ORIGINAL ARTICLE

A Prospective Randomised Double Blind Control Study to Find the Optimum Dosage of Nalbuphine as an Adjuvant to Spinal Anaesthesia

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Abstract

Background: Adequate post-operative pain management is very important to facilitate the functional recovery and enable patients to rehabilitate fast to return to their normal activities. Major limitation is the fixed duration of action of local anesthetic which can be improved with adjuvant like (Opiod). **Aim & Objectives:** To find the onset and duration of sensory and motor block with different doses, and duration of post operative analgesia. **Material &Methods:** This is a prospective randomized double blind control study. 120 patients of ASA I & II physical status patients aged 20- 60 yrs under going lower abdominal and lower limb surgeries under subarachnoid block were allocated randomly to 4 groups A,B,C,D by lottery method . Group A Patients were given inj. Bupivacaine2.5ml(H)+1ml N.S,Group B inj. Bupivacaine (H) 2.5 ml +0.4mg of Nalbuphine diluted to 1 ml of normal saline, Group C inj. Bupivacaine (H) 2.5ml +0.6mg of Nalbuphine diluted to 1 ml of normal saline, Group D inj. Bupivacaine (H) 2.5ml + 0.8mg of Nalbuphine diluted to 1 ml of normal saline. **Results:** Peak sensory level was significantly rapid in group D (0.8mgNalbuphine) which is comparable to group C (0.6 mg Nalbuphine). The two segment regression time of sensory block was statistically significant in group D &C . The time of onset of motor block to reach Bromage 3 was less in group D and C ;statistically significant compared to Group A &B. **Conclusion:** The optimum dose of Nalbuphine to shorten the onset of sensory and motor block and prolong the duration of sensory and motor block and post-operative analgesia is 0.6mg without any increased side effects.

Keywords

Hyperbaric bupivacaine, Nalbhuphine, Subarachnoid block

Introduction

Deposition of drugs in epidural and subarachnoid space paved a new era for pain relief. Major limitation is the fixed duration of action of local anesthetic used. To overcome this limitation various adjuvant are being increasingly used. They act synergistically with local anesthetics e.g. opioids, epinephrine, neostigmine, midazolam, Ketamine, clonidine, dexmedetomidine for prolongation of its action and postoperative analgesia.[1] The use of opioid as adjuvants in regional analgesia techniques has been one of the cornerstones in postoperative pain management in recent decades.[2]. Opioid receptors are abundantly expressed in substantia gelatinosa where substance P release from primary sensory neuron is inhibited by opioids.[3]·The main obstacles for optimal use of opioids are their side effects which include pruritis, nausea vomiting, emesis, constipation, urinary retention, respiratory depression, undesirable sedation and development of tolerance dependence. One of the best ways to control the intrathecal opioid related side effects is the use of mixed agonists-antagonist opioid which binds readily to both mu and kappa receptors..[4] When binds to kappa receptors however it has an agonist effect. In this study

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we tried to establish the effectiveness of intrathecal Nalbuhine as an adjuvant by comparing the optimal dose using 0.4mg, 0.6mg, 0.8mg diluted to 1ml N.S added to 2.5 ml 0.5%(H) bupivacaine to prolong pain relief with minimal side effects in patient undergoing lower abdominal and lower limb orthopedic surgical procedures under SAB.

Aim & Objectives

To find the onset and duration of sensory and motor block with different doses of nalbhuphine. To find the duration of post operative analgesia.

Material & Methods

After receiving approval from the ethical committee, this study was conducted in post graduate department of anesthesia GMC Jammu ,in overall period of one year. The study is prospective randomized double blind control in nature, 120 consenting patients of ASA grade I and II classification, aged (20 - 60) years posted for lower abdominal and lower limb surgeries. Patients were allocated randomly into 4 equal groups. They received normal saline 1ml (Group A),Nalbuphine 0.4mg(Group B) Nalbuphine 0.6mg(Group C) Nalbuphine 0.8mg(Group D) made upto 1 ml volume with 2.5 ml of hyperbaric bupivacaine

Exclusion Criteria

1.Pregnant Females

2.Contraindications to Spinal anesthesia

3.Known hypersensitivity or allergy to local anesthetics/ opioids

The patients were visited preoperatively and history was taken for any medical co morbidity.Clinical examination, Spine examination and routine investigations were done in all patients.

