Section: Anaesthesiology

Original Research Article

COMPARISON OF EFFICACY OF INTRATHECAL FENTANYL AND INTRATHECAL NALBUPHINE AS AN ADJUVANT TO LEVOBUPIVACAINE FOR LOWER ABDOMINAL AND LOWER LIMB SURGERIES

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Abstract

Background: Regional anaesthesia has several advantages over general anaesthesia (GA), including decreased stress response. Spinal anaesthesia is a technique used for lower abdominal and lower limb surgeries. The study aimed to compare the duration of analgesia in terms of the time of the first analgesic requirement of intrathecal levobupivacaine combined with nalbuphine and fentanyl for lower abdominal and lower limb surgeries. **Material and Methods:** This randomised double-blinded study was conducted on 60 patients in the Department of Anesthesiology at Shri Sathya Sai Medical College and Research Institute between May 2017 and October 2018. Group A patients received 3ml of 0.5 % levobupivacaine + 0.8 mg of nalbuphine, a total volume of 3.5 ml, and Group B patients received 3 ml of 0.5 % levobupivacaine + 25 µg of fentanyl, a total volume of 3.5 ml. **Results:** There was no significant difference in age, sex, weight, surgery duration, and sensory loss level between groups. Out of 60 patients in two groups, the sensory and motor block onset was similar. At the same time, the postoperative analgesic requirement was less in patients of group A compared to group B. Hemodynamic parameters were similar in group A and group B. There was a significant difference in analgesic requirement, vomiting, and pruritis between groups. **Conclusion:** Intrathecal nalbuphine combined with levobupivacaine is comparatively better than intrathecal fentanyl combined with levobupivacaine in terms of postoperative pain relief.

INTRODUCTION

Surgical procedures cause severe tissue damage, leading to postoperative pain. Despite efforts to make the intraoperative period pain-free, patients are left to deal with the stress and its effects on their body systems. A pain-free postoperative period reduces morbidity and mortality. Modern medical science offers various postoperative pain relief methods, including epidural catheters, peripheral nerve blocks, and local anaesthetic drug infiltration. Additives like systemic benzodiazepines and synthetic and semisynthetic opioids are simple, effective, and commonly adopted ways of postoperative pain relief. The sub-arachnoid block has been very popular in recent times. Various local anaesthetics have been in use for a long time. Regional anaesthesia has several advantages compared to general anaesthesia (GA), including decreased stress response. Spinal anaesthesia is a technique used for lower abdominal and lower limb surgeries. Levobupivacaine has become popular for central neuraxial blocks in this century.[1-4] The main advantage includes ease of technique and reliability. Till recently, bupivacaine was the only drug used after discontinuation of intrathecal lidocaine use. Levobupivacaine, pure s-enantiomers of bupivacaine, is a safer alternative for regional anaesthesia than its counterpart, with a lower toxicity profile.[5]

Intrathecal opioids were first used for the management of acute pain treatment in 1979. The use of intrathecal opioids as adjuncts has its hold in the recent regional anaesthesia practice. Also, other opioid drugs were used along with bupivacaine to improve the quality of the analgesia, prolong its

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effect and reduce the need for postoperative analgesic drug requirement. Opioid analgesics activate the receptors in the afferent neurons to activate the pain-modulating systems. This activation directly reduces neurotransmission or may stop the excitatory neurotransmitter's release.

