Comparative evaluation of recovery characteristics of fentanyl and butorphanol when used as supplement to propofol anaesthesia

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Abstract

Background and Aim: Narcotics have been used since long as a component of balanced anaesthesia, thus minimizing the anaesthetic requirement both during induction and maintenance as well as attenuating the pressor response during laryngoscopy and intubation. Equally significant is their role in provision of smoother recovery period by minimizing postoperative pain. Other than pain, the factors like postoperative nausea and vomiting (PONV), shivering, sedation and respiratory depression are equally important in recovery from the effects of anaesthetic drugs. The present study aimed at comparing the postoperative recovery characteristics of fentanyl and butorphanol in patients undergoing open cholecystectomy under general anaesthesia. Materials and Methods: The present study configured one hundred adults patients of American Society of Anaesthesiologists (ASA) grade 1 or 2 of either sex scheduled to undergo elective open cholecystectomy and were randomly assigned to receive fentanyl (group F; n = 50) or butorphanol (group B; n = 50). Both group were premedicated with midazolam 0.04 mg/kg intravenously followed by injection fentanyl 2 mcg/kg or butorphanol 40 mcg/kg. Standard induction was done with propofol 2 mg/kg and vecuronium 0.1 mg/kg was used for intubation. Anaesthesia was maintained with propofol infusion and 67% nitrous oxide in oxygen. Intraoperative hemodynamic parameters were observed and recorded. Postoperatively analgesia, sedation, PONV, shivering, respiratory depression and recovery score were observed. Results: The recovery time was less in group F (P > 0.05) while post operative analgesia (P < 0.001) and sedation (P > 0.05) was more in group B. The incidence of respiratory depression was more in group B (P > 0.05). PONV was comparable in both the groups. Postoperative shivering was significantly low in group B (P < 0.05). Conclusion: It is concluded that besides easy availability and lower cost, butorphanol decreased propofol consumption intraoperatively and provided better analgesia and prophylaxis against shivering in postoperative period.

Key words: Butorphanol, fentanyl, propofol, recovery

Introduction

The introduction of thiopental sodium into clinical practice by Waters and Lundy in 1934 marked the advent of modern intravenous anaesthesia. The ideal intravenous anaesthetic drug would provide hypnosis, amnesia and analgesia. Because no single drug is ideal, two or more drugs are used in combination to provide balanced anaesthesia. The choice of adjuvant is of critical importance. It is a common practice among anaesthesiologists to include a small dose of narcotic analgesic as part of anaesthetic technique. These narcotic agents in addition to providing analgesia also minimizes the requirement for potent anaesthetic agent during induction and maintenance of anaesthesia. Narcotics have also been used for attenuation of pressor response during laryngoscopy and intubation and are believed to provide a comfortable recovery from anaesthesia. Ideally the recovery should be smooth and gradual and free from pain, postoperative nausea and vomiting (PONV), shivering, deep sedation or respiratory depression and
should enable a shorter stay in recovery room. In addition, there should not be any major complications related to airway or cardiovascular system during recovery. Delayed recovery not only leads to increased morbidity but also is a potential financial burden both on the hospital as well as the patient.

Different institutes follow different practices of using opioids depending on the indication and availability. Each drug has got its own advantages and disadvantages depending on its pharmacokinetics and pharmacodynamic properties. Though there are numerous studies which have compared different opioids, only a few studies have been carried out to compare the recovery characteristics of fentanyl and butorphanol. In the present study, we have compared the recovery characteristics of above mentioned drugs when used in combination with propofol.

