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Original article

Low-Dose Ketamine in Combination with Midazolam for Diagnostic Upper Gastrointestinal Endoscopy: Case Report

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Abstract

Introduction and objectives: The number of outpatient endoscopic procedures in gastroenterology has increased in recent years. During the pandemic, due to drug shortages, alternative sedation techniques were explored. This study describes the sedation profile and adverse effects of combining low-dose ketamine with midazolam for sedation during diagnostic upper gastrointestinal endoscopy (UGIE). **Materials and methods:** A prospective, observational, descriptive case series study was conducted involving 30 patients aged 18 to 70 years with ASA physical status classification I or II, who underwent diagnostic UGIE. Sedation was induced with 0.03 mg/kg of midazolam and 0.3 mg/kg of ketamine prior to endoscopy. During and after endoscopy, the need for additional sedative medications and the occurrence of major adverse events (e.g., cardiorespiratory arrest or death) and minor events (e.g., desaturation, apnea, laryngospasm, hypertension, tachycardia, coughing, hypersalivation, dizziness, and recall of the procedure) were documented. Procedure duration, recovery time, and depth of sedation were also recorded. **Results:** Effective sedation was achieved in 27 ASA I and II patients without the need for additional sedatives to achieve the endoscopic procedure. The mean procedure time was 7.9 minutes, and the average recovery time was 26.1 minutes. Adverse events were observed in 66% of patients during the procedure (the most frequent being elevated blood pressure in 45.9%) and in 63.4% during recovery (most commonly dizziness in 50%). **Conclusions:** The combination of low-dose ketamine and midazolam appears to be a safe and effective sedation strategy for diagnostic UGIE, with minor adverse effects reported in more than 50% of patients.

Keywords

Gastrointestinal endoscopy, conscious sedation, ketamine, midazolam, safety.

INTRODUCTION

The pandemic caused by the emergence of the SARS-CoV-2 coronavirus (severe acute respiratory syndrome coronavirus 2) in 2020 has led to significant changes in healthcare delivery for patients worldwide. One of the challenges anesthesiologists have faced is the shortage of sedation medications due to the high demand for these drugs in intensive care units (ICUs) for sedating and providing analgesia to patients requiring invasive mechanical ventilation due to the coronavirus. Among the most commonly used medications at risk of shortage in various institutions in Colombia is the hypnotic agent propofol[1,2].

At Hospital Universitario San Ignacio, an average of 1,982 patients per year undergo gastroenterological procedures under sedation administered by anesthesiologists, and of these, approximately 13% (258) require diagnostic upper gastrointestinal endoscopies. Given that diagnos-

tic procedures such as upper gastrointestinal endoscopy must continue to be performed, anesthesiologists have had to explore alternative pharmacological options[3].

Ketamine was first synthesized in 1962 and approved for human use by the Food and Drug Administration (FDA) in 1970. This drug exerts its effects through non-competitive antagonism of N-methyl-D-aspartate (NMDA) receptors, as well as through interactions with opioid, monoaminergic, cholinergic, and purinergic receptors, inhibition of non-NMDA glutamate receptors, and nitric oxide synthase[4]. Its administration induces a dose-dependent dissociative anesthetic state, along with psychodysleptic effects such as visual and auditory hallucinations, vivid dreams, altered time-space perception, and depersonalization.

In the cardiovascular system, ketamine has a stimulant effect mediated by the sympathetic nervous system, resulting in increased heart rate, cardiac output, and blood pressure. It has minimal impact on central respiratory drive, and at low doses, it preserves protective airway reflexes. Additionally, it induces smooth muscle relaxation, leading to bronchodilation and increased secretion production. Furthermore, due to its antagonism of NMDA receptors in the spinal cord, it has a potent analgesic effect that prevents central pain amplification. For these reasons, ketamine has been considered an alternative for anesthetic induction or sedation in patients with hemodynamic instability, airway hyperreactivity, or bronchospasm undergoing various procedures[5]. It has also been studied as part of multimodal analgesia regimens for acute or chronic pain management, asthma exacerbations, certain psychiatric conditions such as depression and substance addiction, and is even known for its recreational use[6].

