Original Article

Preparatory information reduces gastroscopy-related stress in children as confirmed by salivary cortisol

Burcu Volkan, Nevzat Aykut Bayrak[1], Cihat Ucar[2], Duygu Kara[3], Sedat Yıldız[4]

Department of Pediatric Gastroenterology, Erzurum Regional Training and Research Hospital, Erzurum, [1]Department of Pediatric Gastroenterology, Diyarbakır Children's Hospital, Diyarbakır, [2]Department of Physiology, Adıyaman University School of Medicine, Adıyaman, [3]Department of Anesthesia, Erzurum Regional Training and Research Hospital, Erzurum, [4]Department of Physiology, Inönü University School of Medicine, Malatya, Turkey

Abstract

Background/Aims: This study aimed to determine whether the anxiety levels of pediatric patients who undergo endoscopy are reduced after receiving preparatory information about the endoscopic procedure by monitoring their salivary cortisol (s-cortisol) levels.

Patients and Methods: A total of 184 children undergoing gastroscopy under sedoanalgesia were included in the study. All the patients received a brief explanation of the endoscopic procedure. Patients were divided into two groups; Group Unexplained did not receive any further information other than a brief explanation of the procedure, Group Explained received more detailed explanation of the procedure. To determine anxiety levels, saliva specimens were taken on the day before the procedure to examine cortisol levels before and after endoscopy. Anxiety scores before endoscopy were calculated by the modified Yale Preoperative Anxiety Scale. Patients were monitored throughout sedoanalgesia, including during the endoscopy, sedation and recovery, and total propofol dosages were recorded.

Results: Eighty-nine children undergoing gastroscopy (age 11.55 ± 2.52 years; 50.5% girls) constituted Group Explained and 95 children undergoing gastroscopy (age 11.44 ± 2.66 years; 56.8% male) constituted Group Unexplained. The anxiety score, duration of sedation, endoscopy and recovery, propofol dose, pre- and post-endoscopy s-cortisol levels were significantly reduced in Group Explained.

Conclusions: We demonstrated that when endoscopic procedure is explained broadly to a child, the procedural stress is significantly less, as measured by the s-cortisol levels and the anxiety questionnaire. It is important for the attending physician to explain all aspects of examination carefully.

Keywords: Endoscopy, preparatory information, procedural stress, salivary cortisol

Address for correspondence: Dr. Burcu Volkan, Department of Pediatric Gastroenterology, Marmara University, Pendik Regional Training and Research Hospital, Istanbul, Turkey.
E-mail: burcupisgin@yahoo.com

INTRODUCTION

Over the last few decades, upper gastrointestinal endoscopic procedures have frequently been performed worldwide for various pediatric gastrointestinal disorders. However, the procedure can cause severe anxiety, fear, pain and stress in children, which might affect the success of the procedure. Anxiety is an emotional state that causes great discomfort in anticipation of real or imagined hazards and is triggered by stress. In the vast majority of endoscopies,

Access this article online	
Quick Response Code:	Website: www.saudijgastro.com
	DOI: 10.4103/sjg.SJG_493_18

How to cite this article: Volkan B, Bayrak NA, Ucar C, Kara D, Yıldız S. Preparatory information reduces gastroscopy-related stress in children as confirmed by salivary cortisol. Saudi J Gastroenterol 2019;25:262-7.

intravenous (IV) sedation is the most preferred method to relieve anxiety, pain and discomfort associated with the procedure.[1,2] Despite the widespread use of IV sedation, it has not been effective in decreasing the pre-endoscopy anxiety suffered by a child.

The pediatric endoscopist is responsible for minimizing a child's pain and discomfort during the procedure. This objective includes avoiding adverse events related to the procedure and the sedation, as well as alleviating any anxiety and fear before the procedure. Uedo *et al.* demonstrated that music therapy during colonoscopy reduced salivary cortisol (s-cortisol) levels and suggested that music has a marked anxiolytic effect in adults.[3] Hagiwara *et al.* reported that an explanation of the endoscopic procedure before performing the initial endoscopy could reduce anxiety experienced by both children and parents.[4] In particular, before the procedure, children undergoing endoscopy should be informed of the procedure adequately and in an age-appropriate manner.

