Section: Anesthesiology

Original Research Article

AN OBSERVATIONAL STUDY TO EVALUATE NALBUPHINE HYDROCHLORIDE AND CLONIDINE HYDROCHLORIDE AS AN ADJUVANT TO HYPERBARIC BUPIVACAINE FOR SPINAL ANAESTHESIA IN LOWER LIMB SURGERIES

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Abstract

Background: Regional anaesthesia is the most commonly used technique for lower limb surgeries as it is very economical & easy to administer. Its main disadvantage is short duration of action. But still spinal anaesthesia are on increasing trends due to their advantage of postoperative analgesia when used with intrathecal adjuvants. The aim of the study is to evaluate the onset and duration of sensory & motor blockade, hemodynamic response & duration of post-operative analgesia when nalbuphine & clonidine is used as an adjuvant to bupivacaine in spinal anaesthesia for lower limb surgeries. **Materials and Methods:** This observational study includes 60 patients of ASA grade I,II who are posted for lower limb surgeries. Group BN received 2mg(0.2ml) of nalbuphine & Group BC received 30 µg (0.2ml) of clonidine, added to 15 mg 0.5% hyperbaric bupivacaine. **Result:** The time of onset of sensory blockade was earlier inpatients of group BN (4.4 ± 0.77 min. 5.8 ± 1.05 min. Grp BC, p=0.001) and the Onset of motor blockade was earlier in patients of group BN (7.28 ± 0.58 vs 8.08 ±1.20, Grp BC p=0.018). Duration of analgesia is 155 min. vs 245 min. in grp BN, BC repectively. The time to first rescue analgesia inpatients receiving intrathecal clonidine was significantly delayed (282.16± 8.5 vs 244.3 ± 10.42). **Conclusion:** Clonidine was to be more effective & provide longer duration of analgesia and superior as compared to Nalbuphine as an adjuvant to enhance effect of bupivacaine for lower limb surgeries.

INTRODUCTION

The most popular regional anaesthetic technique for the lower limb surgeries is spinal anaesthesia. However, local anaesthetic drugs used alone for spinal anaesthesia do not have the advantage of prolonged postoperative analgesia.[1] For prolongation of postoperative analgesia, reduction of local anaesthetic dose and side effects, various adjuvants, like opioids, midazolam, alpha-2 agonist, and ketamine, have been used along with the local anaesthetics inneuraxial blockade.[2] The surgical stress response peaks during postoperative period and the major effects on all the systems. A pain free and stress-free postoperative period help in early mobilization and recovery, thereby reducing morbidity and mortality. The technique of local anaesthetic along with intrathecal adjuvant administration has been found to provide superior quality of analgesia in variety of surgical procedure.[3]

Nalbuphine is highly lipid soluble, semi-synthetic opioid drug with agonist-antagonist properties. It acts as antagonist at µ-receptors and agonist at κ-receptors.[4]

Its affinity tok-opioid receptors result in analgesia, sedation, and cardiovascular stability with minimal respiratory depression. It provides reasonably potent analgesia to visceral nociception. Intrathecal opioids are transported supra-spinally by bulk cerebrospinal fluid (CSF) flow where they modulate descending inhibitory pain pathways, and a small amount of opioid diffuses into the epidural space with subsequent systemic absorption resulting in centrally mediated analgesia.[5,6]

Clonidine, α2 adrenoceptor agonist, is lipid soluble and can easily penetrates the blood-brain barrier to

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provide effective and extended analgesia by binding to presynaptic C-fibers and postsynaptic dorsal horn neurons, but associated with side effects of hypotension and bradycardia due to decrease sympathetic outflow. The prolongation of sensory and motor block may result from synergism between bupivacaine and clonidine.[7]

The present study was done to evaluate nalbuphine hydrochloride and clonidine hydrochloride as an adjuvant to hyperbaric bupivacaine for spinal anaesthesia in lower limb surgeries.

MATERIALS AND METHODS

We undertook an observational study which was conducted in department of Anaesthesiology, Gandhi medical college, Bhopal. Institutional ethics committee approval was obtained. The study included 60 patients admitted for lower limb surgeries under subarachnoid block.

Inclusion Criteria

Patients of ASA grade I & II, Age group of 18-60 years, Patient undergoing elective lower limb surgery, patient with informed written consent.

Exclusion Criteria

Patient refusal, ASA grade III& IV, patients on anti-coagulation treatment (INR >1.5), patients with infection at the site of injection, with coagulopathy, bleeding diathesis, congenital abnormalities of lower spine & meninges, spine/neurological deformity.

