Original Research Paper

# Comparative study of butorphanol and fentanyl in attenuation of haemodynamic responses in laparoscopic cholecystectomy

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**Abstract:**

Numerous attempts have been made in the past to attenuate the haemodynamic responses occurring during laparoscopic cholecystectomy. The present study compared the effect of two opioids namely Butorphanol and Fentanyl in obtundation of haemodynamic responses in laparoscopic cholecystectomy in terms of Heart rate, BP (SBP, DBP and MAP).

**Materials And Methods :**

This was a randomised study comparing opioid drugs- fentanyl and butorphanol. It was carried out on 50 patients of either sex aged 18 - 60 years scheduled for elective laparoscopic cholecystectomy under GA. Subjects were enrolled into two groups- Group I (n= 25) patients received inj. butorphanol 25 mcg/kg IV, Group II (n= 25) received inj. fentanyl 2 mcg/kg IV before the induction.

**Result :**

At the time of extubation, mean MAP in Group I and II was 99.88 and 95.32 was respectively. This difference is highly significant when compared statistically (p value is 0.005).

**Conclusion:**

With this study, we conclude that the administration of intravenous fentanyl five minutes prior to induction of anaesthesia helps in better obtundation of haemodynamic responses to laparoscopic cholecystectomy than butorphanol.

**Key Words:**

Pneumoperitoneum, Obtundation



**Background:**

Laparoscopic surgeries form an essence of today's surgical practice because of its magnification, dexterity, less cosmetic scar, less post-operative pain and decreased hospital stay because of decreased morbidity and mortality.[1]

However, pneumoperitoneum created to visualise intraabdominal organs along with positional changes (Reverse Trendelenburg position) results in a significant haemodynamic and respiratory changes.[2]

The cardiovascular changes are characterised by decrease in cardiac output and increase in systemic vascular resistance which in turn results in sudden tachycardia, hypertension and increased myocardial oxygen requirement. CO2 (Used for abdominal insufflation) readily absorbed from peritoneal cavity into the circulation resulting in hypercapnia.[3]

These changes though better tolerated in ASA I and II, patients can be detrimental in elderly and ASA III patients particularly with compromised cardiovascular physiology. Various surgical methods like change in nature of insufflating gas, use of low intra-abdominal pressure, use of abdominal wall lift methods have been tried to decrease the haemodynamic alterations associated with pneumoperitoneum, but all with practical limitations.[4]

The inclusion of an opioid can reduce pre-operative pain and anxiety, decrease somatic and autonomic responses to airway manipulation, improve haemodynamic stability, lower requirement for inhaled anaesthetics and provide immediate post-operative analgesia. Each drug has its advantages and disadvantages depending upon its pharmacokinetic and pharmacodynamic profile.[5]

Fentanyl has been identified as an effective agent in this regard. Fentanyl citrate is a synthetic phenylpiperidine opioid and analgesic and chemical congener of pethidine. It is 100 times more potent than morphine. It is a μ (mu) receptor agonist which belongs to G protein-coupled receptor family. Metabolism is mainly via the hepatic route and it has a high first pass metabolism.[6]

Butorphanol is a synthetic opioid derivative. It is a mixed agonist-antagonist and 5 to 8 times as potent as morphine and is available only in the parenteral form. Butorphanol is agonist at K (kappa) receptor and mixed agonist-antagonist at μ (mu) receptor. Whereas duration of action of butorphanol is similar to that of morphine, its plasma $t^{1/2}$ is 2-3 hrs. Duration of analgesia is 3 to 4 hrs.[7]

The primary purpose of the present study is to compare the effects of Fentanyl and Butorphanol in

obtundation of haemodynamic responses during laparoscopic cholecystectomy.

**Materials And Methods :**

**Study Design :**

A prospective, comparative, randomised study. After getting approval from the Institutional Ethical Committee, an informed consent was taken from the patient. This study was conducted on 50 patients aged between 18 - 60 years of either sex and ASA grade I and II scheduled for elective laparoscopic cholecystectomy under general anaesthesia in between June 2016 to Oct 2017.

