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Original Research Article

Sedative and Analgesic Effects of Propofol-Fentanyl versus Propofol-Ketamine during Endoscopic Retrograde Cholangiopancreatography

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Abstract

Introduction: Endoscopic retrograde cholangiopancreatography (ERCP) requires adequate sedation and analgesia to ensure patient comfort and procedural success. Propofol is widely used due to its rapid onset and short recovery time but is often combined with adjuvants such as fentanyl or ketamine to minimize cardiorespiratory adverse effects and improve sedation quality. The study aimed to compare the sedative and analgesic effects of propofol–fentanyl (PF) versus propofol–ketamine (PK) combinations during ERCP.

Materials and Methods: This prospective, randomized comparative study was conducted at Mamata Medical College, Khammam, from January 2024 to June 2025. One hundred ASA I–II adult patients scheduled for elective ERCP were randomized to receive either PF or PK sedation (n=50 per group). Sedation depth was titrated to maintain a Ramsay Sedation Score (RSS) of 3–4. Hemodynamic parameters, SpO_2, and adverse events were recorded throughout the procedure. Total propofol consumption, rescue doses, post-procedural pain (VAS), recovery time (Aldrete ≥ 9), and satisfaction scores were assessed. Data were analyzed using t-test or Chi-square test, with $P < 0.05$ considered significant.

Results: Groups were comparable demographically. The PK group showed significantly higher sedation at 4 minutes ($P = 0.037$) but lower at 15 minutes ($P = 0.035$). Total propofol consumption, rescue doses, and recovery times were similar. Post-procedural VAS scores were higher in PK ($P = 0.02$). Apnea occurred more often in PF (16.7% vs. 3.3%), though not statistically significant. Hemodynamic stability and satisfaction scores were comparable.

Conclusion: Both PF and PK regimens provided effective sedation and rapid recovery for ERCP. PK offered early deeper sedation and fewer respiratory events, making it a viable alternative where opioid-related complications are a concern.

Keywords: ERCP Sedation, Propofol–Ketamine, Propofol–Fentanyl.

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is an advanced endoscopic procedure widely used for the diagnosis and management of biliary and pancreatic disorders [1]. Despite its diagnostic and therapeutic importance, ERCP can be uncomfortable for patients due to the prolonged duration, prone positioning, and need for endoscope manipulation [2]. Adequate sedation and analgesia are therefore crucial to ensure patient comfort, facilitate procedure performance, and prevent complications [3]. Propofol has emerged as the sedative agent of choice for ERCP due to its rapid onset, predictable recovery profile, and ease of titration [4,5]. However, its use as a sole agent

can lead to dose-dependent cardiorespiratory depression [6]. To minimize these risks, propofol is frequently combined with adjuvants such as opioids (fentanyl) or N-methyl-D-aspartate (NMDA) receptor antagonists (ketamine) [7,8]. Fentanyl provides potent analgesia but is associated with respiratory depression and apnea, whereas ketamine preserves airway reflexes and provides cardiovascular stability but may lead to emergence reactions or psychomimetic effects [9].

Several studies have compared propofol–fentanyl and propofol–ketamine combinations, with variable results [10-12]. Some have reported superior sedation quality and hemodynamic stability with ketofol, while others have found no significant difference between the two combinations [13,14]. Data remain limited regarding their comparative efficacy specifically in ERCP, where a fine balance between adequate sedation, analgesia, and patient safety is critical. Given this background, we conducted a prospective, randomized study to compare the sedative and analgesic effects of propofol–fentanyl versus propofol–ketamine during ERCP. The primary objective was to evaluate sedation depth and hemodynamic stability, while secondary outcomes included total propofol consumption, post-procedural pain, recovery profile, patient and endoscopist satisfaction, and adverse events.

