ÖZGÜN ARAŞTIRMA

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The effects of capnography during sedation in pediatric esophagogastroduodenoscopy procedures: A randomized controlled study

Pediatrik özafagogastroduodenoskopi işlemlerinde sedasyon sırasında kullanılan kapnografinin etkinliği: Randomize kontrollü çalışma

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Background and Aims: *Microstream capnography monitors are devices that use nasal sample lines to measure pulse oximeter and end-tidal carbon dioxide values of spontaneously breathing patients. Research suggests that capnography is a more sensitive measure of ventilation than standard modalities. This study aimed to determine whether adding capnography to standard monitoring improves the detection of respiratory depression in children undergoing esophagogastroduodenoscopy with sedation before hypoxemia occurs.* ***Materials and Methods:*** *We enrolled 100 children undergoing esophagogastroduodenoscopy with sedation in a pediatric endoscopy department. All children received standard monitoring and capnography and were randomized to study (n = 50; capnography monitor) and control (n = 50; blind to monitor) groups. The primary outcome was an oxygen desaturation rate < 90%.* ***Results:*** *The control group had higher rates of hypoventilation and oxygen desaturation per minute and received more interventions than the study group. Untimely interventions with hypoventilation were associated with oxygen desaturation < 90%. All episodes of hypoventilation were due to hypopnea; however, medication, gender, and sedation duration were not significantly associated with this outcome.* ***Conclusion:*** *Hypoventilation is common during sedation of pediatric patients undergoing esophagogastroduodenoscopy. Capnography monitoring provides fewer but timely interventions for apnea and hypoventilation and improves the quality of care during sedation. We, therefore, highly recommend the use of capnography monitoring.*

Keywords: *Esophagogastroduodenoscopy procedures, end-tidal carbon dioxide, capnography, hypopnea, hypoventilation, airway interventions*

Giriş ve Amaç: *Mikro-akım kapnografi, spontan soluyan hastalarda nazal hattı ile puls oksimetre, end-tidal karbon dioksit değerlerini izlemek için kullanılan bir cihazdır. Bugüne kadar ki kanıtlar, kapnografi kullanılmasının standart yöntemlerden daha hassas bir ventilasyon ölçümü olduğunu göstermektedir. Çalışmamızda, özofagogastroduodenoskopi yapılan çocukların sedasyonu sırasında standart izlemeye kapnografi eklenmesinin hipoksemi oluşmadan önce solunum depresyonunu tespit edip etmediğini belirlemeyi amaçladık.* ***Gereç ve Yöntem:*** *Pediatrik endoskopi bölümünde özofagogastroduodenoskopi uygulanan 100 çocuğa sedasyon uygulandı. İşleme alınan tüm çocuklara standart monitörizasyon ve kapnografi uygulandı ve randomizasyon ekibin kapnografi monitörünü (çalışma grubu) görüp görmemesi veya monitöre (kontrol grubu) kör olup olmaması durumuna göre yapıldı. Birincil sonuç, oksijen desatürasyon oranı <% 90 idi.* ***Bulgular:*** *Randomize olarak her gruba 50 kişi dahil edildi. Kontrol grubunda hipoventilasyon ve oksijen desatürasyon oranı daha yüksek bulundu. Havayolu müdahale oranları çalışma grubunda kontrol grubuna göre daha az bulundu. Hipoventilasyon ile zamanında yapılmayan müdahaleler oksijen desatürasyonu < 90 ile ilişkilendirildi. Tüm hipoventilasyon atakları hipopneye bağlıydı. Ilaç kullanımı, cinsiyet, sedasyon süresi bu sonuçla anlamlı olarak ilişkili bulunmadı.* ***Sonuç:*** *Özofagogastroduodenoskopi uygulanan pediatrik hastaların sedasyonu sırasında hipoventilasyon sıktır. Kapnografi kullanımı ise apne ve hipoventilasyon durumunda sayı olarak daha az ancak tam zamanında hava yolu müdahalesi sağlayıp, sedasyon sırasındaki kaliteyi artırır. Kapnografi kullanılmasını kesinlikle gerekli buluyoruz.*

Anahtar kelimeler: *Özafagogastroduodenoskopi işlemleri, end tidal karbondioksit, kapnografi, hipopne, hipoventilasyon, havayolu müdahaleleri*

INTRODUCTION

Esophagogastroduodenoscopy (EGD) is a standard test for the diagnosis and treatment of gastrointestinal disorders. Children undergoing EGD need sedation to reduce pain, promote comfort, and complete the procedures (1,2).

