

Original Article:**Comparison of butorphanol and fentanyl for balanced anaesthesia in patients undergoing laparoscopic surgeries under general anaesthesia: a prospective, randomized, double-blind study**

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ABSTRACT

Back ground: Laparoscopic surgeries have advantages like shorter stay and rapid return to normal activities because of small incision and less pain. Pain is an unpleasant sensation in the post-operative period.

Methods: Fifty patients of American society Anesthesiologists (ASA) grade I and II, scheduled to undergo laparoscopic surgery, were randomized into butorphanol group (Group B) (n=25) and fentanyl group (Group F) (n=25). Four minutes before induction of anesthesia, Group B received inj. butorphanol 40 µg/Kg intravenously while Group F received Inj. fentanyl 2 µg/kg intravenously. All patients received general anaesthesia with controlled ventilation. Heart rate, systolic blood pressure (SBP), diastolic blood pressure (DBP), end tidal carbon dioxide (ETCO₂), and oxygen saturation were monitored at different intervals.

Results: The demographic data was comparable in both groups (p<0.05). There was a significant difference between the two groups in pulse rate after 12 minutes after intubation that persisted till the 2nd hour of post-operative period. There was no significant difference in DBP till 9 min after intubation, and then onwards significant changes were noted till 4th hour of post-operative period. Butorphanol provided prolonged analgesia when compared to fentanyl.

Conclusions: We conclude that butorphanol is a better alternative to fentanyl for use as analgesic in laparoscopic surgeries because of its ability to produce prolonged analgesia, and less post-operative complications.

Key Words: *Butorphanol, Fentanyl, Laparoscopic surgery, Pain relief, Sedation*

Rao MH, Satyanarayana V, Srinivas B, Muralidhar A, Aloka Samantaray A, Krishna Reddy AS, Hemanth N. Comparison of butorphanol and fentanyl for balanced anaesthesia in patients undergoing laparoscopic surgeries under general anaesthesia: A prospective, randomized and double blind study. J Clin Sci Res 2013;2:8-15.

INTRODUCTION

Pain is an unpleasant sensation, which produces a reaction consisting of withdrawal response, metabolic response, hormonal response and conscious aversion. The side-effects of pain include peripheral vasoconstriction, reduced functional residual capacity and reduced sputum clearance.^{1,2} Pain relief has many advantages, namely, reduction in metabolic response to trauma, thereby prevent postoperative negative nitrogen balance. Moreover pain-free patients have better mobility with immediate benefits in reduced incidence of chest infections and deep vein thrombosis. Laparoscopy has been promoted aggressively and has advantages like shorter hospital stay, more rapid return to normal activities, less pain associated with the small, limited incisions

and less postoperative ileus compared with the open laparotomy technique.^{3,4} Pneumoperitoneum causes various cardiovascular and respiratory derangements. The purpose of this study was to compare equipotent moderate doses of two different analgesics i.e., butorphanol and fentanyl in healthy adult patients undergoing laparoscopic cholecystectomy and appendectomy under general anaesthesia in terms of intra-operative haemodynamics and post-operative pain relief.

MATERIAL AND METHODS

This prospective, randomized and double-blind study was conducted after obtaining approval from the Institutional Ethical Committee to compare the analgesic efficacy of equipotent moderate doses of butorphanol and fentanyl in patients undergoing laparoscopic surgeries under general anaesthesia.

Received: 30 August, 2012.

