Distress During the Induction of Anesthesia and Postoperative Behavioral Outcomes

Zeev N. Kain, MD*†, Shu Ming Wang, MD*, Linda C. Mayes, MD†‡, Lisa A. Caramico, MD*, and Maura B. Hofstadter, PhD*

Departments of *Anesthesiology, †Pediatrics, and ‡Child Study Center and The Children's Clinical Research Center, Yale School of Medicine, Connecticut

We determined whether children who are extremely anxious during the induction of anesthesia are more at risk of developing postoperative negative behavioral changes compared with children who appear calm during the induction process. Children ($n = 91$) aged 1–7 yr scheduled for general anesthesia and elective outpatient surgery were recruited. Using validated measures of preoperative anxiety and postoperative behaviors, children were evaluated during the induction of general anesthesia and on Postoperative Days 1, 2, 3, 7, and 14. Using a multivariate logistic regression model, in which the dependent variable was the presence or absence of postoperative negative behavioral changes and the independent variables included several potential predictors, we demonstrated that anxiety of the child, time after surgery, and type of surgical procedure were predictors for postoperative maladaptive behavior. The frequency of negative postoperative behavioral changes decreased with time after surgery, and the frequency of negative postoperative behavioral changes increased when the child exhibited increased anxiety during the induction of anesthesia. Finally, we found a significant correlation (r) of 0.42 ($P = 0.004$) between the anxiety of the child during induction and the excitement score on arrival to the postanesthesia care unit. We conclude that children who are anxious during the induction of anesthesia have an increased likelihood of developing postoperative negative behavioral changes. We recommend that anesthesiologists advise parents of children who are anxious during the induction of anesthesia of the increased likelihood that their children will develop postoperative negative behavioral changes such as nightmares, separation anxiety, and aggression toward authority. **Implications:** Anesthesiologists who care for children who are anxious during the induction of anesthesia should inform parents that these children have an increased likelihood of developing postoperative negative behavioral changes.

(Anesth Analg 1999;88:1042–7)

Based on available behavioral and physiological data, the induction of anesthesia may be the most stressful procedure a child experiences during the entire perioperative period (1,2). Many children become agitated, have increased motor tone, cry, and may actively attempt to escape from anesthesia and nursing personnel (1,3). Various interventions, including sedative premedication, parental presence during induction, and preoperative preparation programs, are available to reduce the anxiety of a child during the perioperative period (4–7). Recent data, however, indicate that many anesthesiologists do not use any of these interventions routinely (8,9). Thus, it is likely that a significant number of children in the United States are distressed and fearful during the induction of general anesthesia.

Postoperative negative behavioral changes, such as nightmares and separation anxiety, may occur in up to 60% of all children undergoing general anesthesia and surgery (2,10). These behavioral changes are likely the result of an interaction between the distress the child experiences during the perioperative period and the individual personality characteristics of the child. Variables such as the age and temperament of the child and the state and trait anxiety of the parent have been identified as predictors for the occurrence of negative postoperative behavioral changes (2). There is a paucity of data, however, regarding a possible association between the distress the child experiences during the induction of anesthesia and the occurrence of negative postoperative behavioral changes.

Supported in part by Clinical Associate Physician Grant M1-RR06022, General Clinical Research Centers Program, National Center for Research Resources, NIH, The Arthur Vining Davis Foundations and the Patrick and Catherine Weldon Donaghue Medical Research Foundation.

Presented in part at the American Society of Anesthesiologists annual meeting, October 20, 1997, San Diego, CA.

Accepted for publication February 1, 1999.

Address correspondence and reprint requests to Zeev N. Kain, MD, Department of Anesthesiology, Yale University School of Medicine, 333 Cedar St., New Haven, CT 06510. Address e-mail to kain@biomed.med.yale.edu.

0003-2999/99

The purpose of this investigation, therefore, was to examine whether children who are notably distressed during the induction of anesthesia are more at risk of developing postoperative negative behavioral changes compared with children who appear calm during the anesthetic induction process.

