Optimal level of bispectral index for conscious sedation in awake fiberoptic nasotracheal intubation

Hari Haran Gnanaswaran^a, Gaurav Jain^{a,*}, Ankit Agarwal^a, Ashi Chug^b, Deepak Singla^a

^a Department of Anaesthesiology and Critical Care, All India Institute of Medical Sciences, Rishikesh, 249203, Uttarakhand, India

^b Department of Dentistry and Craniomaxillofacial Surgery, All India Institute of Medical Sciences, Rishikesh, 249203, Uttarakhand, India

ARTICLE INFO

Keywords:

Bispectral index
Conscious sedation
Dexmedetomidine
Fiberoptic intubation

ABSTRACT

Background: Bispectral index (BIS) has been in practice as an objective tool to measure the depth of conscious sedation. The data on adequate levels for awake fiberoptic nasotracheal intubation (AFNI) is however scarce. We aimed to obtain an optimal level of BIS required for achieving the adequate conscious sedation in AFNI procedure.

Methods: In a prospective, observational, outcome assessor blinded cohort trial, 94 consecutive patients with anticipated difficult intubation and undergoing AFNI for any elective surgery were enrolled. The topical anesthesia and sedation were induced with lidocaine and dexmedetomidine, while keeping the patient awake. The sedation levels were targeted to BIS ≤ 90 and Ramsay sedation score (RSS) ≥ 2 to attempt intubation. Propofol bolus were administered if patients get agitated. The primary outcome was “Stable BIS”, the lowest BIS at which intubation could be feasibly performed. A receiver operator characteristic curve, Youden index, and correlation analysis were used.

Results: The optimal criterion for BIS was obtained as ≤ 86 (AUC: 0.80, sensitivity 88.30%, specificity 61.45%, Youden index 49.74). The stable BIS ranged from 80 to 88, while RSS varied from 1 to 3. The BIS and RSS correlated significantly ($r: 0.83$). The stable BIS was independent of any baseline characteristics. Six patients had transient untoward events, none requiring any intervention.

Conclusion: BIS serves as an effective objective tool for titrating the depth of conscious sedation. We advocate a BIS range of 80–86 for feasibly performing the AFNI procedure.

1. Introduction

Awake fiberoptic intubation is a gold standard procedure for managing the difficult airway. Patients undergoing this procedure frequently suffer from an annoying discomfort of foreign body perception and asphyxiation sense, despite giving adequate topical anesthesia to the airway.¹ The addition of conscious sedation improves patient tolerance, decreases anxiety, and obviates the deleterious effect on the systemic haemodynamics.² Oversedation is however linked to complications like airway collapse, hypoxemia and respiratory depression. Thus, titrating the sedation depth to adequate levels is vital; it should be deeper enough to alleviate the patient discomfort but should keep them responsive to avoid the associated complications.

The current practice to achieve the desired level of conscious sedation frequently relies on subjective clinical tools such as Ramsay sedation score (RSS).³ Although applicable in some clinical scenarios,

the subjective methods are susceptible to inter-observer variability and patient cooperation, thus inaccurate in many situations. Bispectral index (BIS), a computer-processed electroencephalogram (EEG) parameter has been in practice as an objective tool to measure the depth of sedation. Although a range of 60–80 is advocated for conscious sedation, the observed range varies widely, with the differing intensity of noxious stimulation according to the invasiveness of the procedure, and also affected by the chosen drug regimen.

Few studies have attempted to define the optimal range of BIS under the conscious sedation, for feasibly performing the bronchoscopy, oral and maxillofacial surgeries, and gastrointestinal endoscopy.^{3–5} However, the data on conscious sedation for awake fiberoptic intubation is sparse. We hypothesized that BIS monitoring could be utilized as an effective tool to guide the conscious sedation for awake fiberoptic nasotracheal intubation (AFNI) procedure. We aimed to obtain the optimal level of BIS required for achieving the adequate conscious

* Corresponding author. Department of Anaesthesiology, All India Institute of Medical Sciences, Virbhadr Marg, Rishikesh, Uttarakhand, 249203, India.

E-mail addresses: drghariharan93@gmail.com (H.H. Gnanaswaran), gauravhld@gmail.com (G. Jain), drankit80@gmail.com (A. Agarwal), ashichug@gmail.com (A. Chug), deepak.anaes@aiimsrishikesh.edu.in (D. Singla).