As per the choice of anaesthesiologist, patients were allocated into 30 patients in each group. Group BN recieved 15mg (3ml) of 0.05% bupivacaine (H) with 2mg(0.2ml) nalbuphine Hcl Group BC recieved 15mg (3ml) of 0.05% bupivacaine (H) with 30 µg(0.2ml) clonidine Hcl After thorough pre-anaesthetic check-up & a common standard anaesthetic regimen was followed for all the patients who included lignocaine sensitivity test. Relevant patient data recorded during the initial assessment & all routine investigation was done. BMI was noted, NBM (nil by mouth) status was confirmed &anti-aspiration prophylaxis was taken. Patient were properly explained on the method of sensory & motor assessments & Visual analogue score.

On the day of surgery, after the pre-operative examination, patient was shifted to the operating theatre. All ASA standard monitors NIBP cuff, pulse oximetry, ECG were attached. Before administration of subarachnoid block, vital parameters were recorded. Then by using 18 G cannula, preloading with ringer lactate 10- 15ml/kg. Local anaesthetic sample was prepared. Patient was put on sitting position. Skin and subcutaneous tissue was infiltrate with 2 ml of 0.2% lignocaine at L3-L4 level. After that subarachnoid block was performed by using 23 G Quincke's needle in the midline at L3-L4 level. The patient received either one of the drug solution which is mention above. Then patient was placed in supine position.

Parameters monitored

Sensory Block Characteristics: Sensory block was evaluated by assessing the peak level dermatome (assessed by loss of pinprick sensation starting at the L1 dermatome and graded according to Gromley and Hill 1996: Normal sensation-0, Blunted sensation- 1, No sensation-2 with grade 2 being considered as the onset of the sensory block) using 23G hypodermic needle.

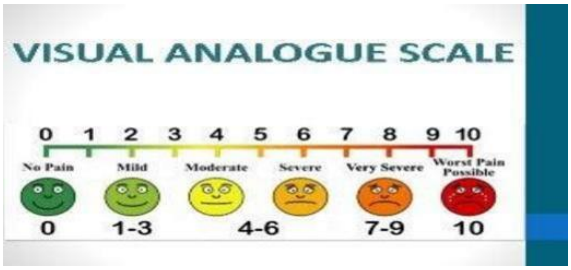
The sensory block characteristics such as onset of the block (sensory block atL1), peak block height, time to reach peak block height, time to reach readiness for surgery (sensory block ≥ T10), time for regression of two segments, time for regression to L1, and time for complete regression to S2 were recorded.

Motor Block Characteristics: Assessment of motor block was done using a modified Bromage Scale.[8] Modified Bromage scale Score 0: No motor block Score 1: Inability to raise extended leg; able to move knees and feet Score 2: Inability to raise extended leg and move knee; able to move feet Score 3: Complete motor block.

The motor block characteristics like: Time to reach modified Bromage score of 3, modified Bromage score at the end of the surgery, and time to reach modified Bromage score of 0 were recorded.

Additional data such as duration of surgery, duration of stay in the Post Anesthesia Care Unit, time to ambulateand time of first postoperative analgesic requirement were recorded.

Time for motor block to regress to modified Bromage Grade I was noted. Duration of analgesia (time from the intrathecal drug administration to the patientstill the patients visual analog scale [VAS],[9] score >3) was noted. All the patients were elaborated about the VAS scoring system strip which consisted of a 10-cm horizontal paper strip with two endpoints labeled "No pain" and "Worst pain ever." Patients were asked to mark on the strip at a point that corresponds to the level of pain intensity they felt when they complained pain..Time for first rescue analgesia was recorded and injection paracetamol 1gm IV was given as rescue analgesia.



A modified Aldrete score was used for discharge criteria from PACU, & Patients were discharged from PACU after achieving a modified Aldrete score ≥ 9-Regular monitoring of BP, PR, Saturation was done at 5, 10, 15, 30, 45, 60, 90, and120 min intervals and postoperatively at 30 min interval until requirement of rescue analgesia.