Methods

Patients aged 1–7 yr (ASA physical status I or II) undergoing elective outpatient surgery and general anesthesia at the Yale-New Haven Children's Hospital were eligible for recruitment. In this longitudinal study, children were observed from the day of surgery until 2 wk after surgery. The primary outcome measure in this study was the presence or absence of negative behavioral changes after surgery. To avoid potential confounding variables, children were excluded from participation if they had experienced a recent stressful life event (see below), any history of chronic illness, history of prematurity, or developmental delay. Premedication was not administrated to any patients, and parental presence during the induction of anesthesia was not allowed. Parental presence during induction was, however, used as a rescue therapy (see below). The study was approved by the Yale University Review Board, and written, informed consent was obtained from all parents.

Detailed reliability and validity data regarding the following behavioral assessment tools were reported previously by our study group (6,11). These behavioral measures were applied to the patient population to either assess baseline characteristics or the outcomes or to serve as covariates in the analysis process.

Temperament, Anxiety, and Compliance

The EASI Instrument of child temperament (EASI) (12) is a parental report instrument that assesses four temperament categories (Emotionality, Activity, Sociability, and Impulsivity) in children and is widely used in the literature.

The State-Trait Anxiety Inventory (STAI) (13) is a self-report anxiety instrument that contains two separate 20-item subscales that measure trait (baseline) and state (situational) anxiety.

The Modified Yale Preoperative Anxiety Scale (mYPAS) (14,15) is an observational instrument of anxiety that contains 27 items in five categories (Activity, Emotional Expressivity, State of Arousal, Vocalization, and Use of Parents) that indicate anxiety in children in the surgical setting.

Primary Behavioral Outcome

The Post-Hospitalization Behavior Questionnaire (PHBQ) (16,17) is a self-report questionnaire for parents that is widely used in the literature and is designed to evaluate maladaptive behavioral responses and "developmental regression" in children after surgery.

Developmental regression refers to loss of previously gained developmental milestones (e.g., loss of bladder control, loss of language abilities—talks "baby talk"). The PHBQ consists of 27 items often cited in the literature as common behavioral responses of children after surgery or hospitalization. Six categories of anxiety are incorporated in this instrument, including General Anxiety, Separation Anxiety, Sleep Anxiety, Eating Disturbances, Aggression Against Authority, and Apathy/Withdrawal. For each item, parents rate the extent to which each behavior changed in frequency compared with before surgery. Response options for each of the 27 behaviors were much less than before surgery (−2), less than before surgery (−1), not changed (0), more than before surgery (+1), or much more than before surgery (+2). This instrument shows good agreement with psychiatric interviews with parents of preschool children ($r = 0.47$) and has been used in several investigations to document behavioral changes as a function of preoperative interventions (18).

One to ten days before surgery, all potential patients were screened for recent stressful life events by using Sandler and Block's modified version of Coddington's Life Event Scale for Children (19). Parents were asked to indicate whether their child had experienced any stressful life events in the month before surgery (e.g., divorce, family moved to new house, parent lost job, started new school). Children who presented with a recent stressful life event were not eligible to participate in the study. After recruitment, demographic data, temperament of the child (EASI), and trait anxiety of the parent (STAI) were obtained. Parents also completed a baseline PHBQ. Approximately half of the children (47%) underwent a behavioral preoperative preparation program that consists of providing information to the child and parent, an orientation tour of the operating room (OR) and recovery room, and modeling/medical play using dolls with child-life specialists.

Using observational (mYPAS) and self-report (STAI) validated anxiety measures, children and parents were evaluated in the holding area and on separation to the OR. If a child exhibited extreme anxiety on separation (as determined solely by the anesthesiologist managing the case), rescue therapy in the form of parental presence during induction was offered to the parents.