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Fifty American Society Anesthesiologists (ASA) grade I and II patients of either gender and in age group of 16-60 years posted for laparoscopic cholecystectomy and appendicectomy were recruited into study. Patients were randomized into two groups of 25 each by computer generated random numbers using the "sealed opaque envelope" technique. All patients were administered oral alprazolam 0.5 mg on the night before surgery. After overnight fasting they were shifted to operation theatre and 18 gauge intravenous (IV) cannula was secured under local anaesthesia and ringer lactate solution was administered. Patients were premedicated with inj. midazolam 20 µg/kg IV and Inj. ondansetron 4 mg IV. Monitors were attached and all baseline parameters like pulse rate, systolic blood pressure, diastolic blood pressure, ECG and oxygen saturation by pulse oximetry (SpO_2) were monitored. An anaesthesiologist who is not involved in the study administered the test drugs in a double-blinded fashion, four minutes before induction of anaesthesia. Group B (n=25) received Inj. butorphanol 40 µg/kg while Group F (n=25) received Inj. fentanyl 2 µg/kg intravenously.

Patients were pre-oxygenated for 3 minutes with oxygen using Bain's circuit. All the patients were induced with Inj. thiopentone sodium 5 mg/Kg, Inj. vecuronium bromide 0.1 mg/Kg intravenously followed by tracheal intubation with cuffed oro-tracheal tube of appropriate size and end-tidal carbon dioxide ($EtCO_2$) was monitored. Anaesthesia was maintained with controlled ventilation with 50% oxygen, 50% nitrous oxide, sevoflurane (0.2%-1.5%) and intermittent inj. vecuronium bromide (0.02 mg/kg) IV. Intra-abdominal pressure was kept between 11-15 mm of Hg. Throughout the course of anaesthesia Heart rate (HR), systolic blood Pressure (SBP), diastolic blood Pressure (DBP), $EtCO_2$ and SpO_2 were monitored after administering the drug, after intubation, every 3 min after intubation till 20 minutes before pneumoperitoneum, at 15 min intervals till 1 hour of pneumoperitoneum, after release of carbon dioxide (CO_2), and after

extubation. After completion of surgery, patients were reversed with Inj. neostigmine 50 µg/kg IV and Inj. glycopyrrolate 10 µg/Kg, IV. In the post-operative period, every patient was monitored for haemodynamic parameters and SpO_2 , sedation score, visual analogue scale⁵ (VAS) for pain relief and post-operative complications. Pain relief was assessed by VAS on a scale of 1 to 10 cm ranging from no pain (0) to worst pain (10). The patients were asked to mark the point in the scale that corresponded level of pain intensity. Distance in cm from lower end of the scale to the mark done by the patient was taken as the numerical index of severity of pain. Inj. tramadol hydrochloride 1.5 mg/kg IV was given when patients complained of pain post-operatively i.e., when the VAS score was more than 5. The sedation score was assessed by the University of Michigan Sedation Scale⁶ (UMSS) postoperatively as: 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; and 5 = very drowsy not responding to severe physical stimulus.

Throughout the study period for following complications namely nausea and vomiting, rashes, excitement, dizziness, urinary retention, respiratory depression, pruritus.

Statistical analysis

Continuous variables such as age, weight, pulse rate, SBP, DBP, SpO_2 , $EtCO_2$, VAS, were compared between butorphanol and fentanyl groups by student's t-test. Sedation score was analysed by chi-square. Comparison of the changes pulse rate, SBP, DBP, SpO_2 , $EtCO_2$ in both groups, intra and inter-group was carried out by paired t-test and unpaired t-test respectively and comparison of VAS was analyzed by unpaired t-test

RESULTS

Both the groups were found to be comparable demographically and with respect to duration of surgery. The pre-operative values, mean heart rate,

SBP, DBP and SpO₂ (%) in group B and in group F were found to be comparable (Table 1). In our study it was observed that the mean duration of surgery in Group B was found out to be 111.17±9.07 minutes and in group F was 112.87±9.48 minutes (p=0.467). There was significant fall in the heart rate in butorphanol group (Group B) starting from 6 min after intubation and this persisted till 45 min after pneumoperitoneum (p<0.05). In fentanyl group (Group F) there was significant fall in the heart rate after intubation and this persisted till, the creation of pneumoperitoneum (Figure 1). However the variations in the pulse rate in both the groups were not up to the extent of bradycardia/tachycardia (i.e., the heart rate remained within 20% of base line values). There was significant difference in heart rate at 12 min after intubation and persisted till second hour of post-operative period between the two groups (p<0.05). There was significant fall in the systolic blood pressure in butorphanol group after intubation and persisted till 20 min after intubation (p<0.05). In fentanyl group (Group F) there was significant fall in the systolic blood pressure started after intubation and persisted till 12 min after intubation (p<0.05). No significant difference was

