Preoperative Anxiety and Intraoperative Anesthetic Requirements

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The purpose of this study was to determine whether larger doses of anesthetics are required in the anxious patient to establish and maintain a clinically sufficient hypnotic component of the anesthetic state. Fifty-seven women undergoing bilateral laparoscopic tubal ligation with a propofol-based anesthetic regimen were enrolled in this cross-sectional study. Trait (baseline) and state (situational) anxiety were assessed in all patients immediately before surgery, and the propofol doses required for the induction and maintenance of anesthesia were recorded. A bispectral index monitor was used to assure that the hypnotic component of the anesthetic state was the same in all patients. We found that patients with high trait anxiety required more propofol for both the induction (2.1 ± 0.4 vs 1.8 ± 0.3 mg/kg; $P = 0.01$) and maintenance of anesthesia (170 ± 70 vs 110 ± 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$; $P = 0.02$), compared with patients with low trait anxiety. State anxiety, however, was not found to affect the propofol doses required for the induction or maintenance of anesthesia. Multiple regression models confirmed that Trait anxiety is an independent predictor for intraoperative propofol requirements ($P = 0.02$). We conclude that increased baseline (i.e., trait) anxiety is associated with increased intraoperative anesthetic requirements. Thus, we suggest that the initial dose of anesthetic administered by an anesthesiologist should be modified based on the anxiety level exhibited by the patient. **Implications:** The goal of this study was to assess the relationship between preoperative anxiety and intraoperative anesthetic requirements. We found that high baseline anxiety predicts increased intraoperative anesthetic requirements. We suggest that anesthesiologists should modify the initial induction dose based on the anxiety level exhibited by the patient.

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Preoperative anxiety is described as an unpleasant state of uneasiness or tension that is secondary to a patient being concerned about a disease, hospitalization, anesthesia and surgery, or the unknown (1). The reported incidence of preoperative anxiety in adults ranges from 11% to 80%, depending on the assessment method. The highest incidence was reported by psychiatrists using a validated psychological questionnaire (2), whereas the lowest was reported in studies using clinical impression only (3). Currently, data exist with respect to the effects of anxiety and fear before surgery on preoperative outcomes, such as heart rate, blood pressure, and neuroendocrinological changes (4), and postoperative outcomes, such as behavioral recovery and pain and analgesic requirements (5,6). There is a paucity of data, however, regarding the effects of preoperative anxiety on intraoperative outcomes. Nonetheless, it is assumed from clinical experience that larger doses of anesthetics are required in the anxious patient to establish and maintain a clinically sufficient hypnotic component of the anesthetic state.

Although some review articles indicate that increased anxiety before surgery is associated with increased intraoperative anesthetic requirements (7,8), this suggestion is based on earlier studies with questionable scientific validity (9–11). Some of these studies did not use validated scales to measure the predictor (i.e., anxiety), and others did not control for potential confounding variables, such as sedative premedication and the surgical procedure (9). Perhaps the most significant limitation of all previous studies, however, is their failure to control for anesthetic depth during the surgical procedure. That is, one can administer various doses of the same anesthetic to achieve "general anesthesia." Thus, the end point to which we titrate the anesthetic must be quantified *a priori.* A new electroencephalograph (EEG) monitor that uses bispectral analysis to generate a single number, termed the bispectral index (BIS), has been

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introduced into clinical practice (12). Bispectral analysis is a signal processing technique that decomposes the EEG and quantifies the level of synchronization in the signal, along with the traditional amplitude and frequency variables. This new monitor has been suggested to serve for measurement and monitoring of the hypnotic component of the anesthetic state (13–16).

Thus, through the introduction of this newer technology and the use of total IV anesthesia, we reexamined the question of whether increased anxiety before surgery is associated with increased intraoperative anesthetic requirements.

Methods

After institutional review board approval, 57 consecutive ASA physical status I or II women undergoing general anesthesia and bilateral laparoscopic tubal ligation were enrolled in this cross-sectional study. Patients with a history of a psychiatric illness, patients taking psychotropic medications, and those undergoing termination of pregnancy and tubal ligation were excluded. On the day of surgery, after recruitment, demographic data—including age, race, gender, marital status, educational level, income, and history of previous hospitalizations and surgery—were obtained. Next, trait and situational anxiety were assessed using the State-Trait Anxiety Inventory (STAI), and coping strategy was assessed using the Monitor-Blunter Style Scale (MBSS). No sedative premedication was offered to any of the patients.

