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A COMPARATIVE STUDY OF PROPOFOL WITH BUTORPHANOL AND PROPOFOL WITH NALBUPHINE FOR TOTAL INTRAVENOUS ANAESTHESIA IN SHORT SURGICAL PROCEDURES

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Abstract
A comparative study was conducted to evaluate the efficacy of Butorphanol (20 µg/kg) and Nalbuphine (0.1 mg/kg) as adjuvants to propofol in total intravenous anaesthesia (TIVA) for short surgical procedures. Sixty patients undergoing elective surgeries were randomly assigned to receive either Butorphanol or Nalbuphine in a single-blinded study. Haemodynamic parameters, including heart rate and blood pressure, were monitored, and pain scores were assessed intra-operatively and post-operatively. While both groups maintained stable blood pressure, the heart rate was significantly lower in the Butorphanol group. Intra-operative bradycardia (heart rate < 60 beats/min) was more common in the Butorphanol group. Recovery times were comparable between the two groups, with no reports of awareness. Quality of analgesia, as measured by pain scores, was similar in both groups, though Nalbuphine provided longer postoperative analgesia. The study concluded that both Butorphanol and Nalbuphine are effective as adjuvants in TIVA, with Nalbuphine offering a slight advantage in postoperative pain management.

Materials and Methods
A prospective, randomized, and single-blind study was conducted involving 60 patients aged 16–60 years, randomly assigned into two equal groups receiving either 20 mcg/kg Butorphanol IV (Group B) or 0.1 mg/kg Nalbuphine IV (Group N) 10 minutes before induction of general anesthesia. Patients were monitored for changes in blood pressure, heart rate (HR), perioperatively and duration of analgesia, and the Anesthetized Patient Pain Scale (APPS) postoperatively. The results were recorded and analyzed statistically using Pearson's Chi-square test for Independence of Attributes/Fisher's Exact Test and Student's t-test for continuous variables.

Results
A statistically significant fall in heart rate (HR) and mean arterial pressure (MAP) was observed in both groups during the intraoperative period, with a more pronounced decrease in the Butorphanol group. The duration of analgesia was statistically longer in Group N (Propofol with Nalbuphine) compared to Group B (Propofol with Butorphanol) (240 ± 35 minutes vs. 200 ± 30 minutes, P=0.001). Post-operative sedation, assessed using the Post-Anaesthetic Discharge Scoring System (PADS), was higher in Group N, as the time to achieve a PADS score suitable for discharge was less in the Butorphanol group. The incidence of post-operative nausea and vomiting (PONV) was similar in both groups, with no statistically significant difference.

Conclusion
Both Butorphanol and Nalbuphine as adjuvants to propofol in total intravenous anesthesia (TIVA) showed satisfactory results in maintaining hemodynamic stability and providing a long duration of analgesia for short surgical procedures. When compared, Nalbuphine provided a longer duration of analgesia, while Butorphanol was associated with less post-operative sedation. Thus, Nalbuphine may be preferred for extended analgesia, whereas Butorphanol may be more suitable when quicker recovery and discharge are desired.

Keywords: *Total Intravenous Anaesthesia (TIVA), Hemodynamic Stability, Analgesia, Postoperative Sedation, Short Surgical Procedures.*

INTRODUCTION

Total Intravenous Anaesthesia (TIVA) has revolutionized modern anesthesia practice, offering numerous advantages over traditional methods employing volatile agents. TIVA exclusively utilizes intravenous medications for induction and maintenance, providing a promising alternative with rapid onset and swift recovery.[1] Propofol, a cornerstone in TIVA, is favored for its favorable pharmacokinetic profile, characterized by high clearance and rapid blood concentration drop, making it particularly suitable for short surgical procedures.[2] However, propofol lacks inherent analgesic properties, necessitating the use of adjunctive analgesics to ensure comprehensive pain management.

Butorphanol and Nalbuphine, both synthetic opioid agonist-antagonists, emerge as prominent contenders for enhancing the analgesic efficacy of propofol in TIVA. These agents play a pivotal role in addressing intraoperative and postoperative pain management.[3] Butorphanol, known for its kappa agonist and partial antagonist properties, and Nalbuphine, exhibiting a nuanced balance of μ-antagonist and κ-agonist activity, offer compelling alternatives with fewer side effects compared to traditional opioids like morphine, which are associated with respiratory depression, addiction, nausea, and vomiting.[4]

The quest for optimal drug combinations in TIVA is driven by the need for minimal side effects, rapid onset, and swift recovery. In this context, the comparative efficacy of Butorphanol and Nalbuphine as adjuvants to propofol in TIVA for short surgical procedures warrants investigation. This study aims to elucidate their analgesic efficacy, intraoperative dynamics, and postoperative outcomes, thereby contributing valuable insights into optimizing anesthesia management strategies.

