Comparative efficacy of butorphanol versus nalbuphine for balanced anaesthesia and post-operative analgesia in patients undergoing laparoscopic surgery

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Abstract
This randomized double blind study was conducted in 60 patients, aged 20-60 years of age, of ASA physical status I and II scheduled to undergo elective laparoscopic surgeries. They were randomized and allotted into two groups. Group B received Inj Butorphanol 20 mcg/kg IV (n=30) and Group N received Inj Nalbuphine 0.2mg/kg IV (n=30), before induction of anesthesia with propofol. Intra-operative haemodynamic stability was assessed by monitioring heart rate, systolic and diastolic blood pressure. Post-operatively, pain was assessed using the VAS scale, and sedation was assessed using the Ramsay Sedation Score.

Heart rate and diastolic blood pressures were lower in Group B after intubation, after insufflation of CO_2, after 30 minutes, after 45 minutes, after extubation and during the post-operative period. Systolic blood pressure was lower in Group B after intubation, after insufflation of CO_2, after 30 minutes and after 45 minutes. VAS pain scores were significantly lower in Group B at 6 hours and 8 hours post-operatively. Ramsay sedation scores were higher in Group B at 1hr, 2hrs, 4hrs, 6hrs and 8hrs post- operatively.

From this study, it was concluded that Inj. Butorphanol 20 µg /kg was more efficacious when compared to Inj. Nalbuphine 0.2mg/kg as an analgesic for use in laparoscopic surgeries because of its ability to produce prolonged analgesia and better hemodynamic stability.

Keywords: Butorphanol, Nalbuphine, Balanced anaesthesia, Post-operative analgesia, Laparoscopic surgery.

Introduction
Nalbuphine[1] is a semi-synthetic opioid agonist-antagonist. Indicated for the relief of moderate to severe pain. It can also be used as a supplement to balanced anaesthesia. Butorphanol[2] is a morphinan-type synthetic agonist-antagonist opioid analgesic. The most common indication for butorphanol is management of moderate to severe pain, as a supplement for balanced general anaesthesia. Butorphanol is also quite effective at reducing post-operative shivering.

Laparoscopic surgeries are also known as minimally invasive surgical procedures which are performed with assistance of video camera and several thin instruments. To perform a laparoscopic surgery, pneumoperitoneum should be created by insufflation with air or carbon dioxide. The created pneumoperitoneum causes several pathophysiological changes during surgery such as increase in systemic and pulmonary vascular resistance and extreme patient positioning.

Laparoscopic surgeries are commonly performed due to advantages like less post- operative pain and faster post-operative recovery. In this study, we compared Butorphanol and Nalbuphine as the analgesic component of balanced anaesthesia for laparoscopic surgeries.

Materials and Methods
After obtaining Institutional Ethical Committee approval, 60 consecutive patients posted for elective laparoscopic surgeries were enrolled for the study.

Inclusion Criteria
1. Male/Female patients of age group 20 to 60 yrs.
2. Patients of ASA physical status I and II.
3. Scheduled for elective laparoscopic surgeries.

Exclusion Criteria
1. Patients taking beta blockers, calcium channel blockers, angiotensin converting enzyme inhibitors.
2. Patients with history of cardiac, pulmonary, heptatic and renal diseases.
3. Patients with difficult airway
4. History of allergy to the study drug.
5. Pregnancy.
6. Patient unwillingness.

Preanaesthetic Evaluation

All patients underwent a routine pre-anaesthetic check-up as per the institutional protocol. An informed valid consent was taken from all the patients. Patients were given tab. Ranitidine 150mg and tab. Alprazolam 0.25mg the previous night. Nil per oral status of 8hrs was maintained for all patients.

Study Groups

The patients were randomized and allotted into two groups using a random number table. Group B received Inj Butorphanol 20 mcg/kg IV (n=30) and Group N received Inj Nalbuphine 0.2mg/kg IV (n=30) before induction.