The STAI is a widely used self-report anxiety assessment instrument (17). The STAI State subscale is designed to measure transitory anxiety states—that is, subjective feelings of apprehension, tension, and worry that vary in intensity and fluctuate based on the situation. The STAI Trait subscale measures relatively stable individual differences in anxiety proneness—that is, differences in the tendency to experience anxiety.

The MBSS was developed for patients undergoing medical procedures and identifies information seekers (high monitor)/information avoiders (low monitors) and distracters (high blunters)/nondistracters (low blunters) (18,19). The MBSS assesses coping style through four scenarios of stressful situations (i.e., "you are on an airplane that is experiencing severe turbulence. . ." etc.).

In the operating room, ASA standard monitors were applied. The EEG was recorded continuously using an Aspect A1000 Spectral EEG monitor (Aspect Medical Systems, Natick, MA). Along with an analog EEG, this device also provides a single BIS value (0–100) thought to be a measure of the hypnotic component of general anesthesia (16). Higher BIS values indicate lighter (more awake) hypnotic states (20). A BIS value of 40–60 indicates loss of consciousness and recall (16). General anesthesia was induced using propofol 1 mg/kg, followed by alfentanil 30 μg/kg. The propofol loading dose was mixed with IV 1% lidocaine at a ratio of 1:10. After observing patients for clinical response and allowing for BIS equilibration (60 s), additional small-increment doses of propofol (10–20 mg) were administered to achieve a BIS value of 40–60. Vecuronium 1 mg/kg was then administered to facilitate endotracheal intubation. Anesthesia was maintained with 50% O_2/N_2O and a continuous infusion of 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ IV alfentanil. A propofol infusion was started at 120–140 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and was adjusted to maintain a BIS value of 40–60. The investigators responded to changes in the BIS by changing the infusion rate by 10%. For example, if the BIS increased from 55 to 65, the propofol rate was increased by 10%. The investigator administering the propofol was blinded to the preoperative STAI state and trait anxiety scores. After surgery, the propofol and alfentanil infusions were discontinued, and the neuromuscular block was reversed using neostigmine and glycopyrrolate. Induction and maintenance doses of all anesthetics and the length of infusion were recorded.

The main association we examined was the amount of propofol required for the induction of anesthesia versus the level of preoperative anxiety as measured by using the STAI. Given previous reports and preliminary data obtained in our institution, a correlation hypothesis of $r = 0.35$ was presumed. For such an r with a two-sided α level of 0.05 and a power of 0.80, at least 55 patients were required to complete this study. Data were analyzed with the use of SPSS version 8.0 (SPSS Inc., Chicago, IL). Demographic data are summarized as the mean ± SD for interval data and by cross-tabulation for nominal data. The association between preoperative anxiety, trait anxiety, and coping style to intraoperative propofol bolus and intraoperative infusion rate was first measured by a Pearson correlation coefficient (r). The cohort of patients was next stratified into three groups based on their state and trait anxiety scores: low-anxiety group (<25% STAI scores; $n = 15$), medium-anxiety group (25%–75% STAI scores; $n = 28$), and high-anxiety group (>75% STAI scores; $n = 14$). Stratification was performed based on Spielberger's manual (17). Induction and intraoperative propofol requirements of the three groups were compared by using a one-way analysis of variance. The Bonferroni *post hoc* analysis was used to locate the differences among the three groups and to correct for multiple comparisons. Finally, a stepwise linear regression analysis was used to determine which of the variables deemed relevant by the literature and our data could predict the intraoperative

Table 1. Characteristics of Study Population

Characteristic	
Age (yr)	30.74 ± 5.19
State anxiety (STAI-S)	44.33 ± 12.27
Trait anxiety (STAI-T)	39.75 ± 8.8
Socioeconomic status[a]	41.92 ± 14.5
Weight (kg)	72.84 ± 18.87
Race (%)	
African-American	35.7
Caucasian	28.6
Hispanic	30.4
Asian	5.4
Previous surgery	
Yes	64.3
No	35.7

Values are mean ± SD.
$n = 57$.
STAI = State-Trait Anxiety Inventory.
[a] Hollingshead Index of Social Position.

anesthetic requirement of propofol. All multiple regression models were performed using the SPSS computer program. Comparisons were considered significant if $P < 0.05$.

