



Original contribution

Assessment of psychological tension after premedication by measurement of salivary chromogranin A

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Abstract

Study Objective: Although some sedatives or analgesics are commonly used for premedication to reduce psychological tension before surgery or anesthesia, it remains unclear which drug is more suitable. Because salivary chromogranin A is a reliable index for estimating psychological tension, this variable was measured during the perioperative period after premedication.

Design: Prospective, randomized control study.

Setting: Operating room at a general hospital.

Patients: Thirty adult female patients undergoing abdominal total hysterectomy were randomly assigned to 3 groups of 10 patients each.

Interventions: On the day before surgery, saliva was collected, and 0.1 mg/kg of midazolam (midazolam group) or 0.02 mg/kg of butorphanol (butorphanol group) was injected intramuscularly 30 minutes before entering the operating rooms. For the control group, no premedication was performed. Saliva was collected as the patient entered the operating room and then the patient received an epidural catheter insertion followed 5 minutes later by collection of the saliva.

Measurements and Main Results: Salivary chromogranin A was assayed using a radioimmunoassay, and revised values calculated from the protein concentration of the saliva were regarded as data. Revised salivary chromogranin A levels increased in the control and butorphanol groups at the time of entrance to the operating room and after epidural treatment compared with the value of the day before surgery, whereas it did not change statistically in the midazolam group.

Conclusions: From the standpoint of reducing psychological tension before surgery or anesthesia, midazolam as a sedative may be more suitable for premedication.

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1. Introduction

Psychological tension increases before surgery or anesthesia, so that the effects of various premedications have been discussed in many reports [1-6]. Furthermore, epidural catheter insertion before induction of general anesthesia

may further increase such psychological tension because it is painful for patients. Questionnaires for evaluation of psychological tension using visual analogue scores (VAS) and state-trait anxiety inventory (STAI) [2,4] or measurement of various stress hormones in urine and blood [7] have been carried out to determine a suitable drug for reducing psychological tension during the perioperative period. However, the results are not conclusive because the former study was subjective and there was some criticism of the

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Table 1 Demographic data

Group	Control (n = 10)	Butorphanol (n = 10)	Midazolam (n = 10)
Age (y)	48 ± 9 (38-64)	47 ± 5 (39-53)	44 ± 9 (35-66)
Height (cm)	157 ± 4 (148-163)	156 ± 4 (148-161)	158 ± 7 (153-166)
Weight (kg)	59 ± 8 (46-74)	57 ± 8 (46-66)	57 ± 8 (46-73)

Values are expressed as mean ± SD (range).

measurement of stress hormones in the latter study [8]. Thus, no premedication seems to be accepted recently. In clinical practice, certain sedatives or analgesics are commonly used for premedication. In our operating rooms (ORs), midazolam and butorphanol are used as a sedative or analgesic, respectively, in relatively healthy patients, expecting an amnesic effect in the former drug and a ceiling effect on respiratory depression in the latter drug. [9,10]. Of these drugs, however, there are many other reports supporting the superiority of midazolam [1,2,5,6,11,12].

Chromogranin A (CgA) was found in 1967 as an acidic glucoprotein, which exists in various endocrine organs and sympathetic nervous systems and is excreted into blood simultaneously with catecholamine release [13]. Chromogranin A also exists in the submandibular gland and is secreted into saliva after stimulation of the sympathetic nervous system [14]. In particular, the CgA in this site responds to psychological stress but not to physical stress [8]. It is therefore considered worthwhile to measure salivary CgA concentrations as an indication of psychological tension. In this report, salivary CgA was measured during the perioperative period to determine a suitable premedication drug for reducing psychological tension before surgery or anesthesia.

2. Patients and methods

The study protocol was approved by our Institutional Committee. After providing informed consent, 30 adult female patients undergoing elective abdominal total hysterectomy for hysteromyoma, classified as ASA-PS 1 or 2 without psychological disorders and menstruation, were randomly assigned to 3 groups of 10 patients each.

On the day before surgery at noon before taking lunch, the patients were placed in a recumbent position for 10 minutes, saliva was collected by holding an absorbent cotton in the mouth for several minutes, and systolic blood pressure and heart rate were recorded. On the day of surgery around noon, 0.1 mg/kg of midazolam or 0.02 mg/kg of butorphanol was injected intramuscularly into the buttocks of either the midazolam or butorphanol group of 10 patients, respectively, 30 minutes before entering the OR. No premedication was performed on the control group. At the time of entering the OR, saliva was collected and systolic blood pressure and heart rate were recorded in the same

way. Subsequently, the patient received an epidural catheter insertion 7 cm cephalad via the L1/L2 interspace using an 18-gauge Tuohy needle under local anesthesia with a 25-gauge needle. The same collection and measurements were carried out 5 minutes after completion of this epidural treatment. Cephalad placement at 7 cm is our regimen to prevent catheter migration from the epidural space [15]. Thereafter, 8 to 10 mL of 1% ropivacaine was injected epidurally according to our formula for estimating anesthetic spread [16], which was then confirmed by ice packed in a surgical glove that also is our routine regimen [17,18]. The patient was given general anesthesia using propofol alone according to our anesthetic protocol [19-21].

The absorbent cotton placed in the patient's mouth was centrifuged to obtain the saliva, which was subsequently stored at -80°C until the CgA assay. The samples were sent to Yanaihara Laboratories (Fujinomiya, Shizuoka, Japan), which is the only laboratory assaying CgA in Japan. Salivary CgA concentrations were assayed by radioimmunoassay [8,22-24] and the raw result (pmol/mL) was revised by dividing by the protein concentration of the saliva in the sample (mg/mL). This revised value of CgA (pmol/mg) was regarded as the level of salivary CgA.

Comparison of patients' demographic data was carried out by 1-way analysis of variance. Changes in systolic blood pressure, heart rate, and revised salivary CgA levels from the day before surgery to the time after epidural treatment in each group were analyzed statistically by repeated-measures 1-way analysis of variance, followed by Fisher protected least significant difference for multicomparison. $P < 0.05$ was considered significant.

3. Results

All patients examined were women, and there was no statistically significant difference in age, height, or weight between the groups (Table 1).

Systolic blood pressure increased only when entering the OR in the control and butorphanol groups, whereas it did not change throughout in the midazolam group. Heart rate did not change in any of the groups (Table 2).

Table 2 Changes in systolic blood pressure and heart rate

	The day before surgery	Entering the OR	After treatment
Systolic blood pressure (mm Hg)			
Control	121 ± 16	137 ± 19*	123 ± 25
Butorphanol	136 ± 25	157 ± 31*	141 ± 27
Midazolam	125 ± 11	126 ± 21	121 ± 18
Heart rate (beats per minute)			
Control	72 ± 8	71 ± 12	68 ± 11
Butorphanol	74 ± 10	79 ± 13	71 ± 10
Midazolam	72 ± 9	75 ± 13	72 ± 13

Values are expressed as mean ± SD.

* $P < 0.05$ vs the value on the day before surgery in each group.

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