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# A Prospective Randomized Comparative Study to Evaluate Effects of Propofol and Fentanyl versus Propofol and Ketamine Sedation in Patients Undergoing Colonoscopy: A Hospital Based Study

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**Abstract:** ***Background and Aim: Colonoscopy is a commonly performed diagnostic and therapeutic procedure that may cause significant discomfort due to mesenteric stretching and colonic spasm, especially at the splenic and hepatic flexures. Adequate sedation improves patient comfort and procedural conditions. This study aimed to compare the efficacy and effects of propofol–ketamine and propofol–fentanyl for monitored anaesthesia care during colonoscopy. Methodology: This prospective randomized clinical study included 72 ASA I–II patients undergoing colonoscopy under sedation. Patients were randomly allocated into two groups of 36 each using a random allocation table. Recovery was assessed by time to first response to verbal command and by Aldrete score recorded every 5 minutes. Endoscopist satisfaction was evaluated using a 3-point Likert verbal rating scale. Results: In Group A, 55.6%, and in Group B, 58.3% of patients were ASA grade II. Group B showed greater respiratory rate fluctuations than Group A, though not statistically significant. Group A demonstrated more variations in mean arterial pressure and $SpO_2$. Mean heart rate, systolic, and diastolic blood pressures were comparable between groups at all time intervals. Endoscopist satisfaction was higher in Group B. Time to first response was shorter in Group A compared to Group B. Conclusion: Rescue propofol requirement was lower in the propofol–ketamine group than in the propofol–fentanyl group. Hemodynamic parameters were stable in both groups. Endoscopist satisfaction was higher with propofol–ketamine, whereas recovery was faster with propofol–fentanyl, as indicated by shorter first response time and earlier attainment of maximum Aldrete score.***

**Keywords:** Colonoscopy, rescue dosage, propofol, fentanyl, ketamine

## 1.Introduction

Colonoscopy is a widely performed diagnostic and therapeutic procedure for evaluation of the large intestine. During insertion of the colonoscope, mesenteric stretching and looping can cause significant discomfort, leading to reflex colonic spasms, particularly at the splenic and hepatic flexures. Poor patient tolerance may reduce cooperation and compromise procedural success[1][2].

Adequate sedation minimizes patient discomfort and provides optimal working conditions for the endoscopist, thereby improving procedural quality[3].

Propofol is a short-acting lipophilic intravenous anesthetic agent commonly used for sedation during colonoscopy. Although it provides rapid onset of sedation and amnesia, it lacks intrinsic analgesic properties. Higher doses may lead to adverse effects such as respiratory depression, hypotension, and injection site pain. Therefore, combining propofol with adjunct agents such as ketamine or fentanyl allows dose reduction while improving analgesia and hemodynamic stability[4].

Fentanyl is a member of the opioid class of medications, which is frequently employed for sedation and pain relief during colonoscopy procedures. It is a good sedative analgesic with hemodynamic stability and reduces the risk of respiratory depression[5].

Ketamine is a sedative and analgesic drug that is recognised for its ability to stabilise blood pressure due to its sympathomimetic properties[6]. Nevertheless, the administration of ketamine as the sole sedative necessitates elevated dosages, thereby increasing the likelihood of psychomimetic effects (such as hallucinations, nightmares, and depersonalisation), excessive salivation, heightened pressure within the skull and eyes, and a comparatively protracted period of recuperation. Additional sedative agents are required to counteract the adverse effects of ketamine. The combined effect of ketamine with propofol is ideal and balanced, particularly in emergency patients with unstable hemodynamics[4][7].

Based on the above background, it was important to carry out research on the complications and sedative effects of these agents on the patients. This study aimed to compare the efficacy and effects of Propofol-ketamine and Propofol-fentanyl in monitored anaesthesia care with sedation for patients undergoing colonoscopy.

