### Procedural Sedation Protocols with or without Ketamine in Pediatric Gastrointestinal Endoscopy: A Retrospective Cohort Study

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#### ABSTRACT

**Objective:** A considerable difference exists in pediatric endoscopy sedation practices with the optimal sedation protocol for gastrointestinal (GI) endoscopy a subject of controversy and to investigate the safety and efficacy of sedation protocols with or without ketamine in procedural sedation for pediatric GI endoscopy.

**Materials and Methods:** A total of 78 pediatric patients who received sedation anesthesia for GI endoscopy were included in this retrospective study. Anesthesia parameters include duration time, doses of anesthetic agents, Ramsay sedation score, respiratory and hemodynamic parameters, recovery time, modified Aldrete recovery scores, and side effects. Study parameters were evaluated with respect to ketamine dose (no ketamine group (NKG), low-dose ketamine group (LDKG,  $\leq 0.75$  mg/kg), and high-dose ketamine group (HDKG,  $\geq 1$  mg/kg).

**Results:** The upper GI endoscopy rate (58.12% vs. 90.0%, p=0.001) was significantly lower in LDKG versus HDKG. No significant changes were observed in blood pressure levels, oxygen saturation, or heart rate compared to baseline levels. No significant difference was noted between study groups in terms of recovery time, modified Aldrete recovery scores, and nausea/vomiting. Final Ramsay sedation scores were significantly higher in NKG (p<0.05) and LDKG (p<0.01) than in HDKG.

**Conclusion:** Our findings indicate a favorable safety and efficacy profile for ketamine as a useful adjunct to procedural sedation for pediatric GI endoscopy, enabling better quality of sedation with a low risk of cardiorespiratory suppression, or serious complications.

Keywords: Children, gastrointestinal endoscopy, ketamine, patient safety

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#### **INTRODUCTION**

Uses of gastrointestinal (GI) endoscopy in the diagnostic work-up as well as treatment of GI disorders have become increasingly common in children.<sup>[1,2]</sup> Given the considerable anxiety and distress caused by such procedures in children, safe and effective sedation is considered a pre-requisite for pediatric endoscopic procedures to facilitate enhanced patient tolerance and successful completion of the procedure.<sup>[1-4]</sup> There is a wide variety of sedative or anesthetic drugs used either alone or in combination for endoscopy procedural sedation, such as benzodiazepines (e.g., midazolam), opioids (e.g., fentanyl), and sedative-hypnotics (e.g., ketamine, propofol).<sup>[3-7]</sup>

Ketamine is a dissociative anesthetic agent with a wide safety margin that provides rapid but short sedation and quick recovery.<sup>[8,9]</sup> It is frequently used for pediatric procedural sedation in combination with benzodiazepines, particularly midaz-



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olam, to limit potential side effects.<sup>[3,4,8,10]</sup> Compared to opioids, ketamine sedation combined with propofol had lower respiratory and circulatory side effects and did not prolong recovery time. However, it is thought to be a good agent for sedation in GI diseases, since ketamine does not inhibit  $\mu$ -receptors, prevents GI obstruction, and does not affect GI function.<sup>[11]</sup>

Propofol is one of the most promising but controversial sedative anesthetics, recommended for use only by anesthesiologists due to the risk of hypotension and respiratory depression at high doses [6]. Nonetheless, the use of propofol at lower doses is considered likely when used in combination with other sedatives that enable a synergistic effect.<sup>[12]</sup>

None of the available agents is considered to fully meet the criteria of an ideal sedative including a predictable dose-dependent sedation with rapid onset and short duration of action, broad therapeutic window, and a favorable safety profile.<sup>[4]</sup> Hence, there is a considerable difference in pediatric endoscopy sedation practices with the optimal sedation protocol for GI endoscopy a subject of controversy.<sup>[2,7]</sup>

During GI endoscopy procedures of pediatric patients, the tolerability of patients under adequate and reliable sedative effect was compared by combining different doses of ketamine with propofol. This retrospective study was therefore designed to investigate the safety and efficacy of sedation protocols with or without ketamine in procedural sedation for pediatric GI endoscopy.