The problems that need to be addressed during sedation are mainly associated with an increased risk of drug-induced respiratory depression, upper airway obstruction resulting in hypoventilation, and apnea. Children are not always able to cooperate; therefore, spontaneous ventilation and sedation depth should be continuously monitored (3-5).

Standard monitoring procedures (electrocardiogram, heart rate [HR], noninvasive blood pressure [NI BP], pulse oximetry [SPO_2], respiratory rate, etc.) are not sufficient to ensure effective control of pulmonary ventilation and deep sedation in children under sedation (6). Alveolar hypoventilation may occur and lead to hypoxemia within several minutes, even in the case of normal oxygen saturation determined by SPO_2.

Capnography, or continuous end-tidal carbon dioxide ($ETCO_2$) monitoring, can detect hypoventilation and apnea before SPO_2 or clinical examination and significantly prevent the delay caused by SPO_2. In pediatric sedation procedures, capnography determines the effect of sedative drugs on respiratory depression and records for early indicators of respiratory failure (6,7). This study aimed to assess the effect of adding capnography to standard monitoring on detecting hypoventilation and hypoxemia during the sedation of children undergoing EGD.

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MATERIALS and METHODS

The study was approved by the Ethics Committee of Ümraniye Training and Research Hospital (B.10.1.TKH.4.34.H.GP.0.01) and conducted in the gastrointestinal pediatric endoscopy department of the hospital between March and May 2019. Informed consent was obtained from the parents of all subjects.

Based on the first digit of their Turkish ID numbers, 100 subjects were equally divided into two groups: study (odd) and control (even). The study group consisted of 50 children that met the following inclusion criteria: (i) aged 3–10 years, (ii) American Society of Anesthesiology physical status I–III, and (iii) scheduled for elective EGD. Exclusion criteria were (i) asthma, (ii) abnormal $ETCO_2$, (iii) airway deformities, (iv) an allergy history to anesthetics, (v) in need of baseline supplemental oxygen or intubation, and (vi) no toleration for capnography.

An 18-gauge intravenous cannula was inserted in all subjects on the dorsal side of their hands, and no premedication was given. In the procedure room, all subjects were placed in a lateral decubitus position, and standard monitoring procedures (electrocardiography, noninvasive systemic blood pressure, SPO_2 and bispectral index [BIS]) were recorded every 5 min. A nurse who did not perform the sedation of the subjects recorded $ETCO_2$ every minute.

A total of 20 mL ketofol was prepared with propofol 10 mg/mL and ketamine 10 mg/mL. The 1:1 combination contained 5 mg propofol/mL and 5 mg ketamine/mL. The induction dose of 1 mg/kg ketofol was administered and followed by a maintenance dose of 0.5 mg/kg infusion. A modified Ramsay sedation scale (RSS) was used to assess sedation before the procedure. When the RSS score was >4, an endoscope was inserted by a pediatric endoscopist. BIS was used to measure the depth of anesthesia/sedation, and RSS was used to adjust the dose of anesthetics throughout the procedure (Figure 1). BIS monitoring was kept in the range of 60 to 80 throughout the procedure. Supplemental oxygen was not used until oxygen desaturation < 90.

	RAMZAY SEDATION SCALE
Score	**Level of Sedation**
1	Patient is anxious and agitated or restless or both
2	Patient is cooperative, oriented, and tranquil
3	Patient responds to commands only
4	Patient exhibits brisk response to light tactile stimuli or loud auditory stimulus
5	Patient exhibits sluggish response to light tactile stimuli or loud auditory stimulus
6	Patient exhibits no response

Figure 1. Ramsay sedation scale

The capnograph was placed within sight of the anesthesiologist for the study group and out of sight for the control group. Alarms on the capnograph alerted the anesthesiologist in the study group to $ETCO_2$ levels <30 and >50 mmHg, the limits for hypopnea and bradypnea, respectively. Alarms on the capnograph were silenced in the control group. All treating staff controlled the main cardiorespiratory monitor. A nurse, blinded to the study, recorded any interventions related to airway management such as verbal or physical stimulation, airway repositioning, bag-valve-mask ventilation, and supplemental oxygen. The nurse did not inform the anesthesiologist of any abnormal values for the control group. The primary outcome of the study was an oxygen desaturation rate of <90. The duration of sedation was defined as the time between the administration of anesthetic and the end of the procedure. Drug infusion was discontinued at the end of the procedure. Recovery time was defined as the time between the termination of drug infusion and the achievement of a modified Aldrete score (9–10; Figure 2). SPO_2 < 90% for more than 10 s was defined as respiratory depression, whereas apnea was defined as the cessation of airflow for at least 20 s.