Procedure Details

Venous access was secured with an 18 gauge intravenous cannula in the dorsum of the non-dominant hand. Ringer lactate solution was started at the rate of 4ml/kg/hr. Non-invasive blood pressure cuff, pulse oximeter and electrocardiography monitor (lead II and V5) were connected and basal parameters like heart rate, blood pressure and oxygen saturation were noted.

Group B or Butorphanol group: these patients were given Inj. Butorphanol 20mcg/kg intravenously 10 minutes before induction.

Group N or Nalbuphine group: these patients were given Inj. Nalbuphine 0.2mg/kg intravenously 10 minutes before induction.

Patients were pre oxygenated for 3 minutes with 100% oxygen followed by induction with Inj. propofol 2mg/kg. Neuromuscular blockade was achieved with Inj. Vecuronium bromide. Patient's trachea was intubated with appropriate sized endotracheal tube. Anaesthesia was maintained with 50% N_2O, 50% O_2 and Sevoflurane 1.5%. A lubricated Ryle's tube was then inserted to decompress the stomach.

Parameters Observed and Analyzed

Hemodynamic stability during the surgery was assessed by the following parameters-Heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), End tidal Carbon dioxide ($EtCO_2$) and oxygen saturation. These were observed and recorded at baseline, after administering the drug, after intubation, insufflation of CO_2, 30 and 45 minutes after intubation. Heart rate and blood pressures were also recorded after extubation, and at 1hr, 2hrs, 4hrs, 6hrs and 8hrs post- operatively.

At the end of surgery, residual neuromuscular blockade was reversed with Inj. Neostigmine 0.05 mg/kg and Inj. Glycopyrolate 0.01 mg/kg intravenously. After extubation, vital parameters, sedation and pain scores were recorded. The VAS scale[3] was used to assess pain and the RAMSAY[4] score was used to assess sedation.

Patient was then shifted to the PACU. Vital parameters, sedation and pain scores were assessed at 1, 2, 4, 6 and 8 hours postoperatively. Patients were given Inj. Fentanyl 0.5mcg/kg intravenously when the VAS score was >3, which was repeated until the pain subsided.

Statistical Tools

The information collected regarding all the selected cases were recorded in Master Charts 1 and 2. Data analysis was done with the help of computer using Epidemiological Information Package (EPI 2008).

Using this software, range, frequencies, percentages, means, standard deviations, chi square and 'p' values were calculated. Kruskal Wallis chi-square test was used to test the significance of difference between quantitative variables and Yate's test for qualitative variables. A 'p' value less than 0.05 was taken to denote significant relationship.

Observations and Results

There was no statistically significant difference found between the two groups with respect to age and gender distribution.

Table 1: Age & sex distribution

Age (in years)	Group B	%	Group N	%	p-value
< 20	2	07	0	00	
21 – 30	10	33	10	33	
31 – 40	5	17	9	30	
41 – 50	13	43	11	36	0.57
Total	30	100	30	100	
Male	18	60	17	56	
Female	12	40	13	44	
Total	30	100	30	100	0.793

The heart rate was comparable between the two groups at baseline and after administering the drug. However, heart rate was significantly lower in group B after intubation, after insufflation of CO_2, after 30 minutes, after 45 minutes, after extubation and during the post-operative period.

Table 2: Heart rate comparison

Variables	Group b		Group n		p - value
	Range	Mean ± SD	Range	Mean ± SD	
Baseline	60 – 112	82.9 ± 12.23	63 – 110	86.20 ± 12.70	0.309
After administering the drug	55 – 90	74.17 ± 12.79	60 – 118	80.23 ± 14.02	0.067
After intubation	54 – 104	76.17 ± 10.27	70 – 118	89.87 ± 3.31	0.003
After insufflation of CO_2	55 – 102	79.03 ± 12.62	68 – 124	89.43 ± 12.44	0.004
After 30 minutes	55 – 105	77.80 ± 11.40	60 – 124	85.97 ± 12.25	0.012
After 45 minutes	55 – 110	77.50 ± 11.90	65 – 127	86.43 ± 12.41	0.000
After Extubation	60 – 95	79.27 ± 8.87	62 - 106	84.27 ± 10.02	0.021
Post Op	60 – 95	79.43 ± 9.23	65 – 123	85.14 ± 10.15	0.004
Grand Mean		78.2838		85.9425	
p-value	0.0241				

The systolic blood pressure was comparable between the two groups at baseline, after extubation and during the post-operative period. However, it was significantly lower in Group B after intubation, after insufflation of CO_2, after 30 minutes and after 45 minutes.

