

## Bispectral Index<sup>®</sup> and the incidence of apnea during monitored anesthesia care<sup>☆</sup>

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### Abstract

**Purpose:** The Bispectral Index (BIS) provides an estimate of depth of consciousness during sedation. If apnea can be shown to correlate with BIS, then a potential improvement in safety during MAC/sedation may be achieved.

**Scope:** Ninety-nine patients undergoing MAC anesthesia were monitored with BIS for level of consciousness, and capnography for apnea detection. The anesthesia provider was blinded to BIS and capnography data. Forty-nine percent of subjects experienced apnea independent of medical history, procedure, or medication. BIS immediately preceding apneic episodes ( $55 \pm 18$ ) was frequently lower than that recommended for an upper limit during general anesthetics ( $<60$ ). The incidence increased as depth of consciousness decreased with a 50% likelihood of developing apnea at a BIS of 56.

**Conclusions:** The incidence of apnea during MAC is high, and incidence increases as BIS decreases.

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**Keywords:** Apnea; Depth of consciousness; Monitored anesthesia care

### 1. Introduction

Apnea is a frequent occurrence during monitored anesthesia care (MAC, or sedation administered by anesthesiologists and anesthesiologists) procedures, with a reported incidence as high as 25% [1]. Due to improvements in surgical techniques and development of improved intravenous sedative agents, conscious and deep sedation are employed increasingly in operating rooms, clinics and offices by anesthesiologists and non-anesthesiologists. Some of these caregivers may have little to no formal training in pharmacology, physiologic monitoring or resuscitation. Although apnea and airway obstruction can be accurately detected by capnography dur-

ing these procedures [1], there have been no studies that examine the ability of new technologies to predict apnea occurrence.

Bispectral Index (BIS) is a parameter derived from the bipolar scalp encephalogram that has been shown to estimate level of consciousness during anesthesia and sedation. Anesthesia providers primarily use BIS to assure that patients are unaware during general anesthesia [2,3]. This study was designed to test the hypothesis that the risk for apnea during MAC procedures may correlate with level of consciousness as measured by BIS.

### 2. Materials and methods

Patients scheduled to undergo procedures with MAC/sedation were enrolled after signing an Institutional Review Board (IRB) approved consent form. In a previous study

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[1], we observed a 26% incidence of apnea for at least 20 s. Assuming similar incidence, we sought to capture data during at least one episode of apnea in at least 25 patients. Therefore, we planned to enroll 110 patients, assuming eight patients would drop out or be otherwise unevaluable. Patients were excluded from study participation if they were pregnant, age <18 years, or could not maintain an SpO<sub>2</sub> of >88% on room air. Drop-out criteria included the need to place an artificial airway to maintain ventilation, or the need to institute artificial ventilation.

All patients were monitored with BIS (A-2000, Aspect Medical Systems, Newton, MA, XP Version 4.0) for level of consciousness, and capnography for apnea detection (NPB-70 handheld capnometer, Nellcor, Pleasanton, CA—sampling rate 50 ml/min). 5-lead ECG and SpO<sub>2</sub> monitoring were displayed continuously for all patients. Non-invasive blood pressure was measured every 2.5 min.

Sedation was administered with propofol ± fentanyl ± midazolam at the discretion of the anesthesia providers (anesthesia residents and nurse anesthetists supervised by faculty anesthesiologists at a large teaching institution), and doses were recorded. All patients received oxygen via nasal cannula with a minimum flow rate of 2 l/min, titrated as needed to maintain SpO<sub>2</sub> >94%. The anesthesia provider was blinded to both BIS and capnography data.

Data were collected at baseline and every 3 min, unless otherwise triggered by apnea for >60 s or SpO<sub>2</sub> <88%. Values for SpO<sub>2</sub> and P<sub>ET</sub>CO<sub>2</sub> were collected during the last minute of each 3 min interval. Apnea or airway obstruction for 60 s, detected using capnography, triggered notification of the anesthesia care provider if the apnea was undetected by routine monitoring. Sixty seconds was specifically chosen due to safety concerns of the IRB.

At the conclusion of the case, the anesthesia provider was asked to determine the deepest level of sedation achieved using standard definitions of sedation/analgesia [4] (minimal, moderate, or deep). This was then correlated with actual incidence of apnea occurrence.

