal buprenorphine adjuvant to bupivacaine and compare it with intrathecal hyperbaric bupivacaine, in surgeries of the lower limb and abdomen.

Material and methods: The prospective randomized study was performed on 80 patients undergoing surgery of the lower limb and abdomen. Patients were arbitrarily divided into groups A and B. Group A received 3ml (15mg) of 0.5% hyperbaric bupivacaine with 0.5ml normal saline. Group B received 3ml (15mg) of 0.5% hyperbaric bupivacaine with 0.5ml (50µg) buprenorphine. The onset and duration of sensory and motor block were noted. Hemodynamic variables, respiratory rate (RR) and oxygen saturation (SpO2) were recorded at different time intervals intra and postoperatively. Post-operative pain, sedation score were also recorded.

Results: In group B the onset of sensory and motor block was significantly faster than group A (P=6e-14, P=1e-14) with the longer duration (P=1e-14, P=3e-14). Time for first rescue analgesia was significantly more in group B (P=1e-14). No significant changes in the RR and SpO2 (P=0.0126, P=4e-05, P=4e-09) was observed at different time intervals when compared in two groups. Patients of group B (92.5%) had excellent analgesia till 6 hours compared to 3 hours in group A (7.5%) and it was statistically significant.

Conclusion: Buprenorphine in a dose of 50µg is a valuable adjuvant to bupivacaine in spinal anaesthesia.

Keywords: Bupivacaine, Buprenorphine, Opioid analgesics, Spinal anaesthesia

INTRODUCTION

Spinal anaesthesia (SA) is commonly used for surgeries of the lower abdomen and lower limbs with bupivacaine being the local anaesthetic agent.[1, 2] However, use of bupivacaine alone in spinal anaesthesia is associated with a shorter duration of action translating to difficult postoperative pain control.[3] Moreover, use of bupivacaine alone in SA produce associated effects such as bradycardia and systemic hypotension.[2] Therefore SA is used with additive drugs to reduce the local anaesthetic requirement, minimize side effects and prolong duration of anaesthesia.[4, 5]

Buprenorphine is a centrally acting lipophilic analog of alkaloid thebaine. It possesses analgesic action at spinal and supraspinal levels.[6] It is reported that buprenorphine increases duration of analgesia to 12-15 hours, without significant effect on blood pressure (BP) and heart rate (HR).[7, 8] Although data exists

regarding use of buprenorphine as an adjuvant to bupivacaine in patients of lower abdominal and lower limb surgeries, the study is aimed to assess the efficacy of 50 µg intrathecal buprenorphine as an adjuvant to bupivacaine and compare it with intrathecal hyperbaric bupivacaine in lower abdominal and lower limb surgeries in terms of onset, duration of action, hemodynamic effects and observe for any side effects or complications.

Material and methods

The prospective randomized study was carried out after approval of the institutional ethics committee. The calculated sample size, n=74 included n=37 for each group. Upon obtaining informed consent, 80 patients (ages 18 to 60 years) of ASA grade I and II scheduled for elective surgeries of lower abdominal, perineal, and lower limbs were included. A sealed envelope simple random sampling procedure allocated the subject into two groups, Group A (n=40) and Group B (n=40). Patients with allergic to the anaesthetic drug, bleeding disorder, dermal infection, neurologic disorders, spinal deformities, and severe cardiopulmonary diseases were excluded from the study. Thorough preoperative investigations were performed prior to the surgery. Patients of both the groups were advised fasting for 6 hours and received diazepam 10mg and ranitidine 150 mg orally as premedication a night before and in the morning on the day of surgery. In the operation theatre, baseline respiratory rate (RR), HR, non-invasive blood pressure (NIBP), ECG, pulse oximetry (SPO2) monitors were attached and baseline parameters noted and were continuously recorded. Patients were preloaded with Ringer lactate. Subarachnoid block at the L3-L4 intervertebral space was performed using a 25-gauge Quincke spinal needle with the patient in the sitting position under all aseptic precautions. After the clear cerebrospinal fluid tap, the drug was injected into the subarachnoid space. Group A (n=40) received 3ml (15mg) of 0.5% hyperbaric bupivacaine with 0.5ml normal saline. Group B (n=40) received 3ml (15mg) of 0.5% hyperbaric bupivacaine with 0.5ml (50µg) buprenorphine. Post anaesthesia vital parameters such as RR, HR, NIBP, and SpO2 at 0, 15, 45, 90, 180, 360, 600, and 1200 minutes were recorded. Pin-prick method was used to test sensory block. The onset and duration of sensory block, the highest level of sensory block and the time for two dermatomal segment regression of sensory level were recorded. The onset of sensory block was determined from the time of injection of the drug into subarachnoid space to loss of sensation tested by the pin prick method. The motor block was quantified using the modified Bromage score (where grade 0 for full flexion of knee and feet, grade 1 – just able to flex knees, full flexion of feet, grade 2 – unable to flex knee, but some flexion of feet possible and grade 3 – unable to move legs or feet).[9] The onset and duration of motor block were recorded. Post-operative pain was quantified using Magill's score characterized by (0-no pain, 1-slight pain, 2-discomfort, 3-unbearable pain, and 4-excruciating pain) at 2 hours, 4 hours, 6 hours, 10 hours, and 20 hours.[10] Sedation was evaluated using the Ramsay sedation scale of (1-anxious, agitated, restless, 2-co-operative, oriented, tranquil, 3-responds to commands only, 4-brisk response to a light glabellar tap or loud noise, 5-sluggish response to a light glabellar tap or loud noise, and 6-no response).[11] Intramuscular diclofenac sodium 75mg was given as a rescue drug when Magill's score was >3.All patients were monitored in the postoperative period for 24 hours and observed for any side effects or complications such as bradycardia, hypotension, drop in RR or oxygen saturation(SPO2),oversedation,prupritus,nausea vomiting , postdural puncture headache/ backache or any other.

