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Original Research Article

Comparative Assessment of Butorphanol, Fentanyl and Nalbuphine for Total Intravenous Anaesthesia in Patients Undergoing Laparoscopic Cholecystectomy

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Abstract:

Background and Aim: Opioids are a class of medicines that can be used to enhance Total Intravenous Anaesthesia (TIVA) in order to address the analgesic component. They not only reduce the need for potent anaesthetic agents during induction and maintenance, but they also allow for a more complete recovery from anaesthesia without excessively prolonging it. The purpose of this study was to assess the efficacy of an agonist antagonist type of opioid as an adjuvant to propofol-based TIVA, thereby replacing agonist opioids, which have higher adverse effect profiles and misuse potential, as well as being scheduled medications that are not widely available.

Material and Methods: After receiving approval from the hospital's ethics council, this prospective randomised trial was carried out in the department of anaesthesia and intensive care at a tertiary centre. A total of 150 patients were involved in this investigation. Patients in Group I received 25 g/kg of intravenous butorphanol, Group II received 2 g/kg of intravenous fentanyl, and Group III received 0.3 mg/kg of intravenous nalbuphine soon before anaesthesia induction. Intravenous propofol 2 mg/kg and vecuronium bromide 100g/kg injections were used primarily for induction. Anaesthesia was maintained with TIVA by infusing propofol according to the Bristol infusion schedule and administering muscle relaxant top-ups on an as-needed basis. The following parameters were recorded: hemodynamic monitoring, recovery characteristics (emergence and recovery time), duration of analgesia, sedation, and any adverse effects.

Results: Butorphanol was reported to have a better stable state of haemodynamics throughout the intraoperative period than fentanyl and nalbuphine. Butorphanol again suppressed the pressor response better, albeit fentanyl also suppressed it to some extent. In terms of recovery metrics, butorphanol and nalbuphine recovered more slowly than fentanyl, whereas butorphanol produced better analgesia than the other two medications.

Conclusion: Agonist-antagonist opioids have the potential to replace agonists due to their extended analgesia, low side effect profile, ease of availability, and lack of abuse potential. Because of their negative effects, abuse potential, and restricted availability as scheduled medications, agonists such as Fentanyl cannot be urged to supplement T1VA.

Keywords: Anaesthesia, Butorphanol, Fentanyl, Nalbuphine.

Introduction

Waters and Lundy's use of thiopental sodium in clinical practise in 1934 heralded the beginning of contemporary intravenous anaesthesia. The ideal intravenous anaesthetic medication would give hypnosis, amnesia, and analgesia. Because no single drug is optimal, two or more medicines are utilised in combination to create balanced anaesthesia. Adjuvant selection is essential. It is usual practise among anesthesiologists to include a tiny amount of narcotic analgesic as part of the anaesthetic method. In addition to delivering analgesia, these narcotic drugs reduce the need for

powerful anaesthetic agents during anaesthesia induction and maintenance. Narcotics have also been used to reduce the pressor response during laryngoscopy and intubation, and they are thought to promote a more comfortable recovery after anaesthesia. [1]

Ideally, the recovery should be smooth and progressive, free of pain, postoperative nausea and vomiting (PONV), shivering, heavy sedation, or respiratory depression, and should allow for a shorter stay in the recovery room. Furthermore, there should be no severe issues connected to the airway or cardiovascular system during rehabilitation. Delayed recovery not only increases morbidity, but it can also be costly for both the hospital and the patient.

Opioids are a class of medications that can be used to enhance Total Intravenous Anaesthesia (TIVA) to address its analgesic component. They not only reduce the need for potent anaesthetic agents during induction and maintenance, but they also provide more complete recovery from anaesthesia without excessively prolonging it. [2]

When administered combined, opioids have a synergistic effect that considerably reduces the dosage of propofol and other sedative-hypnotics required to produce unconsciousness and counteract unpleasant stimulation such as skin incision. [3] Opioids limit heart rate responses to laryngoscopy better than esmolol. [4] Short-acting drugs like fentanyl are frequently utilised for this purpose. However, these agonists can have undesirable effects such as respiratory depression, dizziness, nausea, and vomiting, and their abuse potential limits their availability. Nalbuphine is an opioid that is both an agonist and an antagonist at the receptor. It is said to have a ceiling effect on respiratory depression, cardiovascular stability, longer duration of analgesia, and a lower incidence of nausea and vomiting, making it an effective analgesic during anaesthesia. [5]

The purpose of this study was to assess the efficacy of an agonist antagonist type of opioid as an adjuvant to propofol-based TIVA, thereby substituting the agonist opioids, which have higher adverse effect profiles and misuse potential, as well as being scheduled medications that are not freely available.

