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Comparison of Intravenous Fentanyl and Intravenous Butorphanol in Patients Undergoing Major Abdominal Surgeries Under General Anaesthesia

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Abstract: ***Introduction: Opioids are commonly incorporated in balanced anaesthesia to reduce anaesthetic requirements during both induction and maintenance. Fentanyl and Butorphanol are two different categories of opioids with different mechanism of action but producing a similar analgesic effect. Aim and Objective: The present study is aimed at comparing injection fentanyl 1µg/kg and butorphanol 20µg/kg in balanced anaesthesia with respect to intraoperative haemodynamic changes and postoperative pain relief. Material and Methods: This is double blinded prospective randomised study conducted on 102 patients of either sex, belonging to American Society of Anaesthesiologists (ASA) status I or II and aged between 18-65 years for duration of 18 months (August 01, 2022 to January 31, 2024). These patients were divided into two groups of 51 each, Group A: (Injection Fentanyl) - 1µg/kg I.V and Group B: (Injection Butorphanol) - 20µg/kg I.V. Patients received one of these drugs as a part of balanced anaesthesia and intra-operative haemodynamic changes were recorded. Post-operative sedation and analgesia were also looked for. Results: In our study a statistically significant fall in heart rate was observed at injection of study drug, at 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110 and 120 minutes intra-operatively in group B as compared to group F. No significant changes were seen in systolic blood pressure, diastolic blood pressure and mean arterial pressure in both groups. Post-operatively, there was significant increase in Ramsay sedation score in group B whereas a significant decrease in visual analogue score was observed in group B as compared to group A. There were no significant side effects noted. Conclusion: Our study confirmed that butorphanol showed better haemodyamic stability and pain relief intra-operatively with better attenuation of increase in heart rate throughout the surgery. Hence from our present study we conclude that butorphanol in a dose of 20mcg/kg can be used an alternative to fentanyl in major abdominal surgeries with no major side effects except slight sedation post-operatively.***

Keywords: Butorphanol, Fentanyl, Haemodynamic changes, Postoperative analgesia

1.Introduction

Pain management is a critical component of perioperative care, significantly influencing patient outcomes, recovery time, and overall surgical success [1]. Inadequate analgesia intraoperatively can lead to haemodynamic instability, increased stress responses, and heightened postoperative pain [2]. Among the various pharmacological options available, opioids play a pivotal role in achieving effective pain control [3]. The administration of opioids during general anaesthesia provides several advantages, including attenuation of the stress response to surgical stimuli, improved haemodynamic stability, and enhanced postoperative recovery [4]. However, opioids differ in their pharmacodynamic and pharmacokinetic properties, necessitating careful selection based on patient profile, surgical procedure, and desired outcomes [5, 6]. Fentanyl, a potent synthetic opioid, is widely used in anaesthesia due to its rapid onset, short duration, and minimal histamine release [6]. As a pure µ-opioid receptor agonist, fentanyl provides profound analgesia while maintaining cardiovascular stability [7]. However, its short half-life often necessitates repeated dosing or adjunctive analgesia to sustain pain relief postoperatively. Additionally, fentanyl use has been associated with dose-dependent respiratory depression, nausea, vomiting, and opioid-induced hyperalgesia [8, 9]. Butorphanol, a synthetic opioid with mixed agonist-antagonist properties, offers an alternative to fentanyl in balanced anaesthesia [10]. It primarily acts as a κ-opioid receptor agonist while exerting partialantagonistic effects on µ-opioid receptors [11]. This dual mechanism provides effective analgesia while reducing the risk of respiratory depression and opioid-induced euphoria [12]. Additionally, butorphanol hasbeen reported to have a ceiling effect on respiratory depression, making it a potentially safer option for perioperative analgesia [13]. Despite its advantages, butorphanol's sedative effects and potential for dysphoria at high doses necessitate further investigation [14]. Prior studies have compared fentanyl and butorphanol in various surgical settings, including laparoscopic cholecystectomy, orthopedic procedures, and obstetric analgesia [15-17]. However, data regarding their comparative efficacy in major abdominal surgeries remain limited [18].

This study aims to evaluate and compare fentanyl and butorphanol concerning intraoperative haemodynamic stability, postoperative analgesia, and overall safety profile in patients undergoing major abdominal surgeries under general anaesthesia. By identifying the superior agent in this context, we seek to optimize anaesthetic protocols and improve perioperative pain management strategies.

