Original Research Article

A prospective randomized double blind controlled clinical study comparing epidural butorphanol versus nalbuphine as adjuvants in abdominal hysterectomy

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International Archives of Integrated Medicine, Vol. 7, Issue 3, March, 2020.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 19-02-2020 **Accepted on:** 25-02-2020
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Jayashree, Asrar Hussain, Henna. A prospective randomized double blind controlled clinical study comparing epidural butorphanol versus nalbuphine as adjuvants in abdominal hysterectomy. IAIM, 2020; 7(3): 80-87.

Abstract

Background: Pain is abnoxius stimulus after surgery. This study was undertaken to evaluate the post-operative analgesic benefits in patients administered with epidural butorphanol and nalbuphine as adjuvants with local anesthetic post operatively for abdominal hysterectomy under epidural anaesthesia and to compare their post-operative efficacy.

Material and methods: An RCT was conducted among 80 patients who were divided into two equal groups by computer generated random numbers. One group received Butorphanol and other received Nalbuphine. The sensory block, motor block, duration of analgesia, quality of analgesia and side effects were compared between the two groups.

Results: There was no difference in the pulse rates of patients belonging to both the groups. Not much variation was recorded in systolic and diastolic blood pressures in both the groups. The mean onset of sensory block in Butorphanol group was 5.9 min and 4.6 min in Nalbuphine group. The mean pain score was 1.0 after three hours of injection in the butorphanol group and Nalbuphine group. The duration of analgesia was 7.85 hours in the Butorphanol and 7.88 hours in the Nalbuphine group. Nausea/ vomiting were the main complication among the Butorphanol group and also found in Nalbuphine group. In butorphanol group, the quality of analgesia was good in 93.3% and in Nalbuphine group in 90.0% of the cases.

Conclusion: Both butorphanol and Nalbuphine had comparable efficacy and side effects as adjuvants in epidural anesthesia.

Key words

Epidural anesthesia, Butorphanol, Nalbuphine, Sensory block, Motor block.

Introduction

Pain is an unpleasant sensory and emotional experience which is often associated with actual or potential tissue damage. Anesthesia is provides adequate pain relief in the course of surgical procedure and in the post-operative period. Epidural anesthesia is well established anesthetic technique which is used for most of the surgical procedures [1]. Polypharmacy is often used nowadays as treat approach to ally post-operative pain without associated side effects [2].

Adjuvants are known to minimize the side effects of the local anesthetics and also prolong the duration of intra and post-operative analgesia. Narcotic analgesics have shown to hasten the onset, improve the quality of the block as well as prolong the duration of analgesia. Butorphanol is a lipid-soluble synthetically derived narcotic with weak μ-receptor agonist and antagonist activity and strong k-receptor agonism [3]. It has strong analgesic and sedative properties without respiratory depression. Butorphanol has been frequently used for post-operative analgesia and labor analgesia. This has also got additional properties including lower addiction potential, lesser nausea, vomiting, pruritis and urinary retention. It produces sedation comparable to or more than that of morphine, which is desired in post-operative period [4, 5, 6].

Nalbuphine, a derivative of 14-hydroxymorphine which is structurally related to oxymorphone and naloxone is a strong analgesic with mixed k agonist and μ antagonist properties. The analgesic potency of nalbuphine has been found to be equal to morphine but unlike morphine, it exhibits a ceiling effect on respiratory depression. Nalbuphine has the potential to maintain or even enhance μ-opioid based analgesia while simultaneously mitigating the μ-opioid side effects. Sedation is commonly seen when used in post-operative period as an analgesic [7].

A study comparing the post-operative analgesic effect of administration of butorphanol, nalbuphine, and fentanyl had shown that, the onset of sensory block was significantly earlier in fentanyl group when compared to butorphanol and nalbuphine groups. The duration of anesthesia was significantly longer in butorphanol group than fentanyl and nalbuphine groups. No serious side effects were encountered in any of the groups [6].

This study was undertaken to evaluate the post-operative analgesic benefits in patients administered epidural butorphanol and nalbuphine as adjuvants with local anesthetic post operatively for abdominal hysterectomy under epidural anesthesia and to compare their post-operative efficacy.

Materials and methods

A randomized controlled trial was conducted in the Department of Anesthesiology, Institute of Medical Sciences, after approval from Institution ethical Committee. About 80 patients of ASA grade I and II undergoing epidural anesthesia for abdominal hysterectomy in Obstetrics and Gynecology Department were included as study sample. A Written informed consent was obtained from all the patients. Female patients posted for abdominal hysterectomy under epidural anesthesia, Age group between 30-60 years, Weight between 40-70 kg and ASA physical status I and II were included. Emergency surgeries, Severe anaemia, coagulation abnormalities and bleeding disorders, Patients with previous history of surgeries on spine, Patients with spinal deformity, Patients with history of chronic backache, Patients with active skin lesions over the lumbosacral area were excluded from the study.