Ketamine has been used over time, either alone or in combination with other medications, to achieve varying levels of sedation in adult and pediatric patients undergoing different procedures. Multiple studies in the literature describe the effectiveness and safety of various sedation regimens that include ketamine for gastroenterological procedures in children[7-10]. In contrast, evidence on the use of ketamine for sedation during gastroenterological procedures in adults is scarce. Due to the current situation of the SARS-CoV-2 pandemic and based on the limited evidence available in pediatric patients, this institution began using ketamine as a pharmacological alternative for sedating adult patients undergoing diagnostic upper gastrointestinal endoscopy. The goal was to find a drug combination with rapid recovery, comfort for the patient, anesthesiologist, and gastroenterologist, and a safety profile similar to or better than that of traditionally used medications, without serious adverse effects.

Therefore, the objective of this study is to describe the sedation profile, effectiveness (measured by whether the procedure could be performed and satisfaction with it), and safety provided by the use of low-dose ketamine in combination with midazolam for diagnostic upper gastrointestinal endoscopy in adult patients at Hospital Universitario San Ignacio. Based on the results of this study, we hope to conduct a subsequent randomized study comparing the commonly used medications or combinations (propofol and remifentanil) with the one used in this study (ketamine and midazolam).

MATERIALS AND METHODS

Data collection was conducted at Hospital Universitario San Ignacio between January and March 2022, involving a total of 30 patients for this prospective, descriptive, observational case series study, following the CARE checklist specific to this type of study.

Patients were included during pre-anesthetic evaluation prior to outpatient endoscopic procedures by two principal investigators based on the following inclusion criteria: patients aged 18–70 years, classified as ASA I or II by the American Society of Anesthesiologists, and scheduled for diagnostic upper gastrointestinal endoscopy. Exclusion criteria included pregnancy, active upper gastrointestinal bleeding, emergency procedures, psychiatric or neurocognitive disorders, additional interventions such as variceal ligation or polypectomy, and known allergies to ketamine or midazolam. Initial demographic data—age, sex, identification number, weight, medical history, and ASA classification—were recorded and verified using the hospital's electronic health record system (SAHI).

After obtaining informed consent, standard monitoring was implemented (blood pressure, electrocardiogram, peripheral oxygen saturation [SpO_2], and nasal capnography), alongside oxygenation via nasal cannula (target SpO_2 >90%) and peripheral venous access. Topical anesthesia (lidocaine aerosol) was applied to the oral cavity, followed by midazolam (0.03 mg/kg). After 2 minutes, ketamine (0.3 mg/kg) was administered. Sedation depth was assessed before proceeding with endoscopy. Intraprocedural data included: need for additional medications, major adverse events (e.g., cardiopulmonary arrest, death), and minor adverse events (e.g., desaturation, apnea, laryngospasm, agitation, excessive secretions requiring suctioning, hypertension, hemodynamic changes). Post-procedure monitoring in the recovery room included Aldrete scoring (10/10 for discharge) and documentation of minor adverse effects (e.g., hallucinations, unpleasant recall, dizziness, nausea/emesis). Patients rated sedation satisfaction on a 1–10 numeric scale (0: extremely poor experience; 10: pleasant, repeatable experience).

All procedural and post-procedural variables were recorded in a standardized RedCap (Research Electronic Data Capture) form, using only identification numbers for anonymization to comply with research ethics. Basic analysis was performed, with data presented in tables and figures.

Statistical Analysis

A descriptive analysis was conducted for event frequencies, including patient sedation states (ASA classification for sedation depth), adverse events during procedures/recovery, need for additional medications, and patient satisfaction.

Ethical Considerations

Recruited patients received a full study explanation, had questions addressed, and provided signed informed consent. Procedures adhered to the ethical standards of the 2005 Declaration of Helsinki. The study was approved by Hospital Universitario San Ignacio ethics committee (approval No.: FM-CIE-0753-21).

RESULTS

A total of 30 patients were enrolled, of whom 23 were female (76.6%) and 7 male (23.3%), with various comorbidities (**Table 1**). Ages ranged from 20 to 70 years (mean: 54). Based on comorbidities, patients were classified as ASA I (8 patients, 26.6%) or ASA II (22 patients, 73.3%). Sedation depth achieved with the drug combination was assessed using the ASA sedation scale (**Table 2**): 0% achieved Grade I (anxiolysis), 86.6% Grade II (conscious sedation), and 13.3% Grade III (deep sedation/analgesia). Procedure duration, recovery time (until achieving discharge-ready status per Aldrete score [10/10]), and effectiveness rates are detailed in **Table 3**. The procedure was successfully completed in 100% of patients, with additional medications required in 3 cases (10%). Cases requiring adjunct medications had endoscopic durations exceeding 10 minutes. Atropine was administered once for excessive salivation.