The hypothalamic-pituitary-adrenal (HPA) axis controls physiological stress by regulating the synthesis and secretion of glucocorticoids, especially cortisol.[5] Recent data suggest that the free form of cortisol in serum has a perfect correlation with s-cortisol.[6] S-cortisol has been used to determine the levels of stress in children with various medical conditions.

The purpose of this study was to determine whether the anxiety levels of pediatric patients who undergo endoscopy are reduced after receiving preparatory information about the endoscopic procedure by monitoring their s-cortisol levels.

PATIENTS AND METHODS

Patients and study design

This prospective and randomized study was conducted in the Erzurum Regional Training and Research Hospital and Diyarbakir Children's Hospital, Turkey, between August 2016 and February 2017. Children between the ages of 8–18 years undergoing diagnostic gastroscopy with IV sedoanalgesia for various reasons were included in the study. The sample size was calculated according to the data obtained from the paper written by Wennström *et al.*, which we found to be most similar to ours in terms of study design.[7] Hence, considering an alpha level of 0.05 and the power of the test as 90%, 76 subjects would be required to conduct a similar evaluation. However, we preferred to include 100 patients in each group as some patients might not be eligible to continue after the exclusion criteria were applied. Children with chronic disorders, such as chronic liver, renal, cardiac, or pulmonary diseases, malignancy, congenital malformations, neurological or psychological disorders, and a history of previous surgery or endoscopy were excluded. Patients who received steroids due to respiratory distress or presented with propofol allergy during the procedure and those with inadequate saliva sample/undetectable s-cortisol levels were also excluded. All the patients were determined to be Class I on the American Society of Anesthesiologists (ASA) physical status classification system. The local ethical committee approved the study protocol and written informed consent was obtained from the parents of all the children.

The study team in each center consisted of one pediatric gastroenterologist, one expert pediatric anesthesiologist and two pediatric endoscopy nurses. The expert pediatric anesthesiologist in each center was responsible for sedative drug administration and monitoring the patients throughout the procedure. All the patients received a brief explanation of the endoscopic procedure in the presence of their parents at the time the endoscopy decision, about 1 week before the endoscopy [Table 1]. The patients were randomized according to the order of referral to the outpatient clinic and divided into two groups. The first to present being included in the patient group who was given only brief explanation (Group Unexplained), and the second in the patient group who was given brief and detailed explanation (Group Explained). Group Unexplained did not receive any further information other than a brief explanation of the procedure. Group Explained received a more detailed explanation of the procedure and had their questions answered before the procedure by the pediatric gastroenterologists and the endoscopy nurses on the day of the endoscopy [Table 1].

Sample collection and anxiety scoring

To determine the basal cortisol levels (bSCL), saliva specimens were collected at home in the morning hours (08.00–12.00 AM) the day before the endoscopy and brought by the parents to the hospital. On the day of the endoscopy, the patients arrived at the hospital during the morning hours and the procedure was performed until 12.00 AM. The modified Yale Preoperative Anxiety Scale (mYPAS) was used to evaluate the anxiety levels of the patients and the second saliva sample (pre-SCL) was obtained just before (within 30 min) the endoscopy, at the same time.[8] Propofol was the only drug used for the purpose of sedation. After induction, the repeated bolus method was used, which comprised an initial induction dose of 2 mg/kg, and additional doses of 0.5 mg/kg every 3–5 min until deep sedation could be achieved. The sedation level was assessed by the Ramsey Sedation Score

Table 1: The endoscopy procedure explained to the patients and their parents

Brief explanation	Broad explanation
What is an endoscopy? Why it is required? The procedure will not start before the child goes to sleep. During the endoscopy the child will sleep and will not feel any major discomfort. The endoscope will be passed through the mouth, esophagus, stomach, and the small intestine. The doctor will view pictures of the child's digestive track on a TV monitor. After recovery, the child will be discharged.	The patient will be accompanied by his/her parents to the endoscopy room. An IV line will be placed; the child might feel some pain during this procedure. Then, by IV line, the sedation will be administered and the child will sleep. After sleeping the child will not feel any major pain or discomfort. The procedure will not start before the child goes to sleep. While lying on the left side, the endoscope, a flexible tube with a light and camera attached to it, with the thickness of a small finger, will be passed through the mouth into the esophagus, stomach and upper part of the small intestine. The doctor will view pictures of the child's digestive track on a TV monitor. This procedure will not interfere with breathing. After the procedure, the child will be observed in the recovery area until awake, accompanied by parents. The child might feel a temporary sore throat and bloating after the procedure. When fully recovered (probably within a few hours) the child will be discharged. The child can resume his/her usual diet and daily life next day, at the very latest.