	MODIFIED ALDRETE SCALE
	Criteria Score
Activity	Moves all extremities **2** Moves two extremities **1** Unable to move extremities **0**
Respiration	Breathes deeply, coughs freely **2** Dyspneic, shallow or limited breathing **1** Apneic **0**
Circulation (blood pressure)	20% ± pre-anaesthetic level **2** 20-49% ± pre-anaesthetic level **1** 50%± pre-anaesthetic level **0**
Consciousness	Fully awake **2** Aro usable on calling **1** Not responding **0**
Oxygen Saturation	SPO_2> 92% on room air **2** Supplemental oxygen requirement to maintain SPO_2>90% **1** SPO_2< 90% with oxygen supplementation **0**

Figure 2. Modified aldrete scale

Statistical Method

Frequency analysis was used for nominal and ordinal parameters. Means and standard deviations were used for scale parameters. Differences between categorical parameters were analyzed using the chi-square test and likelihood ratios. Kolmogorov–Smirnov test was used for the normality test with Lilliefors correction. Independent samples t-test was used for

normally distributed data and the Mann–Whitney U test for non-normally distributed data. Statistical Package for the Social Sciences 17.0 for Windows was used to analyze data at a significance level of 0.05.

RESULTS

Researchers contacted 104 children for the study. Four children were excluded because of crying episodes and unavailable study personnel. A total of 100 patients were enrolled, with 50 randomized to each group (study and control). The mean ages of the study and control groups were 8.06 ± 2.22 and 7.32 ± 2.67 years, respectively (p = 0.197). The groups did not differ by gender and weight (p > 0.05).

Table 1 shows the demographic characteristics of the groups. The mean durations of sedation for the study and control groups were 8.68 ± 2.49 min and 6.74 ± 1.75 min, respectively (p = 0.0001). There was no significant difference in the total ketofol dose administered and mean respiratory rate between the groups (p > 0.05). Hypoventilation was observed in nine and ten patients in the study and control groups, respectively (p = 0.799). Oxygen desaturation was observed in two and ten patients in the study and control groups, respectively. This difference was statistically significant (p = 0.014; Table 2).

Two patients in the study group and ten patients in the control group received supplemental oxygen. Verbal and physical stimulation was adjusted for one patient in the study group and three patients in the control group. Shoulder roll was used only for one patient in the study group and two patients in the control group. Head tilt jaw thrust was adjusted for five patients in the control group. The control group received more air way-related interventions than the study group.

Table 3 presents the complications, which did not differ significantly between the groups (p > 0.05). There were no life-threatening adverse events and respiratory arrest. All patients were discharged after recovery.

Tablo 1. Demographic characteristics

	Study	Control	*p*
Age (years)	8.06±2.22	7.32±2.67	0.197[a]
Sex			
Male	25 (50.0)	19 (38.0)	0.227[b]
Female	25 (50.0)	31 (62.0)	
Weight (kg)	29.64±11.19	29.14±14.16	0.845[c]
ASA Class			
I	36 (72.0)	31 (62.0)	
II	9 (18.0)	19 (38.0)	0.004[b]
III	5 (10.0)	—	

[a]Mann-Whitney U test. bChi-square test. cIndependent samples t-test. ASA: American Society of Anesthesiology.

Tablo 2. Mean duration of sedation, total dose of ketofol, mean RR, and episodes of hypoventilation

	Study	Control	*p*
Mean duration of sedation (min)	8.68±2.49	6.74±1.75	0.0001[a]
Total ketofol dose	33.20±10.77	29.12±13.40	0.098[a]
Mean RR (breaths per minute)	21.12±5.70	20.78±5.33	0.721[a]
Any episode of hypoventilation	9 (18.0)	10 (20.0)	0.799[b]
Any episode of oxygen desaturation	2 (4.0)	10 (20.0)	

[a]Mann-Whitney U test. bChi-square test. cIndependent samples t-test. RR: Respiratory rate.

Tablo 3. Complications

	Study	Control	*p*
Aspiration	—	1 (2.0)	0.237[b]
Vomiting	2 (4.0)	2 (4.0)	N/A
Laryngospasm	1 (2.0)	2 (4.0)	0.554[b]
Stridor	2 (4.0)	4 (8.0)	0.395[b]

[a]Mann-Whitney U test. [b]Chi-square test. cIndependent samples t-test.