Material and Methods

After approval from the hospital's ethics council, this prospective randomised study was carried out in the department of anaesthesia and intensive care at a tertiary centre. This study comprised 150 patients from the American Society of Anesthesiology (ASA) grade I of either gender between the ages of 20 and 60, weighting 30-70 kg. Those having a history of hypertension, coronary artery disease, hepatic, renal, and endocrine diseases, as well as those on psychoactive substances or with a history of narcotic misuse and allergy to the trial drug or its contents were excluded from the study.

A regular pre-anesthetic evaluation of patients undergoing study was performed a day before surgery, with special attention paid to basic demographic characteristics, general and systemic physical examination, and routine investigations. They were randomly separated into three groups using a computer-generated random number table. Butorphanol inj. 25g/kg was administered intravenously to Group I. Fentanyl infusions of 2g/kg were administered intravenously to Group II. Nalbuphine injections of 0.3mg/kg were administered intravenously to Group III.

After recording baseline vitals soon before induction, all patients were given injection glycopyrrolate 0.2mg intravenously together with the research medication in the operating room. The patients were preoxygenated for 3 minutes with 100% oxygen before being induced intravenously with inj. propofol 2mg/kg and inj. vecuronium bromide 100 g/kg. This was followed by tracheal intubation after complete muscular relaxation, and patients were ventilated with 50% oxygen in air under IPPV. Soon after induction, an infusion of 1% propofol solution was started according to the Bristol infusion regimen7 based on lean body weight, i.e., 10 mg/kg/hr for the first 10 minutes, followed by 8 mg/kg/hr for the next 10 minutes, and then 6 mg/kg/hr through a controlled infusion system until the end of the surgery. Muscle relaxation was maintained with top-ups of inj vecuronium bromide as needed. A nasogastric tube was inserted, and a normal laparoscopic surgery was performed. The IAP was kept between 10 and 12 mmHg. When skin closure began, the propofol infusion was halted. At the end of the procedure, neuromuscular blockade was reversed with intravenous injections of glycopyrrolate 8g/kg and neostigmine 50g/kg, followed by tracheal extubation when the patient began breathing spontaneously and opened his eyes on command.

Hemodynamic parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean arterial pressure (MAP) were collected intraoperatively.

A continuous record of SpO2, ECG, and ETCO2 was made. The period between when the propofol infusion was terminated and the patient was extubated was recorded as Emergence period, and the time between when the trachea was extubated and when the patient was told his or her name was recorded as Recovery Time. Throughout the procedure, the SpO2 and ETCO2 levels were held between 98-100% and 35-45 mmHg, respectively.

Patients were moved out of the operating room after a successful reversal, and the following parameters were recorded in the postoperative period: Postoperative sedation time: The Modified Ramsay Sedation Scoring System was used to assess the level of sedation in the postoperative phase. Sedation scores were taken starting when the patient was transferred to the recovery ward, then every 15 minutes for the next hour, then every 30 minutes, until the patient reached a sedation score of 2, which was the acceptable level of sedation because the patient was calm and cooperative at this point. The interval between analgesic treatments during induction and the time the patient requested analgesia in the postoperative phase was recorded as the duration of analgesia. Tramadol 1mg/kg i/v SOS injection was used to provide rescue analgesia. Any cases of postoperative nausea and vomiting were documented in the recovery room.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). Quantitative variables were described as means and standard deviations or median and interquartile range based on their distribution. Qualitative variables were presented as count and percentages. For all tests, confidence level and level of significance were set at 95% and 5% respectively

Results

Demographic statistics from both groups were comparable and non-significant. (p>0.05) (Table 1) There was no statistically significant difference between groups for MAP at intervals 0, 1, 3, 4, 5, 6, 7, 8, 9, and 11 with p value > 0.05. With a p-value of 0.05, the MAP at intervals 2 and 10 (after intubation and extubation) demonstrated a statistically significant difference between groups. When mean SBP was compared between groups, the value at interval 2 (after intubation) showed a significant difference with a p-value of 0.05. When mean SBP was compared between groups, the p-value was 0.04 between groups I and II and 0.009 between groups I and III, which was statistically significant. When comparing the groups for mean diastolic blood pressure at interval 10, there was a significant difference with a p-value of 0.003.

