Can Yawning Be Used as an Indicator of Induction of Anesthesia?

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Abstract

Background: We can usually see the yawning at induction of anesthesia, however, it has not been studied as such an indicator of anesthesia. The yawning is one means of changing arousal level, and a sign or marker that such a change is occurring, although its functions are not well understood. The purpose of the present study was to evaluate the yawning whether it could be used as an indicator of induction of anesthesia, using its property as a marker of changed arousal level.

Methods: In 60 adult patients, group 1 was done propofol target controlled infusion (TCI) with Stel-pump software, while group 2 was done thiopental TCI similarly. Clinical indicators of induction of anesthesia were measured as follows: loss of verbal control (LOV), loss of eyelash reflex (LOE), the yawning. In addition, the occurrence of apnea (OOA) were measured, too. We assessed the hypnosis levels of indicators of induction of anesthesia including the yawning and demonstrate their effect site concentrations and elapsed time. Furthermore, we compared the incidences of yawning and apnea between both groups.

Results: Clinical indicators of induction occurred in the order of LOV > LOE > the yawning > OOA in both groups. With respect to BIS, the yawning showed the lowest BIS and the highest effect site concentrations except OOA in both groups. The incidence of the yawning in group 2 was higher than in group 1 (about 82 vs 63%). On the contrary, the incidence of apnea in group 1 was higher than in group 2 (about 79 vs 53%).

Conclusions: As far as the yawning could be shown, we could observe, it approximated most closely to their clinical impression of the 'true' induction in terms of the hypnosis level and its effect site concentration. (Korean J Anesthesiol 2000; 39: S 1–S 6)


INTRODUCTION

Clinical indicators for induction of anesthesia are assessed in routine practice include (1) no response to verbal command, (2) loss of verbal control (patients were asked to count out aloud during induction and the time to achieve induction, defined as loss of verbal control), (3) dropping the syringe (the patient was asked to hold a 20-mL water-filled plastic syringe barrel between the thumb and index finger of the hand during induction), (4) loss of eyelash reflex, (5) pupillary light reflex, (6) isolated forearm technique as a prediction of movement, (7)
bispectral index (BIS) and so on.

We can usually see the yawning at induction of anesthesia, however, it has not been studied as such an indicator of anesthesia. Despite the yawning, it is a common behavioral act in a wide variety of vertebrate species, has widely known as beliefs that it serves as a signal of boredom, it results from a lack of oxygen, and it is a socially contagious act, but its functions are not well understood. In normal, unstressed humans, daily peaks of yawning are associated with transitions from sleeping to waking and from waking to sleeping. The yawning is one means of changing arousal level, and a sign or marker that such a change is occurring.

On the other hand, so far there has been no effective monitor except BIS which can assess the depth of hypnosis and predict the probability of a patient being conscious during general anesthesia.

The purpose of the present study was to assess the hypnosis levels of indicators of propofol or thiopental induction of anesthesia including the yawning and demonstrate their effect site concentrations and elapsed time in order to evaluate the yawning whether it could be used as an indicator of induction of anesthesia.

MATERIALS AND METHODS

Sixty ASA physical status 1, 2 males and females who were 20–50 years of age and scheduled for elective surgery requiring general anesthesia participated in this institutionally approved study after providing written informed consent.

Exclusion criteria were as follows: renal, hepatic, neurologic dysfunction, gross obesity, and upper extremity surgery; use of benzodiazepines, anticonvulsants, alcohol, opioids, or other psychotropic drugs; females who were possibly pregnant; attention position surgery; patients who were having L-tube, Forley catheter.

Patients were not premedicated. Age, sex were recorded and height and body weight were determined by the investigators on the day of the study. The patient was then taken to the operating room where an attending anesthesiologist not involved in the conduct of the study took responsibility for the care of the patient.

The monitoring were routine, consisting of an automated blood pressure cuff, electrocardiogram, pulse oximetry, BIS monitor (model A-2000, Aspect medical systems Inc., USA) with BIS montage (BIS sensor™, Aspect medical systems, USA). Apply Sensor to forehead. The position of circle #1 at center was approximately 1.5 inches above the bridge of the nose and #3 on either temple area was between the corner of the eye and hairline. Before induction, baseline hemodynamic variables were recorded. The first 30 subjects received propofol, and the second group of 30 received thiopental. Intravenous access was in the nondominant hand. In group 1, lidocaine 0.5 mg/kg was administered intravenously to reduce the pain resulting from propofol injection and propofol infusion was started at a propofol target concentration (C₇) 6 µg/ml using Stelpump software (J. F. Coetzee, Department of Anaesthesiology, Faculty of Medicine, University of Stellenbosch, South Africa) with notebook computer, Master-TCI syringe pump (Becton-Dickinson infusion system, Le Grande chemin, France), interface serial cable for serial communication. We selected the Marsh's pharmacokinetic model for propofol TCI from the software.