Preparation of Equipments and Drugs

Premedication :Inj. Ondansteron 4mg i.v, Inj. Glycoprrolate 0.2mg i.v.spinal needle(25 G). Inj. Bupivacaine (H) as 0.5% ampule; each ml contains 5mg. Preloading with RL solution (10ml/Kg) was done .

Under all aseptic precautions 25G spinal needle was inserted in the mid line at L3-L4 or L4-L5 interspace. The appropriate local anesthetic solution was injected over 10-15 seconds.The patient was placed supine immediately after injection.

Intra Operative: Patients were monitored for heart rate (HR), SBP, DBP, Onset and duration of sensory block, onset and density of block (motor block) using modified Bromage scale.

Assessment of Sensory block: The upper and lower spread of sensory block was determined and to assess the height of the block; sensory block was assessed every minute post-injection, for five minutes and at 5-min intervals thereafter until two consecutive levels of sensory block was identical (i.e. fixation of the level), after which assessment was done every 30 minutes.

Assessment of Motor block: Time of onset, degree of motor blockade and duration of motor blockade was recorded. Hemodynamic changes like HR, SBP, DBP was monitored at 0, 1, 3, 5, 10, 15, 20, 25, 30,35, 40, 45, 60, 75, 90, 105, 120 minutes. Duration of Complete Analgesia was assessed using visual analogue scale, which was explained one day prior to the surgery to all patients.

The patients were asked to mark the severity of pain experienced at that time in the post operative period.

The VAS score was serially assessed at 30 min interval starting from 60 min till the patient complaints of pain (VAS score >3) The patients having VAS score more than 3 were administered with rescue analgesia .(Diclofenac 75mg.)

0	1 2 3	4 5 6	7 8 9 10
No pain	Mild pain	Moderate pain	Severe pain

Analysis of variance (ANOVA) was employed for inter group analysis of data and for multiple comparisons, least significant difference (LSD) test was applied. Chi-square test or Fisher's exact test, whichever appropriate, was used for comparison of categorical variables. Graphically the data was presented by bar and line diagrams. A P-value of less than 0.05 was considered statistically significant.

Results

Four Groups were comparable regarding the demographic data and the duration of surgery P> 0.05.

Peak sensory level was significantly rapid in group D which is comparable to group C, but significantly rapid compared to group B and group A (Table 3). The two segment regression time of sensory block was a comparable to group D&C .But difference was statistically significant (P <0.05) compared two group B and A, with the highest duration in group D and lowest in group A.The time of onset of motor block to reach from Bromage 3 was less in group D compare to group C (p 0.13), but

Table 1: Age, weight and duration of surgery (min) distribution of study patients in various groups

	Group	N	Mean	SD	Range	p value
Age (years)	Group A	30	40.9	13.546	24-64	0.649
	Group B	30	43.7	12.413	20-59	
	Group C	30	42.6	11.051	21-60	
	Group D	30	40.1	10.840	24-60	
Weight (kg)	Group A	30	60.1	6.071	48-73	0.346
	Group B	30	59.6	9.651	46-81	
	Group C	30	62.6	10.493	44-80	
	Group D	30	62.4	9.035	45-80	
Duration of Surgery (min)	Group A	30	90.83	21.936	50-120	0.418
	Group B	30	86.0	22.735	40-120	
	Group C	30	85.3	22.740	45-125	
	Group D	30	93.7	21.851	45-120	