All patients were brought into the OR and placed on the OR table. Next, an Spo_2 probe was placed on the child's hand, and a scented anesthesia mask was presented to the child. O_2/N_2O was introduced in a ratio of 3:7 L flow, and halothane was started in a concentration of 0.2%, then increased every three breaths to a maximum of 2.5%. If a child became noncompliant during induction, the mask induction was continued as planned with the child restrained. Once anesthesia was induced, an IV cannula was inserted, and 0.1 mg/kg IV vecuronium was administrated to facilitate intubation. Anesthesia was maintained with O_2/N_2O and isoflurane; IV fentanyl (2–4 μg/kg) was administered. At the conclusion of all herniorrhaphies, the surgeons locally infiltrated the wound with 2–3 mL of 0.25% bupivacaine. Regional anesthesia was not performed on any of the patients in the study, and drugs such as ketamine, atropine, or droperidol were not used. The behavior of the child during induction was evaluated by an independent observer using the mYPAS at two time points: on entering the OR and on introduction of the anesthesia mask to the child.

Immediately on entering the postanesthesia care unit (PACU), the level of each child's "postoperative excitement" was graded according to a 3-point excitement scale (20,20a). This score ranges from 0 (child is lying quietly, with no crying) to 3 (thrashing and/or needs restraint and/or constant crying). The incidence of adverse effects in the PACU was also recorded. Additional pain medication (either 10–15 mg/kg oral acetaminophen or 1–2 μg/kg IV fentanyl) was administered at the discretion of the anesthesiologist. All parents were present in the PACU during their child's recovery period. On Postoperative Days 1, 2, 3, 7, and 14, parents were contacted over the telephone by a research nurse who was blinded to the child's behavior during induction. Parents were asked about behavioral changes in their child (PHBQ) and about their child's pain (visual analog scale). The nurse was able to contact 87% of patients on Day 1, 81% on Day 2, 86% on Day 3, 86% on Day 7, and 71% on Day 14.

The primary association examined in this study was the anxiety of the child during the induction of anesthesia versus the postoperative behavior of the child. Given a null correlation hypothesis of $r_{xy} = 0$, a two-sided α level of 0.05, and a power of 0.80, at least 88 patients were needed to complete this study (21). Descriptive statistics provide an overview of the relationships between the child-parent variables and the anxiety level in the child. Normally distributed data are presented as mean ± SD; skewed data are presented as median (25%–75%). The primary outcome was analyzed using a multivariate logistic regression model in which the dependent variable was the presence or absence of postoperative negative behavioral changes and the independent variables included variables such as anxiety of the child during induction, the follow-up time point after surgery, the type of surgical procedure, surgical history, age of the child, and the presence or absence of a preoperative preparation program. Results are reported as odds ratio (95% confidence intervals). To demonstrate the direction of the association between anxiety during induction and postoperative negative behavior changes over time, the entire cohort was divided into three subgroups: a calm group that included children who scored <25th percentile of the mYPAS on introduction of the anesthesia mask; an intermediate group that included children between the 25th and 75th percentiles of the mYPAS score; and an anxious group that included children who scored >75th percentile of the mYPAS. Statistical significance was assumed for $P \leq 0.05$. Data

Table 1. Baseline Characteristics of Patients

Characteristic	Preparation (+)	Preparation (−)
Age (yr)	5.3 ± 1.9	4.7 ± 1.5
Gender (%)		
Male	60	67
Female	40	33
Previous surgery (%)		
Yes	33	63
No	77	27
Child's temperament[a]		
Emotionality	11.1 ± 4.0	10.5 ± 2.6
Activity	15.1 ± 4.0	15.9 ± 3.9
Sociability	17.6 ± 2.9	17.7 ± 2.9
Impulsivity	12.4 ± 3.4	12.3 ± 4.2
Parental trait anxiety[b]	38.2 ± 7.2	36.0 ± 7.5
Holding area		
Child's anxiety[c]	23.3 (23–55)	28.3 (23–57)
Parental anxiety[b]	44.5 ± 13.7	41.4 ± 8.9

Values are mean ± SD or median (range).
[a] EASI Instrument of Child Temperament.
[b] State-Trait Anxiety Inventory.
[c] Modified Yale Preoperative Anxiety Scale.