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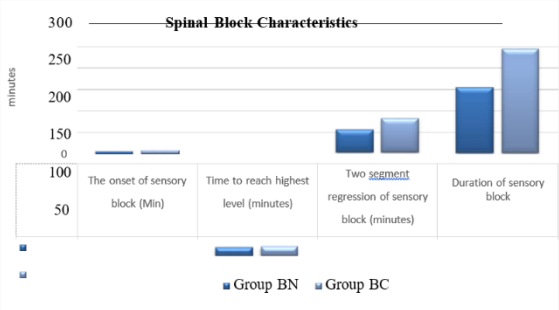
Statistical Analysis: At the end of study, all the data were compiled in a tabulated manner and result were expressed as Mean and Standard Deviation. The categorical variables (qualitative data) like
ASA grading were analyzed with Chi-Square test (for nominal data). The continuous variable (quantitative data) like, age, height, weight, blood pressure, heart rate were analyzed with unpaired Student'st-test. For significance, p <0.05 = significant, p >0.05 = not significant.

RESULTS

In the present study, demographic profile for age, weight, height, ASA grading and duration of surgery were comparable among both the group of which all of them completed the study with no drop outs [Table 1].



Onset of sensory blockade was 4.04 ± 0.52 min in patients of Grp BN & 5.8 ± 0.5 min in Grp BC (p=0.0001). Meantime for two segment regression of sensory block was 55 ±3.0 min in Grp BN and 82.4 ±6.09 min in patients of Grp BC, Meantime for complete regression of sensory block was 271 ±3.0 min in patients of Group BN & 221 ±6.00 min in patients of Group BC & Mean duration of sensory block was 271.15 ± 6.45 min with nalbuphine and 221 ± 8.50 min with clonidine and it also showed statistically significant difference (p=0.0001).
The meantime for onset of motor blockade was 7.28 ± 0.58 min in patients of Group BN & 8.08 ± 1.2 min in patients of Group BC with statistically significant difference(p=0.0018).
Mean duration of complete motor block was 143.43±12.4 min in patients with Group BN and 209.5 ±18.5 min in patients with Group BC with statistically significant difference (p=0.0001) Time to administer 1 st rescue analgesia & time for unassisted ambulation is earlier in (Group BN as compared to Group BC) 75.05±15.75 vs 80.85 ±13.35 respectively [Table 2].
Hemodynamic Profile: The hemodynamic parameters of mean blood pressure, mean heart rate, respiratory rate and oxygen saturation at baseline were comparable. After 5 min of subarachnoid block, the mean heart rate and mean systolic blood pressure showed gradual decline inpatients of both group till 15 min with comparable values. Later on, the mean heat rate and mean blood pressure became stable inpatients of both groups with no statistically significant difference.
Figure 2: Mean Heart Rate
Incidence of hypotension and bradycardia during the intraoperative period was minimal and did not require any medical intervention. No clinically significant incidence of respiratory depression, shivering, nausea or vomiting was observed in any patient during the study period. None of the patient needed supplemented analgesia during surgery.
Figure 3: Mean MAP

Table 1: Demographic variable of patients

Patients characteristics	GROUP BN	GROUP BC	P-VALUE
Age (years)	48.96 ± 9.02	45 ±9.15	0.101
Weight(kg)	62.43 ±5.3	63.2 ±5.5	0.655
Height(cm)	164.6±5.37	162.2±6.58	0.128
ASA Grade I	23	22	0.640
ASA Grade II	7	8	

Sensory and Motor Blockade - Graph 1

Table 2: Showing Motor Blockade Characterstics & PACU Observations

PARAMETER	GROUP BN	GROUP BC	P VALUE
Onset of motor block (min)	7.28 ± 0.58	8.08 ± 1.2	0.0018
Duration of motor block (min)	143.43 ± 12.4	209.5 ± 18.5	0.0001
Duration of stay in PACU(min)	55.20±16.00	46.62 ±7.80	NS
Time to administer 1strescue analgesia (min)	244.3 ±10.42	282.16 ±8.5	0.0001
Time for unassisted ambulation (min)	75.05±15.75	80.85 ±13.35	NS

DISCUSSION

Neuraxial anaesthesia is more popular for lower limb surgeries. The duration of subarachnoid block can be improved by using intrathecal adjuvants in the form of opioid or non-opioid drugs, which act synergistically with local anaesthetic agents to intensifying the sensory block without increasing the level of sympathetic block.
By using intrathecal adjuvants in form of opioid analgesics or non-opioid drugs, the duration of subarachnoid block can be improved because adjuvants act as synergistically with local anaesthetic agents and intensifying the sensory block without increasing the level of sympathetic block as they act independently via different mechanism.

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Demographic data (age, weight, height) and ASA grading and duration of surgery were comparable in this study.

Sensory Block Characterstics: The meantime for onset of sensory blockade was 4.04 ± 0.52 min in patients of Group BN & 5.8 ± 0.5 min in patients of Group BC (p=0.0001).

