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A study to compare the effect of nalbuphine and butorphanol as an adjuvant to intrathecal 0.5% hyperbaric bupivacaine for lower limb surgery

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Abstract---Introduction: Spinal Anaesthesia is routinely used for surgeries performed on lower abdomen, pelvis and lower limbs. Adjuvants allow multiple benefits, most significant being provision of

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post-operative analgesia. Aims: This observational study was conducted to compare intrathecal nalbuphine versus butorphanol with hyperbaric bupivacaine respectively to assess onset and duration of sensory and motor block, hemodynamic parameters, adverse drug reactions and duration of post-operative analgesia. Materials and Methods: Fifty participants between 20-60 years belonging to ASA grade I/II posted for elective surgery were assigned to : group BN (n=25) : Bupivacaine (0.5%) hyperbaric (3ml) + nalbuphine 1mg (0.1ml) + normal saline 0.1ml and group BB (n=25) : Bupivacaine (0.5%) hyperbaric (3ml) + butorphanol 200mcg (0.2ml). Mean period of sensory/motor blockade, hemodynamic parameters, adverse drug reactions and analgesic requirement post surgery were compared. Results: Onset of sensory blockade was comparable while onset of motor blockade was significantly earlier in nalbuphine than butorphanol. Duration of block and post-operative analgesia was significantly higher for nalbuphine. Hemodynamic parameters and adverse effects were comparable. Conclusion: Nalbuphine is more efficacious than butorphanol due to provision of early onset of motor blockade and prolonged period of sensory/motor blockade with delayed requirement of rescue analgesia.

Keywords---Intrathecal, Nalbuphine, Butorphanol, Bupivacaine.

Introduction

Spinal anesthesia is considered to be one of the most popular method of anaesthesia among regional anesthesia routinely used for elective & emergency surgeries.^[1]Single injection of subarachnoid and epidural block is a common technique of choice for surgeries performed on lower abdomen, pelvis, lower limbs and cesarean surgeries. Neuraxial block has a gross variety of indications not just for surgeries but also for acute postoperative pain management along with use for chronic pain relief.^[2]

In comparison to general anaesthesia, subarachnoid block has higher safety and cost efficiency. It also provides avoidance of use of multiple pharmacological agents, airway manipulation, higher risk of aspiration, hemodynamic alterations associated with stress response associated with laryngoscopy and intubation and a longer recovery duration. Also, intra operative as well as post operative analgesia is well provided in subarachnoid block. Considering how spinal anesthesia with sole local anesthetic agent provides post operative analgesia for a short period, a number of intrathecal adjuvants to local anaesthetic agents have been developed to augment the clinical efficiency, duration of blockade and post operative analgesia property.^[3]

Opioids as adjuvants provide analgesic effect by a number of central and peripheral mechanisms, primarily by attenuating C-fibre associated nociception which is not dependant on supraspinal mechanism. This is coined as “synergistic analgesia”.^[4]

In this study, the main aim was to evaluate the action of Nalbuphine(1mg) and Butorphanol(200mcg) added as adjuvant to intrathecal hyperbaric Bupivacaine for elective lower limb surgeries.

Objectives

Primary objectives:

Evaluation of sensory & motor profile:

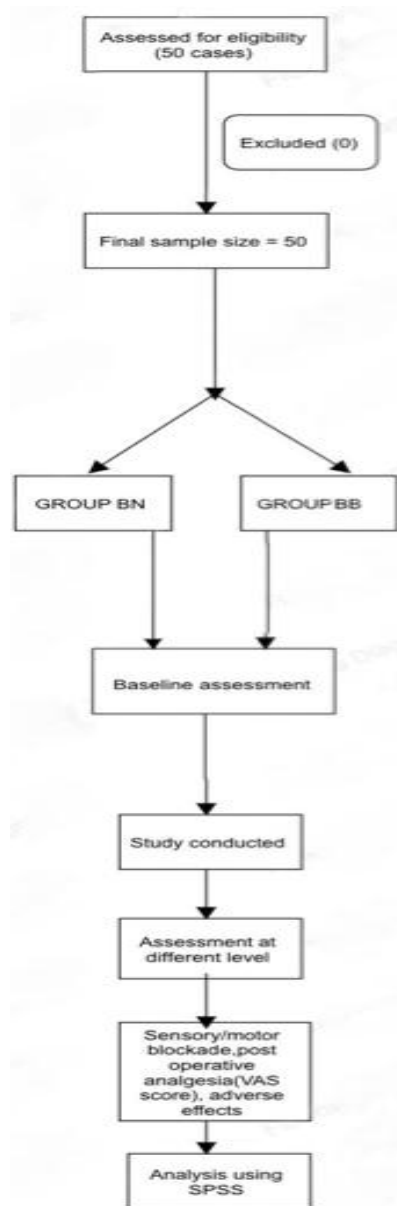
- To compare the mean onset in both groups.
- To compare the duration of blockade in both groups.
- To assess the requirement of analgesia post operatively.