2. Materials And Methods

Study Design and Participants

This prospective, randomised, double-blinded study was conducted over 18 months (August 2022-January 2024) on 102 patients scheduled for major abdominal surgeries under general anaesthesia. Ethical clearance done under institutional ethics committee of Christian Medical College and Hospital Ludhiana on November 5th, 2022, approval number: BMHR-IECCMCL/1122-419/Apprvl-PG-Thesis/Anaesth and informed consent taken from every participant. Patients were divided equally into two groups (n=51 each): Group A: injection fentanyl 1 µg/kg IV and Group B: injection butorphanol 20 µg/kg IV. This study included all ASA I-II patients, aged 18-65 years, scheduled for major abdominal surgery under general anaesthesia whereas exclusion criteria was known hypersensitivity to study drugs, severe cardiovascular, hepatic, or renal dysfunction and history of opioid dependence.

Anaesthesia Protocol

All patients received standard monitoring, including ECG, NIBP, SpO2, and EtCO2. Premedication with IV midazolam (0.03 mg/kg) was administered. Induction was achieved with propofol (2 mg/kg) and vecuronium (0.1 mg/kg) for neuromuscular blockade. Maintenance included oxygen, nitrous oxide, isoflurane, and intermittent doses of vecuronium. The study drugs were administered five minutes before induction. Intraoperative heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and oxygen saturation (SpO2) were recorded at 10-minute intervals. Postoperatively, Ramsay Sedation Score (RSS) and Visual Analogue Scale (VAS) were assessed immediately post-surgery, after 15 minutes and after 30 minutes.

Statistical Analysis

The presentation of the categorical variables was done in the form of number and percentage (%). On the other hand, the quantitative data were presented as the means ±SD and as median with 25th and 75th percentiles (interquartile range). For results, the comparison of the variables which were quantitative in nature were analysed using Independent t test whereas qualitative variables were analysed using Chi-Square test. If any cell had an expected value of less than 5 then Fisher's exact test was used.

3. Results

Demographic and Baseline Characteristics

A total of 102 patients were enrolled and randomized into two groups: Group A (Fentanyl 1 µg/kg IV) and Group B (Butorphanol 20 µg/kg IV). Both groups were comparable in terms of age, gender distribution, body mass index (BMI), ASA status, and surgical duration ($p > 0.05$).

Intraoperative Haemodynamic Parameters

Heart Rate (HR):

A statistically significant reduction in HR was observed in Group B compared to Group A at 10, 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, and 120 minutes intraoperatively ($p < 0.05$). Group B maintained a more stable HR profile throughout the procedure, whereas Group A showed transient tachycardia following intubation and surgical incision.

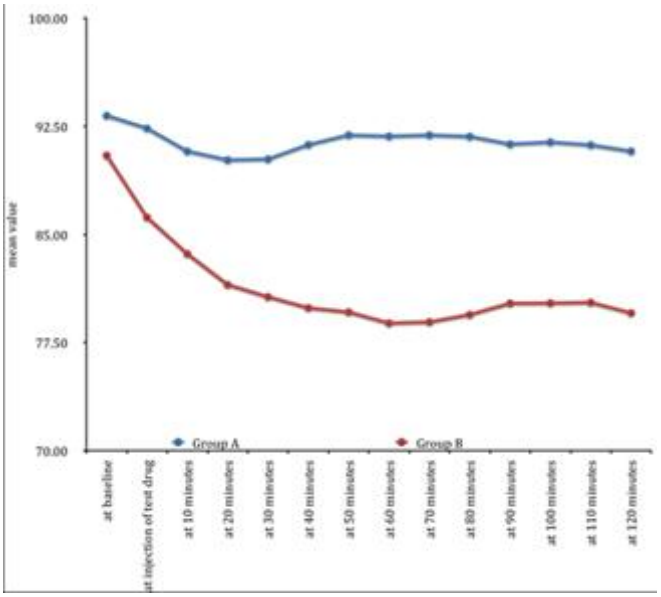

Figure 1: Comparison of intra-operative heart rate (per minute) between group A (blue) and B (red)

Group A - Fentanyl group

Group B - Butorphanol group

No significant difference was seen in intra-operative heart rate (per minute) at baseline (p value=0.335) between group A and B. Mean ±SD of intra-operative heart rate (per minute) at baseline in group A was 93.24 ±15.92 and in group B was 90.47 ±12.75 with no significant difference between them. Significant difference was seen in intra-operative heart rate (per minute) at injection of test drug, at 10 minutes, at 20 minutes, at 30 minutes, at 40 minutes, at 50 minutes, at 60 minutes, at 70 minutes, at 80 minutes, at 90 minutes, at 100 minutes, at 110 minutes, at 120 minutes between group A and B. (p value <.05)

Blood Pressure (SBP, DBP, MAP):

No significant differences were observed in systolic blood pressure (SBP), diastolic blood pressure (DBP), or mean arterial pressure (MAP) between the two groups. Both fentanyl and butorphanol provided effective attenuation of pressor responses, with minimal fluctuations during surgical manipulation.