Table 3: Systolic blood pressure comparison

Variables	Group B		Group N		p - value
	Range	Mean ± SD	Range	Mean ± SD	
Baseline	104 – 160	127.07 ± 14.52	101 – 148	123.43 ± 10.62	0.273
After administering the drug	75 – 171	121.60 ± 22.34	86 – 135	108.47 ± 12.46	0.005
After intubation	90 – 169	125.37 ± 17.95	100 – 180	139.87 ± 18.33	0.006
After insufflation of Co_2	89 – 151	118.43 ± 15.54	98 – 170	131.20 ± 19.06	0.003
After 30 minutes	83 – 160	114.33 ± 15.11	102 – 174	126.21 ± 18.55	0.006
After 45 minutes	87 – 162	115.57 ± 15.71	102 – 176	127.23 ± 18.52	0.010
After Extubation	92 – 164	124.73 ± 15.61	104 – 179	127.20 ± 13.52	0.515
Post Op	92 – 165	126.22 ± 15.44	106 – 170	129.44 ± 13.44	0.524
Grand Mean		121.665		126.6313	
p-value	0.0001				

The diastolic blood pressure was comparable between the two groups at baseline and after administering the drug. However, it was significantly lower in Group B after intubation, after insufflation of CO_2, after 30 minutes, after 45 minutes, after extubation and during the post-operative period.

Table 4: Diastolic blood pressure comparison

Variables	Group B		Group N		p - value
	Range	Mean ± SD	Range	Mean ± SD	
Baseline	62 – 100	80.3 ±9.24	53 – 107	85.27 ± 12.16	0.0802
After administering the drug	54 – 96	77.2 ±10.63	50 – 88	71.37 ± 8.88	0.0612
After intubation	57 – 109	83.53 ± 12.35	60 – 116	89.73 ± 12.51	0.0592
After insufflation of Co_2	61 – 102	76.53 ± 9.95	56 – 106	82.23 ± 12.12	0.0480
After 30 minutes	60 – 100	76.88 ± 9.44	57 – 100	81.14 ± 12.55	0.0410
After 45 minutes	58 – 105	77.76 ± 11.84	56 – 98	79.44 ± 12.41	0.0090
After Extubation	51 – 100	79.70 ± 11.65	60 – 97	78.87 ± 10.92	0.0041
Post Op	53 – 104	79.94 ± 10.98	62 – 100	79.02 ± 10.52	0.0104
Grand Mean		78.98		80.8838	
p-value	0.0001				

Comparing post-operative pain scores between the two groups, there was no significant difference in the VAS pain scores at 1 hour, 2 hours and 4 hours post-operatively. However, patients in Group B had significantly lower VAS pain scores at 6 hours and 8 hours post-operatively.

Table 5: VAS score comparison

Time	Group B	Group N	p-value
	Mean	Mean	
1 hour	3.92	5.00	0.712
2 hours	4.04	4.00	0.629
4 hours	4.42	4.87	0.652
6 hours	4.80	4.92	0.042
8 hours	4.91	5.00	0.025
Grand Mean	4.418	4.758	
p-value	0.0013		

Comparing the post-operative Ramsay sedation scores, the scores were significantly higher in the butorphanol group at 1 hour, 2 hours, 4 hours, 6 hours and 8 hours post-operatively.