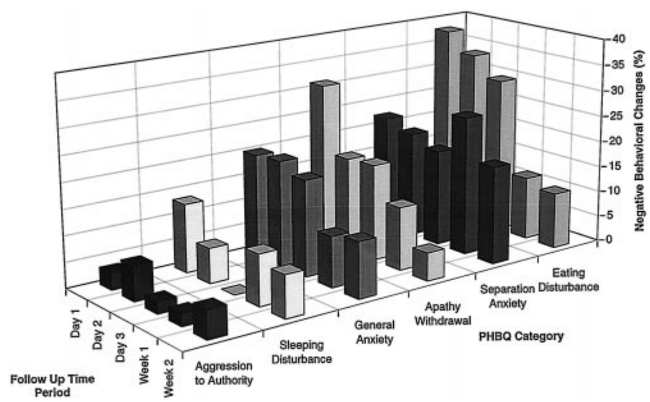

Figure 1. Negative behavioral changes as a function of postoperative time. The behavioral changes were assessed by using the Post-Hospitalization Behavioral Questionnaire (PHBQ).

Table 2. Multivariate Regression Model Relating Potential Predictors for Postoperative Negative Behavioral Changes

Predictor variables	Odds ratio	95% Confidence interval	P
Child's anxiety during induction (categorical)[a]	3.46	1.95–6.15	0.0001
Postoperative time point (per increase of one day)	0.56	0.46–0.68	0.0001
Age (per increase of 1 yr)	0.98	0.84–1.15	0.87
Preoperative preparation program (categorical)[b]	0.94	0.52–1.71	0.86
Prior surgery (categorical)[c]	1.61	0.91–2.86	0.09
Surgical procedure[d]			
PE tubes	0.17	0.10–0.60	0.006
ENT (other)	0.71	0.22–2.3	0.57
General	0.43	0.13–1.42	0.16
Other minor	1.13	0.34–3.68	0.83

PE = pressure-equalizing, ENT = ear-nose-throat.
[a] Anxious children (upper 50%) versus less anxious children (lower 50%).
[b] Participation in the program versus no participation.
[c] Previous surgery versus no previous surgery.
[d] Genitourinary surgery was selected as a reference category and all other surgeries were compared with it.

were analyzed by using SPSS version 6.1.1 (SPSS Inc., Chicago, IL).

Results

Seven children were not recruited to the study because of major life changes (e.g., death in the family and recent divorce). Baseline demographic and clinical variables of the 91 patients who were recruited to the study are shown in Table 1. Most children underwent otolaryngological surgical procedures (34%), followed by minor general surgery procedures (13%) and lower genitourinary procedures (11%). Rescue therapy in the form of parental presence during the induction of anesthesia was necessary for six patients.

Based on parental report, 67% (53 of 91) of the children exhibited new negative behaviors 1 day after surgery (Fig. 1). Of the children, 45% (33 of 71) continued to demonstrate negative behavior changes 2 days after surgery; in 23% (15 of 76), these behaviors persisted 2 wk after surgery (Fig. 1). The specific negative behavior(s) exhibited varied widely among children; however, bad dreams/waking up crying, disobeying parents, separation anxiety, and temper tantrums were common. In addition, children experienced an increased fear of doctors and hospitals.

A multivariate logistic regression model identified three independent predictors for the presence or absence of postoperative negative behavioral changes: 1) a child who was more anxious (upper 50% of mYPAS) had 3.5 times the risk for behavioral problems compared with a child who was less anxious (lower 50% of mYPAS) (95% confidence interval 1.9–6.1); 2) the frequency of negative postoperative behavioral changes decreased significantly with time after surgery (0.56 [0.46–0.68], per postoperative day); and 3) the type of surgical procedure influenced the presence or absence of postoperative behavioral changes (Table 2).