Secondary objectives:

- To compare the hemodynamic changes i.e.(pulse, blood pressure(SBP/DBP), saturation(SPO₂)) in both groups.
- To compare the side effects/complications, if any in both study drugs in both groups.

Methods

After permission and clearance from the ethical committee (SVIEC/ON/MEDI/BNPG18/D19170), this observational study was conducted at Dhiraj (tertiary care) hospital in Department of Anaesthesiology, Vadodara. 50 patients between ages 20 to 60 years of Grade I or II of American Society of Anaesthesiologists (ASA) classification, posted for elective lower limb surgeries between 2019 to 2021 were included in the study. All the patients who participated in the study were explained clearly about the purpose and nature of the study. Written informed consent was obtained.



Table/Figure - 1 Consort Diagram

GROUP BN (Nalbuphine) : Hyperbaric Bupivacaine (0.5%) 3 millilitres + Nalbuphine (1000 micrograms=1 milligram) 0.1 millilitres + Normal Saline 0.1 millilitres (NET VOLUME = 3.2 millilitres)

GROUP BB (Butorphanol) :Hyperbaric Bupivacaine (0.5%) 3 millilitres + Butorphanol (200 micrograms) 0.2 millilitres (NET VOLUME = 3.2 millilitres)

Onset of sensory anesthesia was checked with pin prick sensation and motor blockade was assessed by modified bromage scale.

Preoperative preparation

Pre-operative anaesthetic check-up was done one day prior to surgery. Patients were evaluated for comorbid conditions, general/systemic and airway examination with baseline laboratory investigations noted. All patients were kept nil by mouth for atleast 8 hours before the surgery. Written and informed consent with proper counsel long and addressing queries for each patient was conducted. On the day of surgery, intravenous (i.v.) line was secured with 18 gauge cannula and preloading with 10ml/kg crystalloids was done. On arrival of patient in the operating room standard monitors were attached. Echocardiography (ECG), non-invasive systolic blood pressure (SBP) and diastolic blood pressure (DBP), heart rate (HR) and arterial oxygen saturation (SpO₂) were noted. Patients were pre-medicated with Inj. Glycopyrrolate 0.004mg/kg and Inj. Ondansetron 0.08mg/kg intravenously.

Patient was given sitting position. Under proper aseptic and antiseptic precautions, L4-L5/L3-L4 inter-vertebral space was used to access subarachnoid space in midline/paramedian approach with 23G/25G Quincke type spinal needle. After free flow of clear CSF, drug was administered according to group and immediately supine position was given.

Motor and sensory block parameters were observed. Mean time of onset of sensory and motor block was recorded. HR, SBP, DBP, SpO₂ and sedation were noted at 0, 2, 5, 10, 15, 20, 30, 60, 90, 120 mins. Mean onset time was noted as point of drug administration to absence of appreciation of pin prick at T10 after which surgery was started. Total sensory blockade duration was considered from point of onset of sensory blockade to regression of level by two segments.

Mean onset time assessed via Bromage scale was noted from point of drug administration to complete grade 3 motor blockade. Total motor blockade time noted as the duration till effect reduced to grade 0 blockade.

Sedation was assessed by 'Ramsay Sedation Scale' and sedation score of >3 was considered significant.