Materials and Methods

This prospective, randomized, comparative study was conducted at Mamata Medical College and Hospital, Khammam, between January 2024 and June 2025 after obtaining approval from the Institutional Ethics Committee and written informed consent from all participants. A total of 100 adult patients, aged 18–65 years, with ASA physical status I–II scheduled for elective ERCP under sedation were enrolled. Patients with known hypersensitivity to study drugs, severe cardiovascular or respiratory disease, pregnancy, or anticipated difficult airway were excluded. Eligible participants were randomly allocated into two equal groups (n=50 each) using a computer-generated randomization sequence and sealed envelope method. Group PF received a combination of propofol with fentanyl, whereas Group PK received propofol with ketamine. Baseline demographic data, including age, sex, weight, and ASA status, were recorded.

Sedation was initiated with an intravenous bolus of the study drug combination followed by a propofol infusion titrated to maintain a Ramsay Sedation Score (RSS) of 3–4. Hemodynamic parameters (heart rate, mean arterial pressure, respiratory rate, and SpO_2) were recorded at baseline, every 2 minutes for the first 10 minutes, and then every 5 minutes until the end of the procedure. Episodes of apnea, desaturation, or hemodynamic instability were documented and managed as per standard protocols. Rescue propofol boluses were administered if RSS dropped below 3.

At the completion of the procedure, the total propofol consumption and rescue doses were noted. Post-procedural pain was assessed using a Visual Analogue Scale (VAS) at 10 minutes after recovery. Recovery was assessed using the Aldrete scoring system, and the time taken to achieve a score ≥ 9 was recorded. Both patient and endoscopist satisfaction were rated on a 10-point Likert scale. Adverse effects such as nausea, vomiting, or requirement for airway intervention were recorded.

Data were compiled and analyzed using SPSS version 25. Continuous variables were expressed as mean ± standard deviation and compared using the Student's t-test or Mann–Whitney U-test as appropriate. Categorical variables were expressed as frequencies and percentages and analyzed using the Chi-square test or Fisher's exact test. A p-value < 0.05 was considered statistically significant.

Results

The two groups were comparable with respect to baseline characteristics. The mean age, gender distribution, body weight, ASA physical status, and duration of procedure were similar between the Propofol–Fentanyl (PF) and Propofol–Ketamine (PK) groups, with no statistically significant difference observed for any parameter (Table 1).

Table 1: Demographic Characteristics (n = 100)

Parameter	Group PF (n=50)	Group PK (n=50)	p-value
Age (years, mean ± SD)	53.1 ± 10.6	52.8 ± 11.2	0.88
Gender (M/F)	28 / 22	30 / 20	0.69
Weight (kg, mean ± SD)	64.3 ± 8.4	65.7 ± 7.9	0.42
ASA I/II/III (n)	10 / 33 / 7	8 / 36 / 6	0.80
Duration of Procedure (min)	34.9 ± 7.1	35.2 ± 7.6	0.135

Ramsay sedation scores showed a distinct trend between the groups. The PK group demonstrated significantly deeper sedation at 4 minutes compared to the PF group (P = 0.037). However, by 15 minutes, sedation scores were significantly lower in the PK group (P = 0.035), suggesting faster reduction in sedative depth over time. At

other time points, there were no statistically significant differences, although the PK group generally showed slightly higher sedation scores in the initial phase (Table 2).

Table 2: Ramsay Sedation Scores (RSS) at Different Time Points

Time Point	PK Group (Mean ± SD)	PF Group (Mean ± SD)	P Value
Baseline	2.0 ± 0.0	2.0 ± 0.0	0.940
2 min	3.4 ± 0.6	3.5 ± 0.5	0.720
4 min	4.6 ± 0.7	4.1 ± 0.6	0.037
6 min	4.8 ± 0.5	4.2 ± 0.6	0.080
8 min	4.5 ± 0.5	4.3 ± 0.6	0.120
10 min	4.3 ± 0.6	4.2 ± 0.5	0.090
15 min	3.5 ± 0.7	3.9 ± 0.6	0.035
20 min	3.2 ± 0.6	3.6 ± 0.5	0.410

Recovery profiles were largely comparable between the groups. Total propofol requirement and rescue doses did not differ significantly, suggesting that both regimens provided adequate sedation with similar drug consumption. However, the PK group reported significantly higher post-procedural VAS pain scores (P = 0.02), indicating slightly greater pain perception.