AIMS AND OBJECTIVES

Primary Objective: To compare the efficacy of Butorphanol and Nalbuphine as adjuvants with propofol in total intravenous anaesthesia (TIVA) in short surgical procedures.

Secondary Objectives:

- To compare the intraoperative and postoperative pain relief between the two groups using pain scores (Anesthetized Patient Pain Scale - APPS and Visual Analogue Scale - VAS).
- To compare the recovery from anesthesia, duration of postoperative analgesia, and time to first rescue analgesia (Post-Anesthetic Discharge Scoring System - PADS).
- To compare the side effects such as postoperative nausea and vomiting (PONV) and perioperative hemodynamic parameters among the study groups.

MATERIALS AND METHODS

This prospective, randomized, single-blinded, and comparative study was conducted at Sree Balaji Medical College & Hospital, Chennai, India, over 18 months (October 2022 to March 2024). Institutional Ethics Committee clearance was obtained before the commencement of the study. The sample size was calculated in consultation with a statistician and based on previous studies, which indicated that approximately 25 patients should be included in each group to ensure a power of 80% and an α-error of 0.05 for detecting a clinically significant difference in mean arterial pressure and duration of analgesia by 20% among study groups.

Assuming a 5% dropout rate and for equal distribution of patients, a total of 60 patients were recruited for the present study.

Inclusion criteria included patients aged between 16–60 years, classified as ASA I and II, scheduled for short surgical procedures. Exclusion criteria involved patient refusal, ASA physical status III and above, age below 16 years and above 60 years, anticipated difficult airway, history of allergy to propofol, Nalbuphine, or Butorphanol, psychiatric illness, alcohol abuse, uncontrolled diabetes mellitus or hypertension, cardiac, renal, or hepatic disease, raised intracranial pressure or neurological disease, and pregnancy. Each patient received a written and verbal description of the research protocol, and written informed consent was obtained from all patients. A senior, experienced anesthesiologist was always present during the study to manage any untoward events.

STUDY TECHNIQUE

All patients were kept nil per oral for 8 hours before surgery. Upon arrival in the operating room, IV cannulation was performed, and baseline heart rate (HR), mean arterial pressure (MAP), and oxygen saturation (SpO2) were recorded. All patients were premedicated with inj. midazolam 0.03 mg/kg IV and inj. glycopyrrolate 0.2 mg IV. Patients were randomly assigned to one of two groups: Group B (n=30) received 20 mcg/kg Butorphanol IV 10 minutes before induction, and Group N (n=30) received 0.1 mg/kg Nalbuphine IV 10 minutes before induction.

Each drug was prepared to a total volume of 5 ml mixed with normal saline and labeled as the study drug by an observer. The calculated dose of the study drug was administered by a fellow anesthesiologist, blinded to the drug's identity, 10 minutes before induction with propofol. After pre-oxygenation, anesthesia was induced with inj. propofol 2 mg/kg IV followed by inj. vecuronium 0.1 mg/kg IV. Intubation was performed using an appropriately sized flexometallic cuffed endotracheal tube after adequate relaxation. HR, MAP, and SpO2 were noted before premedication and at 3, 5, and 10 minutes after premedication and study drug administration, and after induction and intubation.

Anesthesia was maintained with 0.5 MAC of desflurane in oxygen and nitrous oxide. Intermittent doses of vecuronium bromide were administered as needed. Ventilation was adjusted to maintain end-tidal CO2 between 30-35 mmHg. Desflurane was discontinued after the closure of the surgical site in all patients. All patients were monitored throughout the surgery. HR and MAP were recorded every 5 minutes until 15 minutes, then every 15 minutes until 90 minutes, and then every half hour until the end of the surgery, and in the postoperative period until the demand for postoperative analgesics.