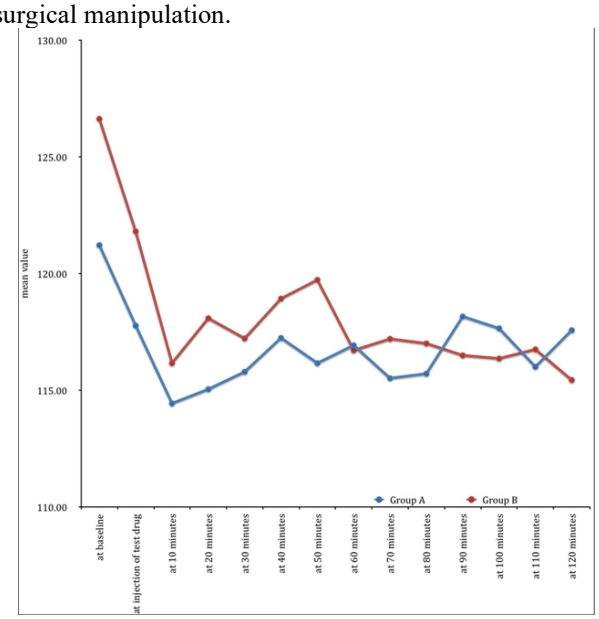

Figure 2: Comparison of intra-operative systolic blood pressure (mmHg) between group A (blue) and B (red)

Group A- Fentanyl

Group B- Butorphanol

No significant difference was seen in intra-operative systolic blood pressure (mmHg) at baseline (p value=0.123), at injection of test drug (p value=0.264), at 10 minutes (p value=0.633), at 20 minutes (p value=0.366), at 30 minutes (p value=0.643), at 40 minutes (p value=0.57), at 50 minutes (p value=0.188), at 60 minutes (p value=0.932), at 70 minutes (p value=0.512), at 80 minutes (p value=0.578), at 90 minutes (p value=0.517), at 100 minutes (p value=0.614), at 110 minutes (p value=0.763), at 120 minutes (p value=0.351) between group A and B.

Oxygen Saturation (SpO2):

Both groups maintained adequate oxygen saturation levels (SpO2 > 96% throughout surgery), with no significant intergroup differences.

Postoperative Sedation and Analgesia

Ramsay Sedation Score (RSS):

Group B exhibited significantly higher RSS immediately post-surgery, after 15 minutes and after 30 minutes, postoperatively compared to Group A ($p < 0.05$). Sedation levels gradually declined and normalized by 4-6 hours, with no cases of prolonged or excessive sedation.

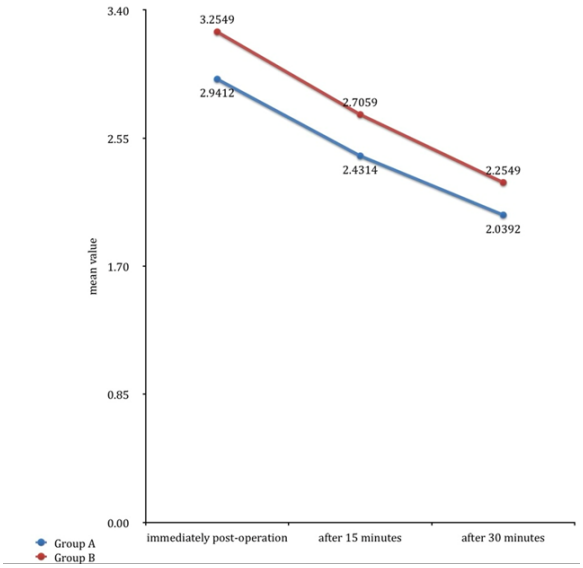

Figure 3: Comparison of Ramsay Sedation Score between group A (blue) and B (red)

Group A- Fentanyl

Group B- Butorphanol

Significant difference was seen in ramsay sedation score immediately post-operation, after 15 minutes, after 30 minutes between group A and B. (p value <.05)

Mean ±SD of ramsay sedation score immediately post-operation, after 15 minutes, after 30 minutes in group B was 3.25 ±0.59, 2.71 ±0.58, 2.25 ±0.44 respectively which was significantly higher as compared to group A (2.94 ± 0.65 (p value=0.012), 2.43 ±0.54 (p value=0.015), 2.04 ± 0.4 (p value=0.011)) respectively.

