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Anxiety of parents and children undergoing gastrointestinal endoscopy correlates with sedative doses

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ABSTRACT

Aim: Sedation is a fundamental component of the pediatric gastrointestinal endoscopy (GIE). The dosing of drugs to be used for sedating the child is an important aspect of the efficacy and safety of procedural sedation. Besides, outpatient procedures are stressful situations for pediatric patients and also their families, and therefore, parental anxiety may affect children indirectly. The first aim of the study was to assess the association between parental anxiety and required sedative dose in children undergoing GIE. The second aim was to assess the factors associated with children's preoperative anxiety.

Material and Method: This study was a prospective, observational, and single-center study performed by the same fellowship-trained pediatric gastroenterology specialist and the same anesthesiology specialist. Parental anxiety was evaluated with the State-Trait-Anxiety-Scale (STAI) and children's anxiety was evaluated with the Modified Yale Preoperative Anxiety Scale (mYPAS). Midazolam, ketamine, propofol, and fentanyl were administered for the children's sedation. There were 2 comparisons in this study, the anxiety of parents according to mean STAI scores, and anxiety of children according to mYPAS scores.

Results: Of 120 children and parents, 87 parents (73%) and 57 children (48%) had high anxiety. Of 120 parents, 111 parents (92%) were mothers of the children. Younger children had higher anxiety levels. Before and the start of the GIE heart rates of children were higher both in the high anxiety group of parents and children. In sedatives, high anxiety parents' children and high anxiety children were required more ketamine dosages. ($p<0,05$)

Conclusion: Parental anxiety affects anxiety in children having GIE, and this increases the required sedative doses. Children's younger age, lower weight and high ASA scores were associated with children's preoperative anxiety.

Keywords: sedation, pediatrics, parent, endoscopy, preoperative anxiety

INTRODUCTION

Gastrointestinal endoscopy (GIE) is a diagnostic and therapeutic procedure used to examine the gastrointestinal tract in the pediatric population by pediatric gastroenterologists. Sedation, which is a fundamental component of pediatric GIE, is a safe and cost-effective alternative to general anesthesia (1). The two primary types of sedation for children undergoing GIE is general anesthesia in the operating room, and intravenous (iv) sedation in the outpatient endoscopy suite. The number of pediatric endoscopies performed in outpatient settings with sedation has increased over the past few decades (2). Children's sedation is different from the adult's, particularly in preschool-aged (3). Even though sedation seems safe in children, it is associated with serious adverse events like; apnea, bradycardia, laryngospasm, pulmonary aspiration, airway obstruction, or even death. An important aspect of the efficacy and safety of procedural sedation is the dosing of drugs to be used for sedating the child. Regardless of the procedure, technical advances in patient monitoring increase patient safety. In particular, the use of pulse oximetry, microstream capnography, and bispectral index (BIS) monitoring is highly reliable measurements for the detection of abnormal ventilation and anesthesia depth during procedures.

Ketamine and propofol are both highly effective and safe in children undergoing both upper and lower endoscopy. Ketamine has its anesthetic, analgesic, and amnestic properties, and propofol is a hypnotic agent for short procedures as it is short-acting and does not accumulate with multiple doses. Ketamine-propofol drug combination is usually used in procedural sedation for children (4).

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These procedures are stressful situations for pediatric patients and also their families. Parents of children undergoing outpatient surgery stay with their children both preoperatively and postoperatively, and therefore, parental anxiety may affect children indirectly (5, 6). This can result in decreased pain threshold and more anesthetic requirements in children during the procedure.

As to former, the literature includes studies on the association between preoperative children's anxiety with parent's occupation, educational background, and anxiety (7-9).

Until now, it has not been possible to identify the association between parental anxiety and the required anesthetic dose in children undergoing GIE. The first aim of this study was to determine the association between parental anxiety and required anesthetic dose in children undergoing GIE. The second aim was to assess the factors associated with children preoperative anxiety.

MATERIAL AND METHOD

This study was a prospective, observational, and single center study conducted between February 1, 2022 and May 1, 2022. The study was carried out with the permission of Umraniye Training and Research Hospital Ethics Committee (Date: 17/06/2022, Decision No:54132726-000-1757). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki. The study was registered to the Clinical Trials, NCT05210829. Children aged between 2-17 years with American Society of Anesthesiology (ASA) Physical Status I and II, who were scheduled to undergo elective outpatient GIE under sedation by the same fellowship-trained pediatric gastroenterology specialist and the same anesthesiology specialist, and their parents were considered for enrollment in this study. Study participation consent was obtained from parents before starting the procedure. An anesthesiology specialist examined all patients before the day of the procedure. The anesthesiology consent form was given by the family.