Tablo 4. Diagnosis

	Study	Control	*p*
Gastritis	13 (26.0)	17 (34.0)	
Celiac	6 (12.0)	4 (8.0)	
Achalasia	—	2 (4.0)	0.31[b]
Weight loss	—	4 (8.0)	
Unexplained anemia	12 (24.0)	5 (10.0)	

[a]Mann-Whitney U test. [b]Chi-square test. cIndependent samples *t*-test.

Table 4 shows the distribution of indications. The most common indication was gastritis in both study (26%) and control (34%) groups. The two groups did not differ by indications.

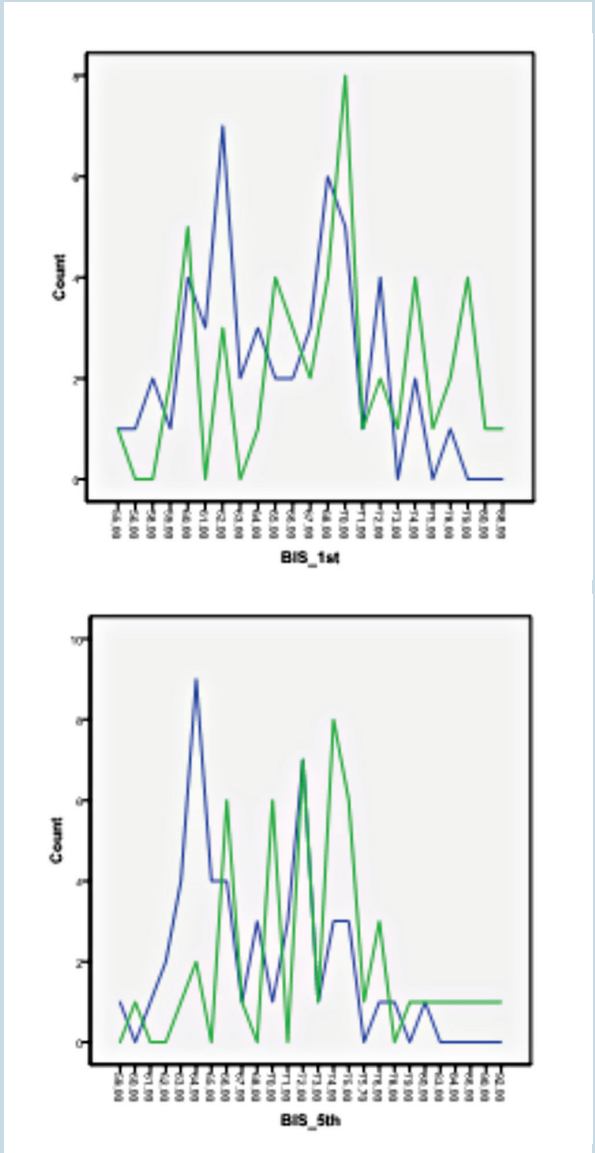

Figure 3. Bispectral index (BIS) distribution at 1-5 min.

The study group had higher SPO_2 at initial and 5 min, NI BP Max at initial, and NI BP Min at 5 min than the control group, whereas the other parameters were higher in the control group than in the study group. There was a statistically significant difference in HR, $ETCO_2$, and BIS at initial and 5 min (Figure 4) and NI BP Min at initial between the two groups ($p < 0.05$; Figure 3; Table 5).

Time-dependent changes were presented in Figures 5 and 6. $ETCO_2$ levels were sharply decreased in the control group with respect to the study group.