and we intended to maintain a sedation level of Ramsey 4–5 during the procedure.[9] The patients were monitored throughout sedation by the anesthesiologist. The duration of endoscopy and sedation, the recovery time and the total administered propofol dosage were recorded. Another saliva sample (post-SCL) was obtained after full recovery, within 2 h after the endoscopy. All saliva samples were collected by having the patient expectorate into a cup.

Analysis of saliva samples

The s-cortisol levels (in ng/ml) were determined using the enzyme-linked immunosorbent assay (ELISA) method. After centrifugation (at 4000 g for 10 min), the clarified saliva supernatants were stored at − 80°C for later ELISA analysis. A cortisol-bovine serum albumin (BSA) stock solution was diluted with a carbonate buffer and 200 μL/well was added to a microtiter plate. The plate was incubated overnight at 4°C and washed with a wash buffer and then blocked by a blocking buffer (200 μL/well). Following the washing steps, the samples (40 μL/well) and diluted primary anticortisol antibody (antiserum) (40 μL/well) were added in duplicate and incubated at 37°C for 45 min. After washing, the biotinylated secondary anti-Rabbit antibody was added (100 μL/well) and the plate was incubated at 37°C for 30 min. Following washing, the streptavidin-peroxidase solution (100 μL/well) was added and the plate incubated for 15 min at 4°C. Then, the plate was washed again, and the substrate solution (150 μL/well) was added and incubated in the dark for 10 min. After incubation, the stop solution (50 μL/well) was added, and the absorbance was measured at 450 nm using a microplate reader. The intra-assay coefficient of variation (CV) was 7.8% and the inter-assay CV was 7.2%. The examiner who studied the saliva samples for cortisol levels was kept blinded.

Data analysis

The data were analyzed with a computer software program (IBM SPSS, version 20, IBM Corp., New York, USA). Continuous variables are presented as mean ± SD. Categorical variables are presented as numbers and percentages. The Student's *t*-test was used to compare the clinical data of the groups. The repeated measured analysis of variance (ANOVA) test was used to compare the changes in s-cortisol levels between the groups. Statistical *P* values < 0.05 indicated statistical significance.

RESULTS

Two hundred consecutive outpatients, fulfilling the eligibility criteria, were asked to participate and were randomized equally into two groups upon the decision to perform endoscopy. Thereafter, five patients from Group Explained and two patients from Group Unexplained were excluded because of undetectable s-cortisol in any of the saliva samples. Also, two patients each from Group Explained and Group Unexplained were excluded because of severe bronchospasm and IV steroid administration. Apart from this, we encountered propofol allergy in four patients of Group Explained and one patient of Group Unexplained, who received IV steroids and were excluded as well. In the end, a total of 184 patients were enrolled after the exclusion criteria were applied.

Table 2: Demographic properties of procedure explained and unexplained group

Parameter	Explained Group (*n*=89)	Unexplained Group (*n*=95)	*P*
Age (years)	11.55±2.52	11.44±2.66	0.773
Sex (% girls)	50.5	56.8	0.460
Basal s-cortisol level (ng/mL)	12.09±12.41	16.12±19.34	0.097

Data were presented as mean±standard deviation

Table 3: Procedural properties and cortisol levels of procedure explained and unexplained group

Parameter	Explained Group (*n*=89)	Unexplained Group (*n*=95)	*P*
Anxiety score	8.34±2.01	10.37±2.76	<0.001
Duration of sedation (minutes)	10.98±2.58	12.19±2.94	0.003
Duration of endoscopy (minutes)	8.51±1.93	9.2±1.94	0.016
Propofol dosage (mg/kg)	3.07±1.07	4.12±1.67	<0.001
Duration of recovery (minutes)	9.2±3.94	11.54±4.12	<0.001
Pre-endoscopy s-CL (ng/mL)	13.29±11.33	38.5±29.02	<0.001
Post-endoscopy s-CL (ng/mL)	13.71±11.44	21.82±20.57	0.001