#### **MATERIALS and METHODS**

#### **Study Population**

A total of 78 pediatric patients (age range: 5 months to 18 years), who received sedation anesthesia for upper and/ or lower GI endoscopic investigation, were included in this retrospective and cross-sectional study conducted at a tertiary case pediatric gastroenterology endoscopy unit. Retrospective examination was performed from the perioperative records of all cases under sedation at a cross-sectional interval of 2 months. An average of 678 gastroscopy and 51 colonoscopy cases were received in the endoscopy unit in 2015. Pediatric patients (age range 5 months to 18 years), who underwent upper or lower GI endoscopy under sedation anesthesia were included in this study. Children who had endoscopic investigation in the presence of their parents without receiving sedation anesthesia and those with mask, laryngeal mask, and/or endotracheal intubation application under general anesthesia were excluded from the study.

The study was conducted in full accordance with local Good Clinical Practice guidelines and current legislation, with per-

mission obtained from our Institutional Ethics Committee (2018-04-07/2018/97) for the use of patient data for publication purposes. The data were retrospectively obtained from all the perioperative file records of the pediatric age group, who were taken under emergency or elective conditions to the GI endoscopy procedure with sedation in November and December in 2015 in the department of anesthesiology and reanimation. All patients who met the inclusion criteria were included in the study. In our study, there were no cases that could not be included due to lack of consent for anesthesia or exclusion criteria during the period examined. A total of ten cases were excluded due to the lack of records in the perioperative period. All perioperative file records and sedative and hypnotic agents used in the sedation procedure that was examined were in compliance with the hospital sedation protocol.

#### **Study Parameters**

Data on patient demographics (age and gender), anthropometrics (weight, height, and body mass index), American Society for Anesthesiology (ASA) physical status, and endoscopic procedure (indication, location, and duration) were recorded for each patient. Anesthesia parameters included duration of anesthesia, first and total doses of anesthetic agents (midazolam, ketamine, and propofol), Ramsay sedation score (during procedure), respiratory and hemodynamic parameters (peripheral oxygen saturation, pulse, systolic, diastolic, and mean arterial blood pressure), recovery time, modified Aldrete recovery scores (0th minute (min), 30th min, 60th min, and 120th min), and side-effects (i.e., nausea-vomiting). Study parameters were also evaluated with respect to ketamine dose (no ketamine group (NKG), low-dose ketamine group (LDKG ≤0.75 mg/kg), and high-dose ketamine group (HDKG  $\geq 1 \text{ mg/kg}$ ).

#### Sedation, Monitoring, and Recovery

Sedation was actively administered by trained and experienced anesthesiologists and endoscopic procedures were performed by the same experienced pediatric endoscopy specialist in the endoscopy unit. By complying with the sedation protocol of our hospital, all our endoscopy cases were oxygenated in the perioperative period with nasal oxygen at a rate of 2–4 L/min. The bolus doses of ketamine (Ketalar, 50 mg/mL, 10 mL; Pfizer, Sandwich, UK), midazolam (Dormicum, 1 mg/mL, 5 mL; Deva Holding, Istanbul, Türkiye), or propofol (Propofol-Lipuro, 10 mg/mL, 20 mL; B. Braun, Melsungen, Germany) were applied before endoscopy and additional incremental doses were administered in case of inadequate initial sedation or the need for a longer procedure. Constant patient monitoring was applied during the procedure for peripheral oxygen saturation, heart rate, respiratory rate, and blood pressure. The effectiveness of sedation during the procedure was evaluated through a modified Ramsay sedation score ranging from 1 (anxious, agitated, and restless) to 6 (no response to glabellar tap or auditory stimulus) depending on the response of the patient to the stimuli. Patients were observed for 2 h after the procedure for sedation-related complications such as a poor oxygen saturation, respiratory distress, apnea, bradycardia, cardiac arrest, and emergency reactions.

The recovery of the patients was assessed using a modified Aldrete score ranging from 0 to 10 depending on the patient's activity, oxygen saturation, consciousness, respiration, and circulation. A score of  $\geq$ 9 was the considered criterion for discharge from the endoscopy unit, while the time between the completion of the process and discharge from the endoscopy unit (the recovery time) was also recorded. Complications during the recovery time (i.e., double vision, dizziness, and nausea/vomiting) were also recorded.