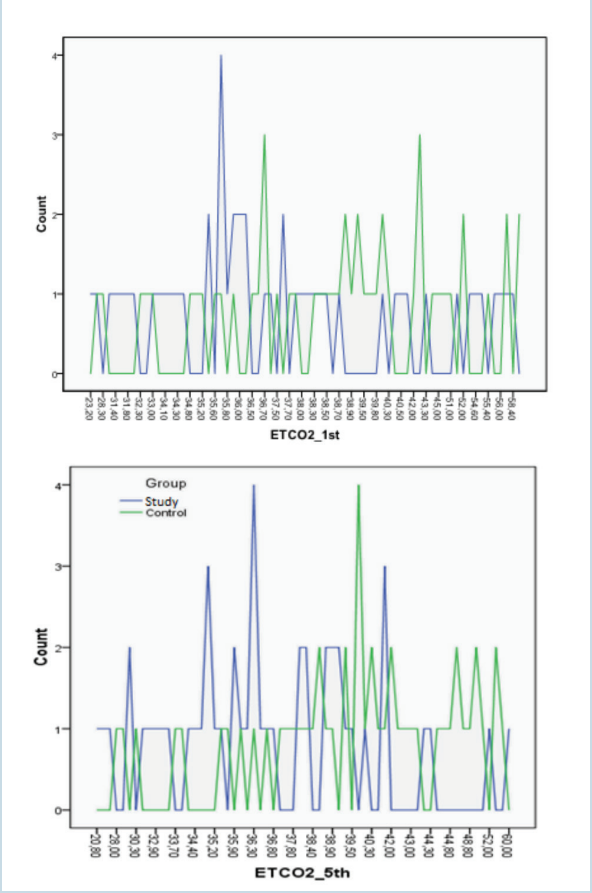

Figure 4. End-tidal carbon dioxide ($ETCO_2$) distribution at 1-5 min.

Tablo 5. Time-dependent changes in circulatory dynamics and categorical BIS scores distribution between groups

	Study	Control	*p*
HR initial	119.44±16.36	**126.12±12.78**	**0.025**[a]
HR 5 min	114.60±15.65	**124.26±13.48**	**0.001**[a]
SPO_2 initial	**96.76±2.26**	96.12±4.13	0.875[b]
SPO_2 5 min	**97.40±1.95**	96.80±2.98	0.710[b]
$ETCO_2$ initial	38.81±8.09	**40.85±7.62**	**0.022**[b]
$ETCO_2$ 5 min	36.77±6.02	**41.01±5.98**	**0.0001**[b]
BIS initial	65.34±5.12	**68.92±6.85**	**0.010**[b]
BIS 5 min	68.16±5.01	**73.01±6.41**	**0.0001**[b]
NI BP Max initial	109.72±9.35	**112.80±9.69**	0.071[b]
NI BP Max 5 min	**62.24±9.59**	59.86±7.50	0.242[b]
NI BP Min initial	107.16±9.81	**111.70±8.64**	**0.010**[b]
NI BP Min 5th min	**59.78±8.90**	57.38±6.63	0.365[b]

[a]Independent samples t-test. [b]Mann-Whitney U test. HR: Heart rate; SPO_2: Pulse oximetry; $ETCO_2$: End-tidal carbon dioxide; BIS: Bispectral index; NI BP: Noninvasive blood pressure.

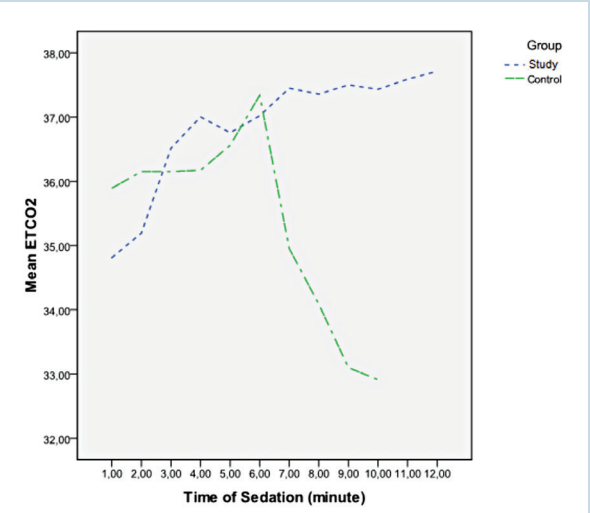

Figure 5. Timely distribution of end-tidal carbon dioxide ($ETCO_2$)

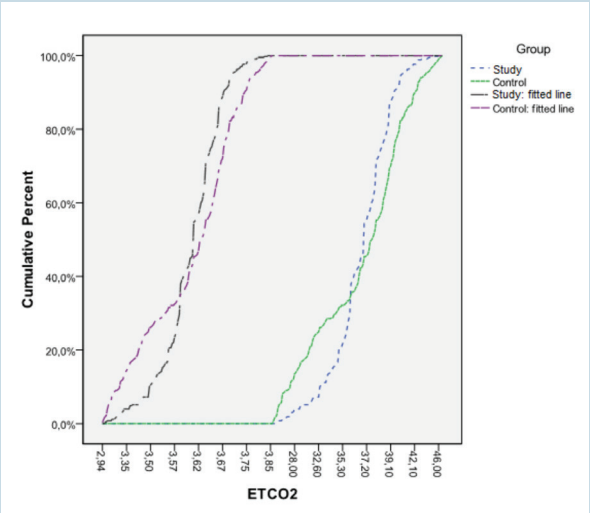

Figure 6. Time-dependent changes in end-tidal carbon dioxide ($ETCO_2$)

DISCUSSION

EGD has started to play a significant role in the diagnosis and treatment of digestive diseases in childhood over the past years, and therefore, there has been a growing interest in the determination of best practices for sedating children undergoing such procedures. The provision of sedation for EGD is, therefore, considered necessary if children are to remain comfortable and safe (8,9).