<https://doi.org/10.1016/j.jobcr.2020.06.004>

Received 18 April 2020; Accepted 19 June 2020

Available online 22 June 2020

2212-4268/ © 2020 Craniofacial Research Foundation. Published by Elsevier B.V. All rights reserved.

sedation in AFNI.

2. Material and methods

After institutional ethical approval and written informed consent, all American Society of Anesthesiologists grade I-II patients of either gender, aged 18–60 years, diagnosed as difficult airway on pre-anesthetic evaluation, and planned for AFNI, for elective surgery under general anesthesia, were included in this prospective, observational, cohort study (Indian Clinical Trial Registry No: CTRI/2018/07/014810). Those with known allergy to study medications, difficult mask ventilation, pregnancy, known hearing or visual problems, mental retardation, end-organ impairment, or any contraindication to nasotracheal intubation were excluded.

All enrolled patients were shifted to the operation theatre, and a standard monitor, BIS sensor, and an intravenous (IV) line were placed. All baseline vitals, RSS, and BIS values were recorded. Medications including Inj. Glycopyrrolate (0.2 mg, IM), Xylometazoline solution (2 drops in each nostril), and Inj. Lidocaine nebulization (4%, 2.5 mL over 15 min), were administered. After an initial 5 min of nebulization, intratracheal Inj. Lidocaine (2%, 2 ml) was instilled, and a bolus dose of Inj. Dexmedetomidine infusion [1 µg/kg, IV] was administered over the next 10 min.

At the end of infusion, if BIS ≤ 90 and RSS ≥ 2, an AFNI was attempted. If intubation was successful feasibly, the corresponding BIS level was recorded. If intubation was not possible due to agitation by the patient, BIS > 90 or RSS < 2, a bolus dose of propofol was given [0.5 mg/kg, IV] over 30 s. After 1 min of propofol dose, both BIS and RSS were reassessed for the above criteria, and intubation was attempted accordingly. This process was repeated until the patient was successfully intubated. At any time-point during the procedure, if any untoward event (hypoxia, hypotension, bradycardia, etc.) occurred, the corresponding BIS level was recorded and the patient was resuscitated. Thereafter, intubation was attempted as per the above protocols. An anesthetist, experienced in performing AFNI, conducted the entire procedure. Another investigator blinded to the procedure recorded the outcome parameters. The primary outcome was the lowest BIS value at which AFNI could be feasibly performed, and defined as “Stable BIS”. The BIS and RSS values were also recorded at baseline, 15 min, and 2 min intervals thereafter, until intubation was feasibly performed.

Taking a 53% sensitivity of BIS for estimating adequate conscious sedation (Russell et al.), with a 20% precision, and 95% confidence interval, we calculated the sample size as 86 (Cochran formula).^{6,7} Considering a dropout rate of 10%, the total sample size was calculated as 94. The statistical analysis was done using SPSS 23.0 (IBM Corp. Armonk, NY, US) and MedCalc software version 19.0.7 (MedCalc Software Ltd, Acaciaaan, Belgium). A Receiver Operating Characteristic (ROC) curve and the Youden index were used to estimate the sensitivity, specificity, predictive value, and the optimal level of BIS for adequate conscious sedation in AFNI. The correlation between stable BIS and baseline demographics were compared using a correlation coefficient. The relation between BIS and RSS was analyzed using Bland Altman plot, and the intraclass correlation coefficient. The relationship between any untoward event and BIS were analyzed by the student's t-test. A P value < 0.05 was considered significant.

3. Results

From July 2018 over a period of 16 months, we included 94 eligible patients, and all of them completed the study successfully. The demographic profile of patients has been summarized in Table 1. The mean time taken for AFNI was 3.5 min. Forty-five patients did not require any propofol boluses, 31 required single bolus, while 18 required two or more doses. The baseline characteristics viz. age, weight, mouth opening, and the modified Mallampati grade of the patient were plotted against the stable BIS in a correlation graph, to see their impact upon

Table 1
Characteristics of included patients.