## 2.Material and Methods

This prospective randomised controlled study was conducted among 72 patients scheduled for colonoscopy under sedation in a tertiary care hospital in Mumbai between August 2022 to April 2024 after obtaining the approval from the institutional ethics committee board and informed consent from all participants. The sampling technique adopted was consecutive sampling. All patients aged between 20-65 years undergoing colonoscopy procedure and belonging to American Society of Anaesthesiologists (ASA) physical status I to II were selected for the study. Exclusion criteria were patient with difficult airway, obstructive sleep apnea, morbid obesity and those with known or suspected to have allergy for study drug. The Institutional Ethical Committee approved the study, and informed consent was obtained from the participants.

The data was assessed using a pre-structured, validated questionnaire. The patients were randomly allocated into two groups containing 36 patients each, by random allocation table. Group A (control group) received midazolam 0.03mg/kg+ fentanyl 1mcg/kg, propofol 2mg/kg. Group B (study group) received midazolam 0.03mg/kg, ketamine 1mg/kg, propofol-2mg/kg propofol. An extra dose of the drug was given based on the following conditions like patient moving during the scope insertion, the patient experiencing pain and discomfort or the endoscopist complaining of difficulty in manoeuvring the scope. On arriving at the anaesthesia room, the standard monitors were connected and the intravenous access was secured. Herat rate (HR) , systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial blood pressure (MAP) and pulse oximetry ($SpO_2$) were monitored continuously. Post-operative recovery time was assessed based on the patient's first response to verbal commands. Recovery was further evaluated using the Aldrete score at five minute intervals until a score of 10 was achieved. Assessment of endoscopist satisfaction was done by a three point Likert verbal rating scale just before shifting the patient to the ward. We administered the intravenous fluids (Ringer lactate at 1ml/kg/hr) during the procedure. All adverse events were recorded and treated.

Hypotension is defined as a decrease in the mean arterial pressure (MAP) less than 50 mm Hg and bradycardia as sudden decrease in pulse rate less than 50 beats/ min. Respiratory depression is defined as a decrease in the respiratory rate less than 10 breaths/ min. Fall in Spo2 less than 90% was considered as oxygen desaturation.

Statistical analysis: The data collected was entered in a Microsoft Excel 2019 spreadsheet followed by analysis using SPSS version 26 (Statistical Package for Social Science) Windows, Version 26.0. (IBM Corp. Released 2019. IBM SPSS Statistics for Armonk, NY, USA). The demographic characteristics were represented using the arithmetic mean, standard deviation and percentages. The bar diagram and pie chart were used as required. The possible associations between the selected variables were found using the Chi-Square test/ Fisher's Exact test. Quantitative, non-parametric data were expressed as median and interquartile ranges. The Inferential statistical test such as the Unpaired t-test or Mann-Whitney U test was used to test for association between variables. A p-value of <0.05 was considered statistically significant.

## 3.Results

In the present study, 72 patients scheduled for colonoscopy under sedation were selected for the study. Using a random allocation table, the subjects were distributed into 2 equal arms (36 subjects each) of the study.

In the Fentanyl group, males (75%) were more than females (25%). Majority of the participants (27.8%) were aged more than 56 years followed by 25% in 36-45 years, 19.4% in 46-55 years, 16.7% in 26-35 years and 11.1% in less than 25 years age. In the ketamine group, majority of the participants were in the 36-45 years age group, followed by 25% in more than 56 years, 16.7% in less than 25 years, 13.9% in 46-55 years and 8.3% in 26-35 years category. The males (58.3%) were slightly more than females (41.7%).

In both the Fentanyl and ketamine groups, the majority of the participants were in ASA Grade II (55.6% and 58.3%). The fentanyl group, the mean weight of the participants was 70.5+14.79 kgs while in the ketamine group it was 61.92+13.21 kgs.