Statistical analysis

Data were analysed using R Studio V 1.2.5001 software. Continuous variables were expressed in mean ± standard deviation (Mean ±SD) whereas, categorical variables were expressed in percentage and frequency. Wilcoxon-sign-rank test and independent-sample t-test were used to find the difference between mean. Chi-square test of association with Yate's continuity correction used to find the difference between the scores. $P<0.05$ was considered statistically significant.

Results

The mean age of the cases (n=80) was 43.15±12.55 years. Baseline data of the cases in both groups were similar. **Table 1**.

Time taken for onset of both (sensory and motor) blocks was significantly less in group B ($P=6e^{-14}$ and

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$P=1e^{-14}$) with increased duration of sensory and motor block ($P=1e^{-14}$ and $P=3e^{-14}$) The time for first rescue analgesia was significantly more in group B (593.5±63.2 min) than in group A (185.3±79.4 min) ($P=1e^{-14}$). **Table 2.**

In group B patients, a significantly increased HR was observed at 15-minutes ($P=7e^{-07}$), 90-minute interval (P=0.0046) and decreased at 600-minute ($P=4e^{-05}$) than group A patients. Whereas, difference in systolic (SBP) and diastolic blood pressure (DBP) were insignificant at any time interval in both the groups. (P>0.05)**Graph-1**

At 5 % level of significance, there is no statistically significant mean difference of RR and

Oxygen saturation (SPO2) in Group-A & Group-B. (P<0.05)**Graph -2**

Significantly higher number of group B patients had Ramsay scale score 2 (co-operative, oriented and tranquil) than group A patient at 45 and 180 minutes (P=0.0005 and P=0.01) but, at 600 minute score 2 was more in group A (P=0.0005). In group B less Magill's pain score was observed with increased duration of analgesia than group A at all-time intervals (P=0.0005). Rescue analgesics were given when the Magill's score was >3 rescue drug was given. **Graph -3**

Graph 4 Shows the incidences of associated complications bradycardia, hypotension, pruritus, nausea vomiting, headache, retention of urine. Incidence of nausea and pruritus was significant with group B patients (P<0.05)

Discussion

Local anaesthesia induced subarachnoid block produces limited postoperative analgesia and deleterious effects such as bradycardia and hypotension. Along with the local anaesthetics, opioids as adjuvants can overcome this limitation.[7] Buprenorphine, a potent lipid-soluble agonist-antagonist of opioid receptors with a long duration of action is apt as an adjuvant for postoperative analgesia.[12, 13] Different doses of buprenorphine ranging from 45µg to 75µg have been used as an adjuvant to bupivacaine in spinal anaesthesia.[4, 7, 14, 15]