Opioid receptors are classified as delta, mu, and kappa receptors. The Opioid agonist usually acts on the mu receptors, and they are usually responsible for spinal and supraspinal analgesia with sedation, nausea, pruritus, respiratory depression, and vomiting. Opioids, an agonist-antagonist, act principally on the kappa receptors alone. The substantia gelatinosa is the site of action. Analgesia with neuraxial opioids is dose-related and specific for visceral pain when compared to somatic pain. Both nalbuphine and fentanyl are opioid analgesics. Fentanyl is also an opioid agonist that acts on μ-opioid receptors.[6] Nalbuphine is one of the synthetic opioid analgesics with agonist-antagonist activity and acts as an agonist at κ-receptors to provide potent analgesia and antagonist at μ-receptors. Nalbuphine, whenever used as an adjuvant to bupivacaine, was found to improve the quality of perioperative analgesia with comparatively lesser side effects and nil neurotoxicity.[7,8]

Aim

The study aimed to compare the duration of analgesia in terms of the time of the first analgesic requirement and to compare the quality of analgesia measured in terms of total analgesic requirement and pain scores, the onset of sensory and motor blockade, duration of motor blockade, and perioperative hemodynamic parameters of intrathecal levobupivacaine combined with nalbuphine and fentanyl for lower abdominal and lower limb surgeries.

MATERIALS AND METHODS

This randomised double-blinded study was conducted on 60 patients in the Department of Anesthesiology at Shri Sathya Sai Medical College and Research Institute between May 2017 to October 2018. The study received Institutional Ethical Committee approval before its initiation.

Inclusion Criteria

The study includes patients in the age range of 18 to 60 years, ASA physical status I and II and patients posted for lower abdominal and lower limb surgeries under spinal anaesthesia.

Exclusion Criteria

Patient refusal, patients allergic to local anaesthesia/ nalbuphine/fentanyl, ASA physical status III or more, patients with coagulation disorder, local site infection BMI >30 and height<140 cm were excluded.

Group A patients received 3ml of 0.5 % levobupivacaine + 0.8 mg of nalbuphine, a total volume of 3.5 ml, and Group B patients received 3 ml of 0.5 % levobupivacaine + 25 μg of fentanyl, a total volume of 3.5 ml.

The outcomes were assessed, including the duration of sensory block (time of onset, duration, and recovery), duration of motor block (time of onset, duration, and recovery), degree of fall in arterial blood pressure, heart rate and pain score using a visual analogue scale (VAS), and adverse effect like vomiting, shivering.

The informed consent was obtained from all the patients. All the patients were assessed for the following parameters, including the time of injection of the drug into subarachnoid space is considered as 0 min, patients were put in the supine position and sensory level was checked by using 26G hypodermic needle by pinprick method, the level was checked by every 2 minutes in first 20 minutes followed by every 5 min for another 20 minutes. Two consecutive readings after 20 minutes can be taken as maximum sensory level. The degree of motor blockade and duration of surgery were assessed using a modified Bromage scale. Intraoperative parameters were monitored, including heart rate, blood pressure, SPO2, and sedation.

Ramsay sedation score and VAS score were assessed, duration when a patient demands rescue analgesia (Injection Diclo 75mg IM on demand when patient complaints of pain), total analgesics are required in 24 hours, observations for postoperative side effects: Nausea was monitored, and vomiting was noted as several emetic episodes. The second episode was treated with metoclopramide 10 mg IV. Patients were observed for 24 hours for postoperative complications like nausea, vomiting, pruritus, shivering, respiratory depression, hypotension, and bradycardia.

Statistical analysis

The data was entered into an Excel sheet and analysed using SPSS (version 16). Descriptive statistics with mean, standard deviation, and proportion (%) were calculated, and statistical tests used were independent sample T Test and Chi-square test as appropriate.

RESULTS

There were 16(26.7%) patients in the age group of <30 years in group A and 14(23.3%) patients who underwent surgery in group B. 6(10%) patients were in the age group of 31 – 40 years in each group from the study participants. In the age group of 41-50 years, 5 and 7 participants were seen in groups A and B, respectively. In both groups, three patients were recorded in the age group of 51-60. There was no statistical significance in age group between the groups (p=0.933).

