Section: Anaesthesiology

Original Research Article

COMPARISON BETWEEN TWO DIFFERENT COMBINATIONS OF KETAMINE-PROPOFOL AND PROPOFOL-FENTANYL FOR SEDATION AND ANALGESIA IN MINOR GYNECOLOGICAL PROCEDURES: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

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ABSTRACT

Background: Procedural sedation and analgesia (PSA) play a critical role in enhancing patient comfort and safety during minor gynecological procedures. The choice of sedative-analgesic combinations affects onset, recovery, hemodynamic stability, and postoperative outcomes.

Objective: To compare the efficacy and safety of two ketamine-propofol combinations (ratios 1:1 and 1:2) with a propofol-fentanyl combination for sedation and analgesia in minor gynecological surgeries.

Materials and Methods: In this prospective, double-blind, randomized trial, 90 ASA I–II female patients undergoing elective minor gynecological procedures were assigned to three groups (n=30 each): Group A (Ketamine:Propofol 1:1), Group B (Ketamine:Propofol 1:2), and Group C (Fentanyl:Propofol). Primary outcomes included induction time, sedation depth (RSS), recovery time, and hemodynamic-respiratory parameters. Secondary outcomes included total drug use, postoperative pain scores, adverse events, and need for rescue analgesia.

Results: Group A had the fastest induction (1.15 ± 0.4 mins) but the longest recovery (11 ± 2 mins), while Group C had the slowest induction (1.65 ± 0.5 mins) and fastest recovery (6 ± 2 mins). Hemodynamic and respiratory parameters remained stable across groups. Group C reported significantly lower postoperative pain scores ($p < 0.001$). Adverse effects and airway interventions were rare and comparable.

Conclusion: All three drug combinations were effective and safe. The propofol-fentanyl combination was associated with faster recovery and superior postoperative analgesia, whereas ketamine-propofol combinations offered quicker induction and more stable oxygenation profiles.

Keywords: Ketamine, Propofol, Fentanyl, Procedural Sedation, Minor Gynecological Surgery, Recovery Time, Analgesia.

INTRODUCTION

Minor gynecological procedures such as dilatation and curettage, endometrial biopsy, and polypectomy are frequently performed in outpatient and day-care settings. Although brief, these procedures can provoke significant anxiety and discomfort in patients, necessitating the use of procedural sedation

and analgesia (PSA) to optimize patient comfort, procedural success, and safety. Compared to general anesthesia, PSA offers a faster onset, better hemodynamic stability, and quicker postoperative recovery, thereby enabling early discharge and greater patient satisfaction.[1]

Among the commonly used sedative-analgesic agents, propofol, fentanyl, and ketamine stand out due to their favorable pharmacokinetic and pharmacodynamic properties. Propofol is a widely used short-acting hypnotic agent known for its rapid onset and smooth recovery. However, it lacks analgesic effects and is associated with hypotension and dose-dependent respiratory depression.[1,2] Fentanyl, a potent synthetic opioid, provides excellent analgesia but carries risks of respiratory depression, particularly when combined with other central nervous system depressants.[3,5]

Ketamine, a phencyclidine derivative, induces a dissociative anesthetic state and possesses strong analgesic properties with minimal impact on respiratory function. It also exhibits sympathomimetic effects, making it especially useful in hemodynamically unstable patients.[2,4] The combination of ketamine and propofol—often termed "ketofol" has been explored as a synergistic blend that balances each drug's adverse effects while providing effective sedation and analgesia.[3,4]

Despite its potential advantages, the optimal ketamine-to-propofol ratio for PSA remains unclear. Studies have shown varying results regarding sedation depth, recovery time, and incidence of side effects.[5,6] Therefore, further comparative evaluation of these combinations in specific clinical settings, such as minor gynecological procedures, is warranted.

This study aims to compare two ketofol ratios (1:1 and 1:2) with a propofol-fentanyl combination in terms of induction characteristics, sedation depth, hemodynamic-respiratory profiles, recovery times, and postoperative analgesia in patients undergoing minor gynecological procedures.

MATERIALS AND METHODS

Study Design and Setting

A prospective, randomized, double-blind controlled trial was conducted at the Department of Anaesthesiology, Konaseema Institute of Medical Sciences and Research Foundation (KIMS), Amalapuram, a tertiary care teaching hospital in Andhra Pradesh to evaluate sedative-analgesic combinations in minor gynecological procedures.

Study Population

A total of 90 adult female patients aged between 18 and 50 years, classified as ASA physical status I or II and scheduled for elective minor gynecological procedures (e.g., dilatation and curettage, endometrial biopsy), were enrolled. Inclusion criteria required a body weight between 40 and 70 kg and Mallampati airway classes I or II.

