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Original Contribution

# Addition of low-dose ketamine to midazolam-fentanyl-propofol–based sedation for colonoscopy: a randomized, double-blind, controlled trial☆

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**Abstract**

**Study Objective:** To evaluate the effects of low-dose ketamine on midazolam-fentanyl-propofol–based sedation for outpatient colonoscopy.

**Design:** Prospective, randomized, double-blinded, placebo-controlled trial.

**Setting:** Gastroenterology unit at a practice and clinical research center.

**Subjects:** Ninety-seven healthy American Society of Anesthesiology physical status 1 volunteers.

**Interventions:** Subjects were randomized to receive midazolam (0.02 mg/kg), fentanyl (1 μg/kg), and ketamine (0.3 mg/kg) and midazolam (0.02 mg/kg), fentanyl (1 μg/kg), and placebo (0.9% sodium chloride) in group K and group C, respectively. In both groups, incremental doses of propofol were used to maintain a Ramsay sedation score of 3 to 4.

**Measurements:** Values of heart rate, blood pressure, oxygen saturation, and respiratory rate were measured. Procedure times, recovery times, drug doses used, complications associated with the sedation, and physician and patient satisfaction were also recorded.

**Main Results:** In group K, mean amount of propofol used and mean induction time ($P < .001$), the need for the use of jaw thrust maneuver and mask ventilation, and the incidence of disruptive movements were significantly lower ($P < .05$) and gastroenterologist satisfaction at the beginning of the procedure was significantly superior ($P < .05$). Mean systolic blood pressures at 4, 6, 8, and 10 minutes ($P < .01$); diastolic blood pressures at 4, 6, and 8 minutes ($P < .05$); respiratory rates at 4, 6, 8, 10, 15, 20, and 25 minutes ($P < .01$); and oxygen saturation at 6, 8, 10, 15, and 20 minutes ($P < .05$) were significantly lower in group C. Patient satisfaction scores, recovery times, and discharge times were similar. No patient in either group experienced unpleasant dreams or hallucination in the postanesthesia care unit and on the first postoperative day.

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**Conclusions:** Addition of low-dose ketamine to midazolam-fentanyl-propofol–based sedation for outpatient colonoscopy resulted in more rapid and better quality of sedation, less propofol consumption, more stable hemodynamic status, and less adverse effects with similar recovery times in adult patients.


## 1. Introduction

Appropriate sedation for an ambulatory colonoscopy should provide rapid onset, cardiopulmonary stability, minimal adverse effects, smooth recovery, and early discharge [1,2]. Although several trials have been performed using different anesthetic agents, the optimal combination has not yet been established [3–9]. In addition, some patients may require much deeper sedation with higher doses leading to cardiorespiratory depression, loss of protective reflexes, and delayed discharge [10,11]. In these circumstances, dissatisfaction with the level of sedation is not uncommon [12,13].

Ketamine is a safe, rapid-acting intravenous anesthetic that has been used to complement sedation for various diagnostic and therapeutic procedures [14–20]. It crosses the blood-brain barrier rapidly and ensures good analgesia while maintaining airway patency, ventilation, and cardiovascular stability [21]. Nevertheless, ketamine was used only in 2 earlier studies for premedication and in a recent study in combination with propofol in adult colonoscopy [22–24].

The purpose of this study was to investigate the effects of small doses of ketamine adjunct to midazolam-fentanyl-propofol–based sedation on the effectiveness, recovery, and the safety profiles; propofol consumption; and patient's and gastroenterologist's satisfaction in adult patients undergoing ambulatory colonoscopy.

## 2. Methods

This study was conducted according to the Declaration of Helsinki; and ethical approval (Ethical Committee No.: KA11/186) was provided by the Ethical Committee of Baskent University, Ankara, Turkey (Chairperson Prof Zeynep Kayhan) on December 8, 2011. Signed written informed consent was obtained from each patient. Exclusion criteria were age outside the range of 18 to 75 years, American Society of Anesthesiology (ASA) physical status class greater than or equal to 3, pregnancy, history of anesthesia or sedation in the last 7 days, psychiatric/emotional disorder, history of addiction to opioids and/or sedatives, previous adverse reactions to medications used in the study protocol, and inability to provide informed consent. Colonoscopies were performed by the same gastroenterologist using the same colonoscope (Fujinon EC-450WL5 colonoscope; Fuji Photo Optical Co Ltd, Saitama, Japan). Sedation and monitoring were performed by 2 anesthesiologists.

Patients were randomly assigned to 1 of 2 sedation protocols (control group [group C] and ketamine group [group K]). The gastroenterologist who performed the colonoscopy procedure and rated the quality of sedation, the anesthesiologist who administrated the drugs and assessed the outcome parameters, and the patients who rated the quality of sedation were blind to the randomization procedure. Blinding was provided by having an independent research nurse. A computer-generated randomization list including 100 patients was prepared and given to the nurse. She had access to the randomization list when the patient was admitted to the colonoscopy suite and met criteria for study inclusion. She provided a 1-mL insulin syringe containing either ketamine 50 mg/mL or 0.9% sodium chloride [NaCl]) and labeled it as "Study Drug." Midazolam, fentanyl, and propofol were also prepared in separate syringes and labeled by the same colonoscopy nurse. Equipment for full resuscitation and reversal agents was available within the gastroenterology unit. Demographic variables were recorded.

In the gastroenterology unit, a 22-gauge intravenous catheter was inserted in the arm; and 0.9% NaCl solution was administered. Standard monitoring, including noninvasive blood pressure, electrocardiogram, and pulse oximetry, was used. Supplemental oxygen (3 L/min) via a face mask was administered during the procedure. All patients were continuously monitored for heart rate, systolic and diastolic blood pressure (SBP and DBP), oxygen saturation ($Spo_2$), respiratory rate, and sedation levels before administration of medicines (baseline) and every 2 minutes for the first 10 minutes and every 5 minutes thereafter until the completion of the procedure and in the postanesthesia care unit (PACU). Sedation level, recovery, and discharge criteria were determined according to the Ramsay Sedation Scale (RSS) and the Modified Post Anesthesia Discharge Scoring System (MPADS), respectively [25,26]. The colonoscopy procedure times were determined as time from first drug administration until start of procedure (induction), time from start of procedure until colonoscope insertion to cecum (cecum intubation), time from start of procedure until colonoscope removal (duration of colonoscopy), time from colonoscope removal until the patient reached RSS = 2 (recovery time), and time from colonoscope removal to achieve MPADS greater than or equal to 9 (discharge time).

In group C, sedation was provided by intravenous midazolam (0.02 mg/kg), fentanyl (1 μg/kg), 0.9% NaCl, and incremental doses of propofol to have a Ramsay sedation score of 3 to 4. In group K, patients received intravenous midazolam (0.02 mg/kg), fentanyl (1 μg/kg), ketamine