#### **Statistical Analysis**

Statistical analysis was conducted using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY). The Pearson Chi-square test (Monte Carlo) and Fisher-Freeman-Halton test (Monte Carlo) with *post hoc* Benjamini-Hochberg correction were used for the comparison of categorical data. The Mann–Whitney U-test (Monte Carlo) and Jonckheere-Terpstra test (Monte Carlo) with *post hoc* Dunn's test were used to analyze parametric variables. Change over time was evaluated through the Wilcoxon signed-rank test (Monte Carlo) and Friedman test (Monte Carlo) with *post hoc* Dunn's test. Data were expressed as "mean-standard deviation," median (minimum-maximum) and percent (%) where appropriate. P<0.05 was considered statistically significant.

#### RESULTS

#### Demographics, Endoscopy, and Anesthesia-Related Characteristics (n=78)

The mean age of patients included in the study was 12.0 (range, 1.0–18.0 years), and female patients were forming 57.72% of the study population. The majority of patients were in the ASA I-II functional class. Dyspepsia (34.61%) and GI bleeding (14.13%) were the most common indications for GI endoscopy investigation, while upper GI endoscopy was performed in 79.54% of patients. Duration of endoscopy and anesthesia procedures was median 14.0 min (range, 2.0–65.0 min) and 18.0 min (range, 4.0–70.0 min), respectively (Table 1).

Ketamine was used in 61 (78.23%) patients with a first dose of median (min/max) 1.0 (0.4–1.3) mg/kg ( $\leq$ 0.75 mg/kg in 38.51%,  $\geq$ 1 mg/kg in 39.72%) (Table 1).

Nausea/vomiting were noted in 14.10% of patients, while the recovery time was median 8.0 min (range, 2.0–20.0 min) (Table 1).

# Demographics, Endoscopy, and Anesthesia Characteristics with Respect to Ketamine Anesthesia

Ketamine first-dose groups, HDKG versus LDKG, were significantly associated with a lower rate of upper GI endoscopy (58.12 vs. 90.0%, respectively, p=0.001), longer duration of endoscopy (median 19 vs. 13 min, respectively, p<0.001), and anesthesia (median 23 vs. 16.5 min, respectively, p<0.001) procedures (Table 2).

The NKG was associated with significantly shorter endoscopy (median 6 min, p<0.01) and anesthesia (median 10 min, p<0.05) procedure durations as compared with both HDKG and LDKG (Table 2).

No significant difference was noted between ketamine groups in terms of patient demographics, recovery time, modified Aldrete scores, and nausea/vomiting rate or scores (Table 2).

The  $30^{th}$  min and  $120^{th}$  min modified Aldrete scores were significantly higher than  $0^{th}$  min scores in each group (p<0.001 for each), while  $30^{th}$  min nausea/vomiting scores were significantly higher than  $0^{th}$  min scores (p<0.05) and lower than  $120^{th}$  min scores (p<0.01) in the HDKG (Table 2).

# Respiratory and Hemodynamic Parameters and Sedation with Respect to Ketamine Anesthesia

A significant decline from baseline to final systolic arterial pressure (SAP), diastolic arterial pressure (DAP), and mean arterial pressure (MAP) values was noted only in the NKG (p<0.001 for each) and LDKG (p=0.003, p=0.015 and p=0.006, respectively), while blood pressure levels remained unchanged from baseline to final measurement in the HDKG (Table 3).

Accordingly, when compared to HDKG and LDKG, final SAP (p<0.001 and p<0.05, respectively) and DAP (p<0.001 and p<0.01, respectively) values were significantly lower in the NKG. The final DAP (p<0.001) and MAP (p<0.01) were also significantly lower in the LDKG than in the HDKG (Table 3).

No significant difference was noted in oxygen saturation or pulse with respect to the presence or dose of ketamine. In addition, despite significant decreases from the baseline for oxygen saturation in the LDKG (p=0.048) and for pulse in both NKG (p=0.017) and LDKG (p<0.001), there was no significant change from baseline levels in oxygen saturation or pulse in the HDKG (Table 3).