Table 1: Comparison of baseline values between Group B and Group F

Baseline	Group B	Group F	p-value
Heart rate	86.66±8.85	88.33±8.64	0.053
SBP	120.08±8.02	122.67±10.1	0.297
DBP	80.66±5.44	80.75±6.2	0.817
SpO ₂	99.08±0.02	99.04±0.03	0.560

SBP=systolic blood pressure; DBP=diastolic blood pressure; SpO₂=arterial oxygen saturation by pulse oximetry

found in systolic blood pressure till 9 min after intubation (p>0.05), and then onwards significant changes (p<0.05) were noted till 4th hour of post-operative period when both groups are compared (Figure 2). In Group B there was significant fall in the DBP after intubation and persisted till 15 min after pneumoperitoneum (p<0.05). In fentanyl group (Group F) there was significant change in DBP started after intubation and persisted till 15 min after intubation (p<0.05). Comparing both the groups, the statistical difference in DBP started at 12 min after intubation (Figure 3) and persisted till 4th hour of post-operative period (p<0.05). Group F patients started feeling pain at 30 min after extubation in comparison to Group B patients who reported pain after 3 hours (Figure 4), and

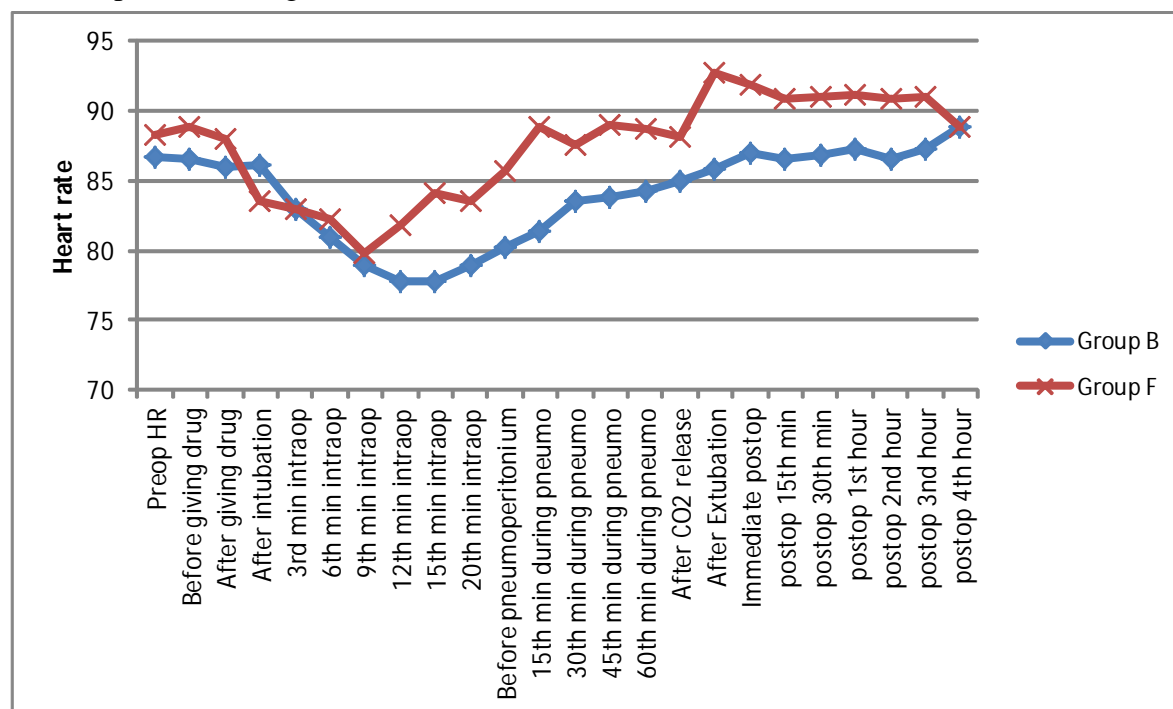


Figure 1: Comparison of heart rate between Groups B and F
HR = hear rate

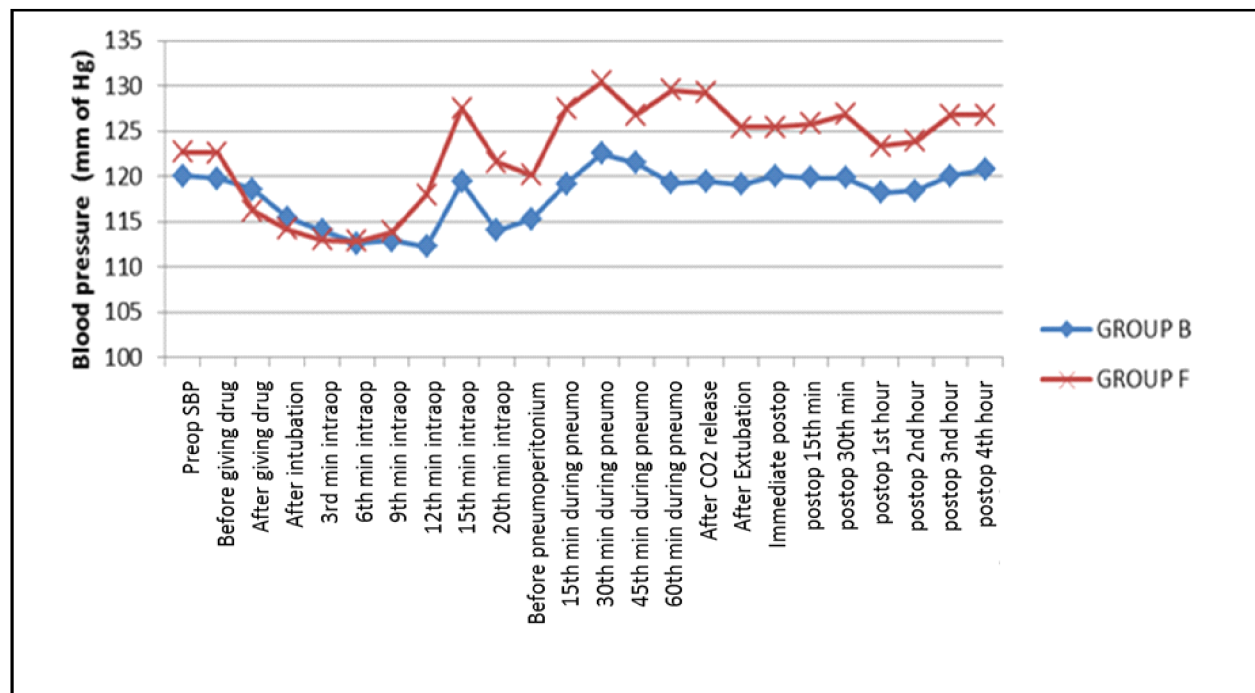


Figure 2: Comparison of systolic blood pressure between Groups B and F
SBP = systolic blood pressure