When the mean duration of anaesthesia (in minutes) was compared between groups, no statistically significant difference was identified with a p-value of >0.05.

Using Bonferroni's test, the mean duration of analgesia (in minutes) revealed extremely significant differences on intergroup comparisons with a p value of 0001. When sedation duration was compared, p values were statistically significant. (p≤0.05) (Table 2)When ET was compared between groups, a p-value of 0.01 was observed, which was statistically significant, however it was >0.05 for groups I and II, which was not statistically significant. When the groups were compared for RT, a statistically significant difference was found between groups I and II. (p≤0.05) There was no statistically significant difference neither between groups II and III, nor between groups I and III. (Table 3)Sedation was observed in 43% of participants in Group I and 46% of patients in Group III. In group II, no patients were sedated. There was only one patient in Group II who reported nausea.

Table 1: Demographic Parameters

Variable	Group I (Mean ± SD)	Group II (Mean + SD)	Group III (Mean + SD)	p value
Age (years)	38.40±10.2	37.10±10.44	39.58±9.67	0.09
Weight (kg)	58.40±8.20	58.39±8.11	61.89 ±6.4	0.54
Gender (M: F)	24:26	21:29	20:30	0.2

Statistically significance at p≤0.05

Table 2: Duration of anaesthesia, analgesia and sedation

Variable	Group I (Mean± SD)	Group II (Mean + SD)	Group III (Mean + SD)	p value
Duration of anesthesia	61.50±10.47	64.30+13.22	65.97+9.47	0.06
Duration of analgesia	120.68± 8.422	71.82±7.11	154.48+18.98	0.003*
Duration of sedation	5.80±1.10	0	12.60+5.22	0.001*

* indicate statistically significance at p≤0.05

Table 3: Recovery Characteristics: Emergence Time And Recovery Time

Variable	Group I (Mean± SD)	Group II (Mean + SD)	Group III (Mean + SD)	p value
Emergence time	4.58+0.20	3.64+0.90	5.09 +1.20	0.001*
Recovery time	1.80+0.47	1.15+0.48	1.49 +0.66	0.001*

* indicate statistically significance at p≤0.05

Discussion

Any anesthesiologist wishes for a smooth recovery in the postoperative period. However, in the presence of postoperative pain, nausea and vomiting, shivering, severe sedation, and respiratory depression, it can be extremely unpleasant. These side effects not only create a delay in recovery due to a prolonged PACU stay, but they can also be a significant psychological and emotional setback for patients and relatives.

TIVA has numerous advantages over traditional breathing approaches. The recent emphasis on the use of intravenous agents in clinical practise stems from the availability of agents with the advantages of rapid onset, pleasant induction, and absence of respiratory tract irritation, stable operating conditions, shorter recovery profiles, and availability of user-friendly infusion delivery systems, simplicity, and the fact that a minimum of equipment and complicated apparatus is required.

When examining the trend of hemodynamic parameters within the individual group, mean HR, MAP, mean SBP, and mean DBP showed a consistent pattern. The readings declined dramatically from baseline at 0 intervals to the post-induction phase at interval 1, then rose at intervals 2 and 3. Following that, there was a progressive fall in the mean HR, MAP, SBP, and DBP at intervals 4, 5, 6, 7, 8, and 9, indicating intraoperative hemodynamic stability, followed by a rise in MAP at interval 10 (after extubation), which was quickly followed by values returning to near baseline levels at interval 11.

Propofol causes considerable myocardial depression, which accounts for the drop in mean HR, MAP, mean SBP, and mean DBP following induction. This fall was higher when paired with fentanyl, butorphanol, or nalbuphine, and hence the combinations were more successful in decreasing the intubation response. In 2013, Neil S Morton [6] expanded on the TIVA approach in paediatric patients. Similarly, Abd-Elazeem Elbakry, Wesam-Eldin Sultan, and colleagues [7] proved that TIVA employing propofol and dexmedetomidine is a better anaesthetic regimen than inhalation anaesthesia. TIVA improved surgical recovery by reducing postoperative side effects and analgesic needs.

