Original Article

Correlation Between Observational Scales of Sedation and Comfort and Bispectral Index Scores

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Abstract

Context. When palliative care patients enter the phase of unconsciousness preceding death, it is standard practice to initiate or continue a subcutaneous infusion of an opioid plus or minus a sedative. The doses are determined somewhat empirically and adjustments are based on clinical assessment and observational measures of sedation and comfort. Following reports that these observational measures could be misleading, this study assesses their validity by comparing them with an objective measure of sedation, the Bispectral Index Score (BIS).

Objective. The objective of this study was to determine the validity of the Richmond Agitation and Sedation Scale (RASS) and the Patient Comfort Score (PCS) in assessing sedation and comfort in unconscious patients.

Methods. Forty eligible and consenting patients were monitored from the onset of unconsciousness (unresponsiveness) until death. Measures of sedation (RASS) and comfort (PCS) were made by the attending nurse every four hours. Correlation coefficients examined the relationship between fourth hourly RASS and PCS and time-matched BISs.

Results. A significant correlation was found between RASS and BIS and PCS and BIS. Sedation and comfort scores were concentrated at the lower end of the respective scales, whereas time-matched BISs were widely scattered with scores ranging from near full awareness to deep sedation.

Conclusions. Compared with BIS, both RASS and PCS appear to be relatively blunt instruments at the lower end of their respective scales. Due caution should be taken interpreting and making clinical decisions based solely on the RASS and PCS and, by extension, other observational measures of patient comfort and sedation. J Pain Symptom Manage 2017;54:186–193.
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Key Words

Unconsciousness, palliative care, observational scales, Bispectral Index Score

Introduction

Although most palliative care patients pass through a phase of unconsciousness before death, we have little knowledge of what they experience nor do we have conclusive proof of the validity of observational scales used to assess their level of sedation and comfort.[1–4] Clinical assessment of unconscious patients relies heavily on subjective evaluations that include observational scales of sedation and comfort. These scales are formulated around the principle that unconscious patients who exhibit none of the recognized markers of pain or distress are comfortable and adequately sedated. Although the reliability of such scales has been tested with palliative care, intensive care (IC), and pediatric patients,[5–7] their validity is now being questioned following reports which suggest unconscious patients may experience distress that goes unrecognized because of the absence of clinical descriptors.[1–3,8] The worst case scenario is

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that patients are more aware than the observational measurements indicate and suffer in silence because of their inability to respond.

Until now, research into the level of sedation and comfort in unresponsive palliative care patients and the validity of observational scales designed to quantify these parameters has not been possible. Included in the list of reasons has been the lack of an objective, noninvasive measure of awareness that is reliable and appropriate for this purpose. The Bispectral Index monitor, a commonly used means of monitoring sedation during anesthesia, fulfills many of these criteria.[9]

Bispectral Index Score (BIS) correlates strongly with levels of sedation, and the technology is a validated and frequently used method of monitoring sedation within the anesthetic setting.[10] The contribution of the Bispectral Index monitor to the care of patients in IC is not as well substantiated and reports of its usefulness in this setting vary considerably.[7,11–17] Apart from two pilot studies[18,19] and a recent validation study,[20] there are no reports that document the reliability and validity of the Bispectral Index monitor with palliative care patients. Both pilot studies suggest the monitor could contribute to patient care and lead to a better understanding of the dying process. The validation study, however, raises questions about the reliability of the monitor after noting a wide range of BISs in patients who, on clinical measures, appeared to be comfortable and deeply sedated.

The present study aims to increase the body of knowledge around the validity and reliability of both the Bispectral Index monitor and two observational scales used to assess sedation and comfort in unconscious palliative care patients.

Methodology

The study was carried out in a 15-bed nonacademic palliative care unit at the Port Kembla Hospital, NSW Australia. Nursing staff attached to the unit were consulted about the implementation of the study. Questions surrounding institutional capacity, increased work load, and the potential clash between research goals and palliative care principles were raised and satisfactorily resolved. Regular in-service training and information sessions were undertaken to ensure competence and proficiency in all aspects of the study.