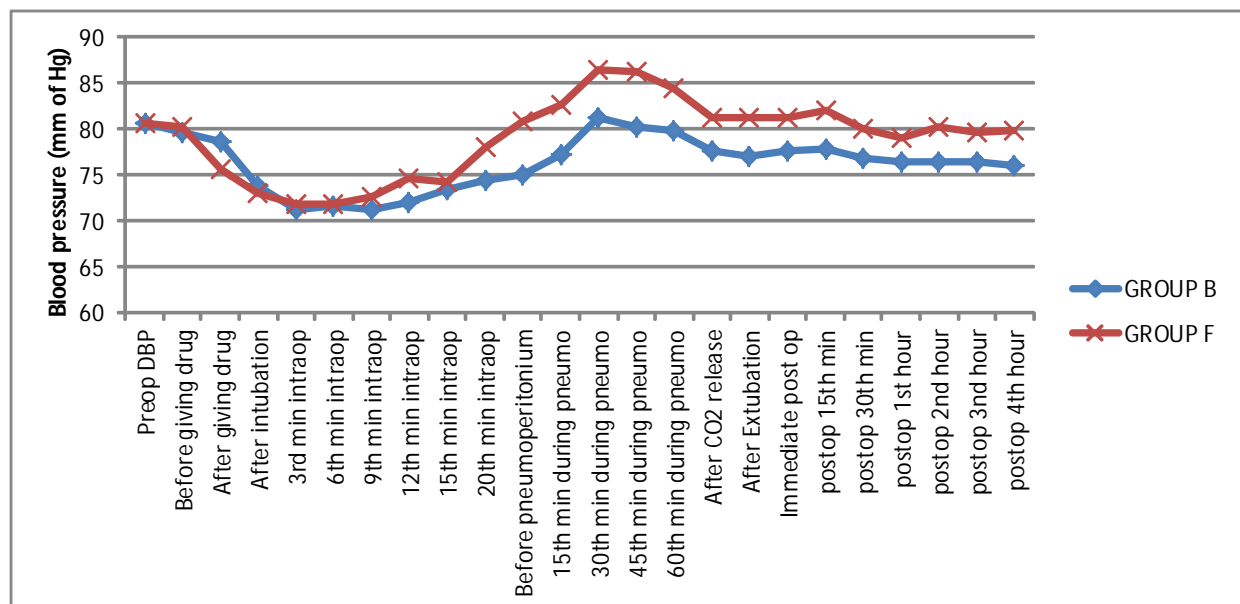


Figure 3: Comparison of diastolic blood pressure between Groups B and F
DBP = diastolic blood pressure