Table 2: Showing ASA status of study patients among various groups

Group	ASA I		ASA II		P-value
	No.	%age	No.	%age	
Group A	30	100.0	0	0.0	0.320
Group B	29	96.7	1	3.3	
Group C	27	90.0	3	10.0	
Group D	28	93.3	2	6.7	

Table 3: Peak sensory level (minutes) and Time to reach Bromage 3 (minutes) in various groups

	Group	N	Mean	SD	95% CI	P-value
Peak sensory level (minutes)	Group A	30	7.2	0.514	6.97-7.36	<0.001*
	Group B	30	5.5	1.434	4.99-6.06	
	Group C	30	4.9	1.341	4.42-5.42	
	Group D	30	4.5	0.878	3.96-4.81	
Time to reach Bromage 3 (minutes)	Group A	30	7.3	0.479	7.15-7.51	<0.001*
	Group B	30	5.8	1.388	5.24-6.27	
	Group C	30	5.1	1.339	4.63-5.63	
	Group D	30	4.7	0.971	4.34-5.06	

statistically significant when compared with group B and A (P value<0.05).The duration of motor block that is the time of regression to Bromage 1 was (255.7±18.2 min) in Group D, in group C(197.2 ±12.42 min) in group B and (185.6±9.8 min) in group A. It was more prolonged in group D and least in group A. Duration of rescue analgesia in group D(268.5±13.7min)was statically significant compared to group C (281.3±11.43min)group B(256.8±9.5min)GroupA(221.0±10.3min) with (p0.05).There were no complaints of nausea vomiting, pruritus, urinary retention and respiratory depression in all groups. Out of 30 patients in Group C, 2 experienced hypotension and 3 experienced bradycardia intra-operatively and out of 30 patients in group D, 7 experienced hypotension and 5 experienced bradycardia intra operatively with no such complaints post-operatively.

Discussion

Spinal Anesthesia is the most common type of anesthesia used for lower limb surgeries, however adding intrathecal opioids to local anesthetic decrease their dose and complications, provide more hemodynamic stability and increase the time required for post operative analgesia[5]. Previous studies[6,7] have shown that nalbuphine increases the duration of analgesia in patients undergoing surgeries under SAB. Nalbuphine is synthetic opioid with agonist and antagonist properties [8]. The mechanism of analgesia relies on its agonistic action on kappa receptor.Nalbhuphine binds to kappa receptors of the brain and the spinal cord areas, which are involved in nociception producing analgesia and sedation without mu side effects[9] .It