The study aimed to assess intrathecal buprenorphine (50µg) adjuvant to bupivacaine and compare it with intrathecal hyperbaric bupivacaine in lower abdominal and lower limb surgeries. In this study, the average age of the patients was 43.15±12.55 years. Patients of both the groups were similar in terms of demographical characteristics such as age, weight and body mass index which was similar to the previous report.[2] Early-onset of analgesia in buprenorphine attributes to high lipid solubility along with higher affinity towards opioid receptors.[16] Here, onset of sensory ($P=6e^{-14}$) and motor block ($P=1e^{-14}$) was significantly faster in group B than group A which is similarly produced by 60µg bupivacaine.[4] This implies, low dose of buprenorphine is enough to produce faster onset. Analgesia duration using 60µg buprenorphine has been documented at 8.2 hours.[16] Similarly, here it was 6 hours and 12 hours in patients administered with 45µg and 60µg of buprenorphine.[7] Furthermore, study of Jejani et al. showed significant increased duration of motor block in buprenorphine (45µg) treated group than control group but no difference was showed in duration of sensory block.[17] In this study significantly increased duration of motor and sensory block was observed in group B than A. The difference in the findings regarding duration of sensory block may be due to the difference in buprenorphine dosage. These findings indicated that buprenorphine adjuvant to bupivacaine produces a dose-dependent prolonged duration of analgesia and duration of sensory block due to a higher affinity towards mu receptors and slow dissociation from the receptors.[7]

Opioid receptors in spinal cord lamina are numerous therefore, direct interaction of opioids to these receptors causes intense analgesia.[18] Intrathecally it acts by inhibiting release of substance P, causes inhibition of nociceptive impulses.[19] After induction of spinal anaesthesia, the time for first rescue analgesia was significantly high in group B (593.5±63.2 min) than group A (185.3±79.4 min) ($P=1e^{-14}$) similar to Dixit.[16] The local anaesthetic causes bradycardia due to sympathetic blockade.[4] Similarly, in group A patients the heart rate was significantly decreased at 15-minutes ($P=7e^{-07}$), 90-minute interval (P=0.0046) and 600-minute ($P=4e^{-05}$) compared to group B patients. This results follow the findings of Vardhan PH et al.[20] Whereas, the study of Amitha S. et al showed no difference between hemodynamic variables (HR, BP) of patients treated

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with 30µg buprenorphine and 5µg dexmedetomidine as an adjuvant to bupivacaine.[21]

Respiratory depression, is an important adverse effects associated with opioids results from vascular uptake by epidural or subarachnoid venous plexuses and circulation to brainstem respiratory center.[22] The study showed a significantly increased respiratory rate at 360, 600, and 1200 minutes and decreased SpO_2 in group B patients. Results of Shaikh SI et al. and Borse YM et al. contrasted due to the difference in considered time intervals.[23, 24] Other complications such as headache, urinary retention, hypotension, bradycardia, nausea and pruritus were similar in both the groups. Ramsay sedation scale was used to assess sedation.[11] A significantly higher number of group B patients had Ramsay score 2 than group A patients at 45 and 180 minutes (P=0.0005 and P=0.01) but at 600 minute score 2 was more in group A (P=0.0005) similar to Ravindran R. et al.[7] In previous studies the incidence of sedation was common in a patient treated with 60µg of buprenorphine.[7] Another study showed a mild sedative effect which is desirable in the perioperative period.[16] Furthermore, Magill's score was used to assess postoperative pain at different time intervals.[10] Majority patients of group B (92.5%) had excellent analgesia till 6 hours compared to 3 hours in group A (7.5%) similarly, at all-time intervals significantly increased duration analgesia was observed in group B compared with group A (Table 4). These findings are similar Dixit S.[16]

Buprenorphine (50µg) adjuvant to bupivacaine produces rapid onset and long-lasting duration of sensory and motor block with minimal hemodynamic and respiratory complications. It produces less sedation and excellent analgesia. These findings imply that buprenorphine at the dose of 50µg can be safely used as an adjuvant to the bupivacaine. The limitations of the study were the small sample size and comparison of its efficacy with the other opioids as well as different doses of buprenorphine was not assessed. A comparative study with various doses of buprenorphine along with a large sample size of the lower lumbar, lower abdominal, and obstetrics surgeries is the further recommendation of the study.

Conclusion

Buprenorphine (50µg) adjuvant to bupivacaine produces rapid onset and longer duration of sensory and motor block with minimal effect on hemodynamic and respiratory rate. Thus buprenorphine can be used as adjuvant to bupivacaine in spinal anesthesia.