Most study participants were females in both groups, with 17(28.3%) female patients in group A and 19 (31.7%) female patients in group B. There were 13 (21.7%) males in group A and 11(18.3%) males in group B. There was no statistical

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significance in the sex group between the groups (p=0.651). 3 and 4 patients were below 50 kgs weight in groups A and B, respectively. Nine patients were between 51- 60 kgs in group A and 11 patients were between 51-60 kgs in group B. In the 61-70 kg weight range, there were 7 and 3 patients and groups A and B, respectively. There were 7 and 8 patients above 80 kgs weight in groups A and B, respectively, and the p-value was not statistically significant (p=0.877). Also, the mean and standard deviation (SD) for weight was 68.21±11.29 in group and 69.14±13.27 in group B.

60-90 mins of surgery were performed among 14 group A participants and 7 participants in group B. The surgery duration for 8 and 15 patients was 91-120 minutes in groups A and B, respectively. Eight patients each in both groups took around 120-150 mins. There was no statistical significance for the duration of surgery between the three groups. Also, the mean value for the duration of surgery in group A was 100.23, an SD of 26.51; in group B, it was 105.13 and 26.08.

The maximum sensory loss was found in T6, T7, T8, and T9 dermatomes in both groups. A smaller number of patients encountered sensory loss in T4 and T5 dermatomes, which is statistically insignificant (p=0.444). [Table 1]

The mean and SD for the onset of sensory function were 6.03±1.21 and 6.25±1.15 in groups A and B, respectively. The mean and SD values for the onset of motor function after anaesthesia were 13.38±1.08 in group A and 13.30±1.07 in group B. time for maximum sensory loss was 13.45±1.11 and 13.23±1.03 in groups A and B, respectively (Table 2).

The mean intraoperative pulse rate was equal in both groups. Systolic blood pressure at various times was not significantly different between the groups. In group A, the mean diastolic blood pressure varied from 72.88±7.19 at 2 mins to 76.10±5.74 at the end of surgery (after 40 mins). In group B, it varied from 74.80±5.09 at 6 mins to 77.88±10.08 at 10 mins, and at the end of surgery, it was 75.38±5.53

At the end of the surgery, the mean arterial pressure was 68.93±6.04 in group A and 68.33±4.75 in group B. There was a significant difference in Spo2 between the groups. The mean value of EtCo2 was 40.55 and SD 2.98 in patients under group A at the end of the surgery. The mean value of EtCo2 at the end of surgery in group A was 40.15 and SD 3.25.

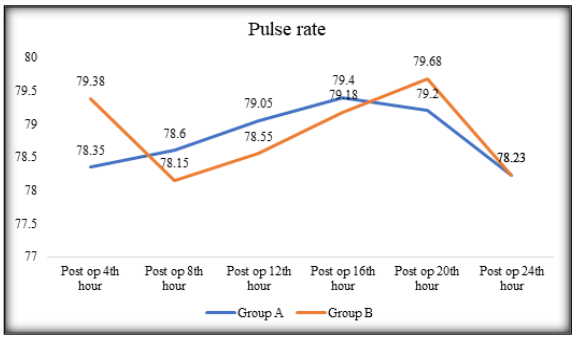

Figure 1: Postoperative pulse rate between the groups

There was little difference in the mean and SD of pulse rate in both groups. [Figure 1]

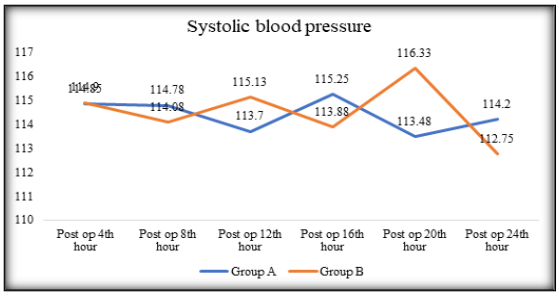

Figure 2: Postoperative systolic blood pressure between the groups

Systolic blood pressure after 24 hours postoperatively was found to be 114.20±8.05 in Group A and 112.75±6.63 in Group B. [Figure 2]