About 80 adult female patients of American Society of Anesthesiologist grade I or II in the age group of 30 – 60 years, undergoing abdominal hysterectomy under epidural anesthesia were enrolled into the study. Patients were familiarized with visual analogue scale (VAS) scoring pre-operatively and were taught to grade their pain on the scale. A thorough pre–anesthetic evaluation was conducted with special emphasis on cardio-respiratory system, nervous system and endocrinal abnormalities. The investigations pertaining to HB%, BT, CT, Blood sugar, Blood urea, Serum creatinine, Urine analysis for albumin, sugar and microscopy, ECG in 12 leads and chest X-ray was conducted on all patients.

Randomization was conducted by using a computer-derived random-number sequence and sealed opaque envelopes, and all investigators were kept unaware of the envelope details throughout the whole study period. The patients were then divided randomly into following two groups according to the epidural medications they received:
Group A (n=40): bupivacaine 0.5% (19 ml) + butorphanol 2 mg (1 ml)
Group B (n=40): bupivacaine 0.5% (19 ml) + nalbuphine 10 mg (1 ml).

Heart rate (HR), non-invasive blood pressure, pulse oximetry (SpO_2) and respiratory rate (RR) were obtained from all the patients at regular intervals. Various block characteristics was observed including, Sensory block, Onset of analgesia, Completion of analgesia, Level of analgesia, Quality of analgesia grades and the motor block was be assessed by using modified Bromage scale. Onset, completion and regression of motor block were also assessed. Sensory block was assessed at 0, 2, 5, 10, 20 and 30 min post-drug injection into the epidural space. In the post-operative period, pain scores were assessed on the VAS scale every hour till 6 hours and then every 2 hours till 24 hours. The data thus obtained was compiled by using and excel sheet. The data was then transferred and analyzed using Statistical package for Social Services (SPSS vs 20). The significance of differences between duration of sensory or motor block in two groups was analyzed by calculating the standard error of difference between two means and by unpaired 't' test. For comparison of incidences of side effects in two groups Chi-square test was used. A 'P' value <0.05 was considered as statistically significant.

Results

The mean age of the Butrophanol group was 43.2 (± 7.0) years and 43.9 (± 7.2) years among the Nalbuphine group. This difference in mean age was not statistically significant between the two groups. Hence, they were comparable with respect to age. Majority of the patients in butophanol and Nalbuphine group belonged to 41–50 years of age. About 50% of the patients of Butorphanol group belonged to ASA grade II and 70% of the Nalbuphine group belonged to grade I. The mean weight Butorphanol group was 56.7 (± 7.3) kg and 58.8 (± 5.1) Kg in Nalbuphine group. This difference in mean weight was not statistically significant between the two groups (**Table – 1**).

In the Butophanol group, the mean pulse rate was 88.4 b/min Butophanol group and reduced to 81.3 after 12 hours of injection of drug. In Nalbuphine group, the mean pulse rate was 88.6 b/min 5 minutes after the injection of drug and reduced to 79.6 b/min after 12 hours of injection of the drug. There was no statistically significant difference in pulse rate levels at any time intervals between the two groups (**Chart – 1**).

The mean systolic blood pressure was 106.7 mm of Hg in Butorphanol group and 109.1 mm of Hg in Nalbuphine group 5 minutes after injection of the drug. The systolicolic blood pressure decreased in both the groups after 20 minutes of injection of the drug and increased and stabilized after 1.5 hours after injection of the drug. The mean diastolic blood pressure 5 minutes after injection of the drug in Butorphanol group was 68.5 mm of Hg and 68.5 mm of Hg in Nalbuphine group. The diastolic blood pressure