**Materials and Methods**

After the approval of hospital’s ethical committee and written informed consent from the patients, a prospective, randomized, double blind study was carried out among hundred American Society of Anaesthesiologists (ASA) grade I and 2 adult patients undergoing elective cholecystectomy. Patients with history of hypertension, coronary artery disease, hepatic, renal and endocrine disorders and patients on psychoactive drugs or with history of narcotic abuse and allergy to the trial drug or its constituents were excluded from the study. In the operation theatre standard monitors including Electrocardiogram (ECG), non-invasive blood pressure (NIBP) and pulse oximetry were applied and baseline parameters recorded. After securing intravenous access patients were preloaded with 15 ml/kg of normal saline. The study drugs were prepared by an anaesthesia-technician either as 25 mcg/ml of fentanyl or 500 mcg/ml of butorphanol. Injection midazolam 0.04 mg/kg (maximum dose of 3 mg) was given as IV premedication followed by the study drug i.e., either 2 mcg/kg of fentanyl or 40 mcg/kg of butorphanol. Induction of anaesthesia was achieved with propofol 2 mg/kg and vecuronium 0.1 mg/kg was used to facilitate tracheal intubation. There was a gap of 7 minutes between administration of study drug and intubation. Hemodynamic parameters were recorded at various intervals. Subsequently, anesthesia was maintained with propofol infusion of 100 mcg/kg/min, and 67% nitrous oxide in oxygen and supplementary doses of vecuronium.

Additional boluses of propofol 20-30 mg were given as and when required judged by light anaesthesia plane, notably a 25% increase in mean arterial pressure or heart rate above base line values, any muscle movement, sweating or lacrimation. Intraoperatively, any untoward incident requiring emergency intervention was recorded and treated symptomatically.

At the end of operation, neuromuscular blockade was reversed using neostigmine 0.05 mg/kg and glycopyrrrolate 0.01 mg/kg and extubation was done when the patients got fully awake. Patients were then shifted to recovery room and monitored.

Postoperatively, pulse rate and blood pressure was measured every 15 min for first hour and then half hourly for next three hours. Patients were also observed every 15 min for respiratory depression (respiratory rate < 8 breath/minute) or hypoxemia (SPO₂ < 92%), PONV, shivering, sedation in addition to postoperative pain. Post operative analgesia was measured by visual analog scale (VAS) at fifteen minutes interval from arrival in recovery room till the patient required rescue analgesic. Injection Voveran was given as rescue analgesic if the patient had VAS > 3. Postoperative nausea was measured on VAS scale (0-10) while emetic episode was defined as a single vomiting or retching event or any combination of these events separated by less than 2 minutes. Injection Ondensetron 4 mg was given as rescue antiemetic. Postoperative sedation was assessed by Ramsay sedation score, till the patient attained a score of 2.

Postoperative shivering was assessed as grade 0 = no shivering, grade 1 = mild fasciculations of face or neck and electrocardiogram (ECG) disturbances in the absence of voluntary activity of the arms, grade 2 = visible tremor involving more than one muscle group, grade 3 = gross muscle activity involving the entire body. Oxygen through venturimask was given to all patients with shivering. Injection Pethidine 0.25 mg/kg was given for grade 2 or 3 shivering.

Overall recovery was assessed by Steward scoring system which awards a score of 0, 1 or 2 points to each of three attributes consciousness, airway and movement. The score was calculated at 15, 30, 60 and 90 minutes. The range of possible scores at each time was 0 to 6. Six points were required for discharge from recovery room.

**Results**

A total of hundred patients were randomly assigned to two groups. The two groups were comparable with respect to demographic characteristics like age, weight, gender ratio and duration of surgery [Table 1].

Pre-operative, pre-induction and maintenance hemodynamic parameters were also comparable in both the groups. Significantly more rises in pulse rate, systolic and diastolic BP was seen in Group F, one minute after intubation [Table 2].
During the intraoperative period, propofol consumption was lower in group B as compared to group F as is also evident clinically from the intraoperative hypertension and tachycardia that occurred in 54% patients in group F and among these lacrimation occurred in 6% patients which was managed by giving additional bolus doses of propofol, while no such episode of lacrimation, sweating or muscle movement occurred in butorphanol group. Mean propofol consumption in group F was slightly higher (406.7 ± 96.36 mg) as compared to 380.5 ± 92.54 mg in group B. The difference however was statistically not significant (P > 0.05).

Recovery time to orientation (on asking name of the patient etc..) which was measured from the time nitrous-oxide was stopped, was less in group F. Mean recovery time was lower (11 ± 3 min) in group F as compared to group B (12.5 ± 3 min). In post anaesthesia care unit (PACU) we assessed recovery by using Steward scoring system. Patients attained maximum Steward score of six earlier in group F as compared to group B but the difference was not statistically significant (P > 0.05). Three patients in the group B and one patient in group F showed delayed recovery [Table 3].