Visual Analogue Scale (VAS) Pain Scores:

Group B reported significantly lower VAS scores at all postoperative time points ($p < 0.05$), indicating superior analgesic efficacy. The mean duration of effective analgesia was longer in Group B, reducing the need for rescue analgesics in the immediate postoperative period.

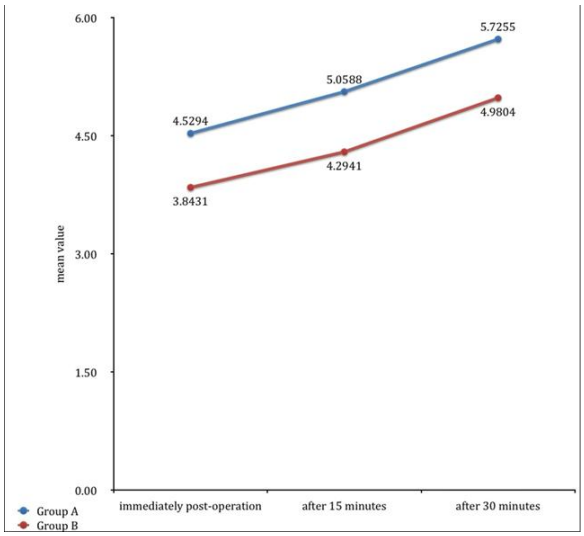

Figure 4: Comparison of Visual Analogue score between group A (blue) and B (red)

Group A- Fentanyl

Group B- Butorphanol

Significant difference was seen in visual analogue score immediately post-operation, after 15 minutes, after 30 minutes between group A and B. (p value <.05) Mean ±SD of visual analogue score immediately post-operation, after 15 minutes, after 30 minutes in group A was 4.53 ±0.81, 5.06 ±0.79, 5.73 ±0.78 respectively which was significantly higher as compared to group B (3.84 ±0.67 (p value<.0001), 4.29 ±0.81 (p value<.0001), 4.98 ±0.65 (p value<.0001)) respectively.

Adverse Effects:

Respiratory depression: None of the patients in either group developed clinically significant respiratory depression. Nausea/Vomiting: Mild nausea was reported in 6% of Group A and 4% of Group B, but it was self-limiting and did not require intervention. Sedation: Group B demonstrated mild sedation postoperatively, which was not associated with any airway compromise or delayed recovery.

Table 1: Comparison of adverse effects between group A and group B

Adverse effects	Group A (n=51)	Group B (n=51)	Total	P value
Confusion	3 (5.88%)	3 (5.88%)	6 (5.88%)	1*
Hallucination	0 (0%)	0 (0%)	0 (0%)	NA
Nausea	3 (5.88%)	5 (9.80%)	8 (7.84%)	0.715*
Vomiting	1 (1.96%)	1 (1.96%)	2 (1.96%)	1*
Constipation	0 (0%)	0 (0%)	0 (0%)	NA
Pruritis	0 (0%)	0 (0%)	0 (0%)	NA
Abdominal pain	0 (0%)	0 (0%)	0 (0%)	NA
Xerostomia	0 (0%)	0 (0%)	0 (0%)	NA
Dizziness	0 (0%)	0 (0%)	0 (0%)	NA
Headache	0 (0%)	0 (0%)	0 (0%)	NA
Hypotension	4 (7.84%)	5 (9.80%)	9 (8.82%)	1*
Bradycardia	3 (5.88%)	3 (5.88%)	6 (5.88%)	1*

Group A- Fentanyl

Group B- Butorphanol

The comparison of qualitative variables analysed using Chi-Square test. Fisher's exact test was used if any cell had an expected value of less than 5

4. Discussion

This prospective, randomized, double-blinded study was designed to compare the effects of intravenous fentanyl and butorphanol as part of balanced anaesthesia in patients undergoing major abdominal surgery. The primary outcomes evaluated were intraoperative haemodynamic stability and postoperative analgesia, while sedation and adverse effects were studied as secondary outcomes.