On the other hand, in group 2, infusion was started at a thiopental C₇ 30 µg/ml using same devices except being changed the pharmacokinetic model of Stanski & Maitre.

Clinical indicators of induction of anesthesia were measured as follows, loss of verbal control (LOV), loss of eyelash reflex (LOE), and the yawning. In addition, the occurrence of apnea (OOA) were measured, too. We assessed the hypnosis level of each event during propofol or thiopental induction of anesthesia using BIS monitor and its elapsed time, effect site concentration and total drug requirements using user interface of Stelpump software. Furthermore, we compared the incidences of yawning and apnea between propofol and thiopental induction groups. When we checked BIS of each event, we took the BIS value of 20 seconds-delay after it because of a delayed response of BIS during such a rapidly changing induction state. Similarly, in the checking of oxygen saturation with pulse oxymetry (SpO₂), we took its value of 10 seconds-delay after each event. Following the onset of unconsciousness, succinylcholine was given to facilitate
tracheal intubation, vecuronium 0.15 mg/kg to maintain muscle relaxation and anesthesia was continued as directed by the attending anesthesiologist.

All data are expressed as mean values ± SD. Data were analysed by chi-square analysis with Yates’ correction, Spearman’s Rank Correlation, paired t-test and ANOVA followed by a post hoc tests as appropriate using 'SPSS for window Release 9.0 (SPSS Inc., USA)’ software. Probability values < 0.05 were considered significant.

RESULTS

The demographic data were no significant differences between two groups in terms of patient age, sex, weight, height and BIS value of preinduction state (Table 1).

Clinical indicators of induction occurred in the order of LOV > LOE > the yawning >> OOA in both groups.

With respect to the elapsed time, aside from OOA, that of LOE and the yawning in group 1 showed significantly longer than that of LOV (P < 0.05) and there was no significant difference between that of LOE and the yawning in the same group. While, in group 2, that of the yawning and OOA showed significantly longer than that of LOV (P < 0.05) (Table 2). There was a strong correlation among the elapsed time of yawning, LOE and LOV in each group. The correlation coefficient (r) were

Table 1. Demographic Data

<table>
<thead>
<tr>
<th>Groups</th>
<th>Sex (m/f)</th>
<th>Age (yr)</th>
<th>Weight (kg)</th>
<th>Height (cm)</th>
<th>BIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (n = 30)</td>
<td>14/16</td>
<td>34 ± 9</td>
<td>62.6 ± 12.1</td>
<td>164.9 ± 6.4</td>
<td>95.9 ± 2.9</td>
</tr>
<tr>
<td>2 (n = 30)</td>
<td>13/17</td>
<td>35 ± 9</td>
<td>60.6 ± 7.8</td>
<td>164.7 ± 7.9</td>
<td>95.9 ± 2.8</td>
</tr>
</tbody>
</table>

Values are mean ± SD. Group 1: propofol infusion was started at a target concentration (Ct) 6 μg/ml using Stelpump. Group 2: thiopental infusion was started at Ct 30 μg/ml using same devices. BIS: BIS values of preinduction state. There was no significant difference between two groups.

Table 2. Comparison of Clinical Indicators of Induction

<table>
<thead>
<tr>
<th></th>
<th>T_EL (sec)</th>
<th>BIS</th>
<th>C_E (μg/ml)</th>
<th>TRIA (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of verbal control (LOV)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>49.9 ± 9.1</td>
<td>80.4 ± 15.0</td>
<td>0.8 ± 0.3</td>
<td>132 ± 21</td>
</tr>
<tr>
<td>Group 2</td>
<td>44.8 ± 7.9</td>
<td>88.4 ± 4.8</td>
<td>6.5 ± 1.6</td>
<td>190 ± 15</td>
</tr>
<tr>
<td>Loss of eyelash reflex (LOE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>61.2 ± 11.1*</td>
<td>70.2 ± 16.3</td>
<td>1.1 ± 0.3*</td>
<td>137 ± 22</td>
</tr>
<tr>
<td>Group 2</td>
<td>51.8 ± 10.2</td>
<td>79.8 ± 10.7*</td>
<td>7.7 ± 2.0</td>
<td>205 ± 24</td>
</tr>
<tr>
<td>Yawning</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>66.3 ± 14.1*</td>
<td>69.8 ± 16.4</td>
<td>1.2 ± 0.3*</td>
<td>139 ± 27</td>
</tr>
<tr>
<td>Group 2</td>
<td>57.4 ± 13.6*</td>
<td>72.7 ± 13.7*</td>
<td>9.3 ± 2.1*</td>
<td>212 ± 22*</td>
</tr>
<tr>
<td>Occurrence of apnea (OOA)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>110.6 ± 14.4†</td>
<td>39.6 ± 13.5†</td>
<td>2.3 ± 0.5†</td>
<td>155 ± 24</td>
</tr>
<tr>
<td>Group 2</td>
<td>113.0 ± 24.2†</td>
<td>57.7 ± 12.9†</td>
<td>16.3 ± 2.6†</td>
<td>299 ± 51†</td>
</tr>
</tbody>
</table>