Table 1. Preoperative Characteristics

Characteristics	n (%)
Total patients	30
Age, years (mean, range)	54 (20-70)
Sex	
- Female	23 (77)
- Male	7 (23)
ASA	
- Grade I	8 (27)
- Grade II	22 (73)
Hypertension	8 (27)
Diabetes mellitus	5 (16)
Cardiac disease (ischemic, valvular, arrhythmic)	3 (10)
Hypothyroidism	7 (23)
Oncologic pathology	3 (10)
HIV	1 (3)
Pulmonary disease (OSAHS, COPD, asthma, PE)	9 (30)
Liver disease	1 (3)
Arthritis	1 (3)
Obesity	3 (10)
None	8 (27)

ASA: American Society of Anesthesiologists; COPD: chronic obstructive pulmonary disease; OSAHS: obstructive sleep apnea-hypopnea syndrome; PE: pulmonary embolism; HIV: human immunodeficiency virus. Table prepared by the authors.

Adverse events during the procedure and recovery are shown in **Figures 1** and **2**. The most frequent were hypertension (45.9% intraprocedural) and dizziness (50% during recovery). Adverse event incidence was 66% intraprocedural and 63.4% postprocedural, though no major events (cardiopulmonary arrest/death) occurred. Mean satisfaction score was 9.5 (range: 6–10), as shown in **Table 3**.

Table 2. ASA Classification of Sedation States

Characteristics	Grade I	Grade II	Grade III	Grade IV
Response	Normal response to verbal stimulus	Purposeful response to verbal/tactile stimulus	Purposeful response to repeated/ tactile/painful stimulus	Unresponsive to painful stimulus
Airway	Unaffected	No intervention needed	May require intervention	Usually requires intervention
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Maintained	Usually maintained	May be impaired

Table prepared by the authors.

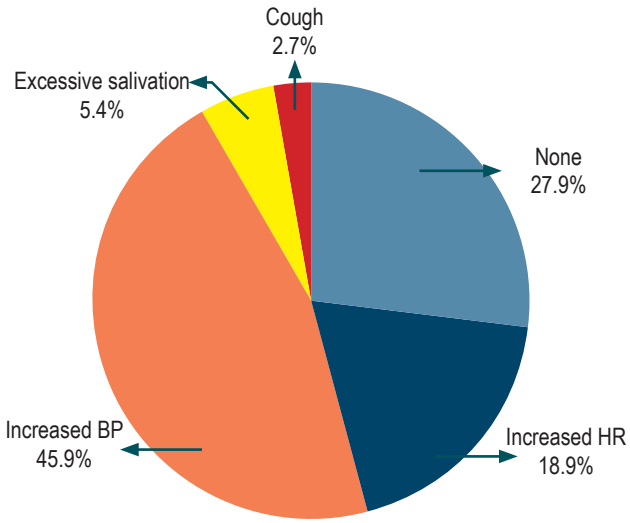

Figure 1. Adverse events during the procedure. Adverse events observed during surgery are shown, with the most frequent being increased blood pressure in 45.9% of cases (orange), followed by increased heart rate in 18.9% (blue), excessive salivation in 5.4%, and cough in 2.7%. All were minor adverse events, with no major events such as cardiopulmonary arrest or death reported. HR: heart rate; BP: blood pressure. Image property of the authors.

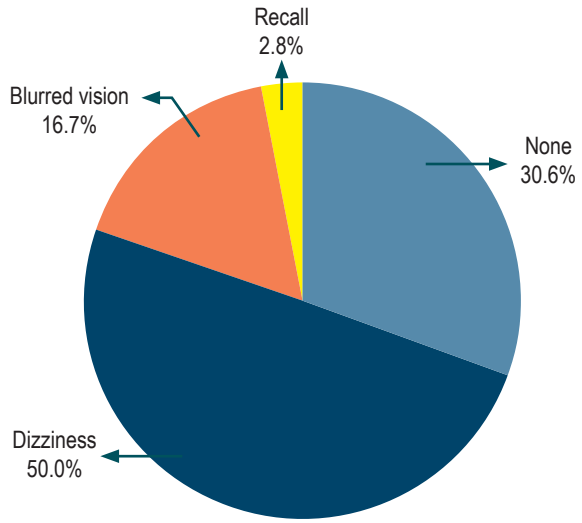

Figure 2. Adverse events during recovery. Adverse events observed during recovery are shown, with the most frequent being dizziness in 50% of cases (blue), followed by blurred vision in 16.7% (orange), and recall in 2.8% of patients. No major adverse events occurred. Image property of the authors.