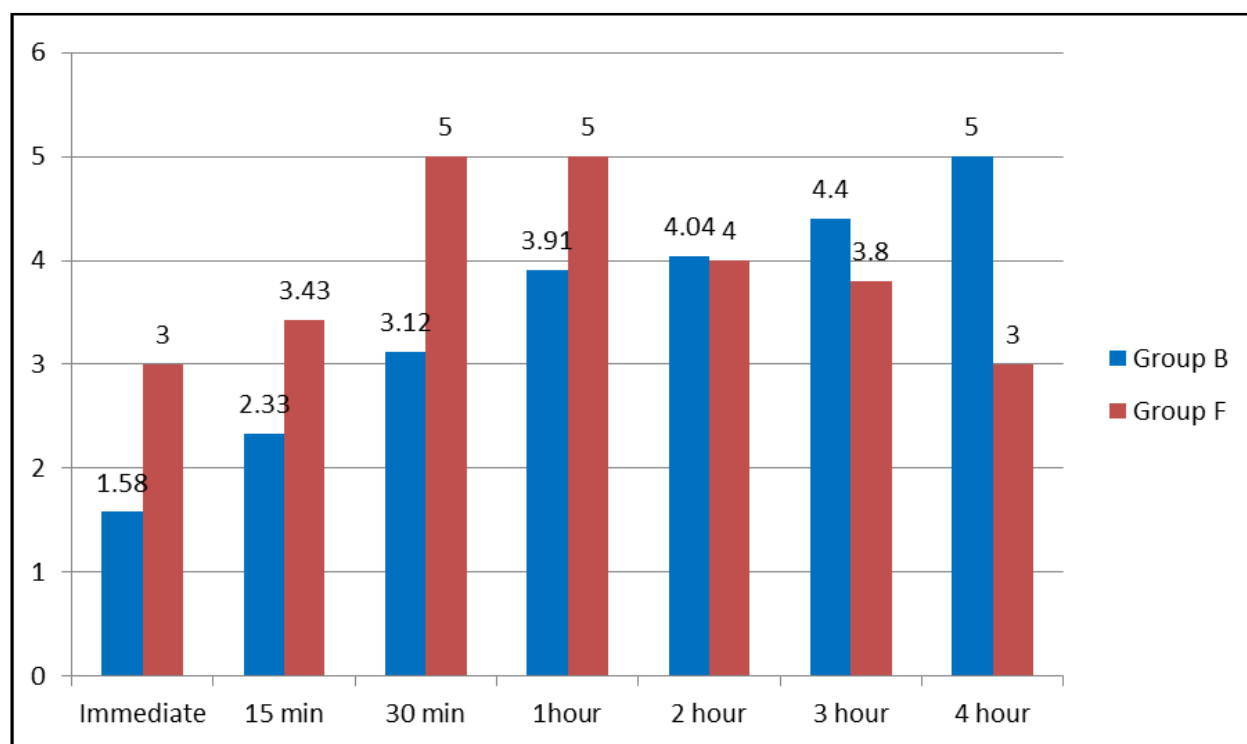


Figure 4: Comparison of VAS score between Group B and F
VAS = visual analog scale

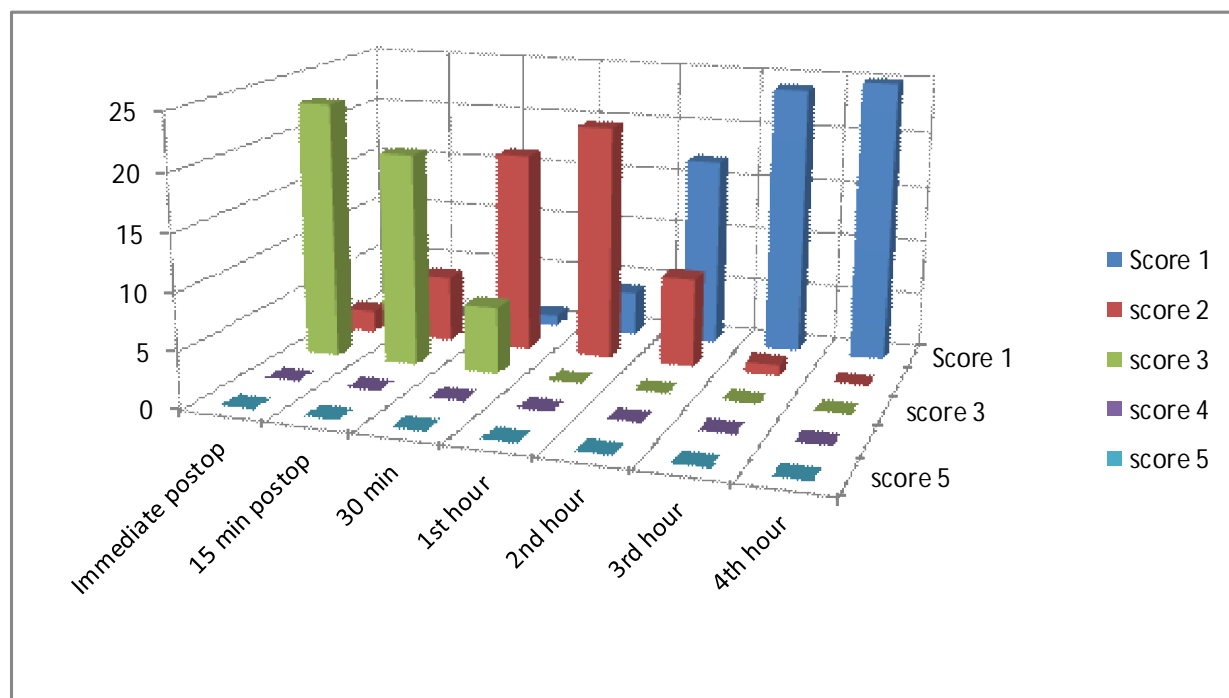


Figure 5A: Postoperative sedation score in Group B patients
Postop = postoperative period