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Patient demographics	n	%	Patient demographics	n	%	
Age (year)			First dose	0.021	0.021 (0.003)	
Mean (SD)	10.6 (5.4)		Mean (SD)	0.021 (0.017/0.030)		
Median (min/max)	12.0	(1.0–18.0)	Median (min/max)			
Gender			Total dose			
Girl	45	57.7	Mean (SD)	0.021	(0.003)	
Воу	33	42.3	Median (min/max)	0.021 (0.017/0.033)		
Anthropometrics, median (min/max)			Ketamine			
Height (cm)	146.0 (	57.0–177.0)	First dose			
Weight (kg)	33.5	(4.0–93.0)	Mean (SD)	0.8 (0.2)		
BMI (kg/m²)	18.6 (	11.8–36.3)	Median (min/max)	1.0 (0.4–1.3)		
ASA status			Total dose			
I	59	75.6	Mean (SD)	0.8 (0.3)		
II	18	23.1	Median (min/max)	1.0 (0	0.4–1.3)	
III	1	1.3	Propofol			
Endoscopy characteristics			First dose			
Duration of procedure (min)			Mean (SD)	1.2	2 (0.4)	
Mean (SD)	18.7 (14.7)		Median (min/max)	1.1 (0.3–2.2)		
Median (min/max)	14.0	2.0–65.0)	Total dose			
Indications			Mean (SD)	1.8 (0.9)		
Dyspepsia	27	34.6	Median (min/max)	1.6 (0.3–4.3)		
GI bleeding	11	14.1	Ketamine first-dose groups			
Location			NKG no ketamine	17	21.8	
Upper GI	62	79.5	LDKG ≤0.75 mg/kg	30	38.5	
Lower GI	10	12.8	HDKG ≥1 mg/kg	31	39.7	
Both	6	7.7	Recovery characteristics			
Sedation anesthesia characteristics			Nausea/vomiting			
Anesthesia duration (min)			Absent	67	85.9	
Mean (SD)	22.7(15.6)		Present	11	14.1	
Median (min/max)	18.0(4.0–70.0)		Recovery time (min)	nin)		
Dose of anesthetic agents (mg/kg)		Mean (SD)	9.3 (4.1)			
Midazolam			Median (min/max)	8.0 (2.0–20.0)		

### SD: Standard deviation; min: minute; BMI: Body mass index; GI: Gastrointestinal; NKG: No ketamine group; LDKG: Low-dose ketamine group; HDKG: High-dose ketamine group

Final Ramsay sedation scores were significantly higher in the NKG (p<0.05) and LDKG (p<0.01) than in the HDKG. In each ketamine group, a significant increase was noted in Ramsay sedation scores from baseline to final measurement (p<0.001 for each) (Table 3).

#### DISCUSSION

Our findings revealed the use of ketamine as a sedation complement for GI endoscopy in most of patients with similar rates of  $\geq 1$  mg/kg and  $\leq 0.75$  mg/kg ketamine doses. Among endoscopy indications, dyspepsia was associated with a higher likelihood of ketamine use, Crohn's disease with the use of  $a \ge 1 \text{ mg/kg}$  ketamine dose and corrosive esophagitis with the use of sedation protocols not involving ketamine.

Overall,  $\geq 1$  mg/kg ketamine doses were more commonly used for lower GI endoscopies, while associated with longer endoscopy and anesthesia duration, a lesser likelihood of a decrease in heart rate, blood pressure and oxygen saturation and lower Ramsay sedation scores when compared to  $\leq 0.75$ mg/kg ketamine doses and no-ketamine protocols.