When compared to butorphanol, nalbuphine showed poor attenuation of pressor response in terms of rise in MAP both at intubation and extubation when compared to MAP, mean SBP, and mean DBP in three groups intraoperatively. At extubation, fentanyl also caused a statistically significant increase in MAP compared to butorphanol. On the contrary, nalbhupine was found to be as effective as fentanyl in reducing haemodynamic response to laryngoscopic and laparoscopic stress in a study conducted by Madhu S, Balarama Reddy P et al [8]. Fentanyl reduces sympathetic outflow and attenuates the cardiovascular response via acting on opioid receptors. According to Ko et al., the optimal timing to administer fentanyl is five minutes before laryngoscopy and intubation. [9] Mixed opioid agonist/antagonists have also been explored, although their efficacy in preventing hemodynamic response to airway manipulation remains unknown. The appeal of drugs with partial antagonist activity stems from the likelihood of reduced abuse potential and a reduction in the severity of side effects, particularly respiratory depression. On a milligramme basis, nalbuphine has the same analgesic effectiveness as morphine. When compared to pure opioid agonists, the most significant advantage of nalbuphine is its ceiling effect on respiratory depression. Nath et al. [10] compared two nalbuphine doses and discovered that the larger the dose, the better the hemodynamic control. When delivered at a dose of 0.2 mg/kg five minutes before laryngoscopy, Chawda et al [11] demonstrated that nalbuphine reduced the hemodynamic response associated with intubation.

When comparing the mean duration of analgesia in our study, it was discovered that nalbuphine (2.5 hrs) had a substantially longer duration of analgesia than butorphanol (2 hrs), which in turn had a longer duration of analgesia than fentanyl (1 hr). As a result, fentanyl has the shortest mean duration of analgesia; in fact, many patients in this group complained of discomfort shortly after extubation and were then supplemented with inj. tramadol 1mg/kg intravenously SOS. Del et al [12] observed the duration of analgesia given by intravenous butorphanol to be about 2 hours (0.5mg dosage) or 2-4 hours (1mg dose).

On comparing ET, data suggested a longer emergence time for nalbuphine and butorphanol than fentanyl. When assessed for RT, higher recovery time seen with butorphanol & nalbuphine than fentanyl. The findings contradicted those of a study conducted by Jenstrup, Nielsen J et al. [13]. In the fentanyl groups, they discovered an emergence time of 10 minutes and a recovery time of 3 minutes, which were both longer than those observed in our study. Despite being significantly longer, the ET obtained by Verma R K, Jaiswal S et al [14] for fentanyl was 4.24±1.04 and for butorphanol was 5.31±0.89, which is quite close to our data. Our study's RT values were compatible with this study's, which were 1.24±0.81 and 2.00±0.61, respectively, with fentanyl and butorphanol.

Sedation was observed as a postoperative adverse effect in the butorphanol and nalbuphine groups, with incidences of 42.9% and 46.2%, respectively. Sedation levels were either 3 or 4, and patients

were easily arousable. The frequency of sedation reported with butorphanol ranges between 30 and 40%, which is congruent with our findings. Pandit SK, Kothary SP, et al [15] observed 44.4% sleepiness with butorphanol compared to 16.6% with fentanyl.

Hussein AE, Youssef et al. [16] found that nalbuphine provided more sedation than morphine. Gan TJ, Ginsberg B, et al [17] found that propofol is more effective than ondansetron in avoiding PONV when used to induce and maintain anaesthesia. Phillips, Mirakhur RK, et al. [18] found a reduced incidence of PONV with TIVA compared to GA using the usual inhalation approach. As a result, the reduced incidence of PONV in our study could be attributed to the administration of propofol. In terms of Recovery Time and Emergence Time, Butorphanol and Nalbhupine demonstrated slower recovery than Fentanyl, although more research is needed to confirm this.

Our study had some limitations, including the fact that we only evaluated ASA PS I/II patients, that stress mediators such as endogenous plasma catecholamines were not measured, and that invasive arterial blood pressure monitoring was not performed.

Conclusion

Because of their extended analgesia, low side effect profile, accessible availability, and lack of misuse potential, opioid antagonist-antagonist series have the potential to replace agonists. Because of their negative effects, abuse potential, and restricted availability as scheduled medications, agonists such as Fentanyl cannot be urged to supplement T1VA.

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