The patient's age, gender, height, weight, ASA score, the procedure to be performed (upper or upper and lower GIE), parent's educational status, occupations, children's anxiety scale, and separation scale were recorded by an anesthesia technician in the waiting room. Parental anxiety scale assessments were done by parents and collected by the anesthesia technician. The anesthesiology specialist did not see the children or parents in the waiting room.

Children's anxiety was evaluated with the Modified Yale Preoperative Anxiety Scale (mYPAS) in the presence of their parents 15 minutes before the procedure. The mYPAS is an observational measurement of children's anxiety with a cutoff score of 30, which is commonly used to define probable anxiety. It has 27 items divided into 5 categories: Activity, Vocalizations, Emotional Expressivity, State of Arousal, and Use of Parent. Higher scores indicate greater anxiety. The mYPAS was adapted for the Turkish population by Hatipoğlu et al. (10). The agitation of the child that occurred when the child separated from their parents was evaluated with the "Parental Separation Anxiety Scale". This four-point scale includes; 1- easy to separate, 2- sobbing but easy to cease, 3- crying loudly and difficult to stop but without holding the parents and not letting them go, and 4- crying loudly and holding the parents and not willing to let them go. Parental anxiety was evaluated with the State-Trait Anxiety Scale (STAI) by parents during the child was in the procedure. This self-report anxiety assessment contains two 20-item rating scales for measuring state (STAI-S) and trait (STAI-T) anxiety. Total scores range from 20 to 80, and higher scores indicate higher levels of anxiety with a cutoff score of 40, which is commonly used to define probable anxiety. The STAI was adapted for the Turkish population by Oner and Le Compte (11).

After recording the children's anxiety and separation scale, a 22G or 24G intravenous line was secured. Cardiac, respiratory, and BIS monitoring for sedation levels were performed. Nasal oxygen administration with end-tidal carbon dioxide ($etCO_2$) monitoring was started. All medications were given according to the protocol in the clinic. For the premedication, iv 0.05 mg/kg midazolam was administered to each patient. For sedation, the initial dose of ketamine was 1 mg/kg and, if necessary, up to a maximum of 2 mg/kg was administered. For moderate sedation, anesthesia will be applied with a BIS value of 60-70. Propofol 0.1 mg/kg, maximum 3 mg/kg sedation was administered if adequate sedation cannot be achieved or if wakefulness occurs during the procedure. It was multimodal sedation, that included both midazolam, ketamine, and propofol. Fentanyl was administered only in colonoscopies. The sedation level was monitored with both Ramsay Sedation Scale (RSS) and BIS. The procedure was not started before the patient had RSS of 5 and BIS between 60-70. Before starting the procedure, the BIS value, the amount of drug administered, the patient's oxygen saturation (SpO_2), heart rate (HR), and $etCO_2$ value were recorded. After the start of the procedure, the same data were recorded again. At the end of the procedure, the duration of the procedure and the total amount of drug administered were recorded, and the patient was transferred to the recovery unit. Nasal oxygen was provided for 30 minutes in the recovery unit, and SpO_2 and HR were monitored. Adverse effects such as laryngospasm, desaturation (SpO_2 <90%), respiratory depression, bradycardia, allergies, hiccups, nystagmus, nausea, and vomiting were recorded. Patients with a Modified Stewart Scale ≥ 6 were discharged from the unit.

Statistical Methods: Power analysis was run in order to evaluate the adequate size of the sample. In order to obtain a statistical power of 80 percent with effect size of 0,71 in the study, we needed to enroll a minimum of 2 × 31 subjects to detect significant differences between groups.

Mean, standard deviation, median, minimum, maximum value frequency, and percentage were used for descriptive statistics. The distribution of variables was checked with Kolmogorov-Simirnov test. Independent Samples t-test and Mann-Whitney U test were used for the comparison of quantitative data. Chi-Square test was used for the comparison of qualitative data. SPSS 28.0 was used for statistical analyses.

Results

Participants were 124 children aged between 2 to 17 years, who were scheduled to undergo GIE, between February 1, 2022, and May 1, 2022 by the same fellowship trained pediatrics gastroenterology specialist and the same anesthesiologist, and their parents. Two patients were excluded due to flu, which was recognized at the endoscopy unit, and two patients were excluded due to being coronavirus positive. One hundred and twenty patients were enrolled in the study. (**Figure 1**) Demographic variables of children and parents were presented in **Table 1**. Of 120 patients, the median age was 12 (7, 16) years with 57% female patients, and 18 patients were ASA II. (ulcerative colitis n= 10, asthma n= 3, diabetes mellitus n= 3, coeliac disease n=2) One hundred and one patients (84%) underwent upper GIE and 19 patients (16%) underwent lower GIE. Of 120 parents, 111 parents (92%) were mothers and 9 parents (8%) were fathers of the children.