Exclusion criteria included

ASA physical status III or higher
Mallampati class III or IV
Weight outside 40–70 kg
Emergency or laparoscopic procedures
History of drug abuse, psychiatric illness, or head injury
Known hypersensitivity to ketamine, propofol, fentanyl, or egg proteins

Randomization and Blinding

Participants were randomly assigned to one of three groups (n=30 each) using the sealed opaque envelope (SNOSE) method. Drug preparations were performed by an anesthesiologist not involved in patient care. All syringes were identical in volume and appearance, ensuring blinding for both the administering anesthesiologist and the outcome assessor.

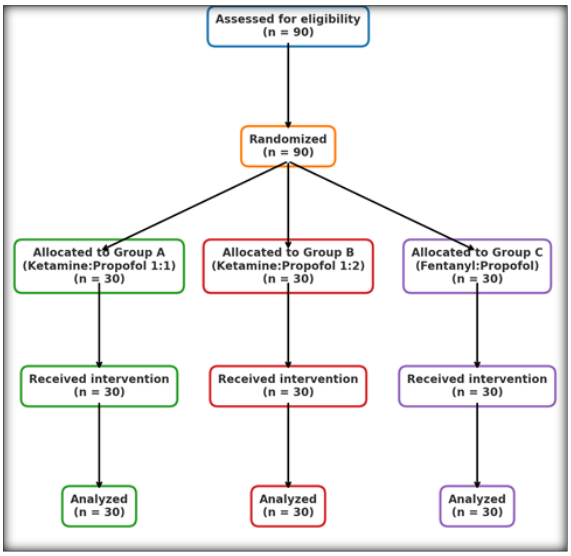

Figure 1: CONSORT Flow Diagram

Group Allocation and Drug Administration

Group A: Ketamine 2 mL (50 mg/mL) + Propofol 10 mL (10 mg/mL) – 1:1 ratio

Group B: Ketamine 1 mL (50 mg/mL) + 1 mL distilled water + Propofol 10 mL (10 mg/mL) – 1:2 ratio

Group C: Fentanyl 2 mL (50 mcg/mL) + Propofol 10 mL (10 mg/mL)

All drug mixtures were administered intravenously in 3 mL boluses until a Ramsay Sedation Score (RSS) of 5–6 was achieved. Additional 1 mL boluses were given as needed during the procedure based on patient movement or signs of discomfort.

Monitoring and Parameters Assessed

Standard monitoring included ECG, NIBP, SpO_2, respiratory rate, and $EtCO_2$. Baseline, intraoperative (every 5 minutes for 15 minutes), and postoperative (at 0, 5, 10, 15 minutes) recordings were made for:

Heart rate
Blood pressure (systolic and diastolic)
SpO_2
Respiratory rate

Ramsay Sedation Score (RSS)
EVANS/PRST score (for anesthetic depth)
Modified Aldrete Score (for recovery readiness)
Wong-Baker Faces Pain Score (for postoperative analgesia)

Outcomes

Primary outcomes included:
Induction time (time to reach RSS 5–6)
Recovery time (time from last drug dose to Aldrete score ≥9)
Depth of sedation
Hemodynamic and respiratory stability

Secondary outcomes included:
Total drug volume administered
Postoperative pain scores
Incidence of adverse events (e.g., hypotension, apnea, nausea, emergence reactions)
Need for rescue analgesia or airway intervention

Statistical Analysis

Data were analyzed using IBM SPSS v23.0. Continuous variables were expressed as mean ± SD and compared using one-way ANOVA. Categorical data were analyzed using the Chi-square test. A p-value < 0.05 was considered statistically significant.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee of KIMS, Amalapuram. Written informed consent was obtained from all participants one day prior to the procedure. Confidentiality was maintained, and all procedures adhered to ethical standards ensuring patient safety and voluntary participation.

RESULTS

A total of 90 adult female patients undergoing minor elective gynecological procedures were enrolled and randomized into three equal groups: Group A (Ketamine:Propofol 1:1), Group B (Ketamine:Propofol 1:2), and Group C (Fentanyl:Propofol). Baseline demographic characteristics, including ASA grade distribution and body weight, were comparable across groups with no statistically significant differences observed (p > 0.05). However, a statistically significant difference in mean age was noted, with Group B showing a slightly higher mean age (p = 0.023). (Table 1)

Sedation and Recovery Outcomes

Group A demonstrated the shortest induction time (1.15 ± 0.4 mins), while Group C required the longest (1.65 ± 0.5 mins), with the difference reaching high statistical significance (p < 0.001). Similarly, the total volume of drug administered was lowest in Group A and highest in Group C (p < 0.001). Recovery time was significantly shorter in Group C (6 ± 2 mins) compared to Group A (11 ± 2 mins), again with a highly significant p-value (p < 0.001). (Table 2)