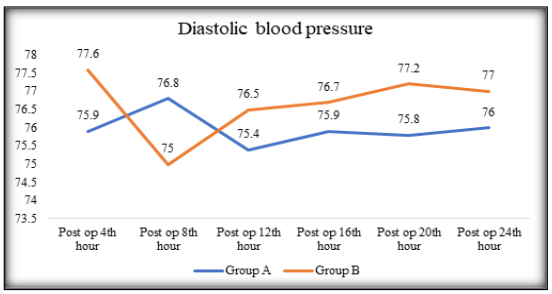

Figure 3. Postoperative diastolic blood pressure between the groups

Diastolic blood pressure after 24 hours postoperatively was found to be 76.00±6.84 in Group A and 77.00±6.38 in Group B. [Figure 3]

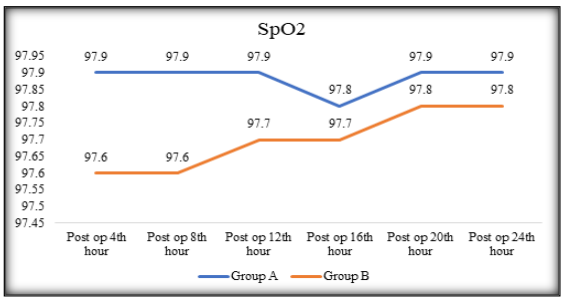

Figure 4: Postoperative spo2 between the groups

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The mean and standard deviation of Spo2 were more than equal in both groups. [Figure 4]

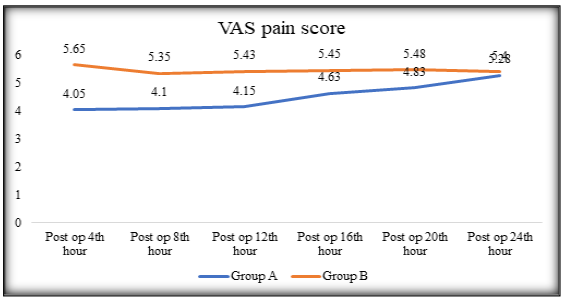

Figure 5: Postoperative VAS pain score between the groups

The mean and SD for pain by visual analogue scale score were found to be higher in patients who received intrathecal levobupivacaine with adjuvant fentanyl than the patients who received intrathecal levobupivacaine with adjuvant nalbuphine. [Figure 5]

The mean value for the first dose of analgesic required at (in hours) in group A was 14.13, and SD was 3.40, whereas in group B, the mean value was 9.76, and SD was 2.60. The difference was highly statistically significant ($p<0.001$). The mean and SD for the number of anaesthetic doses required in group A was 1.45±0.59, and in group B was 2.64±0.87, which was statistically significant ($p=0.001$).

Vomiting was present in 5 (8.3%) patients in group A and 15 (25%) patients in group B, and the difference was found to be statistically significant ($p<0.01$). Among 30 patients in each group, pruritis was noted in 2 patients in group A and 10 in group B, and the difference was statistically significant ($p=0.012$). Shivering was present in 3 (5%) individuals in group A and 7 (11.7%) individuals in group B, but the difference was found to be statistically insignificant ($p>0.05$). Sedation was found in one participant in Group A and Group B, with an insignificant ($p>0.05$). [Table 2]