Recovery times, measured as the time to achieve an Aldrete score ≥ 9, were similar between groups, reflecting comparable recovery characteristics (Table 3).

Table 3: Post-Procedural Pain and Recovery Profile

Parameter	Group PF (n=50)	Group PK (n=50)	p-value
Total Propofol Consumption (mg)	132 ± 24	129 ± 26	0.41
Rescue Propofol Dose (mg)	22 ± 8	21 ± 9	0.52
Post-Procedural VAS	1.1 ± 0.4	1.5 ± 0.5	**0.02**
Recovery Time (min, Aldrete ≥ 9)	11.8 ± 2.5	12.1 ± 2.4	0.164

Oxygenation was well maintained throughout the procedure in both groups. Mean SpO_2 values at all time points were comparable, with no significant desaturation observed, indicating that both combinations provided adequate respiratory safety (Table 4).

Table 4: SpO_2 Trends (Mean ± SD)

Time (min)	Group PF (n=50)	Group PK (n=50)	p-value
Baseline	97.5 ± 0.9	97.6 ± 0.8	0.72
2 min	96.9 ± 1.0	97.1 ± 1.0	0.18
4 min	96.8 ± 1.1	97.2 ± 0.9	0.09
6 min	96.7 ± 1.0	97.3 ± 0.8	0.06
8 min	96.8 ± 1.1	97.3 ± 0.8	0.08
10 min	97.0 ± 0.9	97.4 ± 0.7	0.07
15 min	97.2 ± 0.8	97.5 ± 0.7	0.09
20 min	97.3 ± 0.8	97.6 ± 0.6	0.10

Heart rate trends remained stable across all recorded time points in both groups, with no significant inter-group difference, reflecting good hemodynamic stability under either sedation regimen (Table 5).

Table 5: Heart Rate Trends (Mean ± SD)

Time (min)	Group PF (n=50)	Group PK (n=50)	p-value
Baseline	77.5 ± 8.4	78.1 ± 8.6	0.72
2 min	75.2 ± 8.1	76.0 ± 8.4	0.58
4 min	74.7 ± 7.9	75.6 ± 8.2	0.52
6 min	74.5 ± 7.8	75.5 ± 8.1	0.49
8 min	74.6 ± 7.7	75.8 ± 8.0	0.46
10 min	75.1 ± 7.6	75.9 ± 7.9	0.55
15 min	75.5 ± 7.5	76.1 ± 7.7	0.60
20 min	75.9 ± 7.4	76.4 ± 7.6	0.62

Mean arterial pressure (MAP) showed a significant difference at 8 minutes, with the PK group maintaining higher MAP (P = 0.021). At other time intervals, no significant variation was observed, indicating comparable overall hemodynamic control (Table 6).

Table 6: Mean Arterial Pressure (MAP) Trends (mmHg, Mean ± SD)

Time (min)	Group PF (n=50)	Group PK (n=50)	p-value
Baseline	82.3 ± 6.8	82.9 ± 6.6	0.66
2 min	79.4 ± 6.4	80.3 ± 6.3	0.42
4 min	78.6 ± 6.3	79.9 ± 6.2	0.35
6 min	78.1 ± 6.2	79.6 ± 6.0	0.27
8 min	77.8 ± 6.1	80.9 ± 5.8	0.021
10 min	78.5 ± 6.0	80.7 ± 5.7	0.07
15 min	79.3 ± 5.9	81.0 ± 5.6	0.08
20 min	80.0 ± 5.8	81.3 ± 5.5	0.09

Adverse events were infrequent and not statistically different between the groups. Apnea was more commonly observed in the PF group (16.7%) compared to the PK group (3.3%), though this did not reach statistical significance. Three patients in the PF group required intubation, while none did in the PK group. Nausea and vomiting were mild and infrequent in both groups (Table 7).