Hemodynamic and Respiratory Parameters

Hemodynamic stability was largely preserved across all groups throughout the study. However, at the time of induction, statistically significant differences were observed in heart rate (p = 0.03) and systolic blood pressure (p = 0.04), while diastolic blood pressure differences bordered on statistical significance (p = 0.05) (Table 3). Respiratory parameters revealed significant inter-group differences. In particular, SpO_2 levels at intraoperative and postoperative time points were significantly higher in Group A, and respiratory rate at 15 minutes intraoperatively was also notably higher in Groups A and B compared to Group C (p < 0.001). (Table 4)

Depth of Sedation and Pain Assessment

Ramsay Sedation Scores (RSS) at 15 minutes postoperatively showed significant differences between groups, with Group C exhibiting the lowest sedation score (2.3 ± 0.9), suggestive of faster emergence from sedation (p < 0.001). The Wong-Baker Faces Pain Score also favored Group C, which was associated with milder postoperative pain compared to moderate pain levels in Groups A and B (p < 0.001). (Table 5)

Adverse Events and Intervention Needs

Adverse effects were minimal and showed no significant inter-group variation (p = 0.894). Rescue analgesia was rarely required, with the highest frequency in Group B (10%), though this did not reach statistical significance (p = 0.227). Airway interventions and failed sedation were observed in isolated cases within Groups B and C (3.3% each), but these differences were not statistically significant (p = 0.600). (Table 6)

Table 1: Demographic Characteristics

Parameter	Group A	Group B	Group C	p-value
ASA Grade (I/II)	11 / 19	13 / 17	14 / 16	0.727
Body Weight (kg)	51.9 ± 7.2	51.4 ± 7.9	51.2 ± 7.8	0.937
Age (years)	41 ± 5	45 ± 6	42 ± 4	0.023*

***Statistically significant difference (p < 0.05)**

Table 2: Sedation and Recovery Parameters

Parameter	Group A	Group B	Group C	p-value
Induction Time (mins)	1.15 ± 0.4	1.42 ± 0.4	1.65 ± 0.5	<0.001**
Total Drug Volume (mL)	6 ± 2	8 ± 2	9 ± 2	<0.001**
Recovery Time (mins)	11 ± 2	9 ± 1	6 ± 2	<0.001**

****Highly significant (p < 0.01)**

Table 3: Hemodynamic Variables at Induction

Parameter	Group A	Group B	Group C	p-value
Heart Rate (bpm)	80.1 ± 8.9	74.8 ± 8.4	75.5 ± 7.8	0.03*
SBP (mmHg)	116.3 ± 7.9	110.7 ± 9.1	110.9 ± 10.9	0.04*
DBP (mmHg)	76.7 ± 8.6	71.6 ± 9.6	71.2 ± 10.6	0.05#

***Statistically significant (p < 0.05); #Borderline significance**

Table 4: Respiratory and Oxygenation Parameters

Parameter	Group A	Group B	Group C	p-value
SpO_2 (Intra-op 10 mins)	99.7 ± 0.5	99.5 ± 0.7	98.8 ± 0.8	<0.001**
RR (Intra-op 15 mins)	15.1 ± 1.1	15.1 ± 0.9	14.1 ± 0.9	<0.001**
SpO_2 (Post-op 5 mins)	98.6 ± 0.7	98.3 ± 1.3	97.1 ± 1.2	<0.001**

Table 5: Sedation and Pain Scores

Parameter	Group A	Group B	Group C	p-value
RSS (Post-op 15 mins)	3.3 ± 1.0	3.2 ± 1.0	2.3 ± 0.9	<0.001**
Wong-Baker Pain Score (Post-op)	Moderate	Moderate	Mild	<0.001**

Table 6: Adverse Events and Rescue Interventions

Parameter	Group A	Group B	Group C	p-value
Adverse Effects	4 (13.3%)	3 (10.0%)	3 (10.0%)	0.894#
Rescue Analgesia	2 (6.7%)	3 (10.0%)	0 (0.0%)	0.227#
Airway Intervention	0 (0.0%)	1 (3.3%)	1 (3.3%)	0.600#
Failed Sedation	0 (0.0%)	1 (3.3%)	1 (3.3%)	0.600#