**Inclusion Criteria**

Age Group Ietween 18 - 60 years, undergoing elective laparoscopic cholecystectomy and ASA grade I and II

**Exclusion Criteria**

Patient's refusal, h/o bradycardia, uncontrolled diabetes mellitus, arrhythmias, renal or liver dysfunction, cardiopulmonary disease, allergic to Fentanyl or Butorphanol.

Patients were familiarised with the visual analogue scale (VAS),[8] (0- No pain, 10- Worst pain) a day before surgery.

Patients were randomly allocated using computer generated random number and by picking up a sealed envelope into two groups of 25 patients each Group I and Group II.

All the patients were kept fasting and given tab ranitidine 150 mg and tab Lorazepam 1 mg at 6 am on the day of surgery.

In the operation theatre, routine monitors were attached and baseline pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and saturation of peripheral oxygen ($SpO_2$) were recorded. AII the patients were pre-loaded with 15 mL/kg of ringer lactate of the ringer's lactate solution and given inj. glycopyrrolate 0.2 mg.

Patients in Group I, Group II received inj. Butorphanol 25 mcg/kg IV, inj. Fentanyl 2 mcg/kg IV respectively. Both the drugs (Butorphanol and Fentanyl) were diluted in 10 mL distilled water and injected slowly 5 minutes before the induction of anaesthesia.

After 3 minutes, pre-oxygenation with 100% oxygen using a Bain's circuit and administration of study drugs, induction was done with IV propofol injection till the loss of eyelash and corneal reflex. Inj. succinylcholine IV 1.5 mg/kg was given and patients were intubated. Anaesthesia was maintained with $O_2$-$N_2O$ (50%-50%), Isoflurane 1% and vecuronium bromide 0.1 mg/kg bolus followed by maintenance dose one-fourth of the initial dose as and when required. Positive pressure ventilation was continued. Cardiovascular parameters (Heart rate, SBP, DBP, MAP), $SP0_2$ and $EtCO_2$ were recorded at the following points of time:

Prior to induction (baseline), at the time of endotracheal intubation, every 2 mins interval after the endotracheal intubation till 10 minutes, before the pneumoperitoneum, every 10 mins interval till 60 mins after the pneumoperitoneum, after release of carbon-dioxide (C02) and after extubation.

At the end of surgery, neuromuscular blockade was reversed with neostigmine 50 μg/kg and glycopyrrolate 10 μg/kg intravenously. After satisfying the extubation criteria, patients were extubated and transferred to post-anaesthesia care unit (PACU). In PACU, every patient was monitored for the haemodynamic parameters (HR, SBP, DBP, MAP) and $SPO_2$, sedation score, VAS score for pain relief and postoperative complications if any. Haemodynamic parameters and arterial O2 saturation were monitored every 10 mins post-operatively upto 90 minutes. Any incidence of complications/ adverse event was monitored for next 90 minutes. During the post-operative period, assessment of pain was done with the help of VAS score. VAS score was recorded at 15 and 30 mins, $1^{st}$, $2^{nd}$, $3^{rd}$ and $4^{th}$ hour and duration of analgesia was also recorded (Time interval from the intravenous drug administration upto time when VAS reaches 5). Thereafter, rescue analgesic (IV ketorolac) was given to the patient. The sedation score was assessed by University of Michigan Sedation Scale (UMSS),[9] post-operatively as:

University of Michigan Sedation Scale (UMSS) 1= Awake and alert.

2= Sedated and responding to verbal command.

3= Sedated but responding to mild physical stimulus.

4= Drowsy but responding to moderate physical stimulus.

5= Very drowsy not responding to severe physical stimulus.