Results

Fifty-seven patients were enrolled in this study. Baseline characteristics are presented in Table 1. The patients were women 21–41 (31 ± 5) yr old; 64% had undergone a previous surgery. Self-report anxiety of the patients, as assessed using the STAI before surgery, was 44 ± 12, and the Trait anxiety was 40 ± 9. The average propofol bolus patients required for the induction of anesthesia was 1.85 ± 0.45 (1.0–2.7) mg/kg. An average of 140 ± 50 (80–270) $\mu g \cdot kg^{-1} \cdot min^{-1}$ IV propofol was required intraoperatively for the maintenance of anesthesia. The propofol infusion time ranged from 19 to 103 min (median 36 min), and the duration of surgery ranged from 31 to 120 min (median 48 min).

Univariate Analysis

To examine the associations between demographic and personality variables with intraoperative anesthetic requirements, Pearson correlation coefficients were calculated. As expected, a patient's state and trait anxiety were significantly correlated with each other ($r = 0.53$, $P = 0.0001$). We found that increased preoperative state anxiety was not significantly correlated with the propofol bolus required for the induction of anesthesia ($r = 0.15$, $P = 0.26$), nor was the intraoperative propofol infusion rate required for maintenance ($r = 0.16$, $P = 0.12$). In contrast, a correlation was observed between trait anxiety and the propofol dose required for the induction of anesthesia ($r = 0.30$, $P = 0.03$) (Figure 1A). In addition, a moderate correlation was found between trait anxiety and the intraoperative propofol infusion rate ($r = 0.38$, $P = 0.005$) (Figure 1B). Finally, no correlation was found between coping style and the amount of propofol required for the induction ($r = -0.11$, $P = 0.24$) or maintenance of anesthesia ($r = -0.04$, $P = 0.40$).

Propofol requirements of the three anxiety groups were then compared. The propofol dose required for the induction of the high trait anxiety group ($n = 14$) was larger than that required for induction in the medium trait anxiety group ($n = 28$), which was larger than that required for induction in the low trait anxiety group ($n = 15$) (2.1 ± 0.4 vs 1.8 ± 0.3 vs 1.7 ± 0.5 mg/kg; $P = 0.01$). Bonferroni *post hoc* analysis demonstrated that the high trait anxiety group required significantly more propofol than the low trait anxiety group ($P = 0.01$). Similarly, the dose of propofol required for the maintenance of anesthesia was larger in the high trait anxiety group compared with the medium and low trait anxiety groups (170 ± 70 vs 140 ± 40 vs 110 ± 20 $\mu g \cdot kg^{-1} \cdot min^{-1}$; $P = 0.03$). Bonferroni *post hoc* analysis again demonstrated that the high trait anxiety group required significantly more propofol than the low trait anxiety group ($P = 0.02$).

When the low, medium, and high state anxiety groups were compared, however, no differences were found for the induction (1.7 ± 0.4 vs 1.9 ± 0.5 vs 1.9 ± 0.4 mg/kg; $P = 0.32$) or maintenance propofol doses required (120 ± 50 vs 150 ± 50 vs 140 ± 40 $\mu g \cdot kg^{-1} \cdot min^{-1}$; $P = 0.45$).

Multiple Regression Analysis

To evaluate the unique contribution of each variable to the prediction of intraoperative anesthetic requirements, two stepwise multiple regression models were constructed. In the first, the propofol bolus required for induction was the dependent variable, and the independent variables included trait anxiety, age, social status, previous surgery, and race. We found that the overall model accounted for 25% of the variance, with trait anxiety accounting for 13% of the variance ($F = 3.2$, $P = 0.02$) and race accounting for 10% of the variance ($F = 1.73$, $P = 0.03$). In the second model, intraoperative propofol requirement was the dependent variable, and the independent variables included trait anxiety, age, social status, previous surgery, and race. We found that the overall model accounted for 31% of the variance, with trait anxiety accounting for 16% of the variance ($F = 2.5$, $P = 0.01$) and race accounting for 8% of the variance ($F = 1.8$, $P = 0.02$).