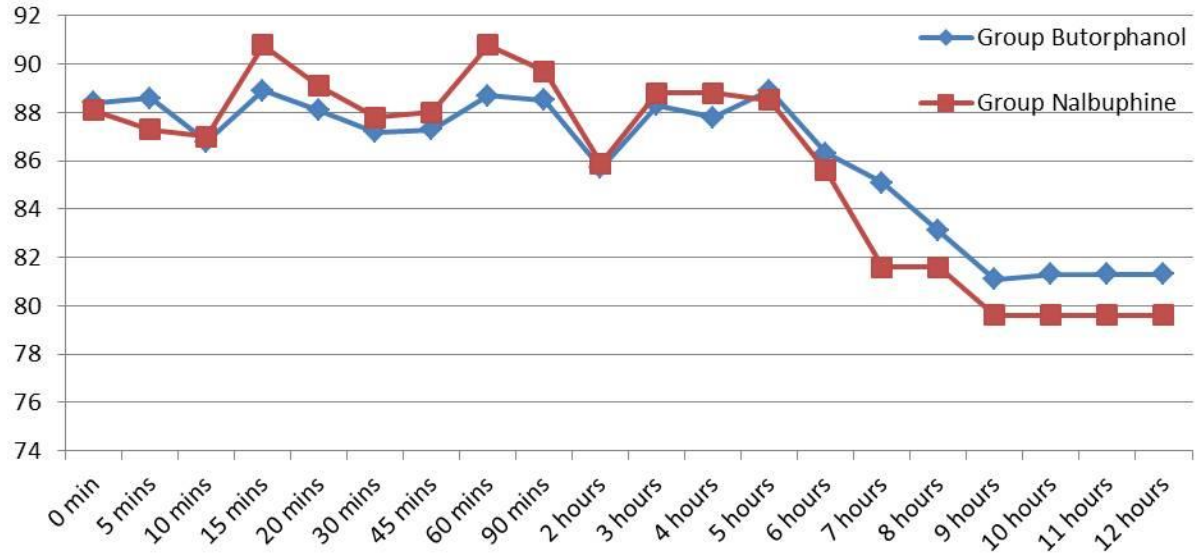
decreased 15 minutes after injection of the drug in all the two groups and stabilized 4 hours after the injection of the drug (**Chart – 2**).

The mean time of onset of sensory block was 5.9 min in Butorphanol group and 4.6 mins in Nalbuphine group which was statistically significant. The mean time of completion of the sensory nerve block was 10.1 min in the Butrophanol group and 9.5 min in the Nalbuphine group which was not statistically significant. The mean motor block score among the butorphanol group was 3.8 min and 3.8 among the Nalbuphine group. The duration of analgesia was 7.7 hours in the Butorphanol group and 7.88 hours in the Nalbuphine group. The pain scores were equal in both the groups after 3 hours and 2.55 in the Butorphanol and 2.37 in Nalbuphine group (**Table – 2**).

Table – 1: Distribution of the study group according to clinical characteristics.

	Age group	**Group**	
		Butorphanol N (%)	**Nalbuphine N (%)**
Age group	**31 – 40 years**	14 (35.0)	14 (35.0)
	41 – 50 years	19 (47.5)	18 (45.0)
	51 – 60 years	7 (17.5)	8 (20.0)
	Mean (± SD)	43.2 (± 7.01)	43.9 (± 7.25)
ASA Grade	**I**	21 (52.5)	26 (65.0)
	II	19 (47.5)	14 (35.0)
Weight	**Mean (± SD)**	56.7 (± 7.3)	58.8 (± 5.1)

Chart – 1: Distribution of the study groups according to pulse rate.



The sensory level was T6 among 55.0% of the Butorphanol group and 62.5% of the Nalbuphine group. Five percent of patients in both the groups noted chills and 12.5% in Butophanol and 7.5% in the Nalbuphine group had nausea/ vomiting (**Table – 3**).

Discussion

The epidural anaesthesia is well established regional anaesthetic technique and commonly used for all the surgical procedures carried on lower abdomen, pelvis and lower limbs [1]. This study was mainly undertaken to study the

efficacy of Butorphanol and Nalbuphine as adjuvants in epidural analgesia.

The mean age of the Butrophanol group was 43.2 years and 43.9 years in Nalbuphine group. Hence they were comparable with respect to age. About 50% of the patients of Butorphanol group belonged to ASA grade II and 70% of the Nalbuphine group belonged to grade I. The mean weight of the Butorphanol group was 56.7 (± 7.3) kg and 58.8 (± 5.1) Kg in Nalbuphine groups.

Chart – 2: Distribution of the study groups according to systolic and diastolic blood pressures.