Values are mean ± SD. Group 1: propofol infusion was started at a target concentration (Ct) 6 μg/ml using Stelpump. Group 2: thiopental infusion was started at Ct 30 μg/ml using same devices. T_EL: The elapsed time of each event from the start of infusion. BIS: BIS value at 20 sec after each event. C_E: The effect site concentration of each event. TRIA: Total requirements of induction agents. *: P < 0.05 compared with LOV. †: P < 0.05 compared with LOV, LOE and yawning.
Table 3. Incidences of Yawning and Apnea during Induction

<table>
<thead>
<tr>
<th>Groups</th>
<th>Yawning</th>
<th>Apnea</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>57%</td>
<td>79%</td>
</tr>
<tr>
<td>2</td>
<td>82%</td>
<td>53%</td>
</tr>
</tbody>
</table>

Group 1: propofol infusion was started at a target concentration (C<sub>T</sub>) 6 µg/ml using Stelpump. Group 2: thiopental infusion was started at CT 30 µg/ml using same devices.

0.812 between the elapsed time of yawning and LOE and 0.762 between that of yawning and LOV in group 1, while, 0.931 between that of yawning and LOE and 0.698 between that of yawning and LOV in group 2 (P < 0.01).

With respect to BIS, the values of LOV, LOE, the yawning, and OOA in each group were significantly lower than preinduction values and their values in group 1 were more reduced than those in group 2. In addition, the yawning showed the lowest BIS and the highest effect site concentrations except OOA in both groups (Table 2).

There was a strong correlation among the BIS values of yawning, LOE and LOV in group 1, while, there was only a marked correlation between that of yawning and LOV in group 2. The correlation coefficient (r) were 0.974 between the BIS values of yawning and LOE and 0.710 between that of yawning and LOV in group 1, while, 0.833 between that of yawning and LOE and 0.325 between that of yawning and LOV in group 2 (P < 0.01).

With respect to oxygen saturation (SpO<sub>2</sub>), there was no significant differences in each group except OOA.

There was no significant hemodynamic changes at the yawning.

The incidence of the yawning in group 2 was higher than in group 1 (about 82 vs 63%). On the contrary, the incidence of apnea in group 1 was higher than in group 2 (about 79 vs 53%) (Table 3).

**DISCUSSION**

After assessment of the indicators of induction of anesthesia including the yawning, we have found that they occurred in the order of LOV > LOE > the yawning >> OOA in propofol and thiopental groups. The yawning showed the most deepest hypnosis levels among indicators except OOA in both groups.

In order to standardise the indicators of induction of anesthesia, the measurements were made as follows, loss of verbal control, loss of eyelash reflex, the yawning. In addition, occurance of apnea were measured, too. Grounds et al<sup>6,7</sup> defined, when the patients were asked to count out aloud during induction, if counting stopped, the patients were asked to open their eyes and if they didn't so were regarded as being unconscious. Besides, abolition of the eyelash reflex is commonly taken as the endpoint when injecting intravenous induction agents. However, in some patients the eyelash reflex was not abolished at the time when anesthesia appeared to have been successfully induced.<sup>4</sup>

When the patient was started infusion of induction agents, the loss of verbal control occurred first and the yawning developed just after the loss of eyelash reflex. Until developing the yawning, the patient was getting hypopneic. Through the yawning, characterized by gaping accompanied by a long inspiration, followed by a shorter expiration, the patient looked like increasing oxygen-CO<sub>2</sub> exchange in the lung, in facial stretching. At this time, we could distinguish yawning from sigh with a look.

Meanwhile, oxygen saturation (SpO<sub>2</sub>) in pulse oxymetry recovered soon after slight decreasing until just before the yawning. Although induction time was too short and such response was delicate and a little bit delayed, we could observe it. Interestingly, if the yawning was developed during induction, the apnea seldom occurred. On the other hand, if the yawning was not developed or even a sigh was developed during induction, we could often see the apnea which was defined as loss of spontaneous breathing for any period of time greater than 10 seconds for convenience. The incidence of the yawning in thiopental group was significantly higher than in propofol group. On the contrary, the incidence of apnea in propofol group was significantly higher than in thiopental group. Cummings et al<sup>18</sup> reported that the occurrence of apnea was not observed in any of the patients who received propofol 2.0 mg/kg.
After 2.5 mg/kg, apnea occurred in 44% of patients with a mean duration of 53 seconds. While, in our study data, the incidence of occurrence of apnea was 79% of patients who received propofol 2.5 mg/kg (155 ± 24 mg per 62.6 ± 12.1 kg). We used TCI instead of bolus doses for induction, which might be cause the different incidence.