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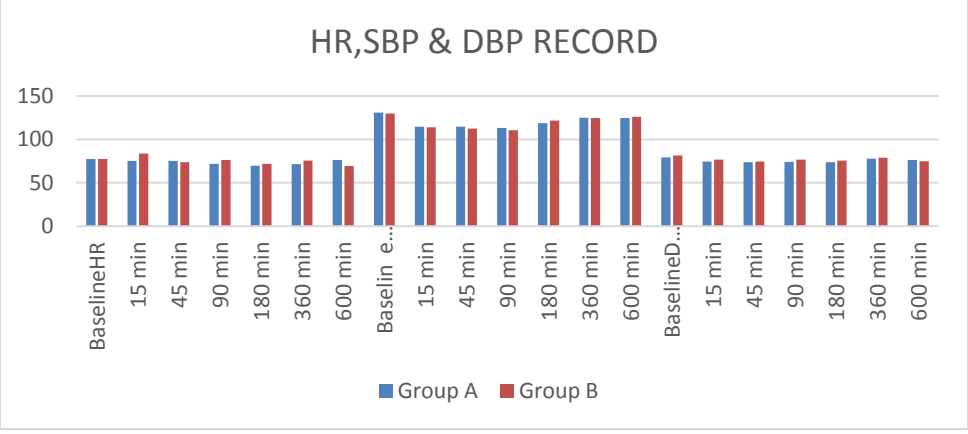
Table 1: Demographical characteristics of the patients

Characteristics	Group A	Group B	P-value
Age (years)	42.7±12.5	43.6±12.16	0.7791
Weight	54.45±7.76	54.3±7.9	0.9265
BMI	20.88±1.4	21.19±1.57	0.4406
Sex (M: F)	20:20	18:22	0.823

Table 2: The Neuro-axial Block characteristics-onset, duration of action & time of first rescue analgesic

The onset and duration of action	Group A	Group B	P-value
The onset of sensory block (seconds)	358.5±48.7	178.48±48.1	$6e^{-14}$
The onset of motor block (seconds)	834±89	434.3±90.4	$1e^{-14}$
Duration of sensory block (minutes)	167.4±26.7	510.5±30.9	$1e^{-14}$
Duration of motor block (minutes)	147.5±26.7	220.5±28	$3e^{-14}$
Time of 1st Rescue Analgesic	185.3±79.4	593.5±63.2	$1e^{-14}$

Graph -1: Haemodynamic variations in two groups (HR.SBP,DBP).



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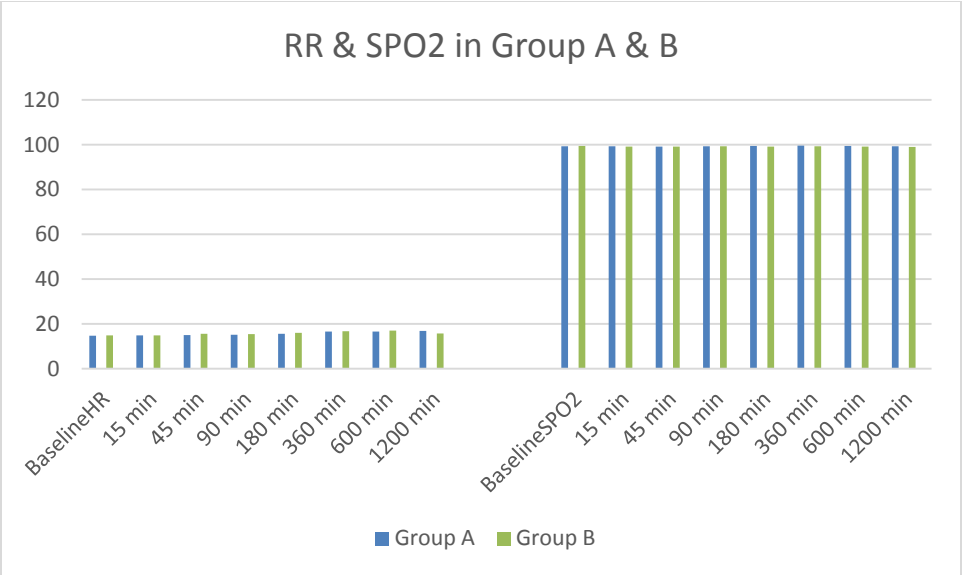
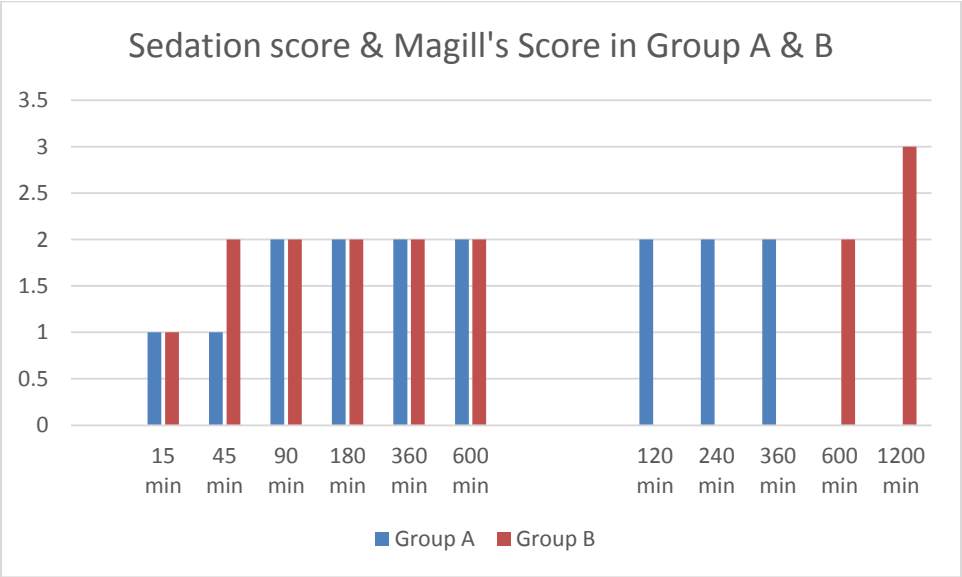
Graph-1 At 5 % level of significance, Heart Rate (HR) variation is statistically significant at 15 min., 90 min. and 600 min. Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) is not statistically significant.