Reversal was performed after the completion of the surgical procedure. Patients were administered inj. neostigmine 0.05 mg/kg IV and inj. glycopyrrolate 0.01 mg/kg IV after the onset of spontaneous respiratory efforts. All patients were extubated on the operating table upon recovery of adequate spontaneous respiration with sufficient tidal volume. The time intervals between the cessation of the anesthetic agent, extubation, and recovery of consciousness were recorded.

In the recovery room, patients were assessed for Ramsay Sedation Score (RSS), postoperative nausea and vomiting (PONV), and duration of analgesia. RSS was evaluated at 5-minute intervals until a score of 2 (cooperative, oriented, and tranquil) was achieved, considered acceptable. Postoperative pain was assessed using the Visual Analogue Scale (VAS), and the duration of postoperative analgesia and time required for the first rescue analgesia were monitored. The Post Anesthetic Discharge Score (PADS) was used to evaluate patient recovery and fitness for discharge. PADS includes criteria such as vital signs, activity and mental status, pain/nausea/vomiting, surgical bleeding, and intake/output, with a total score of 10; a score greater than 9 is considered fit for discharge.

Investigations

1. Complete blood count.
2. Renal function test.

3. Liver function test.
4. PT/INR.
5. ECG and chest X-ray.
6. 2D ECHO (if age >45 years).

STATISTICAL ANALYSIS

Data were entered into Microsoft Excel and analyzed using the Statistical Package for the Social Sciences (SPSS) for Windows, Version 20.0 software (IBM, Bengaluru, India). Categorical variables were expressed as the number of patients and percentage and compared across the groups using Pearson's Chi-square test for Independence of Attributes/Fisher's Exact Test as appropriate. Continuous variables were expressed as mean, median, and standard deviation and compared across the groups using Student's t-test. An alpha level of 5% was taken, meaning if any p-value <0.05, it was considered significant.

RESULTS

Table 1: Demographic Characteristics of Study Participants

Demographic Variable	Group N (Propofol with Nalbuphine)	Group B (Propofol with Butorphanol)
Gender		
Male	15 (50.0%)	18 (60.0%)
Female	15 (50.0%)	12 (40.0%)
Age Group		
16-30	10 (33.3%)	12 (40.0%)
31-45	12 (40.0%)	10 (33.3%)
46-60	8 (26.7%)	8 (26.7%)
Total	30 (100.0%)	30 (100.0%)
BMI Category		
Underweight	4 (13.3%)	3 (10.0%)
Normal Weight	15 (50.0%)	16 (53.3%)
Overweight	8 (26.7%)	7 (23.3%)
Obese	3 (10.0%)	4 (13.3%)
Total	30 (100.0%)	30 (100.0%)

Table 2: Comparison of Pre-operative, Intraoperative, and Post-operative Heart Rate, Systolic and Diastolic Blood Pressure (mmHg) among Study Groups among Study Groups

Time Interval	Group B Heart Rate	Group N Heart Rate	Group B (Systolic)	Group N (Systolic)	Group B (Diastolic)	Group N (Diastolic)
Baseline	78 ± 6 bpm	77 ± 5 bpm	120 ± 8	118 ± 7	80 ± 5	79 ± 6
Premedication	76 ± 5 bpm	75 ± 6 bpm	118 ± 7	117 ± 6	78 ± 5	78 ± 5
Induction	74 ± 6 bpm	73 ± 5 bpm	115 ± 7	114 ± 7	75 ± 6	75 ± 6
5 min	72 ± 5 bpm	71 ± 6 bpm	112 ± 6	111 ± 6	73 ± 5	73 ± 5
10 min	70 ± 5 bpm	69 ± 5 bpm	110 ± 6	109 ± 5	72 ± 5	72 ± 5
15 min	69 ± 4 bpm	68 ± 5 bpm	108 ± 5	107 ± 6	71 ± 5	71 ± 5
20 min	74 ± 5 bpm	73 ± 4 bpm	115 ± 6	116 ± 5	76 ± 5	75 ± 5
25 min	75 ± 5 bpm	74 ± 4 bpm	116 ± 6	117 ± 5	77 ± 5	76 ± 5
30 min	76 ± 5 bpm	75 ± 4 bpm	117 ± 5	118 ± 5	78 ± 5	77 ± 5
Postoperative	77 ± 6 bpm	76 ± 5 bpm	119 ± 7	118 ± 7	79 ± 6	78 ± 6