All data were presented as mean±standard deviation, $P<0.05$ is significant.s-CL, saliva-cortisol level

There were no significant differences between Group Unexplained ($n = 95$) and Group Explained ($n = 89$) in terms of age, sex and the mean levels of basal salivary cortisol [Table 2]. The starting time of endoscopy was between 09.00–11.30 AM for every patient, with a maximum five patients per day in each center; this did not differ statistically between the groups. The anxiety score, duration of sedation, endoscopy and recovery, propofol dose, pre- and post-endoscopy s-cortisol levels were significantly reduced in Group Explained [Table 3]. We found that Group Unexplained had significantly higher levels of pre-endoscopy and post-endoscopy s-cortisol ($P < 0.01$ and $P = 0.02$, respectively) than Group Explained. There was a positive correlation between pre-endoscopy saliva cortisol level and anxiety score ($r = 0.360$, $P < 0.01$) [Figure 1]. We also observed higher mYPAS scores in Group Unexplained than in Group Explained (10.37 ± 2.76 vs. 8.34 ± 2.01). Moreover, the duration of endoscopy and the recovery time were significantly reduced in Group Explained compared to Group Unexplained (8.51 ± 1.93 vs. 9.2 ± 1.94 min and 9.2 ± 3.94 vs. 11.54 ± 4.12 min, respectively). This was also true for the administered propofol dose for adequate sedation (3.07 ± 1.07 vs. 4.12 ± 1.67 mg/kg).

DISCUSSION

In this study, we demonstrated that when an endoscopic procedure is explained broadly to a child, the procedural stress is significantly less, as measured by the s-cortisol levels and the anxiety questionnaire. Additionally, when endoscopy-related stress is reduced, the duration of sedation, endoscopy and recovery, as well as the administered propofol dose, decrease significantly. To the best of our knowledge, this is the first study which evaluated s-cortisol levels to define how the effect of pre-endoscopy preparation relates to the anxiety levels in children.

Cortisol is the key hormone in stress-related homeostasis. Free or protein-bound forms of cortisol exist in serum and the free form is biologically active.[6] During physiological stress, the free form of cortisol increases considerably in serum. Salivary cortisol correlates well with the free form of circulating serum cortisol level and its concentration in the saliva is independent of the saliva volume.[10] Obtaining saliva is simple and non-invasive, and is also recommended by the American-European Endocrinology Societies as one of the major screening tests for the Cushing's syndrome since 2008.[11] Previously, higher s-cortisol and amylase levels had been demonstrated in children undergoing dental procedures.[12–14] In a recent study, children undergoing sedation for invasive procedures had greater increases in s-cortisol levels compared to those undergoing sedation for non-invasive procedures, such as imaging studies.[15] A previous study reported s-cortisol concentrations >28 nmol/L to indicate a high stress response in children.[16] In our study, some patients in both groups had higher s-cortisol levels in different stages of the saliva sampling. While the majority of these patients were in the Unexplained Group, this might reflect a psychological rather than an interventional anxiety, as any endocrine disease state was excluded.

Compared to adults, pediatric patients tend to be more anxious about the endoscopic procedure itself, rather than the underlying disease.[17] This anxiety and stress may arise from fear of discomfort and lack of information or misinformation about the procedure.[18] Anxiety may prolong the procedure and the patient may experience more discomfort. Due to this, the medication necessary for adequate sedation may also increase.[1] Children, especially, need support to help them reduce the level of anxiety and, therefore, improve their tolerance during the procedure. There are studies showing that psychological preparation before surgery can reduce a patient's anxiety regarding

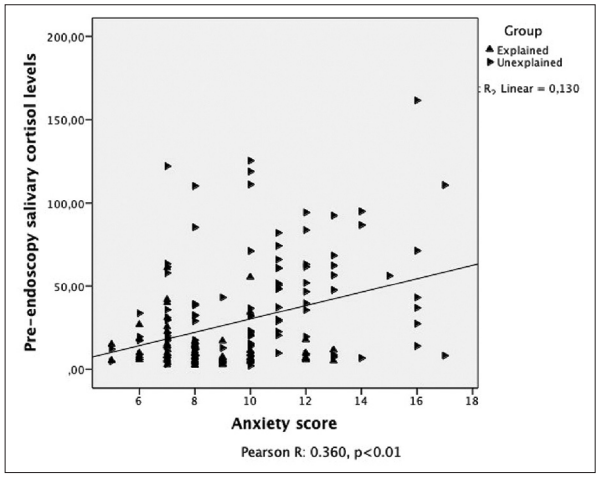

Figure 1: The correlation between pre-endoscopy saliva cortisol level and anxiety score