Graph-2: RR-Respiratory Rate, SPO2-Oxygen Saturation



Graph -2 At 5 % level of significance, there is no statistically significant mean difference of respiratory rate and Oxygen saturation (SPO2) in Group-A & Group-B.(P<0.05)

Graph 3: Sedation Score & Magill's Score in two groups.



Graph 3: Significant difference in sedation scale and Magill's Score in Group B patients.

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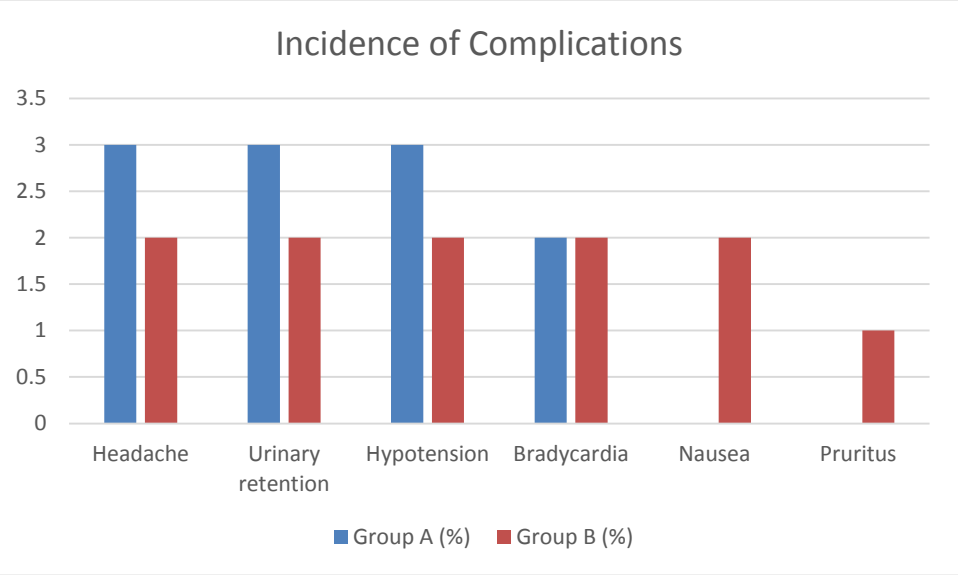
Graph 4: Distribution of complications by Proportion Test, here we found insignificant results except incidence of nausea.



LEGENDS FOR TABLES & GRAPHS

Table 1: Demographical characteristics of the patients

Table 2: The Neuro-axial Block characteristics-onset, duration of action & time of first rescue analgesic

Graph -1: Haemodynamic variations in two groups (HR.SBP,DBP).

Graph-1 At 5 % level of significance, Heart Rate (HR) variation is statistically significant at 15 min., 90 min. and 600 min. Systolic Blood Pressure (SBP) and Diastolic Blood Pressure (DBP) is not statistically significant.

Graph -2 At 5 % level of significance, there is no statistically significant mean difference of respiratory rate and Oxygen saturation (SPO2) in Group-A & Group-B.($P<0.05$)

Graph 3: Sedation Score & Magill's Score in two groups.

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