Respiratory monitoring should include the assessment of two components: oxygenation and ventilation. SPO_2 is a standard tool used to monitor oxygenation in patients under sedation. $ETCO_2$ analysis is used to measure the adequacy of ventilation (10,11).

Respiratory rate and SPO_2 do not always indicate the adequacy of alveolar ventilation during spontaneous breathing in real time. Airway obstruction caused by secretions or by the tongue and epiglottis falling back against the posterior wall of the pharynx does not necessarily reduce the respiratory rate. Inspection of the chest, even if performed by an experienced anesthesiologist, is still a subjective measure and a weak indicator of adequate ventilation (5,12). Arterial desaturation due to hypoventilation or obstruction (especially during oxygen administration) may occur later on.

Capnography is the monitoring of carbon dioxide concentration that may cause hypoxia during EGD. Capnography is, therefore, a particularly important indicator of altered ventilation in pediatric patients with a higher risk of early arterial desaturation due to reduced functional residual capacity (the volume of air present in the lung at the end of passive expiration) (13,14). However, capnography is not routinely recommended for patients receiving sedation. Current practice guidelines for sedation vary from institution to institution (15).

In this study, all episodes of hypoventilation were caused by hypopnea detected by the capnograph ($ETCO_2$ values < 30 mmHg without hyperventilation). Patients had hypoventilation episodes while sedated and increased over time in both groups, but the change in rate was significantly greater in the control group than in the study group (16,17). Capnography was shown to be superior in detecting all types of hypoventilation. An increased volume of dead space leads to low $ETCO_2$ values in hypopnea. Although apnea can be detected through physical examination or monitoring, hypopnea cannot. Burton et al. (2006) and Lightdale et al. (2006) reported that capnography detected apnea in 25% patients, whereas staff detected none as in our study (3,8).

Sedation leads to hypoxemia from hypoventilation over time. Langhan et al. (5) reported that 50% of children had hypopnea and were 6.6 times more likely to have oxygen desaturations during sedation. Oxygen desaturation was observed also in 25% of our subjects during sedation.

Capnography led to a decrease in the number of airway-related interventions in the study group, which might be due to its increased sensitivity for hypoventilation. Langhan et al. (5) reported that capnography decreased the number of staff interventions, which were simple and noninvasive like in our study. Furthermore, the staff was more attentive to the capnography data of the study group and performed interventions timely before reaching cut-off values related to abnormal capnography. The control group received more but delayed interventions because of oxygen desaturation as the anesthesiologist was blind to capnography, which also accounts for the difficulties of detecting hypoventilation.

No serious or less frequent adverse events were recorded. Ketofol was used in all subjects for all EGD procedures in this present study.

Ketofol, which consists of two pharmaceutical drugs, is considered safe when mixed in the same syringe. It provides analgesia, sedation, rapid recovery with hemodynamic stability, and fewer postprocedural complications with minimal respiratory depression (18–20). It also prevents hypopneic hypoventilation, resulting in low postoperative vomiting incidence and earlier discharge (21,22). Various sedative agents can cause different results.

This is one of the first randomized trials to assess the effect of adding capnography to standard monitoring during sedation in upper endoscopies in children. The results showed that capnography reduced hypoventilation episodes and oxygen desaturations.

Furthermore, endoscopy units are positioned in an environment where frequent distractions threaten patients' safety. In terms of patients' safety, its ease of use and interpretation we recommend its routine utilization.

There are several limitations to our present study. Patient morbidity associated with oxygen desaturations is not known. Also, ketofol was used in all patients as it is considered to be safe for sedation and hypopneic hypoventilation. Various sedative agents or combinations can lead to different adverse events.

Hypopneic hypoventilation is common among children and only detectable by capnography. The staff who had access to capnography monitoring performed fewer timely airway-related interventions during sedation, which was due to fewer episodes of hypoventilation and oxygen desaturation. It is recommended that future studies assess the effect of adding capnography to standard monitoring on more serious adverse events.

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