**Statistical Analysis**

The mean comparisons between groups was done by ANOVA with post-hoc test. Categorical variables were compared between groups using Chi-square test Software used was SPSS version 17. A probability level of $p < 0.05$ was considered significant. **Table 1**

| SBP | Group I | Group II | Significance | P value |
|---|---|---|---|---|
| | Mean ± S.D | Mean ± S.D | | |
| Baseline | 125.00 ± 8.21 | 127.16 ± 7.76 | NS | 0.323 |
| Intubation | 128.12 ± 11.15 | 128.04 ± 6.04 | NS | 0.973 |
| 2 | 126.72 ± 7.77 | 115.00 ± 8.08 | HS | <0.001 |
| 4 | 124.04 ± 9.77 | 111.76 ± 8.40 | HS | <0.001 |
| 6 | 126.76 ± 13.27 | 112.40 ± 8.03 | HS | <0.001 |
| 8 | 129.76 ± 11.48 | 112.84 ± 9.54 | HS | <0.001 |
| 10 | 130.56 ± 7.81 | 114.80 ± 6.79 | HS | <0.001 |
| Pneumo | 130.04 ± 641 | 116.76 ± 7.22 | HS | <0.001 |
| 20 | 124.64 ± 7.12 | 116.32 ± 6.93 | HS | <0.001 |
| 30 | 124.12 ± 5.50 | 118.04 ± 6.20 | HS | <0.001 |
| 40 | 123.24 ± 4.65 | 120.04 ± 6.94 | S | 0.062 |
| 50 | 120.33 ± 4.04 | 123.75 ± 5.36 | NS | 0.272 |
| 60 | 127.00 ±5.65 | 122.00 ± 5.65 | NS | 0.365 |
| After CO2 release | 124.52 ± 6.48 | 122.64 ± 4.63 | NS | 0.233 |
| Extubation | 125.60 ± 8.88 | 125.40 ± 3.86 | NS | 0.914 |

**Result:**

As shown in Table 1, both groups showed rise in SBP at the time of intubation when compared to baseline, but this was non-significant (p value is 0.052).

During the pneumoperitoneum mean SBP in Group I was 130, while in Group II was 116. A decrease in SBP was noted in Group II during the pneumoperitoneum. Thereafter, it started rising gradually and returned to baseline at the time of extubation. This difference was highly significant statistically (p value < 0.001). **Table 2**

| DBP | Group I | Group II | P value | Significance |
|---|---|---|---|---|
| | Mean ± S.D | Mean ± S.D | | |
| Baseline | 78.24 ± 7.54 | 79.76 ± 5.23 | 0.655 | NS |
| Intubation | 80.32 ± 8.80 | 79.92 ± 5.00 | 0.975 | NS |
| 2 | 79.64 ± 7.35 | 69.36 ± 5.35 | <0.001 | HS |
| 4 | 78.64 ± 9.72 | 69.52 ± 3.88 | <0.001 | HS |
| 6 | 83.96 ± 10.20 | 71.88 ± 4.72 | <0.001 | HS |
| 8 | 88.32 ± 10.62 | 72.44 ± 4.60 | <0.001 | HS |
| 10 | 88.88 ± 7.47 | 74.80 ± 3.36 | <0.001 | HS |
| Pneumo | 91.20 ± 6.84 | 73.52 ± 4.59 | <0.001 | HS |
| 20 | 84.72 ± 9.44 | 78.96 ± 6.14 | 0.001 | HS |
| 30 | 81.48 ± 4.87 | 77.20 ± 7.95 | 0.028 | S |
| 40 | 82.14 ± 4.38 | 80.17 ± 5.49 | 0.022 | S |
| 50 | 93.66 ± 11.59 | 83.33 ± 5.54 | 0.002 | HS |
| 60 | 95.33 ± 10.06 | 89.00 ± 1.41 | 0.298 | NS |
| After CO2 release | 81.88 ± 5.68 | 81.24 ± 6.14 | 0.931 | NS |
| Extubation | 87.08 ± 5.88 | 80.72 ± 5.71 | 0.001 | HS |

A decrease in mean SBP was noted in Group I during extubation with mean SBP 125.60. Mean SBP in Group II was 125.40 .This difference was statistically non-significant (p value > 0.05).