Instruments and Assessment Tools

The Bispectral Index monitor is a small bedside instrument distributed in Australia by Covidien Pty Ltd. It is a noninvasive and validated means of determining the hypnotic effect of sedative and anesthetic medication.[10] BISs range from 100 (fully awake and aware) to 0 (brain death). Values between 40 and 60 are



Fig. 1. Patient connected to Bispectral Index monitor via adult Quatro sensor. All rights reserved. Used with permission of Covidien.

common with palliative sedation, coma, deep sleep, and anesthesia. Although the monitor is not a measure of nociception, BISs rise when pain or discomfort is sufficiently troublesome to rouse a patient from their sedated or unconscious state.[21]

Each patient is connected to the monitor via an adult Quatro sensor applied to the forehead (Fig. 1). The monitor analyses electroencephalogram input from the frontal cortices and converts this by means of a validated algorithm into a dimensionless score called the BIS. The score is calculated every 15 to 30 seconds and a continuous one-hour record appears on a rolling display together with measures of electromyographic (EMG) activity from the frontalis muscle and signal quality (SQ). BIS, EMG, and SQ are stored, and a minute-by-minute record is available as a PDF download for the duration of each recording. BISs were only considered valid if the SQ was 80% or greater and EMG did not exceed 50 dB.[11] Sensor checks were performed at the commencement of each study and regularly throughout the monitoring period. The sensor was changed if one or more of the electrodes failed the impedance test or if SQ remained below 80% despite corrective measures. Sensors were also changed routinely after 24 hours use.

The observational measures used are the Richmond Agitation-Sedation Scale (RASS) and the Patient

Comfort Score (PCS). The former was chosen because of its ease of interpretation and validity in detecting changes in the level of consciousness associated with medically induced sedation.[5,6,22] It is a 10-point scale with four levels of agitation (+4, combative to +1, restless), one level of calm/alert (0), and five levels of sedation (−1, drowsy to −5, unresponsive). The PCS is an adaptation of a scale described by Breura et al.[23] The score is derived from a numerical rating scale that ranges from 0 to 10, where 0 equates to complete comfort, 1−4 mild discomfort, 5−6 moderate discomfort, and 7−10 severe discomfort. It was chosen for its clarity, minimalism, and good inter-rater reliability in pre-study testing.

Ethical Approval, Eligibility, Consent, and Recruitment

Approval for the study was obtained from the University of Wollongong Human Research Ethics Committee. Patients were eligible for the study if they met the following criteria: 1) older than 18 years, 2) admitted for end-of-life care, 3) conscious, competent, and able to speak and understand English, 4) emotionally stable and in the opinion of the treating doctor neither the patient or family would be distressed by any discussion of the study, 5) not pregnant, 6) not fitted with an internal cardiac pacemaker or defibrillator, 7) not of indigenous descent (the inclusion of Indigenous people required additional approval from The Australian Institute of Aboriginal and Torres Strait Islander Studies Research Ethics Committee. Based on the very small number of Indigenous people previously admitted to the unit we chose not to proceed. This decision was subsequently vindicated with only one person of Indigenous descent being admitted during the study period), and 8) not receiving ketamine (based on reports of paradoxical increases in BIS when ketamine is used as a general anesthetic.[24])

The study commenced on March 31, 2013, and concluded on February 12, 2015. During this time, there were 450 deaths within the unit. Only 102 patients met the eligibility criteria at the time of admission. In 31 instances, the patient, his/her family, or both declined consent. In a further 13 cases, the patient deteriorated before or immediately after discussion with the doctor and was too unwell for the recruiting process to continue. Consent was obtained from the remaining 58 subjects and the designated next of kin. Sixteen of these patients deteriorated suddenly and died before they could be connected to the monitor or were so close to death monitoring was felt to be inappropriate. A further two patients deteriorated and died when the sole Bispectral Index monitor was in use.