Table 1: Demographic data of the study

		Frequency (%)			P value
		Group A	Group B	Total	
Age (years)	< 30	16(26.7%)	14(23.3%)	30(50%)	0.933
	31-40	6(10%)	6(10%)	12(20%)	
	41-50	5(8.3%)	7(11.7%)	12(20%)	
	51-60	3(5%)	3(5%)	6(10%)	
Sex	Male	13(21.7%)	11(18.3%)	24(40%)	0.651
	Female	17(28.3%)	19(31.7%)	36(60%)	
Weight (kg)	<50	3(5%)	4(6.7%)	7(11.7%)	0.877
	51-60	9(15%)	11(18.3%)	20(33.3%)	
	61-70	7(11.7%)	3(5%)	10(16.7%)	
	71-80	4(6.7%)	4(6.7 %)	8(13.3%)	
	> 80	7(11.7%)	8(13.3%)	15(25%)	
Duration of surgery (mins)	60-90	14(23.3%)	7(11.7%)	21(35%)	0.156
	91-120	8(13.3%)	15(25%)	23(38.3%)	
	120-150	8(13.3%)	8(13.3%)	16(26.7%)	
Level sensory loss	T4	3(5%)	2(3.3%)	5(8.3%)	0.444
	T5	4(6.7%)	4(6.7%)	8(13.3%)	
	T6	3(5%)	2(3.3%)	5(8.3%)	
	T7	6(10%)	7(11.7%)	13(21.7%)	
	T8	2(3.3%)	1(1.7%)	3(5%)	
	T9	7(11.7%)	7(11.7%)	14(23.3%)	
	T10	5(8.3%)	7(11.7%)	12(20%)	

Table 2: Onset of sensory, onset of motor, and time for maximum loss between the groups

	Group A	Group B
Onset of sensory	6.03±1.21	6.25±1.15
Onset of motor	13.38±1.08	13.30±1.07
Time for maximum loss	13.45±1.11	13.23±1.03

Table 3: Symptoms between the groups

		Mean ± SD		P value
		Group A	Group B	
Analgesic requirement	The first dose of analgesic is required at (in hours)	14.13±3.40	9.76±2.60	<0.001
	Number of doses required	1.45±0.59	2.64±0.87	0.001
Vomiting	Yes	5(8.3%)	15(25%)	0.01
	No	25(41.7%)	15(25%)	
Pruritis	Yes	2(3.3%)	10(16.7%)	0.012
	No	28(46.7%)	20(33.3%)	
Shivering	Yes	3(5%)	7(11.7%)	0.176
	No	27(45%)	23(38.3%)	
Sedation	Yes	1(1.7%)	1(1.7%)	1
	No	29(48.3%)	29(48.3%)	

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DISCUSSION

This study found no statistical significance in age and weight between groups (p=0.933, p=0.877). Most study participants in both groups were females, with a p-value that was not statistically significant (p-value of 0.651). This result is comparable with the study conducted by Jitendra Agrawal et al., which reported female preponderance was noted in both groups, 25 in Group N and 26 in Group C, with insignificant (p=0.749).[9]

Our study found no statistical significance in the duration of surgery between the two groups. The maximum sensory loss time was 13.45±1.[11] and 13.23±1.03 in groups A and B, respectively. The onset of motor function after anaesthesia was 13.38±1.08 in group A and 13.30±1.07 in group B. The mean and standard deviation for the first dose of analgesic required was 14.13 in group A and 9.76 in group B, with a statistically significant difference (p<0.001). The number of anaesthetic doses required was 1.45±0.59 in group A and 2.64±0.87 in group B. Girgin et al. reported highest sensory block levels achieved were T7 (range T5 – T9) and T6 (range T4 – T9) in groups LF and L, respectively.10 In contrast, Kumkum et al. reported the onset of sensory analgesia at T,[10] (7.25 ± 2.3 versus 9.27 ± 2.79 min). The time to achieve complete motor blockade (19.27 ± 4.7 versus 22.78 ± 5.57 min) was significantly earlier in patients of the LD group.[11]

Our study's mean and standard deviation for intraoperative pulse, systolic, and diastolic blood pressure were similar. There was no statistical significance found which was comparable to the reports of Gagandeep et al., where they reported that mean intraoperative pulse rate, systolic and diastolic blood pressure was more stable in patients receiving a combination of fentanyl and Levobupivacaine.[12]