DBP in both groups increased at the time of intubation, but change is non-significant between the three groups (p value is 0.975).

**Table 2** shows DBP in Group I again increases at pneumoperitoneum. This change is highly significant when compared to Group II (p value is < 0.001).

Mean DBP in subjects of Group I remained significantly higher from the pneumoperitoneum to 50 minutes after the intubation (p value < 0.05).

At the time of extubation, mean DBP in Group I, F were 87.08, 80.72 respectively. The difference between the means was highly significant statistically (p value < 0.001).

MAP in groups increased at the time of intubation, but change is non-significant when compared statistically (p value is 0.868). At the pneumoperitoneum, mean MAP in Group I was 104.16, in Group II was 87.92 and. The difference was highly significant statistically (p value < 0.001). After pneumoperitoneum, mean MAP in Group I is more than Group II. This difference is highly significant when compared statistically (p value < 0.001).

After CO2 release, the difference between the mean MAP becomes non-significant statistically (p value > 0.05).

At the time of extubation, mean MAP in Group I and F was 99.88 and 95.32 respectively. This difference is highly significant when compared statistically (p value is 0.005). **Table 3**

| MAP | Group I | Group II | P value | Significance |
|---|---|---|---|---|
| | Mean ± S.D | Mean ± S.D | | |
| Baseline | 93.76 ± 5.63 | 94.96 ± 5.72 | 0.653 | NS |
| Intubation | 96.20 ± 8.37 | 95.92 ± 4.60 | 0.487 | NS |
| 2 | 95.28 ± 6.26 | 84.52 ± 5.97 | <0.001 | HS |
| 4 | 93.72 ± 8.60 | 83.56 ± 4.27 | <0.001 | HS |
| 6 | 98.32 ± 10.33 | 85.40 ± 3.81 | <0.001 | HS |
| 8 | 102.12 ± 10.05 | 85.88 ± 4.15 | <0.001 | HS |
| 10 | 102.76 ± 6.48 | 88.08 ± 3.27 | <0.001 | HS |
| Pneumo | 104.16 ± 6.00 | 87.92 ± 5.14 | <0.001 | HS |
| 20 | 98.04 ± 7.43 | 91.40± 5.18 | <0.001 | HS |
| 30 | 95.72 ± 3.52 | 90.80 ± 6.16 | 0.003 | HS |
| 40 | 95.90 ± 3.01 | 93.52 ± 4.40 | 0.057 | NS |
| 50 | 102.67 ± 8.62 | 96.83 ± 3.85 | 0.013 | S |
| 60 | 109.00 ± 7.07 | 100.00 ± 1.41 | 0.169 | NS |
| After CO2 release | 96.12 ± 4.24 | 94.96 ± 445 | 0.670 | NS |
| Extubation | 99.88 ± 5.90 | 95.32 ± 4.21 | 0.005 | HS |

As shown in Table 4, pulse rate in both the groups increased at the time of intubation. Mean pulse rate during intubation was 83.24 in Group I, 80.60 in Group II This difference was not significant when compared statistically between the groups (p value is 0.711).

Mean pulse rate was higher in Group I at 4 minutes after the intubation and shows an increasing trend till 40 minutes after the pneumoperitoneum. This difference was highly significant when compared between the three groups (p value < 0.05).

During extubation mean pulse rate in Group I and F were 82.84, 84.48 respectively. The difference in the mean pulse rate during extubation was non-significant when compared between the groups (p value is 0.701).

The difference in the post-op SBP, DBP and MAP between different groups was non-significant when compared statistically (p value > 0.05).