Significant pain was experienced by 56% of patients in group F while only 14% patients in group B required rescue analgesic on shifting to recovery room. This difference is highly significant (P < 0.001). All patients in group F required rescue analgesic within 30 minutes of shifting to recovery room while in group B 54% patients were pain free after 30 minutes of stay in recovery room.

The mean respiratory rate was lower in group B as compared to the fentanyl group upto 3 hours postoperatively. However, there was no incidence of respiratory depression in any patient from either group (respiratory rate < 8 breaths/minute). Postoperatively, hypoxemia (SPO² < 92% on room air) occurred in 6% patients while no such episode occurred in fentanyl group. Incidence of nausea and vomiting was also comparable in both the groups with slightly lower incidence in patients who were administered butorphanol. Of the 18% patients in group F while 12% patients in group B had PONV. Postoperative sedation as assessed by Ramsay sedation score was higher in group B. Two patients had Ramsay grade edation and 1 patient had grade 5 sedation, I patient in group F had grade 4 sedation 30 minutes after shifting to recovery room. Incidence of postoperative shivering requiring treatment with injection pethidine was higher in group F (18%) as compared to group B (4%) which was significant on statistical comparison (P < 0.05) [Table 4].

**Discussion**

A smooth recovery in the postoperative period is the most desired thing by any anaesthesiologist. However it can become very unpleasant in the presence of postoperative pain, nausea and vomiting, shivering, excessive sedation and respiratory depression. These side effects not only cause delay in recovery with prolonged PACU stay but can also be a potential psychological and emotional setback to the patients and the relatives. Based on the background of these facts, the present study was carried out with an emphasis on comparing the recovery characteristics of fentanyl and butorphanol.

Opioids bind to specific receptors located throughout central nervous system and other tissues. The pharmacodynamic properties of a particular opioid depends on the type of receptor to which it is bound, its binding affinity and whether the receptor is activated. The main difference between fentanyl and butorphanol is related to their opioid receptor spectra. Butorphanol is a agonist-antagonist opioid of phenanthrene series. It is a kappa receptor agonist as well as mu receptor antagonist, while fentanyl is primarily a mu receptor agonist. Butorphanol can be given via intramuscular, intravenous or nasal route. It is extensively metabolized in liver, mainly by hydroxylation. Equi potent doses of butorphanol, morphine, pethidine and pentazocine produces same duration of analgesia. Fentanyl a pure agonist can be given through intramuscular, intravenous, transdermal or buccal route. It is extensively metabolized in the liver producing norfentanyl. Fentanyl in different doses can be used to provide analgesia, as component of balanced anaesthesia or surgical anaesthesia in

### Table 1: Demographic profile and duration of anaesthesia

| Parameter | Group F (Mean±SD) | Group B (Mean±SD) |
|-----------|-------------------|-------------------|
| Age (yrs) | 37.23±10.62       | 36.0±10.35        |
| Weight (kg)| 66.20±9.4     | 67.03±8.3         |
| Male:Female ratio | 7.43           | 10.40             |
| Anaesthesia time (min) | 50.10±12.10 | 49.30±10.33       |

### Table 2: Hemodynamic parameters

| Parameter                     | Pulse rate (beats/min) | Systolic BP (mmHg) | Diastolic BP (mmHg) |
|------------------------------|------------------------|-------------------|--------------------|
|                              | Group F | Group B | Group F | Group B | Group F | Group B |
| Preoperative                 | 87.24±7.74 | 85.61±3.95 | 128.89±12.53 | 121.92±10.29 | 79.34±7.51 | 78.92±9.59 |
| Preinduction                 | 85.68±8.16 | 83.40±5.35 | 120.68±7.01 | 119.52±11.51 | 78.12±7.41 | 77.72±9.40 |
| One min after intubation     | 97.62±10.63 | 89.40±7.16 | 135.76±15.13 | 125.08±12.01 | 86.92±7.89 | 81.64±8.35 |
| Maintenance phase            | 88.37±7.17 | 84.63±10.68 | 123.37±12.48 | 118.97±11.24 | 80.36±5.83 | 77.08±9.30 |
All these patients in group 2 had shorter recovery time as compared to group B but this difference was not statistically significant. All patients in both the groups attained Steward score of 6 after sixty minutes of shifting to recovery room. Six percent patients in group B and 2% patients in group F showed delayed recovery. Similar findings had been reported earlier in which no difference in recovery is seen with either butorphanol or fentanyl. All these patients in group B were elderly females and prolongation of drug effect could be both due to pharmacodynamics as well as pharmacokinetic mechanism, while delayed recovery with fentanyl can be explained only by increased individual sensitivity to the opioids.