Table 1. Demographic variables of patients

Variables	Total (n=120)
Age, yr	12 (7, 16)
Preschool (1-5 years)	20 (17)
School-aged (6-17 years)	100 (83)
Child gender Female	69 (57)
Weight, kg	42 (21, 53)
ASA	
I	102 (85)
II	18 (15)
Endoscopy	
Upper	101 (84)
Upper and lower	19 (16)
Parent	
Mother	111 (92)
Father	9 (8)
Parent education level, years	8 (8, 12)
Parent occupation status None	91 (75)

Data are presented as medians (interquartile ranges) or absolute numbers (percentages).

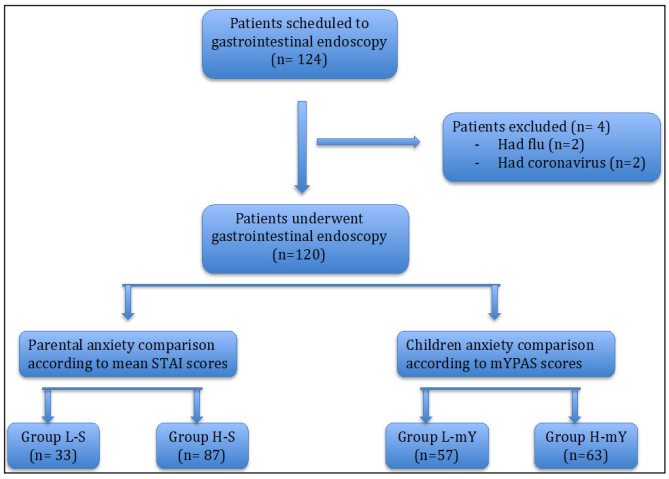

Figure 1. Flow chart

There were 2 comparisons in the current study, the anxiety of parents according to mean STAI scores, and anxiety of children according to mYPAS scores. According to mean STAI scores 87 parents (73%) had higher than 40 points, which indicated high anxiety (Group H-S). Thirty-three parents (27%) had 40 and lower than 40 points in mean STAI score, which indicated low anxiety (Group L-S). Parental education level and occupation status were not significantly different between groups. Mean STAI, STAI-S, and STAI-T scores were significantly different between groups. (p<0,001) There were no significant differences between groups in children's anxiety and separation levels. Before GIE heart rates of children in Group H-S were significantly higher than in Group L-S. (p<0,05) The start of the GIE heart rates of children in Group H-S was not significantly but higher than in Group L-S. (p=0,055) In anesthetic sedatives of children, ketamine dosage was significantly higher (p<0,05) and propofol dosage was not significantly but higher in Group H-S. Group H-S, which parents had more anxiety, children required more ketamine dosage than Group L-S. (p<0,05) There was no serious adverse event in the current study. Nausea and vomiting occurred in 29 patients; 8 (25%) patients in Group L-S, 21 (24%) in Group H-S, and there was no significant difference between groups. (**Table 2**)

In mYPAS score comparison; 57 children (48%) had higher than 30 points, which indicated high anxiety (Group H-mY). All high anxious 57 children's parents were in high anxiety group. Sixty-three children (52%) had 30 and lower than 30 points in mYPAS score, which indicated low anxiety (Group L-mY). Age, weight, and ASA of children were significantly different between groups. (p<0,05) Mean mYPAS scores were significantly different between groups. (p<0,001) Children separation scale, before and the start of GIE heart rates were significantly higher in Group H-mY. In anesthetic sedatives, ketamine dosage was significantly higher (p<0,05) and propofol dosage was not significantly but higher in Group H-mY. (**Table 3**)