Rarely in patients in their twenties, the occurring order of LOE was reversed with the yawning and elapsed time of LOE was very hard to measure for its ambiguity. In such a case, the yawning seems to be more reliable index than LOE.

We tried to apply yawning as an indicator of induction of anesthesia from its property of a marker of changed arousal level, even though it served as a signal of boredom or resulted from a lack of oxygen. On the other hand, even physiological function of yawning is still unknown, it is under the control of several neurotransmitters and neuropeptides at the central level. Among these substances, the best known are dopamine, excitatory amino acids, acetylcholine, serotonin, nitric oxide, adrenocorticotropic hormone-related peptides and oxytocin, that facilitate yawning and opioid peptides that inhibit this behavioral response. Some of the above compounds interact in the paraventricular nucleus (i.e. the hippocampus, the pons and/or the medulla oblongata) of the hypothalamus to control yawning. Furthermore, other neurotransmitters, i.e. gamma-aminobutyric acid (GABA) and noradrenaline, and neuropeptides, i.e. neurotensin and luteinizing hormone-releasing hormone (LH-RH), also influence this behavioral response.¹⁹

This study used the recently developed BIS which has been found to correlate well with sedation and predict a patient’s response to stimulus. We assessed the hypnotic level of three indicators which are standing for unconsciousness during propofol or thiopental induction of anesthesia using BIS monitor. However, the BIS is calculated using 15–30 seconds of EEG data. Such signal averaging will result in a delayed response during rapidly changing states, such as during induction where the hypnotic state moves from awake to unconscious in a few seconds. Changes from an unconscious state to an awake state may sometimes be fairly rapid as well, depending on the anesthetic technique. In either case, a 10–15 second lag in the BIS may be observed as it incorporates the new, rapidly changing information. So we took the BIS value of 20 seconds delay after the moment of each indicator of induction because of a delayed response of BIS during such a rapidly changing induction state, when we checked BIS of each event. Furthermore, in thiopental group, the hypnotic state moved more rapidly from awake to unconscious during induction than in propofol, so we couldn’t have measured the clinical indicators of induction because of such rapidity. Therefore, the infusion was started at a thiopental C₇ 30 μg/ml using Stelpump software with its accompanying devices, which might be equal to half-speed of propofol infusion. We could calculate roughly, if the patient of 50 kg was infused with a thiopental C₇ 30 μg/ml, it took about 2 minutes for 250 mg of total requirements of thiopental. On the other hand, if the same patient was infused with a propofol C₇ 6 μg/ml, it took about 1 minutes for 110 mg of total requirements of propofol. If the speed of thiopental infusion had used to be equal to the speed of propofol, the incidence of the yawning in thiopental group would be more increased due to more rapidly changing arousal level than the result of this study. As a reference, Hung et al¹⁰ described that 15.6 μg/ml is the thiopental C₉₀ (plasma concentration that produced a 50% probability of no movement response for the clinical stimuli) for loss of response to verbal command. Smith et al¹¹ reported that the C₉₀ for propofol alone was 3.3 μg/ml. In our study, we assessed the effect site concentration using user interface of Stelpump software instead of plasma concentration, which might cause the difference from above mentioned study results.

Stelpump was co-developed by Prof Johan Coetzee of the Department of Anaesthesiology and Ralph Pina of SED. It is a software system which enables the anaesthesiologist to simultaneously control two infusion pumps via the PC and the pumps' serial ports i.e. computer-aided-continuous-infusions. Based on patient parameters, the type of drug and the pharmacokinetic model selected for that drug, Stelpump controls drug delivery according to targeted drug concentration in the plasma, targeted concentration in the effect site, or a user-specified constant.
infusion. It also provides graphical feedback to the
anesthesiologist about plasma and effect site concentrations
and pump infusion rates over time. The current released
version (Version 1.07) will drive the Harvard 22, Graseby
3400, Ivac P4000, B-D Module DPS and B-D Pilot Anaes-
thesia syringe pumps, and the imed Gemini PC-2, Baxter
Flo-Gard 6201 and 6301 volumetric pumps. However,
Stelpump is an experimental device for experimental use
only under the aegis of an appropriate institutional review
board. Use only to assist in the evaluation of drugs and
methods of drug delivery.

Conclusively, with this study, we considered that the
yawning was not only a compensatory reflex of oxygen-
CO2 exchange for hypopnea but also a sign of changing
arousal level. As far as the yawning could be shown, we
could observe, it approximated most closely to their clin-ical
impression of the 'true' induction in terms of the
hypnosis level and its effect site concentration, although
the incidence of it was not perfect and the combined effect
of several clinical indicators was thought to be more
meaningful than that of single one.

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