Table 2. Demographics, endoscopy, and anesthesia characteristics in study groups							
	NKG (n=17)		LDKG ≤0.75 mg/kg (n=30)		HDKG ≥1 mg/kg (n=31)		р
	n	%	n	%	n	%	
Demographics							
Gender							
Girl	8	47.1	19	63.3	18	58.1	0.583 <sup>p</sup>
Воу	9	52.9	11	36.7	13	41.9	
Age (year)	9	(1/18)	13 (1	.50/17)	12	(1/18)	0.159 <sup>b</sup>
Anthropometrics							
Height (cm)	110 (66/168)		153.50 (57/173)		148 (59/177)		0.196 <sup>b</sup>
Weight (kg)	18	18 (8/69)		45 (4/93)		35 (11/55)	
BMI (kg/m²)	19.3 (1	1.9/24.5)	19.4 (1	19.4 (11.8/36.3)		17.6 (13.7/31.6)	
ASA class							
I. I.	11	64.7	23	76.7	25	80.6	0.420 <sup>f</sup>
II	5	29.4	7	23.3	6	19.4	
III	1	5.9	0	0	0	0	
Endoscopy characteristics Location							
Upper GI	17	100.0	27	90.0**	18	58.1	0.001 <sup>f</sup>
Lower GI	0	0.0	3	10.0	7	22.6	
Both	0	0.0	0	0.0	6	19.4	
Duration of procedure (min)	6 (2/	'19)***,++	13 (4	4/65)**	19 (1	10/60)	<0.001 <sup>b</sup>
Anesthesia characteristics							
Anesthesia duration (min)	10 (4	10 (4/45)***,*		16.5 (5/70)**		23 (14/64)	
Anesthesia dose (mg/kg)							
Midazolam							
First dose	0.02 (0.02/0.03)		0.02 (0.02/0.03)		0.02 (0	.02/0.03)	0.628 <sup>b</sup>
Total dose	0.02 (0.02/0.03)		0.02 (0.02/0.03)		0.02 (0	.02/0.03)	0.719 <sup>b</sup>
Propofol							
First dose	1.58 (0.77/2.22)		1 (0.25/1.74)		1.06 (C	).91/2.17)	0.112 <sup>b</sup>
Total dose	1.90 (0.77/2.92)		1.21 (0.25/3.57)		2 (0.91/4.35)		0.480 <sup>b</sup>
Ketamine							
First dose	-		0.66 (0.36/0.75)		1.05	(1/1.30)	<0.001 <sup>u</sup>
Total dose	-		0.66 (0.36/0.75)		1.05	(1/1.30)	<0.001 <sup>u</sup>
Recovery characteristics							
Recovery time (min)	7 (	(4/15)	10	(2/20)	8 (4	4/20)	0.729 <sup>b</sup>
Modified Aldrete scores							
0 <sup>th</sup> min	9	(8/9)	8	(7/9)	9	(7/9)	0.349
30 <sup>th</sup> min	10 (10/10) <sup>qq</sup>		10 (10/10) <sup>qq</sup>		10 (1	0/10) <sup>qq</sup>	0.999
120 <sup>th</sup> min	10 (10/10) <sup>qq</sup>		10 (10/10) <sup>qq</sup>		10 (1	0/10) <sup>qq</sup>	0.999
p value for intra groups <sup>ff</sup>	<(	0.001	<(	0.001	<0	.001	
Nausea/vomiting							
No	17	100	26	86.7	24	77.4	0.096
Yes	0	0	4	13.3	7	22.6	
Nausea/vomiting score							
O <sup>th</sup> min	0	0 (0/0)		0 (0/0)		0.1 (0/1)	
30 <sup>th</sup> min	0.1	0.1 (0/1)		0.1 (0/3)		0.3 (0/3)ª	
120 <sup>th</sup> min	0	0 (0/0)		0 (0/0)		0/0) <sup>t</sup>	0.999
p value for intra groups <sup>f</sup>	0.999		0.058		<0	.001	

Data are expressed as median (minimum/maximum) if not stated otherwise min; minute, GI; gastrointestinal. P: Pearson Chi-square Test (Monte Carlo); b: Jonckheere-Terpstra Test (Monte Carlo) – post hoc Dunn's Test; <sup>f</sup>: Fisher Freeman Halton (Monte Carlo) – post hoc Benjamini-Hochberg correction; <sup>u</sup>: Mann–Whitney U-test (Monte Carlo); <sup>ff</sup>: Friedman Test (Monte Carlo) – post hoc Dunn's Test; <sup>\*\*:</sup> p<0.01; <sup>\*\*\*:</sup> p<0.001; compared to HDKG; <sup>+</sup>: p<0.05 and <sup>++</sup>: p<0.01; compared to LDKG <sup>e</sup>: p<0.05 and <sup>ee</sup>: p<0.001 compared to 0-minute group; <sup>1</sup>: p<0.01 compared to 30-min group. NKG: No ketamine group; LDKG: Low-dose ketamine group; HDKG: High-dose ketamine group; ASA: American Society for Anesthesiology; GI: Gastrointestinal