Table 2. Parental anxiety comparison according to mean STAI scores

Variables	Group L-S (n=33)	Group H-S (n=87)	p value
Age, yr	13 (7, 16)	12 (7, 16)	0,846[m]
Preschool (1-5 years)	7 (22)	13 (15)	0,356[x2]
School-aged (6-17 years)	25 (78)	75 (85)	
Child gender			
Female	15 (47)	54 (61)	0,156[x2]
Weight, kg	46 (26, 53)	40 (20, 53)	0,381[m]
ASA			0,106[x2]
I	31 (94)	71 (82)	
II	2 (6)	16 (18)	
Endoscopy			0,970[x2]
Upper	28 (85)	73 (84)	
Upper and lower	5 (15)	14 (16)	
Parent			0,210[x2]
Mother	28 (85)	83 (95)	
Father	5 (15)	4 (5)	
Parent education level, years	8 (8, 12)	8 (8,12)	0,158[m]
Parent occupation status			0,115[x2]
None	21 (66)	70 (80)	
Parental STAI scores			
STAI-S	32 (26, 39)	49 (45, 54)	**<0,001[m]**
STAI-T	36 (31, 39)	45 (43, 50)	**<0,001[m]**
Mean	34 (31, 37)	48 (44, 51)	**<0,001[m]**
Children mYPAS	28 (28, 42)	28 (28, 46)	0,426[m]
Children separation scale			0,596[x2]
I	27 (82)	60 (69)	
II	2 (6)	13 (15)	
III	2 (6)	7 (8)	
IV	2 (6)	7 (8)	
Children before GIE			
HR	99 (81, 111)	107 (90, 120)	**0,034[m]**
SpO_2	100 (100, 100)	100 (100, 100)	0,273[m]
$EtCO_2$	36 (35, 40)	37 (26, 39)	0,855[m]
Children start of the GIE			
HR	100 (82, 112)	102 (93, 117)	0,055t
SpO_2	100 (100, 100)	100 (100, 100)	0,419[m]
$EtCO_2$	40 (26, 44)	38 (36, 40)	0,339[m]
Ketamine, mg/kg	1 (1, 1.4)	1.2 (1, 2)	**0,008[m]**
Propofol, mg/kg	0.3 (0, 0.5)	0.5 (0.1, 0.8)	0,127[m]
Fentanyl, mcg/kg	0 (0, 1)	0 (0, 1)	0,516[m]
GIE time, min	7 (6, 10)	8 (7, 12)	0,248[m]
Nausea and vomiting	8 (25)	21 (24)	0,898[x2]

Data are presented as medians (interquartile ranges) or absolute numbers (percentages). P-values in bold represent statistically significant results (P < 0.05). t: independent sample t-test, m: Mann-Whitney U test, X^2: Chi-square test, STAI: state trait anxiety scale, mYPAS: modified yale pediatrics anxiety scale, GIE: gastrointestinal endoscopy, HR: heart rate, SpO_2: oxygen saturation, $EtCO_2$: end-tidal carbon dioxide

Table 3. Children anxiety comparison according to mYPAS scores

Variables	Group L-mY (n=63)	Group H-mY (n=57)	p value
Age, yr	14 (11, 17)	8 (5, 13)	**<0,001[m]**
Preschool (1-5 years)	3 (5)	17 (30)	
School-aged (6-17 years)	60 (95)	40 (70)	
Child gender			
Female	33 (52)	36 (63)	0,233[x2]
Weight, kg	48 (39, 56)	23 (18, 45)	**<0,001[m]**
ASA			**0,005[x2]**
I	59 (94)	43 (75)	
II	4 (6)	14 (25)	
Endoscopy			0,625[x2]
Upper	54 (86)	47 (82)	
Upper and lower	9 (14)	10 (18)	
Parent			0,849[x2]
Mother	58 (92)	53 (93)	
Parent education level, years	8 (8, 12)	8 (8,12)	0,401[m]
Parent occupation status			0,601[x2]
None	49 (78)	42 (74)	
Children mYPAS	28 (28, 28)	45 (36, 65)	**<0,001[m]**
Children separation scale			**<0,001[x2]**
I	62 (98)	24 (42)	
II	1 (2)	15 (26)	
III	0 (0)	9 (16)	
IV	0 (0)	9 (16)	
Parental STAI scores			
STAI>40	45 (71)	43 (75)	0,620[x2]
STAI-S	45 (37, 51)	47 (41, 52)	0,185[m]
STAI-T	44 (37, 48)	44 (38, 48)	0,877[m]
Mean	44 (36, 49)	45 (40, 50)	0,351[m]
Children before the GIE			
HR	98 (85, 110)	110 (92, 121)	**<0,001[m]**
SpO_2	100 (100, 100)	100 (100, 100)	0,176[m]
$EtCO_2$	37 (36, 39)	37 (35, 39)	0,886[m]
Children start of the GIE			
HR	98 (85, 109)	113 (94, 123)	**<0,001[m]**
SpO_2	100 (100, 100)	100 (100, 100)	0,612[m]
$EtCO_2$	38 (36, 40)	38 (35, 40)	0,563[m]
Ketamine, mg/kg	1 (1, 1.5)	1.5 (1, 2)	**0,008[m]**
Propofol, mg/kg	0.3 (0, 0.7)	0.5 (0, 0.9)	0,631[m]
Fentanyl, mcg/kg	0 (0, 0)	0 (0, 0)	0,313[m]
GIE time, min	8 (7, 12)	8 (6, 11)	0,614[m]
Nausea and vomiting	11 (17)	18 (32)	0,071[x2]