In the present study complaint of pain was significantly less in group B as compared to group F. It has been demonstrated earlier that administering a small dose of fentanyl (100 mcg) at the time of induction failed to provide effective postoperative analgesia in patients undergoing ambulatory gynaecologic laparoscopy. Similar observations were made in another study in which author noted significant postoperative pain in 40% patients receiving fentanyl and in only 17% patients in the butorphanol group (P < 0.05). This difference could possibly be due to rapid redistribution of fentanyl. In addition to relatively uncommon postoperative respiratory complication of airway obstruction and aspiration, hypoxemia can occur in postoperative period. In this study 3 cases of post operative hypoxemia were seen in group B. In the earlier studies no episode of hypoxemia or respiratory depression was seen in any of the patients in two groups. All the three cases of hypoxemia in our study occurred in elderly females. Butorphanol clearance is decreased in geriatric patients resulting in prolonged elimination-half life and this could be the reason for postoperative hypoxemia.

PONV not only lead to patient discomfort but rarely can cause pulmonary aspiration when patients are recovering from the effects of anaesthetic drugs. The incidence of nausea and vomiting in our study is much less as compared to earlier studies which reported an incidence up to 61% with fentanyl in outpatient laparoscopic procedures. The lower incidence of PONV in our study could be attributed to antiemetic effect of propofol which we have used both for induction as well as maintenance of anaesthesia.

The incidence of sedation was much less in our study than that reported earlier. Propofol was used in the present study both for induction and maintenance as compared to thiopentone and isoflurane used by the authors in previous study. Post anaesthesia shivering is another complication which can occur in 5-65% of patients in recovery period depending on age, sex, anaesthetic agent used for induction and maintenance of anaesthesia and duration of surgery. Shivering not only causes physical discomfort but also causes precipitous rise in oxygen consumption which may be poorly tolerated by a patient with diminished cardiorespiratory reserve. In the present study incidence of shivering was significantly less in group B. In fact butorphanol has been used previously for its antishivering properties as an alternative to pethidine.

Based on observations made in the present study it can be concluded that use of butorphanol is associated with less anaesthetic (propofol) consumption, better post operative analgesia with a better protection against post operative shivering. The only major drawback with butorphanol was postoperative hypoxemia and sedation in geriatric patients.

### Table 3: Number of patients showing maximum steward score of 6/6 at various time intervals

| Time intervals in minutes | Group F | Group B | P value |
|---------------------------|---------|---------|---------|
| 15                        | 7       | 4       | >0.05   |
| 30                        | 26      | 20      | >0.05   |
| 60                        | 49      | 47      | >0.05   |
| 90                        | 50      | 50      | >0.05   |

### Table 4: Postoperative parameters

| Parameters                                      | Group F (%) | Group B (%) | Significance |
|------------------------------------------------|-------------|-------------|--------------|
| PONV                                           | 18          | 12          | P>0.05       |
| Sedation (grade 4 or 5 after 30 minutes)        | 2           | 6           | P>0.05       |
| Respiratory depression or hypoxemia            | Nil         | 6           | P>0.05       |
| Shivering                                      | 18          | 4           | P<0.05       |
| Pain                                           | 56          | 14          | P<0.001      |

PONV: Post operative nausea and vomiting

very high doses. We used equipotent doses of both drugs as has been used earlier. Patients in group F had shorter recovery time as compared to group B but this difference was not statistically significant. All patients in both the groups attained Steward score of 6 after sixty minutes of shifting to recovery room. Six percent patients in group B and 2% patients in group F showed delayed recovery. Similar findings had been reported earlier in which no difference in recovery is seen with either butorphanol or fentanyl. All these patients in group B were elderly females and prolongation of drug effect could be both due to pharmacodynamics as well as pharmacokinetic mechanism, while delayed recovery with fentanyl can be explained only by increased individual sensitivity to the opioids.

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