In the Fentanyl group, more rescue doses were administered as compared to the Ketamine group. Proportion of patients in fentanyl group who needed a rescue dose of propofol were 83.33% (30) and 8.33% (3) in ketamine group. This difference was found to be statistically significant ($p<0.001$). (Table 1, Figure 1)

The ketamine group had more fluctuations in the respiratory rate compared to the fentanyl group while the Fentanyl group showed more fluctuations in MAP from the baseline as compared to the ketamine group. Both the groups were comparable in terms of HR, SBP, DBP at different time intervals. Minor fluctuations were observed in the ketamine group; however, these differences were neither clinically nor statistically significant. (Table 2, Figure 2)

On assessing the endoscopist's satisfaction at the end of the procedure, it was found that the satisfaction was more with Ketamine group than with Fentanyl group. (Table 3)

Assessment of the time to first patient response showed a shorter response time in the fentanyl group (mean = 54.17 ± 23.86 seconds) compared with the ketamine group (73.56 ± 16.67 seconds). This difference was statistically significant ($p < 0.001$). (Table 4)

On assessing the Aldrete score among both groups, it is seen that the time required was less with Fentanyl group (Mean= 66.389 + 28.98 sec) as compared to Ketamine group (Mean = 121.9+19.45 sec). This difference was found to be statistically significant ($p<0.001$). (Table 5)

## 4.Discussion

Colonoscopy is a common clinical procedure. Due to mesentery stretching, inserting the colonoscope may induce discomfort and limit patient compliance[1][2].

Lipophilic intravenous anesthetic propofol has a short half-life. It is used in colonoscopies. Although sedative and amnesic, it has no analgesic effect. A propofol overdose may produce injection site discomfort, temporary blood flow and cognitive abnormalities, and respiratory depression. Thus, adding fentanyl and ketamine in little amounts is wise[4].

The current research involved 72 individuals. Equally and randomly allocated to the Fentanyl and Ketamine with propofol trial arms. Fentanyl 75% and ketamine 58.3% men dominated both research arms. Most individuals in the fentanyl group were over 50-60 years old, whereas those in the ketamine group were 40-50. Most participants (55.6% and 58.3%) had ASA Grade II. In this research, the fentanyl group averaged 70.5+14.79 kgs and the ketamine group 61.92+13.21 kgs. This difference was significant (p=0.011).

In the study by Pandey et.al, the mean age of the participants in the ketamine group was 31.1+ 12.3 yrs and fentanyl was 29.7+ 11.2 yrs which was statistically not significant (p=0.546). 10 of the 50 participants in the ketamine group had ASA grade II while 5 of the 50 of the fentanyl participants were ASA grade II (p=0.09). The non-significant p-values showed that the 2 groups were comparable in terms of the mean age, weight, and sex ratios[8].

In the present study, patients receiving propofol–ketamine required significantly fewer rescue doses of propofol compared with those receiving propofol–fentanyl. This finding suggests superior analgesic supplementation with ketamine, allowing better procedural tolerance with lower sedative requirements. Another study by Tang et.al to assess the feasibility to use fentanyl or ketamine for gynecologic procedures found that the mean (SD) rescue dose of propofol was 0.4 (0.5) mg/kg in group Ketamine + fentanyl compared with 1.6 (0.6) mg/kg in group Fentanyl only. This difference was found to be statistically significant ($p<0.001$)[9].

In the present study, hemodynamic parameters such as respiratory rate (RR), MAP and $SpO_2$ were compared for the two drugs at intervals of 5 minutes to evaluate the difference in the values. It was seen that the fluctuations in the RR was more in ketamine group as compared to the fentanyl group. The MAP & SpO2 changes were slightly more in Fentanyl group, but clinically & statistically not significant.

Singh Bajwa et al. found that PR increased in ketamine patients after anesthesia and dropped somewhat in fentanyl patients. Both groups' PR progressively reverted to baseline after anesthesia maintenance, with significant differences ($P < 0.05$). The Fentanyl group had a drop in blood pressure (systolic and diastolic) during anesthesia induction, whereas the Ketamine group had a small rise ($P < 0.05$) after induction and intubation. SpO2 changed little in either research group[10].