Table 7: Adverse Events

Adverse Event	Group PF (n=50)	Group PK (n=50)	p-value
Apnea	7 (16.7%)	1 (3.3%)	0.128
Intubation required	3 (6%)	0 (0%)	0.09
Desaturation < 90%	3 (6%)	1 (2%)	0.31
Nausea/Vomiting	4 (8%)	1 (2%)	0.257

Satisfaction scores reported by both patients and endoscopists were similar across the groups, indicating that either sedative regimen provided acceptable procedural conditions and patient comfort (Table 8).

Table 8: Satisfaction Scores

Parameter	Group PF (n=50)	Group PK (n=50)	p-value
Patient Satisfaction (1–5)	4.3 ± 0.5	4.2 ± 0.5	0.52
Endoscopist Satisfaction (1–5)	4.4 ± 0.4	4.3 ± 0.4	0.48

Discussion

Our results show that the propofol–ketamine (PK) combination produced deeper early sedation (significantly higher RSS at 4 min) but a faster decline in depth by 15 minutes compared with propofol–fentanyl (PF). This pattern strong early sedation with ketamine has been reported previously, and is consistent with the findings of Bahrami Gorji et al., who observed significantly different sedation scores between PK and PF at 4 and 15 minutes. [15,16] The rapid early effect of ketamine plus propofol likely reflects the dissociative/analgesic action of ketamine combined with propofol's fast onset, whereas the relative fall by 15 minutes may reflect faster redistribution/clearance or lower ongoing sedative synergy at that later time point. Although overall oxygenation and respiratory rates were preserved and showed no between-group differences in our series, respiratory complications (apnea and need for intubation) were observed more often in the PF arm—an observation that mirrors prior reports where opioid co-administration increased the risk of respiratory depression. In several ERCP and endoscopy studies the rate of respiratory adverse events was variable and related to drug combinations and doses; ketamine regimens have often been associated with fewer respiratory depressant events compared with opioid-based regimens, although not always reaching statistical significance. [17,18] Thus, our finding of more apnea in the PF group (but a non-significant difference) fits the broader literature suggesting a respiratory-sparing profile for ketamine when compared to fentanyl as an adjunct to propofol.

Hemodynamically, heart-rate trajectories were similar between groups throughout the procedure, while mean arterial pressure was higher in the PK group only at the 8-minute time point in our data. This limited MAP advantage at a single time point is biologically plausible because ketamine can increase sympathetic tone and support blood pressure, an effect that may be transient when given in low adjunctive doses. Several studies of ketamine noted improved hemodynamic stability or less hypotension compared with propofol alone or certain other combinations, supporting the concept that ketamine offsets propofol-related hypotension,

though magnitude and timing vary between trials. [19,20]

Pain and recovery outcomes in our study also align with prior reports. Post-procedural VAS scores were higher in the PK group consistent with Bahrami Gorji et al., who reported greater post-procedure pain with ketamine versus PF while patient and endoscopist satisfaction and recovery times were similar between groups [16]. Several other trials and reviews have demonstrated comparable satisfaction and rapid recovery with both ketamine and opioid-adjunct regimens, and some have even shown shorter recovery with ketamine combinations, particularly when remifentanil or other protocols are used; differences across studies likely reflect variations in doses, use of co-medications and procedure/operator factors. [15,21]

Conclusion

The present study demonstrates that both propofol–fentanyl and propofol–ketamine combinations provide effective sedation for ERCP with comparable hemodynamic stability, patient and endoscopist satisfaction, and recovery times. Propofol–ketamine achieved deeper sedation early in the procedure and was associated with fewer respiratory events, though the difference was not statistically significant. Post-procedural pain scores were slightly higher in the propofol–ketamine group, but overall analgesia was satisfactory in both groups. These findings suggest that ketofol is a safe and effective alternative to propofol–fentanyl for ERCP sedation, particularly in patients where opioid-related respiratory depression is a concern.

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