A univariate data representation indicated that on Postoperative Days 1–14, children in the anxious group had more negative behavioral changes compared with children in the calm group or the intermediate group (Fig. 2). Figure 3 demonstrates that genitourinary surgery was associated with the most postoperative negative behavioral changes and that pressure-equalizing tube placement was associated with the least postoperative negative behavioral changes.

Finally, we found a significant correlation (r) of 0.42 (P = 0.004) between the anxiety of the child on introduction of the anesthesia mask and the excitement score on arrival to the PACU—children who were more anxious during the induction of anesthesia had a higher excitement score on entrance to the PACU.

Discussion

We found that extreme anxiety during the induction of anesthesia is associated with increased occurrence of postoperative negative behavioral changes. We do not suggest a cause-effect relationship, but rather an association between two phenomena. We recommend that anesthesiologists advise parents of children who are anxious during the induction of anesthesia of the increased likelihood that their children will develop postoperative negative behavioral changes, such as nightmares, separation anxiety, and aggression toward authority.

Although many studies have assessed children's reactions to medical procedures and subsequent behavior (17,22), few have evaluated the relationship between children's reactions to specific hospital stressors and the later development of problems. This is

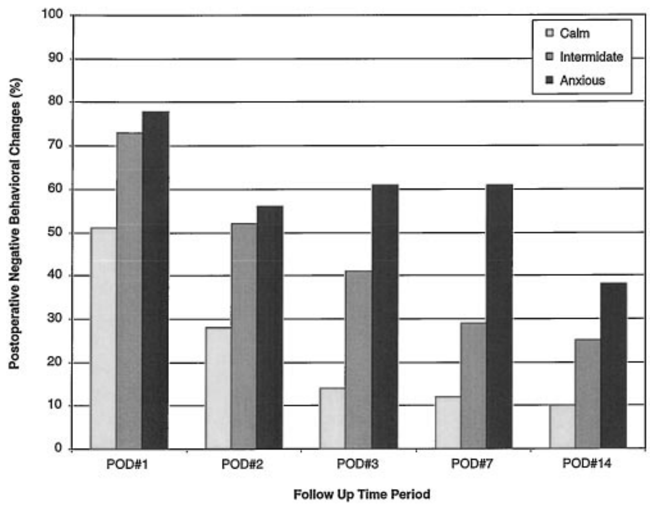

Figure 2. Patients with postoperative negative behavioral changes as a function of both postoperative time and anxiety during the induction of anesthesia.

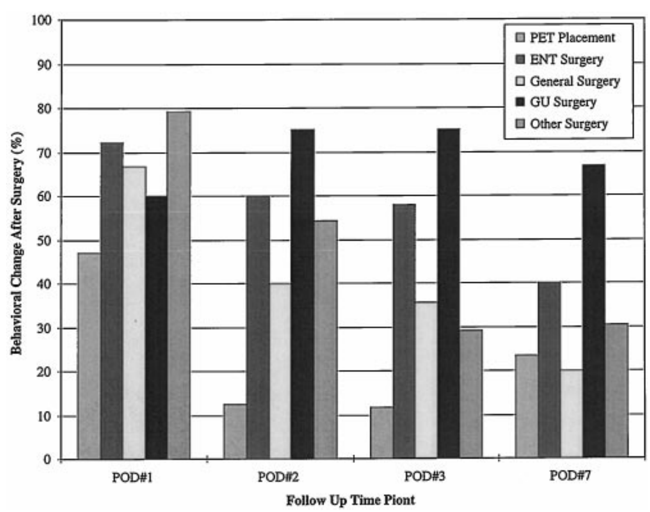

Figure 3. Patients with postoperative negative behavioral changes as a function of follow-up time point and surgical procedure. POD = postoperative day, PET = pressure-equalizing tube, ENT = ear-nose-throat, GU = genitourinary.

hardly surprising considering that a child undergoing anesthesia, surgery, and possibly admission is exposed to multiple stressors, which makes it very difficult to identify the isolated effect of each stressor. Two recent investigations, however, have suggested that a significant predictor for negative postoperative behavioral changes is the behavior of the child in the preoperative holding area (2,23).