### 2.1. Statistical analysis

Categorical data were analyzed using Pearson's chi-squared test. The relation between potential predictive variables (BIS value, patient demographics, and type of procedure, sedative and analgesic) and the occurrence of apnea was assessed by logistic regression analysis using SigmaStat for Windows Version 3.0 (SPSS, Chicago, IL).

## 3. Results

Ninety-nine patients who ranged in age from 19 to 78 years (51 ± 13 years) and weighed from 49 to 170 kg (83 ± 19 kg) were studied. There were 48 females and 51 males. Eighty-

Table 1

Apnea as related to BIS mean, minimum and maximum values

Apnea	N	BIS (M ± S.D.)	BIS <sub>min</sub> (M ± S.D.)	BIS <sub>max</sub> (M ± S.D.)
Y	49	71 ± 14	48 ± 17	91 ± 11
N	50	83 ± 12	67 ± 17	96 ± 5

Table 2

Temporal pattern of BIS as a function of apnea event

Time to apnea	BIS <sub>min</sub> (N)	BIS <sub>min</sub> (M ± S.D.)	BIS <sub>min</sub> (Min)	BIS <sub>min</sub> (Max)
>3 to <6 min before	47	73 ± 19	32	98
<3 min before	47	55 ± 18	25	91

three percent of patients received midazolam, 85% received propofol, and 35% received fentanyl, with most receiving a combination of medications. Medication given was not predictive of apnea occurrence (19 of the 36 subjects receiving fentanyl became apneic (53%), 37 of 83 for midazolam (45%), and 46 of 86 for propofol (53%). Orthopedic, vascular, pain, and gastroenterology procedures were included in the study protocol.

Forty-nine (49.5%) of 99 patients experienced 60 s of apnea. None of the episodes of apnea were detected by the anesthesia provider. All were detected by capnography. No subjects required ventilation or airway placement, and thus none met dropout criteria. Average time to apnea was 15 ± 13 min after onset of sedation. Twenty patients desaturated to below 90%, 3 in the non-apnea group, and 17 in the apnea group (6 prior to and 11 after apnea occurrence). Lowest saturation reached was 88%. There were no differences in heart rate or blood pressure throughout the study.

Patients that became apneic had mean BIS of 71 ± 14, compared to 83 ± 12 in the group that did not experience apnea. Mean, minimum and maximum BIS data related to apnea are shown in Table 1. Average BIS during the 3 min immediately preceding apnea was 55 ± 18, and BIS for the immediately preceding 3 min averaged 73 ± 19 as shown in Table 2. Anesthesia provider ability to correlate subjective depth of sedation with risk of apnea was poor as shown in Table 3.

## 4. Discussion

As previously shown, the incidence of apnea during MAC has been shown to be high [1], and although it can be reliably detected by capnography, apnea cannot be reliably predicted with current standard monitors. With recent studies highlighting the increased risk of morbidity and mortality during office-based procedures [5], many of which are performed under IV sedation, it is important to identify means of improving patient safety. We therefore designed this study to examine the correlation between a processed-EEG measure of consciousness and apnea.

Table 3

Sedation level as assessed by anesthesia providers as related to BIS mean, minimum and maximum values and incidence of apnea

Apnea	Sedation judgment	N	BIS (M ± S.D.)	BIS <sub>min</sub> (M ± S.D.)	BIS <sub>max</sub> (M ± S.D.)
Y	Minimal	10	77 ± 10	58 ± 17	92 ± 9
Y	Moderate	30	70 ± 14	48 ± 17	90 ± 11
Y	Deep	9	66 ± 18	36 ± 14	92 ± 13
N	Minimal	30	88 ± 6	73 ± 14	97 ± 4
N	Moderate	17	79 ± 12	60 ± 15	95 ± 6
N	Deep	3	62 ± 22	40 ± 26	96 ± 2
All groups		99	77 ± 14	57 ± 20	93 ± 8

The Bispectral Index Score (BIS) is a derived parameter from the scalp electroencephalogram used for monitoring level of consciousness during administration of anesthetics and hypnotics [6]. BIS has been shown to correlate well with anesthetic depth and sedation for a number of agents [7]. Kim et al. showed that BIS values at apnea occurrence following induction of anesthesia with propofol or thiopental were  $40 \pm 14$  or  $58 \pm 13$ , respectively [8]. The minimum, maximum and range for BIS data was not supplied, but onset of apnea during induction of general anesthesia appears to correlate with that obtained in our sedation study. Typically, BIS values of 65–80 are indicative of loss of conscious information processing and recall. Although BIS has been extensively studied during sedation, the impact of sedation depth on apnea has not.