Sandhya et al. found that the mean SBP dropped following induction in both the PK (119.08 ± 4.10) and PF (114.62 ± 6.47) groups. Afterwards (mean ± SD), both groups maintained steady SBP at 5, 10, 15, 20, 25 minutes and after treatment. The PK group received an IV bolus of propofol and fentanyl, resulting in a significant difference in SBP immediately after induction compared to the PF group (P=0.0001). Propofol causes hypotension via vagotonic action, whereas fentanyl decreases baroreceptor reflex. No significant variation in SBP was seen at various time intervals following infusion ($P \geq 0.05$)[11].

According to a research by Nazemmroaya et al., the MAP in the fentanyl with propofol (fenofol) group was 104.63 ± 12.81 before surgery, decreased to 91.69 ± 9.30 during surgery, and climbed to 97.96 ± 21.96 after surgery. The MAP variations over time in the fenofol group were statistically significant ($P = 0.003$), whereas the ketamine with propofol (ketofol) group's change was negligible ($P = 0.083$). Patients in the ketofol group had a substantially higher mean MAP state (91.69 ± 9.26, $P = 0.007$) than those in the fenofol group (91.69 ± 9.30), although both groups' postoperative MAP status was similar ($P > 0.05$). No significant change in HR or arterial SPO2 was observed between the two groups or throughout the procedure ($P > 0.05$)[12].

Nalini et al. found that the PK group's HR, SBP, and DBP readings did not substantially alter from baseline during anesthesia. After five and ten minutes, PF patients had significant decreases in SBP and DBP, but not HR, which was not statistically significant. No individuals had bradycardia or hypotension over 20% of baseline. SPO2 dropped up to 92% in seven of thirty PF patients, or 23.3%, despite oxygen supplementation. SPO2 differences across groups were notable. No desaturation below 90% required airway opening after chin lifts and jaw thrusts[8].

In this research, it was seen that the endoscopist's satisfaction was more after the use of ketamine on the patients. Similar to our study, in Heidari et al.'s research, the average satisfaction score for KF and PR was 7.69 (CI = 7.16-8.21) and 8.65 (CI = 8.25-9.05)[13].

The reaction time following the surgery was shorter for the fentanyl group (mean 54.167 + 23.86 seconds) than the ketamine group (73.56 + 16.67 sec) in our study. Singh Bajwa et al. found that Fentanyl improved recovery time (Mod. Alderete scores) over Ketamine. Two patients (4%) in the Ketamine group exhibited excitement postoperatively, whereas none in the Fentanyl group had dreams, hallucinations, euphoria, etc. Fentanyl's shorter duration of action may explain its improved alertness ratings compared to ketamine's greater sedation[10].

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**Tables**

**Table 1** Summary of the number of rescue propofol doses administered

| Variables | n | No. of extra propofol doses [n (%)] | | | | | | Chi-square | p-value |
|---|---|---|---|---|---|---|---|---|---|
| | | 0 (0) | 1 (5mg) | 2 (10mg) | 3 (15mg) | 4 (20mg) | 5 (25mg) | | |
| **Group A** | 36 | 6 (16.7) | 4 (11.1) | 14 (38.9) | 5 (13.9) | 6 (16.7) | 1 (2.8) | 42.626 | **<0.001*** |
| **Group B** | 36 | 33 (91.7) | 2 (5.6) | 1 (2.8) | 0 (0) | 0 (0) | 0 (0) | | |