A number of previous investigations provide data regarding the effects of the induction of anesthesia on postoperative behavior. In 1958, Eckenhoff (24) reported that "unsatisfactory" inductions are associated with significantly more negative postoperative personality changes compared with "smooth inductions" (57% vs 13%). Eckenhoff, however, did not control for confounding variables such as sedative premedication, anesthetic techniques, and the use of inpatients as subjects. The use of inpatients is particularly problematic because it is difficult to establish whether the personality changes observed were related to the induction of anesthesia or some other perioperative events. Furthermore, the behavioral instruments that were used to assess both the predictor variable (i.e., anxiety of the child during induction) and the primary end point (i.e., personality changes) were not validated, and no reliability data are provided about the instruments used.

Some 20 yr later, Meyers and Muravchick (25) compared postoperative behavioral responses in a group of children who underwent a "steal induction" versus a group of children who underwent an "awake" induction. One month after the children's discharge from the hospital, the investigators reported that the rate of behavioral changes was 88% in the awake group and 58% in the steal group. The steal group, however, was premedicated with atropine and droperidol, whereas the awake group was not premedicated. All subjects were asleep upon arrival in the OR. As with the earlier investigation, all children were also hospitalized, the primary end point of the study was not clear, and the behavioral instruments used were not validated.

In contrast to previous studies, the present investigation tried to avoid potential confounding variables, such as recent stressful life events, sedative premedication, parental presence during induction, and anesthetic drugs associated with behavioral sequelae. Moreover, only validated behavioral tools were used to assess both anxiety during the induction of anesthesia and the behavioral outcomes after surgery. This is the first study to document specific behaviors that may occur in children who are very anxious during the induction of anesthesia, the results of which are of particular importance because parents can be advised which behaviors may be expected.

Several methodological issues related to this study should be clarified. First, although we found that children who are markedly anxious during induction of anesthesia are significantly more likely to develop postoperative negative behavioral changes, it is important to emphasize that we have demonstrated not a cause-effect relationship, but rather an association between two phenomena. It is plausible that anxious children would have developed postoperative negative behavioral changes regardless of their anxiety during the induction of anesthesia. One method to directly answer this question is to conduct a randomized, controlled trial that includes matched pairs identical in all aspects except in their anxiety level during the induction of anesthesia. Such an experiment is clearly impossible to perform.

Second, our lack of control over the participation in the preoperative preparation program may represent a methodological design flaw. The standard of care in our institution is to offer participation in this voluntary preparation program to all patients who can be contacted before surgery. Our usual participation rate in the preoperative preparation program ranges from 40% to 60%. All patients participating in this study were offered participation in the preparation program—participation was voluntary. Although it is important that our study group has demonstrated in two separate trials that preoperative preparation programs are not effective in reducing the incidence of postoperative negative behavioral changes (7,26), this issue should have been controlled for in this investigation. To overcome this limitation, we included this variable in multivariate analysis. All analyses performed revealed that participation in the preparation program did not affect the outcome assessed.

In conclusion, we demonstrated that children who are anxious during the induction of anesthesia are also likely to develop postoperative negative behavioral changes. We do not suggest a cause-effect relationship, but rather an association. Anesthesiologists should make parents aware of the possibility that their child may develop negative behaviors in the 2 wk after surgery if their child was very anxious during the induction of anesthesia.

The authors thank Paul G. Barash, MD, for his critical review of this manuscript.