S. No.	Parameter	Values (n = 94)
1.	Age (Years)	36.82 ± 13.68
2.	Weight (kg)	55.50 ± 10.44
3.	Male	67 (71%)
4.	ASA	Grade 1 71 (76%)
		Grade 2 23 (24%)
5.	MMP	Grade 2 7 (7%)
		Grade 3 32 (34%)
		Grade 4 55 (59%)
6.	Mouth opening	< 1 cm 23 (25%)
		1–2 cm 51 (54%)
		> 2 cm 20 (21%)
7.	Type of surgery	ENT 14 (15%)
		Burn and plastic 7 (7%)
		Dental 28 (30%)
		Surgical Oncology 45 (48%)
8.	Number of propofol boluses	0 45 (48%)
		1 31 (33%)
		≥ 2 18 (19%)
9.	Time taken for intubation minutes)	3.50 ± 2.07
11.	BIS	Baseline 100 (95–100)
		15 min 88.5 (84–94)
12.	Stable BIS	Median (range) 84.5 (80–88)
		80–82 19 (20%)
		83–85 44 (47%)
		86–88 31 (33%)

Data is presented as mean ± standard deviation, number (percentage) or median (range). ASA indicates American society of Anesthesiologists; MMP: Modified Mallampati grade; BIS: Bispectral Index; ENT: Ear, nose, throat.

the results. None of the above parameters, however, showed any correlation with the observed values of stable BIS (Fig. 1).

In total, 354 BIS values (range 76–100) were obtained from the 94 included patients. Under sedation, 260 BIS values (range 76–94) were noted. The median value of stable BIS was 84.5 (range: 80–88), with 67% values with the range of 80–85. The area under the ROC curve demonstrated a moderate discriminatory power of BIS [0.80, confidence interval (CI): 0.74–0.84] in judging adequate conscious sedation in the process of AFNI (Fig. 2). The optimal criterion value for BIS was obtained as ≤ 86 at a Youden index of 49.74 (sensitivity 88.30%, specificity 61.45%). The predictive profile for the entire range of BIS values is shown in Table 2. The RSS values ranged from 1 to 3. The RSS of “3” and “2” corresponded to a mean BIS level of “83.3” and “86.5”, respectively.

A Bland Altman plot was plotted with the standardized mean of BIS and RSS, which indicated a good agreement between the two scores (Fig. 3). Since the above scores represent the degree of sedation in the opposite directions (RSS of “6” and BIS of “0” donate maximum sedation), the RSS was coded as inverse values (i.e. 1 as 6, 2 as 5, 3 as 4, 4 as 3, 5 as 2 and 6 as 1) to compare them with the corresponding BIS by intraclass correlation coefficient. It showed a value of 0.83 (CI 0.79–0.86), indicating good reliability between the above scores.

Overall, 3 patients had an episode of bradycardia (heart rate < 50), 2 developed hypotension (systolic blood pressure < 90 mm Hg), and one had hypertension (systolic blood pressure > 140 mm Hg), during the procedure. These episodes were transient, recovered spontaneously, and all the patients were thereafter intubated. The mean BIS levels at the onset of the above events (84.0 ± 1.78) were compared with all other BIS values (89.82 ± 6.41). It indicated a risk of untoward events at lower BIS values (P = 0.03).

4. Discussion

This study measured the optimal level of BIS as ≤ 86 for feasibly performing the AFNI procedure under conscious sedation. The stable BIS values varied over a range of 80–88, were safe and without any

Fig. 1. Correlation between baseline variables and the stable Bispectral index (BIS) values. “r” denotes correlation coefficient; Fig. 1A: Age; Fig. 1B: Weight; Fig. 1C: Modified Mallampati grade (MMP); Fig. 1D: Mouth opening. A $P < 0.05$ considered significant.

Fig. 2. Receiver operating characteristic curve for Bispectral index values under sedation. A $P < 0.05$ considered significant.

significant side-effects. A decrease in BIS value corresponded to a higher degree of specificity, although parallel fall in sensitivity was also observed.

The BIS algorithm had been derived from a large database of participants receiving various anesthetic drug regimens. The recommended range for conscious sedation varies widely according to the procedure. Bower AL et al. observed a BIS range of 75–85 with a 0.96 probability for getting an observer assessment of alertness/sedation score ≥ 3 in interventional gastrointestinal procedures.⁸ Bell JK et al. similarly

Table 2

Predictive profile of various Bispectral index scores.