the procedure. These preparation procedures usually consist of verbal explanations,[4,17] guidebooks,[19] leaflets,[20] informative videos[21] and visual illustrations.[22] However, visual illustrations have been shown to reduce only the parents' anxiety, but not the child's.[22] We thought that videos and illustrative materials could be more frightening for children and may cause more anxiety. For this reason, we preferred a broad verbal explanation and answering questions in a detailed and age-appropriate manner, rather than using any visual materials.

Wennström *et al.* reported that perioperative dialogue corresponded to low postoperative s-cortisol levels and reduced postoperative morphine consumption for pain control in children undergoing outpatient surgery.[7] In another study, maternal presence during anesthesia induction and recovery period was associated with reduced stress and decreased s-cortisol levels in children undergoing throat surgery.[23] It was also reported that adult patients listening to music during colonoscopy had a lower pain score and s-cortisol levels than the control group.[3] In a recent meta-analysis, music therapy was found beneficial in anxiety control in several endoscopy procedures in adults, except colposcopy and bronchoscopy.[24] Similar to our results, studies involving psychological preparation before gastrointestinal endoscopy demonstrated that decreased anxiety levels were observed in children and their parents, who received an explanation about the procedure before endoscopy, and the dose of medication required for procedural sedation was decreased as well.[4,16,25] In concordance with the literature, we observed that the control group, which was not given preparatory information, had higher levels of pre-endoscopy and post-endoscopy s-cortisol, along with the mYPAS scores, than the test group, which received a broad explanation of the procedure. Additionally, the duration of endoscopy and the recovery time, as well as the administered propofol dose for adequate sedation were significantly reduced in the test group.

There are some limitations to this study that should be mentioned. First, our study did not measure any pre-endoscopy knowledge (family, friend, or media experience) about gastroscopy. Despite our attempts to answer all questions and correct any misinformation and misunderstanding regarding the procedure, there might be some bias in our data if the patient hesitated to ask some questions. Second, we did not measure parental anxiety, which might influence the child's stress. Moreover, we did not conduct a post-endoscopy questionnaire addressing whether the detailed explanation was found to be satisfactory by the patient.

In conclusion, we have determined that detailed preparatory information given to the child between the ages of 8–18 years helps to significantly alleviate procedural stress, measured by s-cortisol levels and an anxiety questionnaire. Moreover, when endoscopy-related stress is reduced, the duration of all stages of the procedure, as well as the administered propofol dose, decreases significantly. Therefore, it is important for the attending physician to explain all aspects of the examination carefully. Further studies with larger groups should aim to evaluate a standardized, age-appropriate psychological preparation method for children undergoing endoscopy.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Thomson A, Andrew G, Jones DB. Optimal sedation forgastrointestinal endoscopy: Review and recommendations. J Gastroenterol Hepatol 2010;25:469-78.
2. Van Beek EJ, Leroy PL. Safe and effective procedural sedation for gastrointestinal endoscopy in children. J Pediatr Gastroenterol Nutr 2012;54:171-85.
3. Uedo N, Ishikawa H, Morimoto K, Ishihara R, Narahara H, Akedo I, *et al.* Reduction in salivary cortisol level by music therapy during colonoscopic examination. Hepato gastroenterology 2004;51:451-53.
4. Hagiwara S, Nakayama Y, Tagawa M, Arai K, Ishige T, Murakoshi T, *et al.* Pediatric patient and parental anxiety and impressions related to initial gastrointestinal endoscopy: A Japanese multicenter questionnaire study. Scientifica 2015;797564:1-7
5. Chrousos GP, Kino T, Charmandari E. Evaluation of the hypothalamic-pituitary-adrenal axis function in childhood and adolescence. Neuroimmunomodulation 2009;16:272-83.
6. Törnhage CJ. Salivary cortisol for assessment of hypothalamic-pituitary-adrenal axis function. Neuroimmunomodulation 2009;16:284-9.
7. Wennström B, Törnhage CJ, Nasic S, Hedelin H, Bergh I. The perioperative dialogue reduces postoperative stress in children undergoing day surgery as confirmed by salivary cortisol. Paediatr Anaesth 2011;21:1058-65.
8. Jenkins BN, Fortier MA, Kaplan SH, Mayes LC, Kain ZN. Development of a short version of the modified Yale Preoperative Anxiety Scale. Anesth Analg 2014;119:643-50.
9. Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. Br Med J 1974;2:656-9.
10. Gallagher P, Leitch MM, Massey AE, McAllister-Williams RH, Young AH. Assessing cortisol and dehydroepiandrosterone (DHEA) in saliva: Effects of collection method. J Psychopharmacol 2006;20:643-9.
11. Guignat L, Bertherat J. The diagnosis of Cushing's syndrome: An Endocrine Society Clinical Practice Guideline: Commentary from a European perspective. Eur J Endocrinol 2010;163:9-13.
12. Furlan NF, Gavião MB, Barbosa TS, Nicolau J, Castelo PM. Salivary cortisol, alpha-amylase and heart rate variation in response to dental treatment in children. J Clin Pediatr Dent 2012;37:83-7.
13. Curcio WB, Abreu LG, Carrada CF, Ribeiro Scalioni FA, Ribeiro RA. Relationship between salivary cortisol levels and children's behavior during a dental examination. J Dent Child 2017;84:80-5.