Table 3. Outcomes

Item	
Mean procedure time, min (range)	7.9 (5-25)
Procedures without adjunct medications (%)	27 (90%)
Procedures with adjunct medications (%)	3 (10%)
Satisfaction score (1–10), mean (range)	9.5 (6-10)
Procedure completion rate (%)	100%
Recovery time, min (range)	26.1 (15-50)

Table prepared by the authors.

DISCUSSION

This study evaluated the feasibility of performing diagnostic upper gastrointestinal endoscopy in ASA I and II patients using low-dose ketamine and midazolam, with adequate patient satisfaction. The procedure was successfully completed using midazolam + ketamine in 90% of cases, while the remaining 10% required additional propofol doses–two of these cases were associated with endoscopic durations exceeding 10 minutes. ASA Grade I and II sedation levels were achieved, providing an adequate plane for successful low-complexity outpatient diagnostic procedures.

No major adverse events occurred during procedures or recovery. Minor intraprocedural adverse events occurred in 66% of cases, predominantly blood pressure increases >20% from baseline (without emergency criteria in any case), directly related to ketamine's catecholamine-mediated mechanism. Minor recovery-phase adverse events occurred in 63.4% of cases, with dizziness being most prevalent (50%). No patients experienced emesis. Despite >50% prevalence of minor events during and after procedures, mean patient satisfaction was 9.5, with a 100% procedural success rate by gastroenterologists. Average recovery time was <30 minutes–appropriate for outpatient procedures and comparable to other widely used sedation methods.

Several small descriptive studies have been published evaluating ketamine's use and safety, either alone or in combination with other medications, for inducing sedation in patients undergoing endoscopic procedures[7-9]. Most of these studies were conducted in pediatric populations, assessing various sedation protocols with ketamine doses ranging from 0.5 to 1 mg/kg. While the results are not definitive, these studies agree that ketamine–whether used alone or in combination–achieves adequate conditions for endoscopic procedures performed by gastroenterologists, with proper hemodynamic stability typically characterized by increased blood pressure and heart rate, and without major respiratory complications. Some cases reported minor procedural complications such as excessive

salivation, stridor, and laryngospasm, which were easily managed and did not lead to adverse outcomes[10]. Notably, this study used lower ketamine doses than those described in the literature, with similar effectiveness and no negative respiratory outcomes.

This study suggests that low-dose ketamine combined with midazolam is effective and provides an adequate safety profile compared to other commonly used combinations like propofol, remifentanil, and fentanyl. A key benefit of this technique is that none of the patients developed hypoxemia (defined as SpO_2 <90%), a complication reported with various combinations of the aforementioned medications, potentially offering a safer alternative during drug shortages.

Although this is not a randomized clinical trial, the findings may be generalizable to the broader population and represent an excellent option for ASA I and II patients when resources are limited, as during the SARS-CoV-2 pandemic. Beyond study design limitations, potential measurement bias may exist since the evaluating anesthesiologists were study participants. Additionally, the sample size was small. Finally, while procedures were successfully completed in 100% of cases, endoscopist satisfaction was not assessed.

Currently, no studies compare propofol versus ketamine for low-grade diagnostic outpatient endoscopic procedures in adults. This study, therefore, opens possibilities for future research, particularly randomized clinical trials comparing low-dose midazolam-ketamine combinations with standard medications like propofol to determine effectiveness, safety, and satisfaction among patients, gastroenterologists, and anesthesiologists across low- and high-risk populations.

CONCLUSIONS

Low-dose ketamine-midazolam sedation may be a reasonable alternative for low-complexity endoscopic procedures given its effectiveness and safety profile, particularly the low hypoxemia incidence. This makes it potentially suitable for high pulmonary-risk patients (e.g., morbid obesity, obstructive sleep apnea-hypopnea syndrome [OSAHS], difficult airway), while offering competitive recovery times and costs. However, optimal sedation duration proved insufficient for procedures exceeding 10 minutes.

Conflict of Interest Statement

The authors declare no conflicts of interest.

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