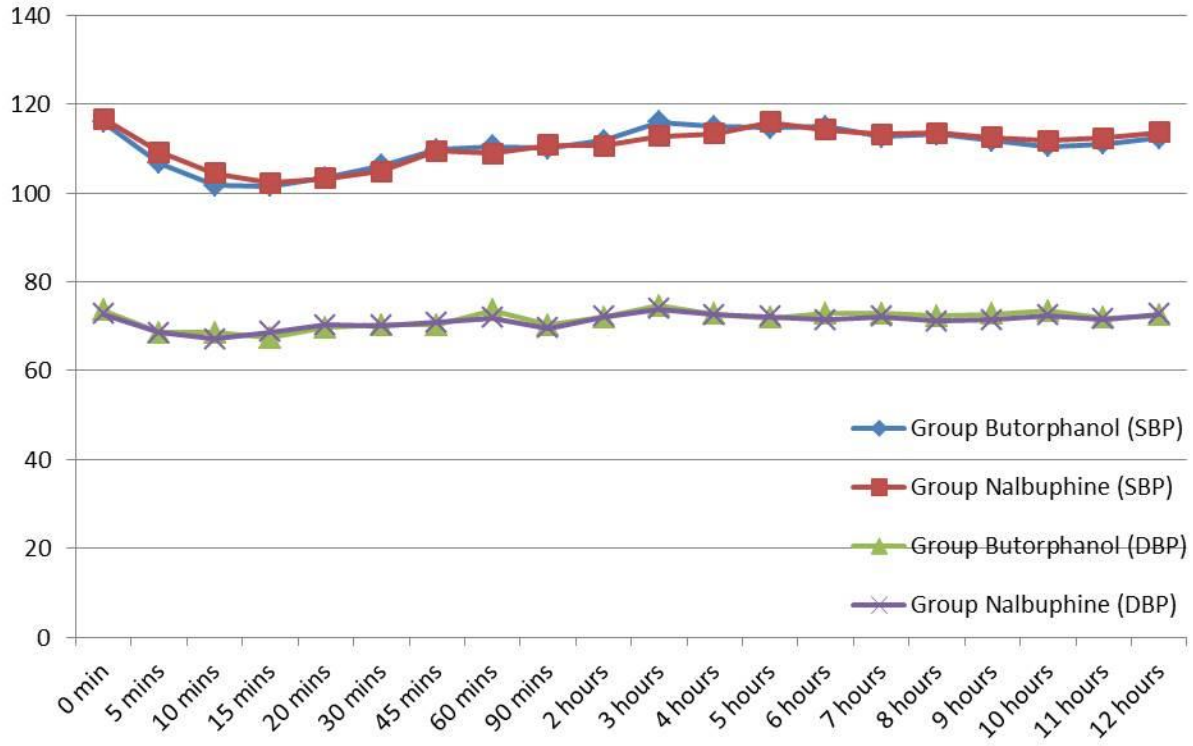


Table – 2: Distribution of the study groups according to time of sensory block, motor block and pain scores.

Mean (± SD)	Group		T value	P value
	Butorphanol	Nalbuphine		
Time of onset of sensory block (mins)	5.9 (± 2.1)	4.6 (± 1.6)	3.032	0.003, Sig
Time of completion of sensory block (mins)	10.9 (± 3.1)	10.0 (± 2.8)	1.323	0.19, NS
Motor block at the start of surgery (Bromage scale)	3.8 (± 0.4)	3.8(± 0.4)	0.582	0.562, NS
Duration of analgesia	7.75 (± 1.1)	7.86 (± 1.07)	-0.455	0.651, NS
Pain score after 3 hours	1.0 (0)	1.0 (0)		
Pain score after 6 hours	2.55 (± 0.60)	2.37 (± 0.74)	0.886	0.38, NS

In the Butophanol group, the mean pulse rate was 89.4 b/min Butophanol group and reduced to 80.6 after 12 hours of injection of drug. In Nalbuphine group, the mean pulse rate was 89.5 b/min 5 minutes after the injection of drug and reduced to 80.1 b/min after 12 hours of injection of the drug. In a study by Gosavi, et al.; the heart rate remained stable throughout intra-operative and recovery period in groups B and BB while in group BC it dropped from the baseline 30 to 45

min after caudal block and remained near this level throughout the surgery [8]. In a study by Karia, et al., the pulse rate of Ropivacaine and Butorphanol group was comparable at all the time intervals and were clinically and statistically significant [9]. In a study by Banerjee, et al., no change in pulse rate was observed in Butophanol, fentanyl and nalorphine groups [6].

Table – 3: Distribution of the study groups according to sensory level, side effects and quality of analgesia.