**Table 2** Hemodynamic parameters in the study groups

| Hemodynamic parameters | Variables | Baseline | 0 min | 5 min | 10 min | 15 min | 20 min | 25 min | 30 min |
|---|---|---|---|---|---|---|---|---|---|
| RR | Group A | 17 | 15.9 | 16.67 | 17.03 | 16.84 | 17.45 | 19.25 | 19 |
| | Group B | 17.14 | 17.33 | 17.14 | 17.42 | 17.45 | 18.13 | 20.67 | 22 |
| MAP | Group A | 97.4 | 90.3 | 88.5 | 86.2 | 87.47 | 90.1 | 91.5 | 79 |
| | Group B | 89.36 | 89.69 | 88.92 | 87.46 | 85.57 | 87.86 | 87.33 | 86 |
| HR | Group A | 76.2 | 76.19 | 72.1 | 73.36 | 75 | 75.62 | 79.2 | 78 |
| | Group B | 83.1 | 84.67 | 81.64 | 81.2 | 81.4 | 81.6 | 87.3 | 90 |
| SBP | Group A | 129.36 | 116.69 | 115.94 | 111.75 | 113.68 | 116.76 | 115.37 | 97 |
| | Group B | 118.33 | 116.42 | 115.08 | 116 | 113.48 | 114.36 | 109.5 | 118 |
| DBP | Group A | 81.56 | 77.14 | 74.8 | 73.5 | 74.2 | 76.67 | 79.56 | 70 |
| | Group B | 74.56 | 76.2 | 75.69 | 73.8 | 72.65 | 74.71 | 72.67 | 70 |
| SPO2 | Group A | 99.86 | 99.86 | 99.9 | 99.8 | 99.9 | 99.85 | 99.7 | 100 |
| | Group B | 99.86 | 99.83 | 99.8 | 99.8 | 99.8 | 99.7 | 99.67 | 100 |

**Table 3** Endoscopist satisfaction after the procedure

| Variables | Endoscopist satisfaction | | | | Fisher's exact test | p-value |
|---|---|---|---|---|---|---|
| | Yes | | No | | | |
| | N | % | n | % | | |
| **Group A** | 22 | 61.1 | 14 | 38.9 | 2.742 | 0.098 |
| **Group B** | 15 | 41.7 | 21 | 58.3 | | |

**Table 4** First response time (in seconds)

| Variables | n | Mean | SD | 95% CI | | Independent t-value | p-value |
|---|---|---|---|---|---|---|---|
| | | | | Lower | Upper | | |
| **Group A** | 36 | 54.167 | 23.86 | -29.06 | -9.71 | -3.997 | **<0.001*** |
| **Group B** | 36 | 73.56 | 16.67 | | | | |

**Table 5** Aldrete score (in seconds)

| Variables | n | Mean | SD | 95% CI | | t-value | p-value |
|---|---|---|---|---|---|---|---|
| | | | | Lower | Upper | | |
| **Group A** | 36 | 66.389 | 28.98 | -66.58 | -44.47 | -10.017 | <0.001 |
| **Group B** | 36 | 121.917 | 19.45 | | | | |

## Figure Legends

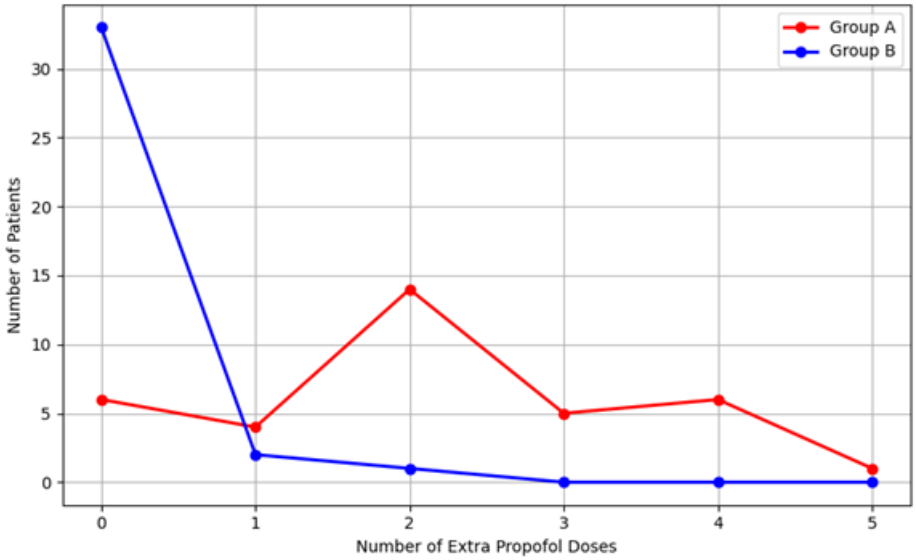


**Figure 1** Distribution of extra propofol dose requirements in Group A (red) and Group B (blue). Group B demonstrated a markedly reduced need for additional propofol doses compared with Group A.