Duration of analgesia is 155 min (Group BN).& 245 min (Group BC) when bupivacaine was used in combination with nalbuphine and clonidine, respectively. These results coincide with results of Chopra and Talwars study.[10]

The total duration of analgesia in nalbuphine group was less when compared to Fareed Ahmed et al,[11] in which the total duration of analgesia was 199.8 ± 25.9 min. The present study demonstrated that clonidine produces a longer duration of postoperative analgesia when compared tonalbuphine.

The time duration for the two segment regression of sensory level in nalbuphine group was 55 min as compared to 82 min in clonidine group which was statistically significant. Sethi et al,[12] found that addition of 1 µg/kg of clonidine to bupivacaine prolonged the time for two segment regression. This prolongation of two segment regression and time to first rescue analgesia was supported by Fareed Ahmed. et al,[[11] and Tiwarietal.[13]

Motor Block Characterstics: In the present study faster onset of sensory &motor block was comparable between nalbuphine & clonidine Group. Onset of Motor block (7.28 ± 0.59 min.) Nalbuphine and (8.08 ± 1.2 min.) in clonidine group, while Bansaletal.[7] demonstrated faster onset of sensory and motor block with nalbuphine.

The duration of motor block was 143.43 ± 12.4 & 209.5 ± 18.9 min in patients of nalbuphine, and clonidine group, respectively. Our results demonstrate that the duration of motor block is longer in clonidine Group.

Degree of sedation was comparable between two Groups. Time for 1st analgesic requirement (0.0001) & early ambulation is seen earlier in Nalbuphine Group.

Time for 1 st rescue analgesia requirement is 244.3 ±10.42 min. (Grp BN) Vs 282.16 ±8.5 min, (Grp BC) (stastically significant) & time for unassisted ambulation is shorter in Group BN 75.05±15.75 min as compared to Group BC 80.85 ±13.35 min.

VAS in nalbuphine group and clonidine group were comparable, but use of rescue analgesia was more in thenalbuphine group (statistically significant). from the present study we state that addition of clonidine and nalbuphine intrathecally to hyperbaric bupivacaine significantly decreases the total dose of rescue analgesic given in 24 h postoperatively. The present study results coincides with study done by Culebraset al,[14] & Chopra and Talwar.[10]

The addition of clonidine and nalbuphine intrathecally to hyperbaric bupivacaine significantly decreases the total dose of rescue analgesic given in 24 h postoperatively. (IV Paracetamol 1 gm was given as rescue analgesic when patients experienced pain equivalent to VAS score>3.) The present study inference coincides with that established by Chopra, Talwaretal.[10]

In our study clonidine group had better post operative analgesia compared to both nalbuphine and control group. Boussofaraetal,[15] & showed that intrathecal clonidine improved the postoperative VAS as compared to the control group.

Hemodynamic Parameters & Adverse Effects: The haemodynamic parameters like heart rate and blood pressure were monitored peri- operatively. In present study, the baseline heart rate was 90.77±7.45 bpm,in nalbuphine group and 95.67± 6.04 bpm in the clonidine group, respectively. Heart rate was maintained for the first 30 minutes. However, beyond 25-30 minutes, there was significant reduction in heart rate more in the clonidine group.

The present study demonstrated no clinically significant difference in hemodynamic parameter and adverse effects (hypotension, bradycardia, nausea, vomiting and pruritus) among the groups. Low dose clonidine is not associated with hemodynamic instability as evidence by Dutta et al,[16] Reduced incidence of opioid – related side effects in nalbuphine group is supported by Mukherjeeetal.[17]

There is no clinical significant difference in hemodynamic parameters and adverse effects (nausea, vomiting,) among two groups., these results supported by Bansal et al.[7] Low-dose clonidine is not associated with hemodynamic instability as evidenced by Dutta et al.[16]

Opioid-related side effects were not encountered significantly in nalbuphine group due to its mu (µ)-antagonist property. Respiratory depression, Pruritis was not observed in any patient during this study. Reduced incidence of opioid-related side effects in nalbuphine group is supported by Mukherjee et al,[17] Mostafa et al.[18]

Thus our study demonstrated that clonidine produce longer duration of post – operative analgesia when compared with nalbuphine, with minimal hemodynamic changes & adverse effects which was supported by Bansal et al.[7]

CONCLUSION

From the observation & results of this study we concluded that clonidine 30 µg as an adjuvant to hyperbaric bupivacaine results in extending the duration of sensory & motor block & enhancing the postoperative analgesia following lower limb surgeries with comparable minimum haemodynamic alterations.

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