Mean VAS score in Group I and F at 15 minutes postoperatively was 1.44, 2.40 and 2.72 respectively. This difference was highly significant when compared statistically. **Table 4**

| PR | Group I | Group II | P value | Significance |
|---|---|---|---|---|
| | Mean ± S.D | Mean ± S.D | | |
| Baseline | 82.24 ± 8.84 | 78.76 ± 7.36 | 0.306 | NS |
| Intubation | 82.24 ± 8.29 | 80.60 ± 8.29 | 0.711 | NS |
| 2 | 84.68 ± 8.84 | 79.96 ± 7.59 | 0.055 | NS |
| 4 | 87.32 ± 8.28 | 80.36 ± 7.18 | <0.001 | HS |
| 6 | 86.32 ± 8.72 | 80.80 ± 8.48 | 0.004 | HS |
| 8 | 87.16 ± 9.28 | 79.92 ± 8.58 | <0.001 | HS |
| 10 | 87.52 ± 10.31 | 81.08 ± 9.51 | 0.002 | HS |
| Pneumo | 90.20 ± 6.99 | 81.80 ± 8.75 | <0.001 | HS |
| 20 | 86.20 ± 9.01 | 78.96 ± 5.96 | <0.001 | HS |
| 30 | 87.28 ± 8.28 | 78.44 ± 5.76 | <0.001 | HS |
| 40 | 86.33 ± 11.15 | 80.91 ± 5.41 | 0.002 | HS |
| 50 | 83.67 ± 7.09 | 77.83 ± 3.53 | 0.138 | NS |
| 60 | 85.33 ± 6.02 | 82.00 ± 8.48 | 0.535 | NS |
| After CO2 release | 84.60 ± 10.84 | 82.80 ± 6.77 | 0.401 | NS |
| Extubation | 82.84 ± 9.17 | 84.48 ± 6.36 | 0.701 | NS |

AS score in Group II showed an increasing trend over the next 3 hours. This difference was highly significant statistically when compared with other groups (p value < 0.001). The reason being short duration of action of fentanyl, 30 - 60 minutes.

At the end of four hours post-operatively, Group I was having VAS score of 4.60, Group II was having 3.92 . This difference was highly significant when compared statistically (p value < 0.001).

**Discussion**

Pneumoperitoneum during laparoscopic surgery leads to significant haemodynamic changes such as increase in MAP and systemic vascular resistance and a decrease in cardiac output. These haemodynamic changes can be detrimental due to associated risk of myocardial ischaemia or cerebral haemorrhage; therefore, these should be attenuated.

Rao et al 2013[9] compared butorphanol and fentanyl in patients undergoing laparoscopic surgeries and concluded that no significant difference was observed in systolic blood pressure till 9 minutes after intubation similar to present study. Our results are similar to Balasubramaniam et al[10] (2016) who observed that the DBP after intubation in Group I becomes comparable to the preoperative DBP at the third minute after intubation. The DBP in Group II becomes significantly lower than the preoperative DBP at the tenth minute after intubation. Verma et al[11] (2006) conducted a study on total intravenous anaesthesia in laparoscopic cholecystectomy and compared butorphanol with fentanyl. They found out that butorphanol and fentanyl both showed a decreasing trend in MAP at the time of pneumoperitoneum when compared to baseline, but this decrease was statistically not significant (p value > 0.05). However, in the present study Group I depicted an increasing trend in the MAP at the time of pneumoperitoneum.

Patel et al[12] in 2016 compared intravenous butorphanol with intravenous fentanyl in general anaesthesia and concluded that rise in pulse rate was more in fentanyl group when compared with butorphanol group. The difference between the group was statistically significant for 5 minutes after intubation. Thereafter, it was insignificant for upto 30 minutes.

Complications like nausea, vomiting, bradycardia, hypotension, chest wall rigidity, pruritus and respiratory depression were recorded.

It is concluded that sympathetic activation during pneumoperitoneum is attenuated by both the drugs- butorphanol and fentanyl. Fentanyl was more effective than butorphanol in obtunding the haemodynamic response during pneumoperitoneum.

**Conflict of Interest**: None

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