comparison of both the groups was found to be significant till 4th hour of post-operative period ($P < 0.001$). Rescue analgesia was given in the form of Inj. tramadol hydrochloride when the VAS score was 5 or more out of 10; this was taken as an end point of pain relief. In the post-operative period, in group B sedation remained for longer period for about 3 hours after extubation, while in case of group F sedation remained for 30 min only after extubation (Figures 5A and 5B). There were complications like nausea, vomiting, and rashes in few of the cases (*vide infra*). The incidence of nausea was 1 out of 25 in Group B and 3 out of 25 in Group F where as occurred vomiting in 1 out of 25 in Group B and 3 out of 25 in Group F. There was incidence of rash (4%) in case of Group F; no rash occurred in Group B subjects.

DISCUSSION

Presently laparoscopic surgery has replaced many of the open surgeries because of its advantages like smaller incision, fast recovery, less incidence of complications and relatively less painful. There are various haemodynamic, respiratory, and stress response changes in laparoscopic surgery due to creation of pneumoperitoneum.⁷⁻¹⁰ In balanced

anaesthesia, ideal opioid would permit rapid titration to the effect, successfully prevent unwanted responses to various stimuli, require little supplementation, does not depress cardiovascular function, permit the return of adequate spontaneous ventilation in timely manner and produce residual if not complete post-operative analgesia with minimal side effects. Both the group of drugs have haemodynamic stability, analgesia, sedation and decreases the requirement of other anesthetic drugs and is available at low cost. So we have chosen butorphanol and fentanyl to study the analgesia and haemodynamic changes in both the groups.

Patients in the age group of 16 to 60 years were selected because the variability of haemodynamic changes decreases with an increase in age and younger patients show more extreme changes. The changes in the heart rate were comparable in both the groups. There were very minimal changes in pulse rate in both the groups till 12 min after intubation. Comparing the mean pulse rate in both the groups from 12 min after intubation till second hour of post operative period was found out to be significant ($p = 0.041$). There was no significant