Data are presented as medians (interquartile ranges) or absolute numbers (percentages). P-values in bold represent statistically significant results (P < 0.05). t: independent sample t-test, m: Mann-Whitney U test, X^2: Chi-square test, STAI: state trait anxiety scale, mYPAS: modified yale pediatrics anxiety scale, GIE: gastrointestinal endoscopy, HR: heart rate, SpO_2: oxygen saturation, $EtCO_2$: end-tidal carbon dioxide

DISCUSSION

The results of this study indicate that parental anxiety was associated with children's required anesthetic doses for sedation in GIE. All high anxious children (n=57) had high anxious parents. In 87 high anxious parents, 30 parents had low anxiety children. In our study, Group H-S required more ketamine and propofol than Group L-S. Likewise our study, other studies administered both ketamine and propofol with or without premedication to children in procedural sedations [4, 12, 13]. In a study with 125 children, who had a procedure in the emergency department, only ketamine was administered as a sedative agent and required more doses (1.5- 2 mg/kg) than in our study, in which we used multimodal sedatives (14). In addition, there was a formulation for the estimated dose of propofol to induce sedation in children, but it was hard to use in daily practice (15). This formulation included lots of calculations including body surface area. However, the optimal level of sedation differs according to the procedure. For example, in upper endoscopy, the major goal of sedation is to avoid gagging, and in colonoscopy, the goal of sedation is to avoid visceral pain (16).

In our study, we did not see any serious adverse effects of sedation like; desaturation, bradycardia. We believe that using multimodal sedation in outpatient settings protects children from serious adverse events. In one study, they used only ketamine sedation in children undergoing upper GIE and recorded 9.5% laryngospasm (17). Another study showed 20% of transient apnea in the use of only propofol for upper GIE (18). In adverse events, nausea

and vomiting were occurred in 29 children. Children with high anxiety showed higher incidence of nausea and vomiting without a significant difference (32% vs. 17%, p=0,071). In the literature there are conflicted results; Li et al. (19) showed no association between preoperative anxiety and postoperative nausea and vomiting, and Kallar and Jones (20) presented an increased preoperative anxiety results with a postoperative nausea and vomiting.

We did not find any significant difference in mYPAS scores in the comparison of parental anxiety. Similar to our results, Bumin and Uyar (21) showed that maternal anxiety levels did not have a significant association with children's anxiety. In contrast to our results, Cui et al. (9) a found positive correlation between mYPAS of the children and STAI-S score of parents in the younger aged group, but no significant difference in STAI-T scores of groups.

Before and the start of the GIE heart rates were higher in both Group H-S and Group H-mY. Supporting our results, previous literature showed that children's heart rate was positively associated with children's anxiety (22).

We showed that younger ages in children had more preoperative anxiety levels. This finding was consistent with other studies in the literature, which showed younger age was associated with higher preoperative anxiety in children (9, 22, 23). In addition, the current study showed that higher preoperative children anxiety, which included younger ages, was associated with higher preoperative separation levels. Previous literature proved that there was a correlation between age and the separation level of children. This finding might be a result of the older ages being more independent and they might have more prior experience of separation anxiety (24, 25).

The current study showed ASA II children were significantly higher preoperative anxiety levels in the comparison of children's anxiety. Similar to our results, Facco et al. (26) showed the level of anxiety was significantly related to the ASA physical status in adults. Patients belonging to ASA II and III had significantly higher anxiety levels than ASA I patients.

There are some limitations in the current study. One limitation was that we did not examine other factors that could affect the anxiety of the parents, such as parents' cognitive ability, children's or their sibling's previous surgery history. Another limitation was we did not record postoperative children's recovery time or parents' postoperative anxiety levels.

In conclusion, parental anxiety affects anxiety in children having GIE, and this increases the required sedative doses. Multimodal sedative administration might protect children from serious adverse events. These findings encourage further studies to investigate sedative doses and anxiety in both children and their parents in outpatient procedures.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study was carried out with the permission of Umraniye Training and Research Hospital Ethics Committee (Date: 17/06/2022, Decision No:54132726-000-1757).

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper and that they have approved the final version.

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