S. No.	BIS	Sensitivity (%)	Specificity (%)	LR +	LR -	+ PV	-PV
1.	< 76	0	100.00	0	1.00	0	63.8
2.	≤ 76	0	99.40	0	1.01	0	63.7
3.	≤ 78	0	98.80	0	1.01	0	63.6
4.	≤ 79	0	98.19	0	1.02	0	63.4
5.	≤ 80	6.38	96.99	2.12	0.97	54.5	64.7
6.	≤ 81	9.57	96.99	3.18	0.93	64.3	65.4
7.	≤ 82	21.28	94.58	3.92	0.83	69.0	68.0
8.	≤ 83	28.72	92.17	3.67	0.77	67.5	69.5
9.	≤ 84	51.06	80.12	2.57	0.61	59.3	74.3
10.	≤ 85	68.09	75.30	2.76	0.42	61.0	80.6
11.	≤ 86	88.30	61.45	2.29	0.19	56.5	90.3
12.	≤ 87	95.74	51.20	1.96	0.08	52.6	95.5
13.	≤ 89	100	34.34	1.52	0	46.3	100
14.	≤ 90	100	27.11	1.37	0	43.7	100
15.	≤ 91	100	9.04	1.10	0	38.4	100
16.	≤ 92	100	3.61	1.04	0	37.0	100
17.	≤ 93	100	3.01	1.03	0	36.9	100
18.	≤ 94	100	0	1.00	0	36.2	100

BIS signifies Bispectral index; LR: Likelihood ratio; PV: Predictive value.

recommended an optimal BIS range of 80–85 for performing the endoscopies.³ The studies on oral and maxillofacial surgeries have concluded a BIS range of 80–85 for adequate conscious sedation.^{4,9} The literature on interventional bronchoscopy, however, recommends a BIS range of 40–75, corresponding to deeper hypnotic levels as required for the general anesthesia.^{5,10} As AFNI required the placement of endoscope tip within the trachea much proximal to the carina, we hypothesize that it avoided any stimulation to the carina and the bronchial tree, as occurs routinely during the interventional bronchoscopy procedure. Thus, AFNI required a lighter sedation plane, which is desirable in a difficult airway and corresponded to a BIS range of 80–88.

To achieve the required level of conscious sedation, we utilized

Fig. 3. Bland Altman plot of agreement between the Bispectral index (BIS) and Ramsay sedation score (RSS).

dexmedetomidine to exploit its favorable profile viz. anxiolysis, sedation, analgesia and preservation of respiratory efforts.¹¹ The patient agitation, however, necessitated the administration of propofol, a short-acting hypnotic, to produce an immediate short-lasting effect.³ The bolus doses allow more frequent drug administration with less concern of complications. Though it allowed consciousness level to decrease briefly, all the patients remained responsive to verbal commands and had no respiratory difficulty. Since BIS values are derived from the analysis of cerebral cortical electrical epochs of 15–30 s duration, a noticeable change is expected after the same period. We recorded the RSS and BIS values at “1 min” after the drug administration, taking into consideration the above fact and the time duration for the onset of action of propofol. We observed a significant correlation between the BIS values and the RSS at all time points of the study. This further validates the reliability of the obtained stable BIS scores during the AFNI procedure. These results are in coherence with previous trial conducted to evaluate the compliance between the BIS and RSS under the different settings.¹²

The effect of baseline characteristics, especially age on the BIS values for a particular depth of sedation, has not been well addressed. Katoh et al. showed that BIS at which response to verbal commands was suppressed is not affected by the age of the patient.¹³ In contrast, Lysakowski et al. observed that during a loss of consciousness under the propofol induction, all EEG based parameters including BIS and entropy were significantly higher in the elderly age group as compared to the younger patients.¹⁴ There has also been an inter-individual variability in the sensitivity to the hypnotic effects of propofol. It is related to patient body weight as a result of common weight-based drug administration.¹⁵ Dexmedetomidine, on the other end, has no significant sex or age-related effects on the pharmacokinetic profile.¹¹ We observed that stable BIS was independent of any of the baseline characteristics for predicting the depth of sedation. We believe that exclusion of pediatric or elderly patients together with minimal need of propofol boluses might have contributed to the above results. Another cause could be the difference in the effects of baseline characteristics on stable BIS, under the lighter sedation and the general anesthesia, respectively.

The complication rates are expected to increase with deeper levels of sedation. Avci S et al. predicted an average BIS score of 70.8 for predicting the associated complications.¹² We observed only a few untoward events at a BIS range of 76–94, none requiring any intervention. The included patients belonged to the non-geriatric age group and had no systemic comorbidities. The above factors might have also

contributed to minimal complication in this study. Further data on larger sample size is however required to define the optimal BIS range that provides suitable conscious sedation, with minimal untoward effects. Future studies can also test this hypothesis on the other population groups.

There were some limitations of the study. The investigator performing the AFNI procedure was not blinded to the sedation protocols. Since the procedure required the administration of propofol boluses as per need, it was not possible to achieve optimal blinding conditions. The outcome parameters were however blinded, so avoid any associated bias. The BIS values may be affected by other unaccounted factors such as frontalis muscle activity, hypothermia, sleep, blood glucose levels, and noise. Although we performed the AFNI procedure in an elective controlled environment excluding all the possible influencers, the above factors may still affect the results. The variation in the study protocols may also modify the obtained stable BIS values.