References

1. Schwartz BH, Albino JE, Tedesco LA. Effects of psychological preparation on children hospitalized for dental operations. J Pediatr 1983;102:634–8.
2. Kain ZN, Mayes LC, O'Connor TZ, Cicchetti DV. Preoperative anxiety in children: predictors and outcomes. Arch Pediatr Adolesc Med 1996;150:1238–45.
3. Kain Z, Mayes L. Anxiety in children during the perioperative period. In: Bornstein M, Genevro J, eds. Child development and behavioral pediatrics. Mahwah, NJ: Lawrence Erlbaum, 1996: 85–103.
4. Zuckerberg AL. Perioperative approach to children. Pediatr Clin North Am 1994;41:15–29.
5. Ullyot SC. Paediatric premedication. Anaesthesia 1992;39:533–6.
6. Kain Z, Mayes L, Wang S, et al. Parental presence during induction of anesthesia vs. sedative premedication: which intervention is more effective? Anesthesiology. 1999;89:1147–56.
7. Kain ZN, Mayes LC, Caramico LA. Preoperative preparation in children: a cross-sectional study. J Clin Anesth 1996;8:508–14.
8. Kain Z, Ferris C, Mayes L, Rimar S. Parental presence during induction of anesthesia: practice differences between the US and Great Britain. Paediatr Anaesth 1996;6:187–93.
9. Kain ZN, Mayes LC, Bell C, et al. Premedication in the United States: a status report. Anesth Analg 1997;84:427–32.
10. Kotiniemi LH, Ryhanen PT, Moilanen IK. Behavioural changes in children following day-case surgery: a 4-week follow-up of 551 children. Anaesthesia 1997;52:970–6.
11. Kain ZN, Mayes LC, Caramico LA, et al. Parental presence during induction of anesthesia: a randomized controlled trial. Anesthesiology 1996;84:1060–7.
12. Buss AH, Plomin R. Theory and measurement of EAS. In: Temperament: early developing personality traits. Hillsdale, NJ: L. Erlbaum, 1984.
13. Spielberger CD. Manual for the State-Trait Anxiety Inventory (STAI: Form Y). Palo Alto, CA: Consulting Psychologists Press, 1983.
14. Kain Z, Mayes L, Cicchetti D, et al. Measurement tool for pre-operative anxiety in children: the Yale Preoperative Anxiety Scale. Child Neuropsychol 1995;1:203–10.
15. Kain Z, Mayes L, Cicchetti D, et al. The Yale Preoperative Anxiety Scale: how does it compare to a gold standard? Anesth Analg 1997;85:783–8.
16. Vernon DT, Schulman JL, Foley JM. Changes in children's behavior after hospitalization. Am J Dis Child 1966;111:581–93.
17. Thompson R, Vernon D. Research on children's behavior after hospitalization: a review and synthesis. Dev Behav Pediatr 1993; 14:28–35.
18. Visintainer MA, Wolfer JA. Psychological preparation for surgical pediatric patients: the effect on children's and parents' stress responses and adjustment. Pediatrics 1975;56:187–202.
19. Sandler I, Block M. Life stress and maladaptation of children. Am J Comm Psychol 1979;7:425–40.
20. Keegan N, Yudkowitz F, Bodian C. Determination of the reliability of three scoring systems to evaluate children after general anaesthesia. Anesthesiology 1995;50:200–2.
20a. Kain Z, Mayes L, Wang S, et al. Effect of premedication on postoperative behavioral outcomes in children. Anesthesiology 1997;87:A1032.
21. Bornstein M, Cohen J. Statistical power analysis: a computer program (correlation module). Mahwah, NJ: Lawrence Erlbaum Associates, 1988.
22. Vernon D, Thompson R. Research on the effect of experimental interventions on children's behavior after hospitalization: a review and synthesis. Dev Behav Pediatr 1993;14:36–44.
23. Lumley MA, Melamed BG, Abeles LA. Predicting children's presurgical anxiety and subsequent behavior changes. J Pediatr Psychol 1993;18:481–97.
24. Eckenhoff JE. Relationship of anesthesia to postoperative personality changes in children. Am J Dis Child 1958;86:587–91.
25. Meyers EF, Muravchick S. Anesthesia induction technics in pediatric patients: a controlled study of behavioral consequences. Anesth Analg 1977;56:538–42.
26. Kain Z, Caramico L, Mayes L, et al. Preoperative preparation programs in children: a comparative study. Anesth Analg. 1998; 87:1249–55.