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Preoperative anxiety and pain sensitivity are independent predictors of propofol and sevoflurane requirements in general anaesthesia

H. K. Kil[1], W. O. Kim[1], W. Y. Chung[2], G. H. Kim[1], H. Seo[3] and J.-Y. Hong[3]*

[1] Department of Anesthesiology and Pain Medicine, Anesthesia and Pain Research Institute and [2] Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea
[3] Department of Anesthesiology and Pain Medicine, Asan Medical Center, Ulsan University College of Medicine, 388-1 Pungnap 2-dong, Songpa-gu, 138-736 Seoul, Republic of Korea

* Corresponding author. E-mail: jenyhongg@hanmail.net

Editor's key points

- Preoperative factors (e.g. anxiety, pain sensitivity) may impact on the perioperative period and long-term outcomes.
- Propofol doses correlated with state and trait anxieties dependent on anaesthetic depth.
- Postoperative pain was most strongly correlated with preoperative pain sensitivity, rather than anxiety.
- Identifying patients preoperatively who are likely to require higher anaesthetic and analgesic doses should aid individualized postoperative management.

Background. Psychological factors are thought to drive inter-patient variations in anaesthetic and analgesic requirements. This cross-sectional study investigated whether preoperative psychological factors can predict anaesthetic requirements and postoperative pain.

Methods. Before total thyroidectomy, 100 consecutive women completed the Spielberger's State–Trait Anxiety Inventory (STAI) and the pain sensitivity questionnaire (PSQ). Target-controlled propofol was administered for induction of anaesthesia, and sevoflurane–oxygen–air was given to maintain equal depths of anaesthesia, as determined by bispectral index (BIS) monitoring.

Results. Patients with higher anxiety scores (state and trait) required greater amounts of propofol to reach light (BIS=85) and moderate (BIS=75) levels of sedation, but only trait anxiety was significantly associated with propofol requirements in reaching a deep level of sedation (BIS=65). The MAC-hour of sevoflurane was significantly correlated only with PSQ scores. The postoperative pain intensity was significantly correlated with both STAI and PSQ.

Conclusions. Preoperative anxiety and pain sensitivity are independent predictors of propofol and sevoflurane requirements in general anaesthesia. Anaesthetic and analgesic doses could be modified based on the patient's preoperative anxiety and pain sensitivity.

Keywords: anaesthesia, general; anxiety; pain threshold; propofol, sevoflurane

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Psychological factors are thought to drive inter-patient variations in anaesthetic requirements and postoperative pain experiences, even for the same surgical procedure.[1–4] The main psychological factors of interest in this area have been preoperative anxiety and pain sensitivity.[5–7] Although many studies have assessed the effects of anxiety on perioperative variables such as haemodynamic changes and neuroendocrinological responses, pain, and analgesic requirements,[5 8 9] less is known about the effects of pain sensitivity on intraoperative outcomes. In addition, studies showing associations between high levels of anxiety and increased anaesthetic requirements have been of questionable scientific validity, were limited to only the hypnotic component of propofol-based anaesthesia, or failed to control anaesthetic depth during the surgical procedure, thus yielding inconsistent results.[3 10–12]

Before operation determined pain sensitivity has been shown to predict acute postoperative pain intensity, although this may also depend on the specific pain sensitivity test chosen.[13 14] Recently, Ruscheweyh and colleagues[15] demonstrated that experimental pain intensity predicted by the pain sensitivity questionnaire (PSQ) was better than that by

pain-associated psychological factors. PSQ is an easy and safe self-rating instrument for non-invasive assessment of preoperative pain sensitivity by rating imaginable painful situations occurring in daily experiences.

We therefore evaluated whether increased preoperative anxiety and pain sensitivity are associated with (i) increased requirements for propofol to reach phased levels of sedation, (ii) increased requirements of sevoflurane to maintain an equal depth of anaesthesia, and (iii) increased postoperative pain intensity.

Methods

The study protocol was reviewed and approved by the Institutional Review Board of Yonsei University Health System Clinical Trial Center (Seoul, Republic of Korea) (IRB number: 4-2010-0117). It was registered with ClincalTrials.gov (Registration Number: NCT01149239). All participants provided written informed consent. This cross-sectional study enrolled 100 consecutive women (ASA classification I) with euthyroid status undergoing elective total thyroidectomy. Patients with a history of psychiatric illness and those taking psychotropic medications, and also patients with neurological disorders or significant cardiovascular, respiratory, and hepatic diseases were excluded.