In conclusion, BIS serves as an effectual objective tool for calibrating the depth of conscious sedation. Considering a practical difficulty in maintaining a static BIS value due to its fluctuating nature, we advocate a BIS range of 80–86 for feasibly performing the AFNI procedure.

Source of support

No funding.

CRediT authorship contribution statement

Hari Haran Gnanewaran: Conceptualization, Writing - original draft, Writing - review & editing. **Gaurav Jain:** Conceptualization, Writing - original draft, Writing - review & editing. **Ankit Agarwal:** Writing - original draft, Writing - review & editing, Data curation. **Ashi Chug:** Formal analysis, Writing - original draft, Writing - review & editing. **Deepak Singla:** Formal analysis, Writing - original draft, Writing - review & editing.

Declaration of competing interest

Nil.

References

1. Mavridou P, Dimitriou V, Manataki A, Arnaoutoglou E, Papadopoulos G. Patient's

- anxiety and fear of anesthesia: effect of gender, age, education, and previous experience of anesthesia. A survey of 400 patients. *J Anesth.* 2013;27:104–108.
2. Ni YL, Lo YL, Lin TY, Fang YF, Kuo HP. Conscious sedation reduces patient discomfort and improves satisfaction in flexible bronchoscopy. *Chang Gung Med J.* 2010;33(4):443–452.
 3. Bell JK, Laasch HU, Wilbraham L, England RE, Morris JA, Martin DF. Bispectral index monitoring for conscious sedation in intervention: better, safer, faster. *Clin Radiol.* 2004;59(12):1106–1113.
 4. Mishra N, Birmiwai K, Pani N, Raut S, Sharma G, Rath K. Sedation in oral and maxillofacial day care surgery: a comparative study between intravenous dexmedetomidine and midazolam. *Natl J Maxillofac Surg.* 2016;7(2):178.
 5. Fadaizadeh L, Hoseyni MS, Shajareh E, Heydari G, Ardehali SH. Use of bispectral index score for interventional bronchoscopy procedures. *Tanaffos.* 2015;14(4):246–251.
 6. Russell IF. The ability of bispectral index to detect intra-operative wakefulness during isoflurane/air anaesthesia, compared with the isolated forearm technique. *Anaesthesia.* 2013;68(10):1010–1020.
 7. Kasiulevičius V, Šapoka V, Filipavičiūtė R. Sample size calculation in epidemiological studies. *Gerontol.* 2006;7(4):225–231.
 8. Bower AL, Ripepi A, Dilger J, Boparai N, Brody FJ, Ponsky JL. Bispectral index monitoring of sedation during endoscopy. *Gastrointest Endosc.* 2000;52(2):192–196.
 9. Taniyama K, Oda H, Okawa K, Himeno K, Shikanai K, Shibutani T. Psychosedation with dexmedetomidine hydrochloride during minor oral surgery. *Anesth Prog.* 2009;56(3):75–80.
 10. Lo YL, Lin TY, Fang YF, et al. Feasibility of bispectral index-guided propofol infusion for flexible bronchoscopy sedation: a randomized controlled trial. *PLoS One.* 2011;6(11):1–7.
 11. Kim KH. Safe sedation and hypnosis using dexmedetomidine for minimally invasive spine surgery in a prone position. *Korean J Pain.* 2014;27(4):313–320.
 12. Avcı S. Evaluation of the compliance between EEG monitoring (Bispectral Index™) and Ramsey Sedation Scale to measure the depth of sedation in the patients who underwent procedural sedation and analgesia in the emergency department. *Turkish J Trauma Emerg Surg.* 2018;25(5):447–452.
 13. Katoh T, Bito H, Sato S. Influence of age on hypnotic requirement, bispectral index, and 95% spectral edge frequency associated with sedation induced by sevoflurane. *Anesthesiology.* 2000;92(1):55–61.
 14. Lysakowski C, Elia N, Czarnetzki C, et al. Bispectral and spectral entropy indices at propofol-induced loss of consciousness in young and elderly patients. *Br J Anaesth.* 2009;103(3):387–393.
 15. Rüsch D, Arndt C, Eberhart L, Tappert S, Nageldick D, Wulf H. Bispectral index to guide induction of anesthesia: a randomized controlled study. *BMC Anesthesiol.* 2018;18(1):1–10.