Discussion

Our goal was to assess the relationship between preoperative anxiety and intraoperative anesthetic requirements, controlling for the hypnotic component of

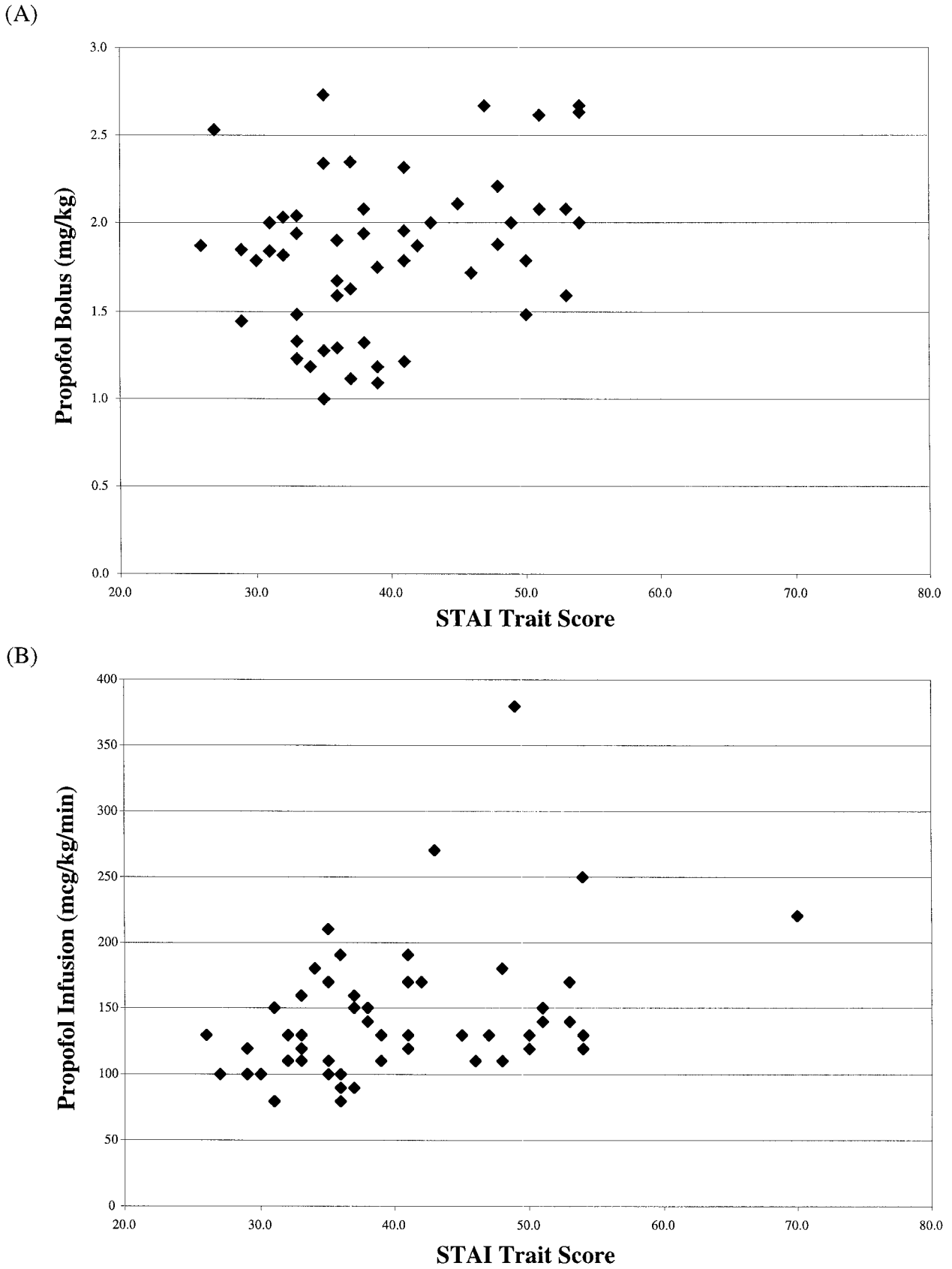

Figure 1. Correlation coefficient between trait anxiety and intraoperative anesthetic requirements. STAI = State-Trait Anxiety Inventory.

the anesthetic state and surgical procedure. We found that situational (i.e., state) anxiety immediately before surgery is not associated with intraoperative anesthetic requirements. In contrast, high baseline (i.e., trait) anxiety does predict increased intraoperative anesthetic requirements.