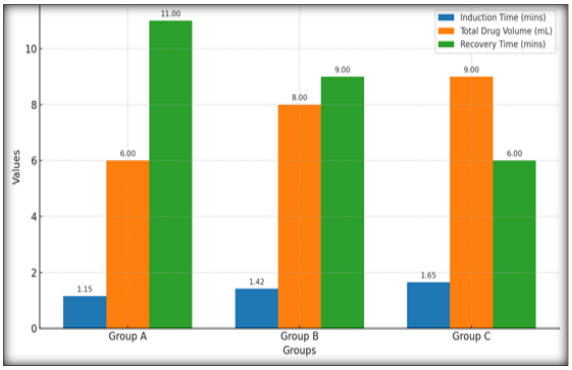

Figure 2: Sedation and Recovery Parameters Across Study Groups

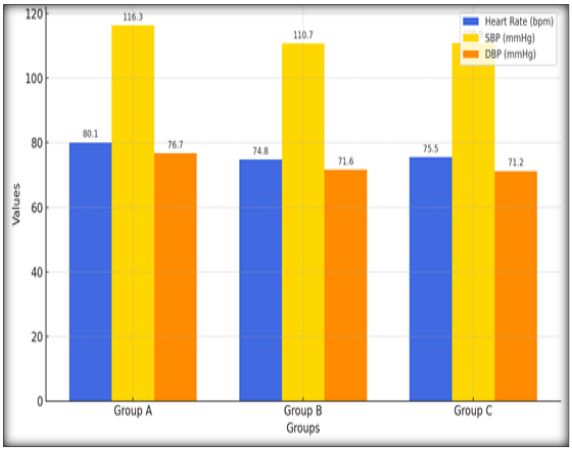

Figure 3: Hemodynamic Variables at Induction

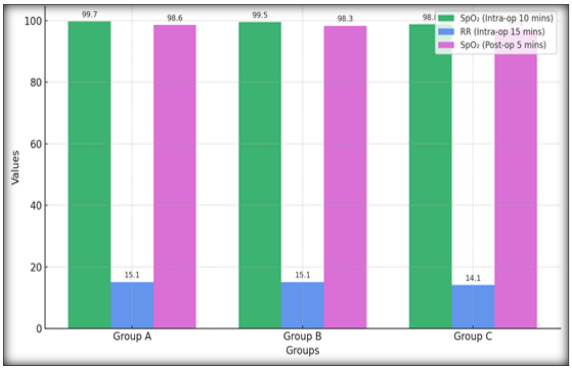

Figure 4: Respiratory and Oxygenation Parameters

DISCUSSION

This prospective, randomized, double-blind trial evaluated and compared the efficacy, safety, and recovery profiles of two ketamine-propofol ratios (1:1 and 1:2) with a fentanyl-propofol combination in patients undergoing minor gynecological procedures. The findings confirm that all three drug regimens provided effective sedation and analgesia with minimal adverse effects, consistent with prior evidence supporting the safety of such combinations for procedural sedation.[9,12]

Group A (ketamine:propofol 1:1) demonstrated the shortest induction time but the longest recovery duration, likely due to the prolonged dissociative and sedative effects of ketamine. This aligns with findings from Padhi et al., who observed similar recovery delays with higher ketamine proportions in gynecologic procedures.[9] In contrast, Group C (fentanyl:propofol) exhibited slower induction but significantly faster recovery and better postoperative pain control, making it ideal for day-care procedures requiring early discharge. These results are supported by Padmanabhan et al., who noted

enhanced recovery profiles when fentanyl was combined with propofol.[11]

Hemodynamic variables remained stable in all groups, with Group A exhibiting superior oxygen saturation and respiratory rate maintenance, attributed to ketamine's sympathomimetic and respiratory-preserving effects.[10] Raman et al. also reported favorable hemodynamic stability with ketofol during laparoscopic surgery.[8] The minimal adverse events observed across all groups are consistent with existing literature, including a meta-analysis by Bellolio et al., which reported low complication rates for procedural sedation in emergency and surgical contexts.[12]

Overall, the propofol-fentanyl combination offered better postoperative analgesia and faster recovery, while ketofol, particularly in a 1:1 ratio, ensured rapid induction and preserved respiratory stability features especially beneficial in settings with limited airway management resources.[7,8]

Limitations

The study was limited by its single-center design, small sample size, and exclusion of high-risk patients. Long-term outcomes, patient satisfaction, and cost-effectiveness were not evaluated, which may limit the generalizability of the findings to broader populations.

CONCLUSION

This study concludes that all three drug combinations—ketamine-propofol 1:1, ketamine-propofol 1:2, and fentanyl-propofol—are effective and safe for procedural sedation and analgesia during minor gynecological procedures. The ketamine-propofol 1:1 combination provided the fastest induction with stable hemodynamic and respiratory profiles but had a longer recovery time. The fentanyl-propofol group showed superior postoperative analgesia and significantly faster recovery, making it more suitable for outpatient settings where early discharge is desired. Minimal adverse events and comparable safety across groups support the clinical utility of each regimen. Choice of combination may be tailored based on patient characteristics, procedural needs, and desired recovery profiles to optimize sedation outcomes.

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