improves quality of block and offers prolonged and long lasting postoperative analgesia .It has low incidence of adverse effects known for other opioids e.g. respiratory depression, nausea, vomiting, pruritis.Sapate M *et al*., [10] There have been few studies of varying quality that support the utility of neuraxially administered opiods in managing post-operative pain[11,12]. In this prospective randomized controlled study we compared the use of intrathecal (H) bupivacaine 0.5% without additive [control group],with the use of 0.4 mg, 0.6 mg,0.8 mg with 2.5ml of 0.5% [H] bupivacaine for lower abdominal and lower limb surgeries. Our choice of doses depend on a previous study by Mukherjee A *et al.*[13] who studied 100 patients undergoing lower limb orthopedic surgeries using Nalbuphine with different doses of intrathecally 0.2 mg, 0.4 mg, 0.8 mg, added to 0.5% hyperbaric bupivacaine. They concluded that the duration of sensory block and the duration of effective analgesia were prolonged with 0.4 mg and 0.8 mg doses but the side effects were higher with 0.8 mg dose. Similar results were obtained in present study where there was a progressive increase in duration of both sensory and motor block with increasing concentrations of dose with more side effects like hypotension and bradycardia with 0.8 mg. Dubey R and Bisht S [14] conducted a study to evaluate the efficacy of Nalbhuphine vs fentanyl as intrathecal adjuvant. 100 patients were posted for elective total abdominal hysterectomy and were randomly divided into two groups FB and FN group. FB group received 15 mg of 0.5% Bupivacaine and 25 microgram of fentanyl. Group NB received 15 mg of 0.5% bupivacaine and 1mg Nalbuphine . Their results showed that time to attain peak sensory and motor block was significantly faster in group FB. Duration of motor block was comparable in both the groups. Time for sensory block to regress by two segment was significantly longer in group NB than in group FB. The time to first analgesic requirement in group NB was 460 minutes compared to 283 minutes in group FB . Our study results showed that the time to reach peak sensory block was decreased with increasing concentration of dose of nalbuphine .Time to reach Bromage 3 motor block also decreases with increasing concentration of doses of nalbuphine . One group of patients was given 3 ml of heavy bupivacaine 0.5% + 0.8 mg of Nalbhuphine intrathecally and the other group was given 3 ml of hyperbaric bupivacaine 0.5% + normal saline They found that the intrathecal nalbuphine provided significantly faster onset of sensory block and shorter peak sensory time compare to Bupivacaine alone and provides effective post operative analgesia and prolongs the duration of 1st rescue analgesia. These results are in contrary to Sapate M *et al.*, [15] In their study they have shown that onset of sensory block and peak time for sensory block was not affected by adding nalbuphine intrathecally ,but in our study we found that as compared to control groups,with nalbhuphine has shorter onset of sensory and motor block and prolonged duration of analgesia. Our study shows effective analgesia increases with increasing the dose of nalbuphine. Time of rescue analgesia requirement with vas score 0 -3 in group A was 221.00± 10.37min [mean ± SD], group B 256.8 ± 9.51 min [mean ± SD], group C 281.3 ± 11.4 min [mean ± SD], group D 268.50± 13.72 min [mean ± SD]; group C shows maximum duration of request for rescue analgesia. patients in group C have had much satisfactory analgesia intraop period as there was less side effects compared to group D and this may have a psychological effect post operatively which may have resulted in late requirement for 1st rescue analgesia post operatively compared to Group D. Culebras X *et al.*,[16] performed the comparative study to evaluate post operative analgesia and adverse effects after using 3 doses i.e 0.2 mg, 0.8 mg, 1.6 mg of intrathecal nalbuphine [or] morphine 0.2 mg given for C-section along with bupivacaine. The largest duration of complete and effective analgesia among the nalbuphine treated groups were provided by 0.8 mg added to bupivacaine. Neither pruritis nor post-operative nausea vomiting were observed with nalbuphine from 0.2 mg and 0.8 mg. They concluded that 0.8 mg of intrathecal improves intraoperative analgesia and prolong early postoperative analgesia without increasing the risk of side effects but in our study .0.6mg showed better post operative analgesia and lesser side effects as compared to 0.8 mg intrathecal nalbhuphine group .In the same direction we observed that by comparing the control group A with other groups 0.4 mg, 0.8 mg 0.6 mg intrathecal Nalbuphuine with bupivacaine, the request of first rescue analgesia was prolonged in groups with adjuvant nalbuphine with maximum duration for request of analgesia in group C 281.3 ± 11.43 min [mean]. Similar results were also demonstrated by Tiwari AK, Tomar GS, Aggarwal J. [17] who showed significant increase in post- operative analgesia in patients given 0.2 mg, 0.4 mg nalbuphine intrathecally. None of our patients in each group in our

study had any significant side effects like respiratory depression, pruritus, urinary retention ,postoperative nausea vomiting. According to our study results 2 patients in group C and 7 patients in group D experienced bradycardia intraoperatively which was managed with injection atropine 0.5 mg IV stat but neither of them experience same complication post-operatively. Along with this ,3 patients in group C and 5 patients in group D experience hypotension intraoperatively which was managed with fluids and direct vasoconstrictors with no such complication postoperatively. Thus it is concluded that optimal dose of Nalbuphine as an adjuvant to 0.5% Bupivacaine is 0.6mg which decrease onset of both motor and sensory block, prolongs the duration of analgesia with minimal side effects.

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Conflicts of Interest
There are no conflicts of interest.

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