On the day of surgery, patient characteristic data were obtained from each patient's medical records. All patients fasted for at least 6 h before surgery and received no premedication. A 20 G i.v. cannula was inserted into a large antecubital vein and Ringer's lactate solution 10 ml kg^{-1} was administered for 1 h. In an isolated calm preparing room, patients completed the Spielberger's State–Trait Anxiety Inventory (STAI)[16] and PSQ.[15] The investigators were blinded to the results during the study period.

In the operating theatre, patients underwent standard monitoring, with the bispectral index (BIS; BIS A-1050 Monitor®, Aspect Medical Systems, Newton, MA, USA) used to measure the depth of anaesthesia.[17] To decrease artifacts, subjects were asked to close their eyes and not speak or move during the brief BIS assessment period. As BIS values are affected by noise disturbances, all non-attendant persons were asked to leave the room and any unnecessary lights were turned off.[18]

Heart rate (HR), systolic arterial pressure (SAP), diastolic arterial pressure (DAP), peripheral oxygen saturation (Sp_{O_2}), and BIS index were measured at baseline. All subjects were administered 5 litre min^{-1} oxygen via a nasal probe to maintain Sp_{O_2} above 95%. Using the Schneider pharmacokinetic model that runs on a microcomputer connected to an infusion pump (Fresenius Kabi Co., Orchestra Base Orima and DPS Module System, France), propofol 2% (Fresenius Kabi Co., Germany) was administered via a target-controlled infusion system to a preset target concentration of 2.5 μg ml^{-1} until the patient reached the three desired levels of sedation, as determined by BIS indices of 85 (light sedation), 75 (moderate sedation), and 65 (deep sedation).[19] If the BIS index did not reach the next, deeper level within 3 min, target concentrations were increased by increments of 0.5 μg ml^{-1}. Propofol requirements to reach each BIS index were recorded. Positive pressure ventilation was available as required in the event of desaturation (Sp_{O_2} <90%). When a patient reached a BIS index of 65, the propofol infusion was stopped and positive ventilation was started. After tracheal intubation with fentanyl 1 μg kg^{-1} and rocuronium 0.6 mg kg^{-1}, anaesthesia was maintained with sevoflurane in 50% oxygen–air at a flow rate of 4 ml min^{-1}. During surgery, sevoflurane concentration was adjusted to provide an equal depth of anaesthesia, as assessed by a BIS index of 40–50, while rocuronium was infused continuously at a rate of 10 mg kg^{-1} min^{-1} with additional doses when T1 of the train-of-four exceeded 15%. No other opioids were administered during surgery. The MAC-hour of sevoflurane was recorded.

Postoperative pain at rest was assessed by an independent investigator using a visual analogue pain score (VAS, 0–10) at 1, 24, and 48 h after surgery. Rescue fentanyl (0.5 μg kg^{-1}) was i.v. administered when postoperative pain VAS ≥5. The incidence rates of postoperative side-effects, including nausea, vomiting, pruritus, dizziness, and headache, were recorded and treated if necessary. Intra- and postoperative parameters were assessed by an independent anaesthesiologist blinded to assessments of preoperative anxiety and pain sensitivity.

The main association we examined was that between the amount of propofol required for induction of anaesthesia and the level of preoperative anxiety on the STAI. The number of patients required was based on previous results,[3] which found that increased state anxiety (r^2=0.285, P=0.006) and trait anxiety (r^2=0.233, P=0.146) were predictors of propofol dose necessary for sedation. We calculated that a total of 95 patients were required with a two-tailed α value of 0.05 and a power of 80%. To control for protocol omissions, we enrolled 100 women. All data are expressed as mean (SD) or number of patients (%). Microsoft Excel version 10.1 (Microsoft Inc., Redmond, WA, USA) was used as a database for data collection and manipulation. All statistical analyses were performed with a statistical software package (SPSS/PC+; SPSS, Inc., Chicago, IL, USA). Normality was determined using the Kolmogorov–Smirnov and Shapiro–Wilk tests. Linear regression analysis was used to determine whether STAI and PSQ scores were associated with propofol and sevoflurane requirements, and the association between psychological variables and postoperative pain intensity. A P-value of <0.05 was considered statistically significant.

Results

All patients successfully completed the STAI and PSQ. Patients' baseline characteristics, preoperative psychological variables, and intraoperative data are summarized in Table 1.

We found significant correlations between state and trait anxieties, whereas neither was associated with PSQ score (Fig. 1). Increased age was associated with lower PSQ