Haemodynamic Stability

The haemodynamic response to surgical stress, including airway manipulation, surgical incision, and ongoing nociceptive stimuli, is primarily mediated by sympathetic activation, resulting in tachycardia and hypertension. Uncontrolled intraoperative haemodynamic fluctuations may increase myocardial oxygen consumption, potentially compromising high-risk patients [1-3]. Opioids are integral to balanced anaesthesia because of their potent analgesic properties and their ability to attenuate these haemodynamic responses [4, 5]. Our study demonstrated that butorphanol provided superior haemodynamic stability compared to fentanyl, particularly in controlling intraoperative heart rate. The κ-agonist activity of butorphanol is believed to modulate autonomic responses more effectively, blunting the sympathetic surges typically seen during surgical stimuli [10, 11]. These findings are consistent with prior studies by Arora et al. and Patel et al., who also demonstrated superior control of heart rate and stable haemodynamics with butorphanol administration [14, 15]. Rao et al. further validated these observations, noting sustained haemodynamic control during laparoscopic cholecystectomy using butorphanol compared to fentanyl [16]. Fentanyl, although widely accepted for its rapid onset and short duration of action, primarily acts on μ-receptors, providing profound analgesia but not consistently attenuating the sympathoadrenal responses during high-intensity surgical manipulation [6-8]. Studies by Stanley and Paul et al. have emphasized that even at appropriate doses, fentanyl may require adjunctive measures to completely suppress laryngoscopic and surgical pressor responses [6, 7].

Postoperative Analgesia

Effective postoperative pain control remains one of the most significant determinants of recovery following major abdominal surgery. Poorly controlled postoperative pain can impair respiratory mechanics, delay ambulation, prolong hospitalization, and increase the risk of chronic post-surgical pain [2, 3]. In our study, butorphanol offered superior postoperative analgesia, as indicated by lower VAS pain scores over multiple time points and a longer interval before rescue analgesia was required. The mixed agonist-antagonist pharmacological profile of butorphanol is likely responsible for these prolonged analgesic effects [10-12]. Ahire et al. demonstrated similar benefits of butorphanol, reporting extended analgesic duration compared to fentanyl following outpatient laparoscopic surgery [10]. Arora V et al also supports the superior analgesic profile of butorphanol, particularly in managing moderate to severe visceral pain, which is common in abdominal surgeries [14]. Fentanyl's shorter half-life necessitates more frequent redosing or adjunctive analgesics in the postoperative period, as also noted in the literature by Vardanyan et al. and Angst et al [8, 9]. Furthermore, the potential for opioid-induced hyperalgesia with fentanyl underscores the need for alternative agents with more favorable profiles for longer-term pain control [9].

Sedation and Safety Profile

Sedation is an expected property of both fentanyl and butorphanol due to their central nervous system depressant effects. In our study, butorphanol produced statistically significant but clinically acceptable postoperative sedation, which resolved spontaneously within a few hours without requiring intervention. The mild sedation observed in Group B aligns with the κ-receptor agonist effects of butorphanol, which modulate arousal centres in the brainstem without excessive respiratory depression. Pasternak and Khan have highlighted that butorphanol's ceiling effect on respiratory depression offers a margin of safety compared to pure μ-agonists like fentanyl [12, 13]. Importantly, none of the patients in either group developed clinically significant adverse events such as respiratory depression, hypoxia, or prolonged recovery times. Both drugs were well tolerated, supporting their use as safe components of balanced anaesthesia when administered in carefully titrated doses.

Clinical Implications

The findings from this study have several important clinical implications: Butorphanol may be especially useful in patients who are at risk of tachyarrhythmias or those with limited cardiovascular reserve where haemodynamic stability is paramount. The prolonged postoperative analgesia provided by butorphanol may reduce the need for additional opioids postoperatively, thus potentially lowering the risk of opioid-related complications, including nausea, vomiting, ileus, and opioid-induced hyperalgesia. Butorphanol may serve as an attractive alternative to fentanyl in resource-limited settings due to its lower abuse potential and often easier regulatory handling [17, 18].

Strengths and Limitations

A strength of this study is its prospective, randomized, double-blinded design which minimizes bias.

Additionally, we used clearly defined dosing regimens reflective of real-world clinical practice. However, this study also has limitations. The study population excluded high-risk ASA III and IV patients, and therefore, the findings may not be generalizable to higher-risk cohorts. We also limited postoperative follow- up to early recovery; longer-term analgesic outcomes were not assessed. Future larger-scale studies evaluating these drugs in higher-risk patients, across diverse surgical procedures, and assessing chronic postoperative pain outcomes would further elucidate the role of butorphanol in modern anaesthetic practice.

5. Conclusions

This study shows that both fentanyl and butorphanol are effective for intraoperative and postoperative analgesia in major abdominal surgeries. Compared to fentanyl, butorphanol offers better haemodynamic stability during surgery and provides longer-lasting postoperative pain relief with fewer requirements for additional analgesics. Mild sedation was noted with butorphanol, but it was short-lived and not associated with respiratory issues. Overall, butorphanol appears to be a safe and effective alternative to fentanyl, especially in surgeries where stable haemodynamics and prolonged analgesia are important. Further research with larger groups and varied surgical settings would help confirm these benefits.

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