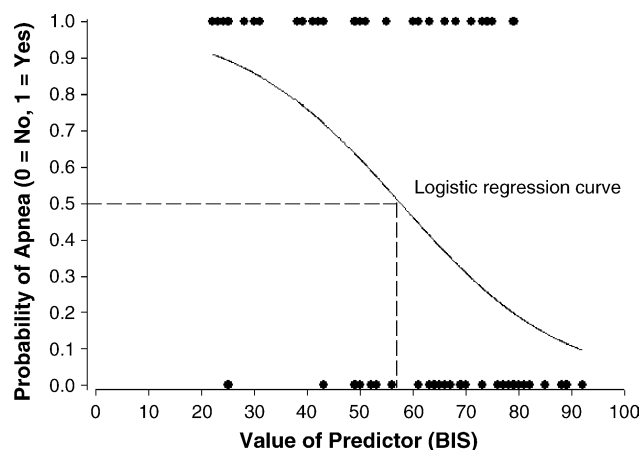
The “levels of sedation/analgesia” as defined by the ASA include minimal, moderate, and deep levels, and criteria for each are reproduced in Table 4 [4]. Deep sedation is associated with ventilation that “may be inadequate”, and “airway intervention may be required”. This is clearly undesirable, especially when sedation is administered by personnel without formal training in resuscitation and airway management. A continuum of sedation exists during sedative medication administration. The more sedated one becomes, the more likely one is to experience airway difficulties. Since BIS measures consciousness, it follows that the risk of apnea should increase below a certain BIS level.

In our study, we have found that the average BIS of patients that became apneic was lower than those in patients that did not experience apnea ( $71 \pm 14$ , compared to  $83 \pm 12$ ). More importantly, the BIS immediately preceding apneic episodes ( $55 \pm 18$ ) was frequently lower than that recommended for an upper limit during general anesthetics (<60). As depth of consciousness decreased, the incidence of apnea increased.

Table 4

Definitions of general anesthesia and levels of sedation/analgesia (approved by ASA House of Delegates on October 13, 1999, and amended on October 27, 2004 [4])

	Minimal sedation (anxiolysis)	Moderate sedation/analgesia (“conscious sedation”)	Deep sedation/analgesia	General anesthesia
Responsiveness	Normal response to verbal stimulation	Purposeful response to verbal or tactile stimulation	Purposeful response following repeated or painful stimulation	Unarousable even with painful stimulus
Airway	Unaffected	No intervention required	Intervention may be required	Intervention often required
Spontaneous ventilation	Unaffected	Adequate	May be inadequate	Frequently inadequate
Cardiovascular function	Unaffected	Usually maintained	Usually maintained	May be impaired



Apnea Group BIS value < 3 minutes before event  
No-apnea Group BIS value = minimum during procedure

Fig. 1. Probability of apnea as a function of BIS.

When probability of apnea was plotted against BIS, logistic regression analysis revealed that the likelihood of apnea development was 50% at a BIS of approximately 57, as shown in Fig. 1.

The ASA Practice Guidelines for Sedation and Analgesia by Non-Anesthesiologists discuss level of consciousness monitoring, but limit the discussion to the clinical assessment of patient response to verbal command [4]. Based on our findings and previous recommendations as outlined by the aforementioned ASA guidelines, we recommend that processed-EEG monitoring be further studied in large patient populations to further delineate risk factors for development of apnea. Although we found no difference based on patient age, sex, or other comorbid conditions, a much larger sample size with a broad variety of clinically uti-

lized sedatives is warranted. Considering that the risk of processed-EEG monitoring is minimal, the additional monitoring of depth of consciousness that these monitors provide may add value during sedation cases. Indeed, education about the benefits of depth of consciousness monitoring may be even more appropriate for non-anesthesia providers.

In conclusion, we have shown that apnea during procedural sedation is common, and that it is more likely to occur as level of consciousness is progressively depressed, with BIS prior to apnea frequently in the range of general anesthesia (i.e. <60). With apnea frequently associated with oxygen desaturation (20% of our study population desaturated to below 90% despite use of supplemental oxygen), monitoring depth of consciousness with processed EEG may result in an improvement in patient safety during procedural sedation.

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