14. Rodrigues Gomes SS, Barretobezerra AC, Maia Prado AC. Salivary biomarkers, vital signs and behaviour of pre-school children during their first dental visit. Eur J Paediatr Dent 2013;14:279-83.
15. Hsu AA, von Elten K, Chan D, Flynn T, Walker K, Barnhill J, *et al.* Characterization of the cortisol stress response to sedation and anesthesia in children. J Clin Endocrinol Metab 2012;97:1830-5.
16. Gröschl M, Rauh M, Dörr HG. Circadian rhythm of salivary cortisol, 17alpha-hydroxyprogesterone, and progesterone in healthy children. Clin Chem 2003;49:1688-91.
17. Mahajan L, Wyllie R, Steffen R, Kay M, Kitaoka G, Dettorre J, *et al.* The effects of a psychological preparation program on anxiety in children and adolescents undergoing gastrointestinal endoscopy. J Pediatr Gastroenterol Nutr 1998;27:161-5.
18. Jones MP, Ebert CC, Sloan T, Spanier J, Bansal A, Howden CW, *et al.* Patient anxiety and elective gastrointestinal endoscopy. J Clin Gastroenterol 2004;38:35-40.
19. Tanaka K, Oikawa N, Terao R, Negishi Y, Fujii T, Kudo T, *et al.* Evaluations of psychological preparation for children undergoing endoscopy. J Pediatr Gastroenterol Nutr 2011;52:227-9.
20. van Zuuren FJ, Grypdonck M, Crevits E, Walle CV, Defloor T. The effect of an information brochure on patients undergoing gastrointestinal endoscopy: A randomized controlled study. Patient Educ Couns 2006;64:173-2.
21. Callaghan P, Chan HC. The effect of videotaped or written information on Chinese gastroscopy patients' clinical outcomes. Patient Educ Couns 2001;42:225-30.
22. Riddhiputra P, Ukarapol N. Effect of systematic psychological preparation using visual illustration prior to gastrointestinal endoscopy on the anxiety of both pediatric patients andparents. J Med Assoc Thai 2006;89:231-5.
23. Ozdogan HK, Cetinalp S, Kuran G, Tugal O, Tahiroglu M, Herdem UE, *et al.* The effects of maternal presence during anesthesia induction on salivary cortisol levels in children undergoing tonsillectomy and/or adenoidectomy. J Clin Anesth 2017;39:64-6.
24. Wang MC, Zhang LY, Zhang YL, Zhang YW, Xu XD, Zhang YC. Effect of music in endoscopy procedures: Systematic review and meta-analysis of randomized controlled trials. Pain Med 2014;15:1786-94.
25. Lewis Claar R, Walker LS, Barnard JA. Children's knowledge, anticipatory anxiety, procedural distress, and recall of esophagogastroduodenoscopy. J Pediatr Gastroenterol Nutr 2002;34:68-72.