Table 3. Respiratory and hemodynamic parameters and sedation in study groups							
	NKG (n=17) ≤0.75 mg/kg (n=30)	LDKG ≥1 mg/kg (n=31)	HDKG	p⁵			
SpO <sub>2</sub>							
Baseline	100 (93/100)	100 (98/100)	100 (99/100)	0.284			
Final	100 (98/100)	100 (98/100)	100 (98/100)	0.762			
Change from baseline	0 (0/5)	0 (-2/2)	0 (-1/1)	0.685			
p value for intra groups <sup>w</sup>	0.509	0.048	0.068				
Pulse (bpm)							
Baseline	120 (86/146)	114.50 (82/158)	112 (70/146)	0.226			
Final	111 (82/141)	105 (86/141)	110 (86/140)	0.706			
Change from baseline	-8 (-21/13)	-7.50 (-30/11)	-2 (-26/27)	0.065			
p value for intra groups <sup>w</sup>	0.017	<0.001	0.996				
Systolic arterial pressure							
Baseline	107 (90/144)	117.50 (92/143)	117 (91/136)	0.232			
Final	105 (89/125)***,+	114.50 (91/128)	115 (95/126)	0.001			
Change from baseline	-5 (-24/3)**,+	-2.50 (-24/9)*	1 (-22/11)	0.002			
p value for intra groups <sup>w</sup>	<0.001	0.003	0.665				
Diastolic arterial pressure							
Baseline	68 (62/89)	67 (53/90)	72 (51/84)	0.601			
Final	63 (0/75)*	63 (57/76)***	70 (55/83)	0.001			
Change from baseline	-7 (-68/10)***,++	-2.50 (-18/6)	0 (-15/22)	0.004			
p value for intra groups <sup>w</sup>	<0.001	0.015	0.376				
Mean arterial pressure							
Baseline	83 (74.67/104)	81.83 (68.67/107.67)	87.67 (65.67/101.33)	0.328			
Final	77.33 (72/91.67)**	80 (70.67/93.33)**	85 (68.33/95.33)	0.001			
Change from baseline	-5.67 (-16/6)**,+	-2.17 (-19/4.33)	-0.67 (-13.33/15.33)	0.003			
p value for intra groups <sup>w</sup>	0.001	0.006	0.503				
Ramsey sedation score							
Baseline	1.6 (1/2)	1.8 (1/2)	1.7 (1/2)	0.653			
Final	3.9 (3/5)*	4.0 (3/5)**	3.6 (3/5)	0.019			
Change from baseline	2.3 (1/4)*	2.1 (1/3)	1.9 (1/4)	0.043			
p value for intra groups <sup>w</sup>	<0.001	<0.001	<0.001				

Data are expressed as median (minimum/maximum). <sup>b</sup>: Jonckheere-Terpstra Test (Monte Carlo) – post hoc Dunn's Test; <sup>w</sup>: Wilcoxon Signed-Ranks Test (Monte Carlo); <sup>\*</sup>: p<005, <sup>\*\*\*</sup>; p<0.01; <sup>\*\*\*\*</sup>: p<0.001; compared to HDKG; <sup>+</sup>: p<0.01; compared to LDKG. NKG: No ketamine group; LDKG: Low-dose ketamine group; HDKG: High-dose ketamine group; Sp0,: Peripheral oxygen saturation

Preservation of heart rate, blood pressure, or oxygen saturation levels during sedation anesthesia with  $\geq 1 \text{ mg/kg}$ ketamine doses in our cohort supports the safety of ketamine based on its cardiovascular and respiratory protective effects.<sup>[13,14]</sup> In fact, an initial dose of 1–1.5 mg/kg of ketamine is recommended, due to a decrease in its efficacy at lower doses.<sup>[3,10]</sup>