In our study, the mean value and standard deviation of Spo2 were significantly different between the groups. There was little difference in the mean and SD of pulse rate in both groups. After 24 hours postoperatively, systolic blood pressure was found to be 114.20±8.05 in group A and 112.75±6.63 in group B. Diastolic blood pressure after 24 hours postoperatively was found to be 76.00±6.84 in group A and 77.00±6.38 in group B. Similar to our study, Agrawal et al. reported mean pulse rate (min), SBP (mmHg), DBP (mmHg) and Spo2 (%) were comparable between groups (p>0.05). MAP (mmHg) was significantly higher in Group N compared to Group C.[13]

In our study, the mean and SD for pain by visual analogue scale score were found to be a little higher in patients who received intrathecal levobupivacaine with adjuvant fentanyl than in patients. The mean value for the first dose of analgesic required at (in hours) in group A was 14.13, and SD was 3.40, whereas in group B, the mean value was 9.76, and SD was 2.60. The difference was found to be highly statistically significant (p=0.000). Agrawal et al. reported a VAS score of 38.56±1.79 at 16 hours in Group N, whereas Group D had a VAS score of 42.83±0.99 at 12 hours, and Group C had 49.46±1.132 at 8 hours (p< 0.001). At 24 hours, VAS scores of groups N, D, and C were 15.17±1.497, 15.67±1.309 and 15.67±1.714, respectively.13 Another study conducted by Jitendra Agrawal et al. VAS score was 38.56±1.79 at 16 hours in Group N, and Group C had 49.46±1.132 at 8 hours (p<0.001).[9]

In our study, the mean and SD for the number of anaesthetic doses required in group A were 1.45±0.59; in group B, they were 2.64±0.87, which was statistically significant (p=0.001). Akan et al. reported the time taken for administration of the first analgesic request was lesser in the fentanyl group when compared with the other groups (p<0.05). During the first 24 hours of the postoperative period, 58% of patients, 48% of patients, and 45% required a dose of the analgesic drug in groups I, II, and III, respectively (p>0.05).[14] Salama et al. reported for the first time that the postoperative analgesic requirement was significantly longer in the LN group (384± 23.1 min) compared to the L group (202.20 ± 23.42 min) (p>0.001). The total dose of postoperative supplementary analgesia (intravenous paracetamol infusion) in the first 12 hours was significantly lesser in the LN group (200.5 ±65.5 mg) in comparison with the L group (355.25 ± 69.9 mg) (p<0.05).[15]

Saleh et al. reported that the time to first analgesia was significantly higher in Group L +N (p<0.01) compared to another group. The mean time for first rescue analgesia was 5.9± 1.0 hours and 11.2 ± 1.6 hours in Group L and Group L+N, respectively. On comparing the pain scores of the two groups at 2, 4, 6, 12, and 24 postoperative hours, it was found that there was a statistically significant difference between Group L+ N and Group L at 4, 6, and 12 h with higher pain scores in the (Group L) than in the other Group (L + N). Vomiting was present in 5 (8.3%) patients in group A and 15 (25%) patients in group B, and the difference was found to be statistically significant (p<0.01).[16]

In our study, among 30 patients, pruritis was noted in 2 patients in group A and 10 in group B. The difference was found to be statistically significant (p<0.01). Shivering was present in 3 individuals in group A and 7 in group B, but the difference was not statistically significant (p>0.05). Akan et al. reported no differences between groups regarding side effects (p>0.05).[14]

CONCLUSION

The duration of postoperative analgesia and the effective analgesic time was more prolonged in the nalbuphine group than in the fentanyl group, with a statistically significant difference. As regards the

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side effects, they were less in the nalbuphine group than in the fentanyl group, with no statistically significant difference. We concluded that intrathecal nalbuphine combined with levobupivacaine is comparatively better than intrathecal fentanyl combined with levobupivacaine in terms of postoperative pain relief. Thus, doses of analgesics required during the postoperative period were less, with no difference in hemodynamic parameters like pulse rate, systolic and diastolic blood pressure, and oxygen saturation.

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