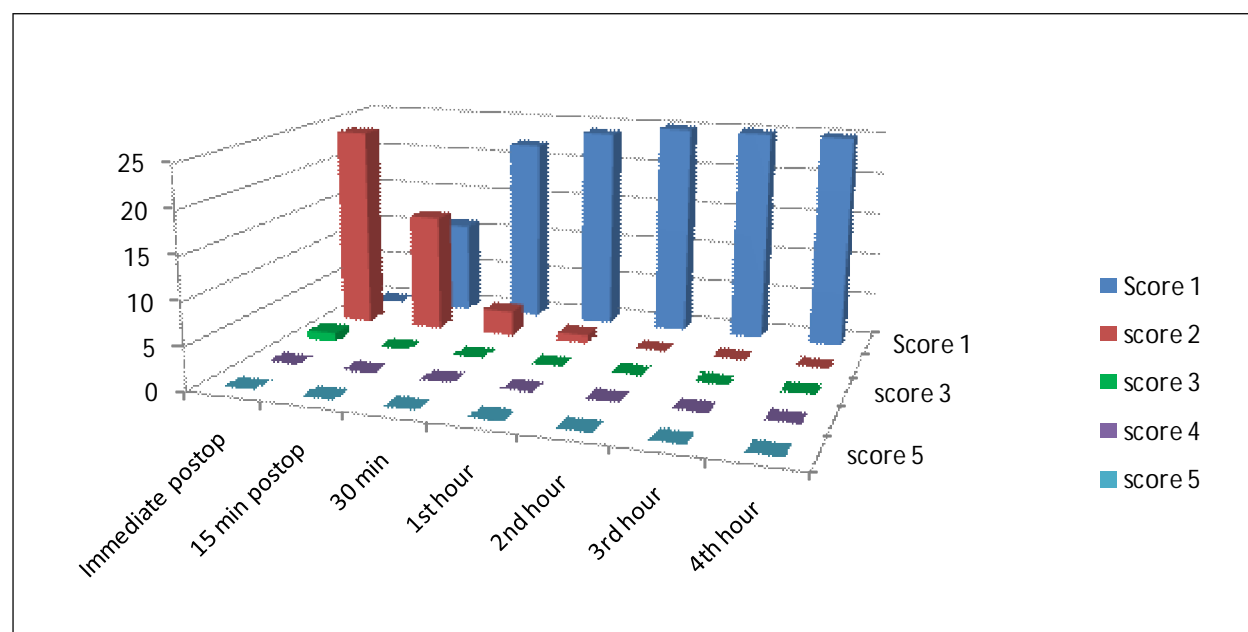


Figure 5B: Postoperative sedation score in Group F patients
Postop = postoperative period

difference in the pulse rate at fourth hour of post operative period ($p=0.92$). Fall in pulse rate in Group B was more in comparison to Group F throughout peri-operative period. The deviation in pulse rate in both the Groups was not to the extent of bradycardia or tachycardia ($\leq 20\%$ of pre-operative value). In the study by Pandit et al¹¹ the only statistically significant change occurred 2 minutes after tracheal intubation in fentanyl group when pulse rate was significantly higher than the base line values. Where as such a rise in pulse rate was not noted in butorphanol group.¹¹ In Group F there was higher rise in SBP after creation of pneumoperitonium till post-operative period than in comparison to group B (Figure 2). There were no significant changes in SBP in another study.¹² Higher fall in diastolic blood pressure was seen in case of group B than in comparison to group F (Figure 3). There was no incidence of hypotension or hypertension in both the groups. The amount of inhalational agent used in Group F was more in comparison to Group B. Similar observations were in another study.¹³ In case of Group F, in order to control blood pressure we started propofol drip in 12% of cases when blood pressure was not controlled even after inhalation concentration beyond 2% and the rise in pulse rate and blood pressure were greater than 20 % of the base line values. The changes in EtCO₂ in Group B and Group F were not found to be statistically significant ($p>0.05$). There were no significant changes in SpO₂ in both the groups in intra and inter group study. The sedation in group F was found upto 1 hour and in Group B was found upto 3 hours in post operative period. So it was found that postoperatively sedation was more in case of Group B than in comparison to Group F. On analyzing postoperative pain relief on VAS, Group B showed analgesia upto 3 hours as compared to Group F showed pain relief upto 1 hour and difference was statistically significant ($p<0.05$) (Figure 4). In a study¹⁴ the emergence time, recovery profile and postoperative sedation was found to be less in fentanyl group where as

postoperative analgesia was more in butorphanol group.

Both groups were comparable as far as incidence of nausea [2 out of 25 (Group B) and 3 out of 25 (Group F)], vomiting [1 out of 25 (Group B) and 3 out of 25 (Group F)] and rashes [0 out of 25 (Group B) and 1 out of 25 (Group F)]. However, post-operative nausea and vomiting were easily treated with Inj. ondansetron 4 mg IV, and rashes in group F, were treated with inj. chlorpheniramine maleate 5 mg intravenously.

We found that butorphanol and fentanyl were cardiostable, but there was significant fall in heart rate and diastolic blood pressure in patients who received butorphanol as premedication as compared to the patients who received fentanyl, in which there was rise in heart rate and blood pressure intraoperatively, however the rise in heart rate and blood pressure were not up to the 20% of pre-operative value. However post-operative sedation and analgesia remained for longer duration in butorphanol group as compared to fentanyl group. Thus, we conclude that butorphanol was a better alternative to fentanyl as an analgesic for use in laparoscopic surgeries because of its ability to produce prolonged analgesia, and less post-operative complications.

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