Table 6: Ramsay sedation score

Variables	Group B		Group N		p-value
	Mean	SD	Mean	SD	
Pre-Op	1.72	0.67	1.17	0.41	0.0074
Post-Op 0 hour	2.76	0.62	2.03	0.59	0.0010
Post-Op 1st hour	2.41	0.51	1.62	0.42	0.0012
Post-Op 2nd hour	2.39	0.43	1.63	0.51	0.0002
Post-Op 4th hour	1.94	0.59	1.17	0.32	0.0001
Post-Op 6th hour	1.42	0.47	1.04	0.07	0.0004
Post-Op 8th hour	1.39	0.43	1.09	0.02	0.0120
Grand Mean	1.91		1.31		
p-value	0.0024				

Discussion

In our study, we found that Butorphanol and Nalbuphine were both cardio stable. However, Heart rate was significantly lower in group B (Butorphanol group) after intubation, after insufflation of CO_2, after 30 minutes, after 45 minutes, after extubation and during the post-operative period. Systolic and Diastolic Blood Pressures were significantly lower in Group B after intubation, after insufflation of CO_2, after 30 minutes and after 45 minutes. This shows that Butorphanol is more effective than Nalbuphine in attenuating the sympathetic response to direct laryngoscopy and endotracheal intubation and in blunting the surgical stress response.

Rao satyanarayana V, Srinivas B, Muralidar A et al[5] compared butorphanol and fentanyl for balanced anaesthesia in patients undergoing laparoscopic surgeries under general anaesthesia. Fifty patients of ASA I & II scheduled for elective laparoscopic surgery were randomized to butorphanol group and fentanyl group. There was significant rise in systolic & diastolic blood pressure after intubation in fentanyl group compared to butorphanol group.

R.K. Verma, S. Jaiswal, et al[6] compared butorphanol and fentanyl in total intravenous anaesthesia in laparoscopic cholecystectomy. In this study, patients received either inj. fentanyl 2 µg/kg or butorphanol 25µg/kg. All the patients were induced with inj. propofol and muscle relaxation with vecuronium. Anaesthesia was maintained by oxygen and propofol infusion. Suppression of sympathetic response to laryngoscopy and intubation was found to be better with Butorphanol than Fentanyl.

The above two studies had concluded that Butorphanol was more efficacious than Fentanyl in attenuating the haemodynamic stress response to direct laryngoscopy and endotracheal intubation

Tariq M A, Iqbal Z, Qadirullah, et al[7] studied the efficacy of nalbuphine in preventing hemodynamic response to laryngoscopy and intubation. The nalbuphine group showed significantly lesser increase in mean arterial pressure and heart rate compared to control group after laryngoscopy and orotracheal intubation. They concluded that nalbuphine prevents marked rise in heart rate and mean arterial pressure associated with laryngoscopy and intubation.

In our study, there was no significant difference in the VAS pain scores between the two groups at 1 hour, 2 hours and 4 hours post-operatively. However, patients in Group B (Butorphanol Group) had significantly lower VAS pain scores at 6 hours and 8 hours post-operatively. This shows that Butorphanol provides longer duration of analgesia compared to Nalbuphine. Also, the Ramsay sedation scores were significantly higher in the Butorphanol group at all the time points post-operatively. There was no significant effect in oxygen saturation post-operatively.

F.N. Minai and F.A. Khan, et al[8] compared morphine and nalbuphine for intraoperative and post operative analgesia. They concluded that nalbuphine in a dose of 0.2mg/kg provided better analgesia and greater hemodynamic stability, as a component of balanced anaesthesia in lower abdominal surgery, with a lower incidence of nausea and vomiting in postoperative period compared to morphine 0.1 mg/kg.

The previous literature, however does not contain any study comparing Butorphanol and Nalbuphine for balanced anaesthesia. In our study, both Nalbuphine and Butorphanol provided good analgesia. The duration of analgesia was longer with Butorphanol than with Nalbuphine.

Conclusion

From this study, it is concluded that Inj. Butorphanol 20 µg /kg is more efficacious than Inj. Nalbuphine 0.2mg/kg as an analgesic for use in laparoscopic surgeries because of its ability to provide prolonged analgesia and better hemodynamic stability.

Conflict of Interest: None.

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