Previous studies published in the psychological and anesthesia literature have yielded contradictory findings. Williams et al. (9) suggested that highly anxious patients require a greater amount of sodium thiopental to induce anesthesia than less anxious patients. This study, however, did not use validated measures to assess preoperative anxiety and did not control for potentially confounding variables, such as sedative premedication, surgical procedure, and depth of anesthesia (9). Goldman et al. (11) assessed state anxiety in 53 women presenting for gynecological surgery who underwent the induction of general anesthesia using alfentanil and methohexitone. The investigators reported that preoperative anxiety seems to correlate with the amount of methohexitone required, but this relationship was not statistically significant. As with the study by Williams et al., the investigators did not define the end point for administering additional methohexitone boluses in their patients.

At the onset of the present investigation, we realized the various methodological limitations of previous studies. These limitations may in part be explained by the fact that previous means to assess anesthetic depth were either not precise or too complex to interpret (e.g., EEG); therefore, it was difficult to determine exact anesthetic requirements. "State of anesthesia" is suggested to consist of a triad: unconsciousness and lack of recall, analgesia, and muscle relaxation (22). It is now recognized that because individual anesthetics provide a unique spectrum of pharmacological actions, the concept of "anesthetic depth" must be revised to reflect the three components of the anesthetic state (16). As the BIS monitor has been reported to measure the hypnotic component of the anesthetic state (15,22,23), we decided to incorporate this technology into our study. That is, using the BIS monitor allowed us to compare the anesthetic requirements necessary to maintain the same hypnotic state (i.e., predefined end point) for the same surgical procedure. In addition, BIS monitoring has been reported to be particularly useful when used with patients undergoing propofol-based anesthetics (16).

We also recognized *a priori* that 1) a validated measure to assess anxiety must be used; 2) the anesthetic technique must be well defined; and 3) the surgical procedure must be controlled. The best known tool for anxiety evaluation is Spielberger's STAI, which has been used in more than 1000 research studies published in peer-reviewed literature (24). In fact, the STAI was referred to recently in a major anesthesia journal as the "gold standard" for measuring preoperative anxiety (25). In this investigation, we used the STAI to assess both the situational (state) and the baseline (trait) anxiety of the patients. Our anesthetic technique was well defined *a priori* and consisted of only one variable (propofol dose), which was easily defined and measured. We also controlled for the surgical procedure and enrolled only healthy women undergoing laparoscopic tubal ligation with no history of effective disorders.

Several limitations concerning the design of our study must be addressed. First, the anesthetic technique used for patients in this study included N_2O, alfentanil, and propofol. Although the propofol infusion rate was changed based on the BIS value, the N_2O and alfentanil concentrations were administered in a fixed dose throughout the procedure. By using N_2O and alfentanil, we may have decreased the variability in the study population, and a greater difference among the groups might have been found if N_2O and alfentanil had not been added as a baseline anesthetic dose. Neither N_2O (26) nor alfentanil (27) have been reported to affect the BIS value significantly. Second, we responded to changes in the BIS value by changing the IV infusion rate of propofol. Although the propofol infusion titration technique has clinical relevance, this method does not assure that brain concentrations of propofol change as the IV infusion rates change. Measuring blood concentrations of propofol or using a target-control infusion system with a three-compartment pharmacokinetic model (28) would have been more appropriate for this study design.

In conclusion, we demonstrated that there is a moderate correlation between baseline anxiety and the amount of propofol required for the induction and maintenance of anesthesia. Thus, we suggest that the initial dose of induction drug administered by an anesthesiologist should be modified based on the anxiety level exhibited by the patient.

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