		Group		χ^2 Value	P value, Sig
		Butorphanol N (%)	Nalbuphine N (%)		
Sensory level	**T4**	17 (42.5)	15 (37.5)	1.316	0.518, NS
	T5	1 (2.5)	0		
	T6	22 (55.0)	25 (62.5)		
Side effects	**Chill**	2 (5.0)	2 (5.0)	0.559	0.756, NS
	Nausea/ Vomiting	5 (12.5)	3 (7.5)		
Quality of analgesia	**Fair**	5 (12.5)	4 (10.0)	0.125	0.723, NS
	Good	35 (87.5)	36 (90.0)		
	Total	40 (100)	40 (100)		

Not much variation was recorded in systolic and diastolic blood pressures were encountered in this study in both Butorphanol and Nalbuphine groups. In a study by Gosavi, et al., the blood pressure remained stable throughout the intra-operative period in both the groups but demonstrated a significant rise in 3 hours after surgery in Bupivacaine group which was significant compared to group BB and BC [8]. In a study by Karia, et al., the systolic blood pressure of Ropivacaine and Butorphanol group was comparable at all the time intervals and were clinically and statistically significant. The diastolic blood pressure of Ropivacaine and Butorphanol group was comparable at all the time intervals and were clinically and statistically significant [9].

The mean time of onset of sensory block in Butorphanol group was 5.9 min and 4.6 min in Nalbuphine group. In a study by Karia, et al., the onset of sensory block was 13.83 min and in butorphanol group was 9.36 min [9]. The mean onset of sensory block in control group was 7.5 min, 7.2 min in 0.8 mg of Nalbuphine, 7.4 min in 1.6 mg of Nalbuphine group and 7.1 min in 2.4 mg group of Nalbuphine group respectively [10].

The mean time of completion of the sensory nerve block was 10.9 min in the Butorphanol group and 10.0 min in the Nalbuphine group. In a study by Ahmed et al, mean duration of sensory block was 117.8 min in control group, 133.8 min in 0.8 mg group, 133.8 min in 1.6 mg group and 199.8 min in 2.4 mg group [10].

The mean motor block score among in the butorphanol group was 3.8 and 3.8 among the Nalbuphine group. In a study by Karia, et al., the onset of motor block was 17.17 min and in butorphanol group was 13.03 min [9]. The mean time of the onset of motor block was 8.5 min in control group, 8.4 min in 0.8 mg group, 8.5 min in 1.6 mg group and 8.2 min in 2.4 mg group [10].

The mean pain score after three hours of injection of the drug was 1.0 in the butorphanol group and Nalbuphine groups. In a study by Gosavi, et al., the mean pain score in the Bupivacaine group was less than 2 in recovery period but had a significant value in postoperative time and during 1st, 2nd and 3rd hour respectively. Hence all the patients needed post-operative analgesia [8]. In a study by Banerjee et al, the pain recorded was significantly lower in Butorphanol group and Fentanyl group than

Nalorphine group. All patients in fentanyl group, and nalorphine group required analgesic supplementation within first 2 – 4 hours and 4 – 6 hours [6].

The duration of analgesia was 7.85 hours in the Butorphanol group and 7.88 hours in the Nalbuphine group. In a study by Gosavi, et al., the mean duration of analgesia was 460.6 min in clonidine group compared to 378.8 in butorphanol group and 275.8 min in bupivacaine group [8]. In a study by Karia, et al., the mean duration of analgesia in ropivacaine group was 275 min and in Butorphanol group was 408 min [9].

Nausea/ vomiting was the main complication among the Butorphanol group followed by Chills in 5% of the patients. The nausea/ vomiting and chills were present in 7.5% of the patients in Nalbuphine group. In a study by Gosavi, et al., 2 patients in BB group had pruritus compared to none in BC group. About 7 patients in Butorphanol group had vomiting while only 2 patients in clonidine group did vomit. About 2 patients in BB group had prolonged urinary retention and 4 patients in BC group had urinary retention requiring catheterization [8]. In a study by Karia, et al., the bradycardia was present in 2 cases, hypotension in 3 cases and sedation in 2 cases [9]. In a study by Banerjee, et al., 12% in Butrophanol group, 16% of patients in fentanyl group and 48% of the patients in Nalorphine group had nausea and vomiting [6]. In a study by Ahmed et al, hypotension was present in 3 patients of control and lower dose of Nalbuphine and 6 patients in higher doses of anesthesia group. Bradycardia, nausea/ vomiting and pruritis were the other side effects [10].

In butorphanol group, the quality of analgesia was good in 93.3% of the cases and in Nalbuphine group, the quality of analgesia was good in 90.0% of the cases.

Conclusion

There were no significant changes in hemodynamic parameters including heart rate, systolic and diastolic blood pressures between Butorpanol and Nalbuphine. The mean time of onset of sensory block and mean time of completion of sensory block was better in Nalbuphine group. The mean onset of motor block was also comparable between the two groups, the pain score was better in Butorphanol and Nalbuphine group. Hence, both the drugs had equal efficacy and effectively used as adjuvants.

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