Table/Figure 2 : Ramsay Sedation Scale ^[14]

Clinical Score	Patient Characteristics
1	Awake; agitated or restless or both
2	Awake; cooperative, oriented, and tranquil
3	Awake but responds to commands only
4	Asleep; brisk response to light glabellar tap or loud auditory stimulus
5	Asleep; sluggish response to light glabellar tap or loud auditory stimulus
6	Asleep; no response to glabellar tap or loud auditory stimulus

Side effects and complications were noted and treated. Bradycardia was defined as fall in heart rate < 55 /minute and it was treated with Inj. atropine sulphate 0.6mg i.v. Hypotension was defined as mean arterial Pressure or less than 60 mm Hg and was treated with Inj. mephentermine 6mg i.v. along with intravenous fluids. Nausea/emesis was managed with inj. Ondansetron 4mg intravenously. After the patients were shifted to recovery room, HR, SBP, DBP, SpO₂, sedation and complications, was monitored. Patient's pain score was assessed by visual analogue scale (VAS). Duration of analgesia was considered from the time of intrathecal injection to when VAS ≥ 4 . Inj diclofenac sodium 75mg intravenously was given for rescue analgesia.

Statistical analysis

The data was entered into Microsoft Excel spreadsheets and the master chart was tabulated. The collected data were analyzed by unpaired student t test, chi square test and results obtained in the form of range, mean and standard deviation. p-value was calculated using MedCalc. A value of $p < 0.05$ was considered statistically significant.

Results and Observation

Both groups were comparable in terms of demographic parameters ($p > 0.05$). Mean onset time of sensory block was 2.72 ± 0.65 minutes for group BN and 2.96 ± 0.71 minutes for group BB. This finding was not significant. ($p > 0.05$) Mean duration of sensory block for group BN was 133.2 ± 23.4 minutes and for group BB was 110.8 ± 21.20 minutes which was highly significant. ($p = 0.0009$)

Both the onset and duration of motor block in our study was statistically significant, the onset being faster for nalbuphine group (5.64 ± 1.1 minutes) than butorphanol (7.08 ± 0.87 minutes) and duration of block being prolonged more in nalbuphine group (280 ± 29.29 minutes) than butorphanol group (240 ± 23.45 minutes).

Table/Figure 3: Onset and duration of sensory blockade.

	Group BN Mean \pm SD (in minutes)	Group BB Mean \pm SD (in minutes)	p-value	Significance
Onset of sensory block	2.72 ± 0.65	2.96 ± 0.71	0.2186	Not significant ($p > 0.05$)
Duration of sensory block	113.2 ± 23.40	110.80 ± 21.20	0.0009	Highly significant
Onset of motor block	5.64 ± 1.10	7.08 ± 0.87	< 0.0001	Highly significant
Duration of motor block	280.80 ± 29.29	240.00 ± 23.45	< 0.0001	Highly significant

TABLE/FIGURE 4 : Duration of analgesia (in minutes)

	Duration of analgesia (in minutes)		p-value	Significance
	Group BN	Group BB		
Mean± SD	416.00±40.82	364.80±55.76	0.0005	Highly significant

Duration of analgesia was analysed in either groups and it was concluded that the duration was 416±40.82 minutes in group BN and 364.8±55.76 in group BB and this was highly significant. (p=0.0005) The hemodynamic parameters remained statistically non significant both intra and post operatively for both groups (p>0.05) The adverse event profile was comparable for both groups and none of the patients developed significant sedation (sedation score >3).

Discussion

Spinal anesthesia is usually preferred for most surgical procedures of the lower abdomen and lower limbs. Using bupivacaine as sole agent in provision of spinal anaesthesia results in a shorter duration of anaesthesia and post operative analgesia. Addition of opioid agents to local anesthetic agents as adjuvants enhances the quality and duration of anaesthesia and post operative analgesia thereby providing a pain free and less stressful recovery post operatively with early ambulation. Intrathecal opioids act synergistically with the local anesthetic agent without augmentation of sympathetic and motor blockade.