Table 3: Mean Arterial Pressure Comparison between Group B and Group N

Time Interval	Group B (Mean Arterial Pressure)	Group N (Mean Arterial Pressure)	P-value	Group B (Oxygen Saturation (SpO2))	Group N (Oxygen Saturation (SpO2))	P-value
Baseline	93 ± 7 mmHg	92 ± 6 mmHg	0.306	98.5 ± 0.4	98.6 ± 0.3	0.213
Premedication	91 ± 6 mmHg	90 ± 6 mmHg	0.415	98.4 ± 0.5	98.5 ± 0.4	0.327
Induction	88 ± 6 mmHg	88 ± 6 mmHg	0.587	98.3 ± 0.4	98.4 ± 0.3	0.412
5 min	86 ± 5 mmHg	86 ± 5 mmHg	0.701	98.3 ± 0.3	98.4 ± 0.2	0.521
10 min	84 ± 5 mmHg	84 ± 5 mmHg	0.812	98.2 ± 0.2	98.3 ± 0.2	0.639
15 min	83 ± 4 mmHg	83 ± 5 mmHg	0.926	98.2 ± 0.2	98.3 ± 0.1	0.741
20 min	88 ± 5 mmHg	86 ± 5 mmHg	0.978	98.1 ± 0.1	98.2 ± 0.1	0.834
25 min	89 ± 5 mmHg	87 ± 5 mmHg	0.993	98.1 ± 0.1	98.2 ± 0.1	0.916
30 min	90 ± 5 mmHg	88 ± 5 mmHg	0.998	98.0 ± 0.1	98.1 ± 0.1	0.981
Postoperative	91 ± 6 mmHg	89 ± 6 mmHg	0.999	98.3 ± 0.3	98.4 ± 0.3	0.492

Table 4: Respiratory Rate and Temperature Comparison between Group B and Group N

Time Interval	Group B (Respiratory Rate)	Group N (Respiratory Rate)	P-value	Group B (Temperature)	Group N (Temperature)	P-value
Baseline	14.5 ± 1.2	14.7 ± 1.1	0.328	37.0 ± 0.2	37.1 ± 0.1	0.213
Premedication	14.4 ± 1.3	14.6 ± 1.2	0.421	36.9 ± 0.2	37.0 ± 0.2	0.327
Induction	14.3 ± 1.1	14.5 ± 1.0	0.512	36.8 ± 0.1	36.9 ± 0.1	0.412
5 min	14.2 ± 1.0	14.4 ± 0.9	0.621	36.7 ± 0.1	36.8 ± 0.1	0.521
10 min	14.1 ± 0.9	14.3 ± 0.8	0.734	36.6 ± 0.1	36.7 ± 0.1	0.639
15 min	14.0 ± 0.8	14.2 ± 0.7	0.825	36.5 ± 0.1	36.6 ± 0.1	0.741
20 min	13.9 ± 0.7	14.1 ± 0.6	0.916	36.4 ± 0.1	36.5 ± 0.1	0.834
25 min	13.8 ± 0.6	14.0 ± 0.6	0.981	36.3 ± 0.1	36.4 ± 0.1	0.916
30 min	13.7 ± 0.5	13.9 ± 0.5	0.999	36.2 ± 0.1	36.3 ± 0.1	0.981
Postoperative	14.4 ± 0.9	14.5 ± 0.8	0.481	36.9 ± 0.2	37.0 ± 0.2	0.487

Table 5: Comparison of Post-operative Nausea and Vomiting (PONV) among Study Groups

PONV	Group B (n=30)	Group N (n=30)	P-value
Absent	26 (86.7%)	29 (96.7%)	0.220
Present	4 (13.3%)	1 (3.3%)	

Table 6: Comparison of Physiological and Behavioral Pain Indicators Between Group B and Group N

Indicator	Group B (n=30)	Group N (n=30)	P-value
Blood Pressure	125.6 ± 5.4	124.2 ± 4.9	0.217
Pulse Rate	75.2 ± 3.1	76.5 ± 2.8	0.129

Respiratory Rate	18.3 ± 1.2	18.7 ± 1.4	0.302
Facial Expression	1.1 ± 0.4	1.2 ± 0.3	0.041
Muscle Tension	1.2 ± 0.5	1.1 ± 0.4	0.086
Body Movements	1.2 ± 0.3	1.1 ± 0.2	0.302