In this regard, the more common use of lower ketamine doses for upper GI endoscopy in our cohort seems nota-

ble given the association of ketamine with a higher likelihood of hypoxia and desaturation as well as complications during upper versus lower GI endoscopy.<sup>[8,14]</sup> Hence, our findings indicate a more favorable course in terms of hemodynamic and respiratory parameters when ketamine is included in the sedation anesthesia protocol and support ketamine as a useful adjunct to conscious sedation for pediatric endoscopic procedures enabling better quality and depth of sedation.<sup>[2,15]</sup> Similarly, data from previous pediatric studies indicated endoscopy with a low-dose midazolam and ketamine combination to be a suitable sedation protocol with effective sedation and low major complications rates<sup>[2,7,10,16,17]</sup> as well as more stable hemodynamic parameters and a lower incidence of respiratory adverse events with the addition of ketamine to propofol compared to propofol alone.<sup>[6,18-20]</sup> Data from two recent meta-analyses of procedural sedation in children and adults also concluded that the risk ratios, and respiratory adverse events significantly favored the combination of ketamine and propofol compared with propofol alone.<sup>[21,22]</sup>

Nausea/vomiting occurred in 13.34% and 22.61% of children with  $\leq$ 0.75 mg/kg and  $\geq$ 1 mg/kg bolus ketamine doses in our study. This supports the reported rates of ketamine-associated vomiting in the literature, ranging from 3.5 to 28.4%, and more often in GI tract procedures.<sup>[3,17,23]</sup>

No significant difference was noted in recovery time, modified Aldrete recovery scores, and nausea/vomiting rates according to the presence or dose of ketamine in sedation protocols in our cohort. This supports the wide margin of safety of the ketamine dose as well as the concomitant anxiolytic and analgesic effects, increasing the success of ketamine-based combinations in children with a less predictable response to sedatives.<sup>[2-4,8,24]</sup>

Although nausea/vomiting rates were similar between sedation anesthesia protocols with our without ketamine in our cohort, a fluctuation in nausea/vomiting was noted in the HDKG with an increase in scores from the baseline to 30<sup>th</sup> min followed by a decrease to basal values at 120<sup>th</sup> min of the observation period. Similarly, in a past study evaluating the four doses of ketamine (0, 0.25, 0.5, and 1 mg/kg) in combination with a dose of propofol in sedation for pediatric gastroduodenoscopy, authors reported a significant increase in the incidence of nausea/vomiting with the 1 mg/ kg dose of ketamine.<sup>[6]</sup>

Lack of emergence reactions (pleasant dream-like state, hallucinations, and delirium) in our cohort under ketamine-based anesthesia protocols seems consistent with a higher likelihood of these reactions in adults than in children and when ketamine is used alone in large doses.<sup>[2,25,26]</sup>

Moreover, lack of other side effects such as laryngospasm, recovery agitation, apnea, and respiratory depression under ketamine anesthesia in our cohort seems also to be related to the fact that the majority of our patients were ASA I-II class patients, supporting a consideration of safe sedation if the child's ASA classification conforms to classIor II.<sup>[4]</sup>

#### Limitations of Study

The retrospective single-center design seems to be a major limitation of the present study, which prevents the temporality between cause and effect from being established as well as our findings being generalized to the overall pediatric GI endoscopy population. Another limitation is that as a cross-sectional study, when a limited time interval was examined, all pediatric cases were included in the study, regardless of age range, we think that large-center studies are needed to examine close age ranges.

#### **CONCLUSION**

Our findings indicate a favorable safety and efficacy profile for ketamine as a useful adjunct to procedural sedation for pediatric GI endoscopy, enabling better quality of sedation with a low risk of cardiorespiratory suppression or serious complications.

#### Disclosures

**Ethics Committee Approval:** The study was approved by the Bakırköy Dr. Sadi Konuk Training and Research Hospital Clinical Research Ethics Committee (No: 2018-04-07, Date: 26/02/2018).

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