On reviewing available literature, we found comparative paucity of use of butorphanol intrathecally as well for the optimum dosage of butorphanol with variations noted from 25-200 mcg in most of the studies. N. Gopal Reddy et al (2015)^[5], Kumkum Gupta et al(2015)^[6]and B. Durga Venkatram et al (2019)^[7]used butorphanol as an adjuvant at a dose of 200mcg and Vishva Darshanbhai Shah et al (2020)^[8] used 300 mcg of butorphanol without any significant side effects. In the present study, we have used nalbuphine 1 mg and butorphanol 200 mcg as intrathecal adjuvants to 15 mg (3ml) hyperbaric bupivacaine (0.5%) and both groups were observed to be comparable with regards to the demographic profile (age, gender, weight, A.S.A. grade) which was found to be not significant (p value > 0.05).

The time onset of sensory blockade was comparable & statistically non significant in both groups(p value > 0.05). The average period of sensory block (2 segment regression) was notably higher with nalbuphine which was statistically significant (p=0.0009). The mean duration of analgesia was statistically significant and prolonged in nalbuphine group. (p=0.0005)

Similar to our study, Sandip Sinha et al (2018)^[9] used a lower dose of nalbuphine (0.4mg) and butorphanol (25mcg) in infraumbilical surgeries and observed a comparable onset of sensory blockade with duration of regression by two segments being significant and delayed with nalbuphine. Also, mean duration of analgesia was prolonged in nalbuphine which was highly significant (p<0.05). B. Durga Venkatram et al (2019)^[7] noted mean time of sensory onset between nalbuphine (0.8mg) and butorphanol (200mcg) was comparable and statistically

non significant while duration of sensory blockade was more prolonged for nalbuphine which was highly statistically significant. Regarding duration of analgesia, Shahedha Parveen et al (2015)^[10] observed a similar duration of requirement of rescue analgesia with nalbuphine(1mg) as an adjuvant compared with plain bupivacaine in her study while B. Durga Venkatram et al (2019)^[7] noted that the mean duration of analgesia with nalbuphine was significantly higher than butorphanol. Pallavi Ahluwalia et al (2015)^[13] and Vishva Darshanbhai Shah et al (2020)^[8] used similar drugs in infraumbilical surgeries and observed a shorter duration to rescue analgesia with nalbuphine(0.8mg) and butorphanol (300mcg) respectively as compared to ours.

Sagar S M et al (2013)^[11] compared nalbuphine (0.8mg) and butorphanol(25mcg) to bupivacaine without adjuvants and in contrast to our observations, they observed that the two segment regression time was non significant in nalbuphine group compared to butorphanol group and both having high significance($p < 0.001$) against the group given hyperbaric bupivacaine without adjuvant. Also, the mean duration of analgesia was similar in both groups with adjuvants used in this study. In the present study, both the onset & time period of motor block was statistically significant, the onset being faster for nalbuphine group than butorphanol ($p < 0.0001$) and duration of block being prolonged in nalbuphine group than butorphanol group ($p < 0.0001$).

Akash Nirmal et al (2019)^[12], Pallavi Ahluwalia et al (2015)^[13], Sandip Sinha et al (2018)^[9], B. Durga Venkatram et al (2019)^[7] had similar findings with respect to onset and duration of motor blockade. In contrast to our study, Sagar S M et al (2013)^[11] observed that mean duration of onset of motor blockade with nalbuphine compared to butorphanol was statistically non-significant. Also, the duration of motor block for nalbuphine was statistically not significant as well. In the present study, the variation in vital parameters for both groups was statistically non-significant both preoperatively and postoperatively. ($p > 0.05$) Sedation was assessed by Ramsay sedation score where patients in both group had score of 2 or 3 intraoperatively, being statistically insignificant. Other intraoperative side effects (hypotension, bradycardia, nausea and vomiting) were comparable in between both groups.

Study Limitation: Plasma level of drug was not measurable. Sample size for the above study was limited.

Funding : None

Conclusion

Opioid adjuvants likely nalbuphine (1mg) and butorphanol (200 mcg) when added to hyperbaric bupivacaine for elective lower limb surgeries has multiple advantages like early motor blockade onset, longer duration of sensory/motor blockade and longer duration of post operative analgesia. Both drugs when compared had minimal adverse effect profile with significant differences in the above said parameters, and of the two, nalbuphine was comparatively better than butorphanol as an adjuvant for spinal anesthesia for elective lower limb orthopaedic surgery.

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