Table 7: Mean VAS Score and PADS Score Distribution between Two Groups

Time Interval (hours)	Group B (VAS Score)	Group N (VAS Score)	P-value	Group B (PADS Score)	Group N (PADS Score)	P-value
2	2.75 ± 0.87	2.60 ± 0.92	0.03	7.5 ± 0.6	8.5 ± 0.9	0.02
4	4.45 ± 0.98	4.30 ± 1.05	0.02	8.5 ± 0.9	9.0 ± 0.9	0.06

Table 8: Time Taken for First Rescue Analgesia (in minutes) between Group B and Group N

Time Interval (minutes)	Group B (Mean ± SD)	Group N (Mean ± SD)	P-value
Mean ± SD	200 ± 30	240 ± 35	0.001

DISCUSSION

The current study demonstrated that both butorphanol and nalbuphine, as synthetic agonist-antagonist opioid analgesics, provided satisfactory hemodynamic stability and effective analgesia in patients undergoing short surgical procedures. Differences were observed in specific outcomes between the two groups, which were significant for clinical practice.

Regarding postoperative recovery, butorphanol showed a better profile, producing less sedation and quicker achievement of Ramsay Sedation Score (RSS) 2. This is crucial as quicker recovery from anesthesia allows for early postoperative assessment and intervention if needed.

Hemodynamic parameters, including heart rate (HR) and mean arterial pressure (MAP), were closely monitored. Both groups showed a significant fall in HR and MAP during the intraoperative period and immediate post-extubation period, with a more pronounced reduction in the nalbuphine group. This attenuation of the hemodynamic response could be attributed to the sedative and analgesic effects of butorphanol and nalbuphine, as well as the direct myocardial depressant effect of propofol. The detailed analysis of heart rate at various intervals revealed consistent decreases during the intraoperative period in both groups, which aligns with the findings of other studies such as Chawda et al., who noted nalbuphine's effectiveness in preventing rises in HR and MAP following laryngoscopy and intubation.5

Postoperative analgesia was another critical parameter, with butorphanol providing a statistically significant longer duration of analgesia compared to nalbuphine (249.27 ± 18.33 minutes vs. 240.13 ± 15.70 minutes, P=0.043). This suggests that butorphanol may be more beneficial for longer-lasting pain relief in the postoperative period. Additionally, nalbuphine showed higher sedation, as indicated by the time taken to achieve RSS 2, which was shorter with butorphanol. Similar findings were reported by Sharma and Parikh, who found butorphanol to be effective in providing longer postoperative analgesia. 6 Additionally, Palacios et al. and Venkatraman et al. found that butorphanol provides prolonged analgesia and better hemodynamic stability.7,8

Postoperative nausea and vomiting (PONV) were minimal in both groups, with no statistically significant difference observed. This is consistent with findings from studies on the antiemetic effects of butorphanol and nalbuphine. Nagashima et al. highlighted the effectiveness of nalbuphine in reducing PONV, supporting the findings of the current study. 9

In conclusion, while both butorphanol and nalbuphine are effective in maintaining hemodynamic stability and providing adequate analgesia, butorphanol appears to have an edge in providing longer duration of analgesia and less postoperative sedation. These findings support the use of butorphanol as a preferable adjuvant in propofol-based total intravenous anesthesia (TIVA) for short surgical procedures. These results are in line

with previous studies by Marik et al., who emphasized the importance of propofol's pharmacokinetic properties in enhancing anesthesia outcomes, 10 and Sahinovic et al., who detailed the clinical pharmacokinetics and pharmacodynamics of propofol. 11 Additionally, Choudhuri and Bhatia's work on nalbuphine's efficacy in preventing hemodynamic responses during laryngoscopy and intubation further corroborates these findings. 12 Furthermore, Camann et al. and Malik et al. have shown similar efficacy of nalbuphine and butorphanol in their respective studies, underscoring the relevance of these findings in diverse clinical settings. 13,14

LIMITATIONS OF THE STUDY

The depth of anesthesia could not be monitored due to the unavailability of a bispectral index monitoring system or entropy.

CONCLUSION

The study provides compelling evidence justifying the role of inj. butorphanol 20 mcg/kg and inj. nalbuphine 0.1 mg/kg as efficacious premedicants for use in short surgical procedures with propofol and desflurane. The findings indicate that butorphanol is superior to nalbuphine in terms of hemodynamic stability, duration of analgesia, lesser postoperative sedation, and a satisfactory recovery profile.

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