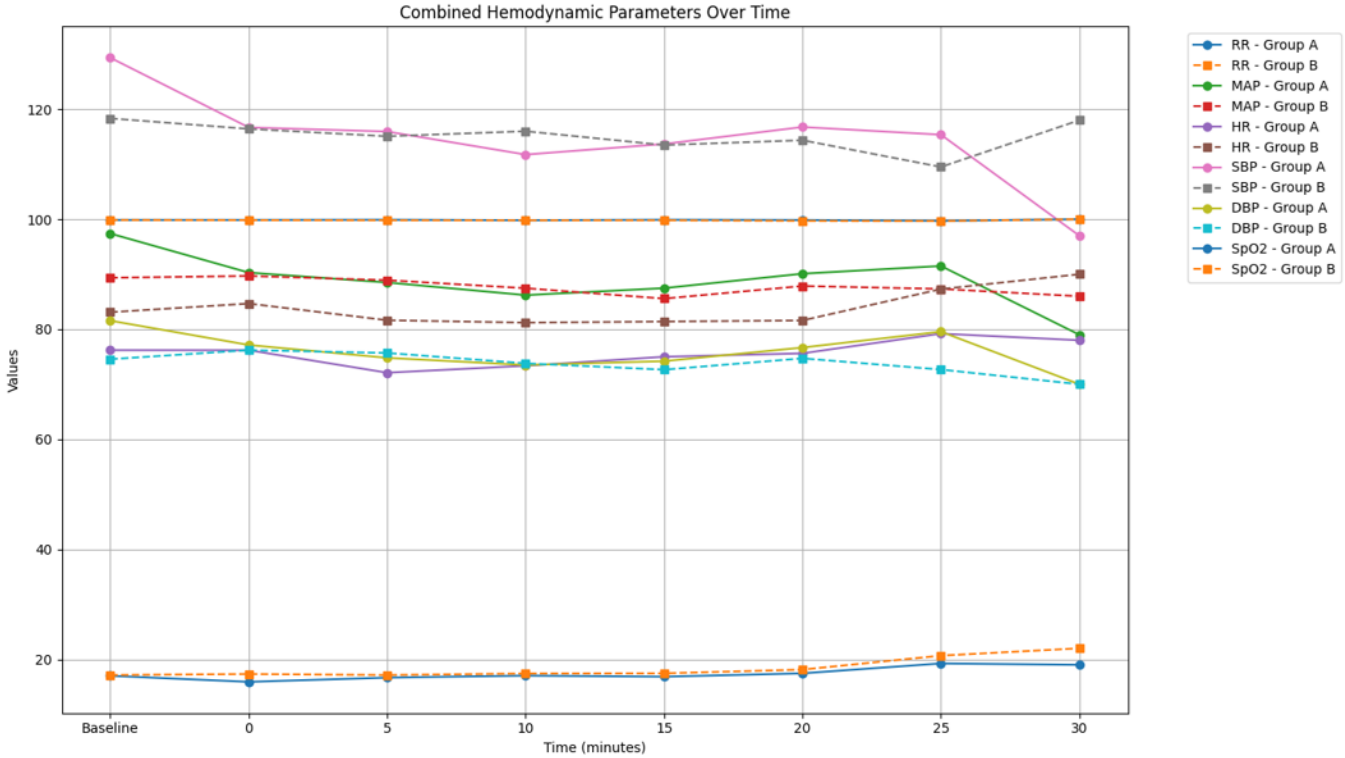


**Figure 2** Hemodynamic parameters (RR, MAP, HR, SBP, DBP, and $SpO_2$) recorded at baseline and at intervals up to 30 minutes in Group A and Group B.