Study Design

The 40 eligible and consenting patients were monitored from the onset of unconsciousness (unresponsiveness) until death. Measures of sedation (RASS) and comfort (PCS) were made by the attending nurse every four hours. Results were recorded on a specially designed chart together with the exact time of each assessment to allow comparisons with time-matched BISs. Nurses were blinded to the BIS at the time of all assessments to avoid potential bias. Periodic sensor checks were made outside assessment times and the investigating team notified if the check failed or if a message appeared on the screen alerting nurses to the presence of excessive artifact. All decisions regarding patient care and treatment were made independent of BISs. The stored BIS, EMG, and SQ for each minute of monitoring was downloaded before a change or removal of the sensor and the data analyzed after the patient had died.

Statistical Analysis

Each patient was assigned a numerical code to maintain anonymity of the data. The link between the code number and patient could only be accessed by one of the researchers (MB). Descriptive statistics on the main measures, BIS, EMG, RASS, and PCS are provided. Correlation coefficients examining the relation between four-hourly measurements of BIS vs. RASS and vs. PCS were performed using the method of Bland and Altman for calculating correlation coefficients with repeated within-subject observations.[25] The *P*-value for the relation between types of observation was determined by the F-test in the analysis of variance required by the Bland and Altman method to remove the within-subject variance from the final correlation coefficient. *P* was considered significant at values where $P < 0.05$. BIS recordings for four-hourly measurements met quality standard (SQ ≥80) in 97% of readings. The equivalent quality standard for EMG readings was 99%.

Results

The characteristics of the study population, median scores for BIS, EMG, RASS, and PCS based on 297 readings of the four-hourly data, and medications in use at the time of death are listed in Table 1. Thirty-five patients in the study population had a solid tumor, three had leukemia, another multiple myeloma, and one patient had a nonmalignant condition (cerebrovascular accident). An opioid together with midazolam was administered to all patients by a continuous subcutaneous infusion. A smaller number of patients received additional medications which included one or more of the following: haloperidol, hyoscine

Table 1
Characteristics of the Study Population ($n = 40$), Results of BIS, EMG, RASS, and PCS Scores From Four-Hourly Readings and Subcutaneous Medications at Time of Death

Characteristics	Variable	Range
Mean age (yrs)	74	41–97
Female/male	15/25	
Mean length of inpatient stay (days)	29.8	3–95
Mean duration of sedation (days)	3.6	1–14
Mean duration of unconsciousness (hours)	22.4	<1–91

Main Outcome Measures	Median	Interquartile Range (Q1–Q3)
BIS	54	42–67
EMG	36	31–41
RASS	−5	−5 to −4
PCS	0	0–0

Medication	Number of Patients[a]	Mean ± SD
Opioids (s.c. morphine eq. mg/day)	40	80.2 ± 70.3
Midazolam (mg/day)	40	25.0 ± 8.7
Haloperidol (mg/day)	21	2.9 ± 2.6
Hyoscine hydrobromide (mg/day)	10	2.1 ± .5
Hyoscine butylbromide (mg/day)	8	52.5 ± 14.8
Clonazepam (mg/day)	6	8 ± 0
Phenobarbitone (mg/day)	5	1840 ± 456.1

BIS = Bispectral Index Score; EMG = electromyography; RASS = Richmond Agitation and Sedation Scale; PCS = Patient Comfort Score.
[a]Total numbers of medications add to more than 40 as all patients received multiple medications.

hydrobromide, hyoscine butylbromide, clonazepam, and phenobarbitone (Table 1). Breakthrough medications were administered as required. The most common breakthrough agents included an opioid, midazolam, and hyoscine hydrobromide.

The varied time course of the four-hourly BIS recordings in the 24 hours preceding death are plotted in Figure 2 for the 17 patients who had at least 24 hours of observation. Correlation coefficients examining the relation between four-hourly measurements of BIS vs. RASS and vs. PCS were performed using 297 pairs of observations for the 40 patients. Scatter plots with linear regression for BIS vs. RASS and BIS vs. PCS are shown in Figures 3a and 3b. The relation between BIS and RASS showed a correlation coefficient of 0.42, which was highly significant $P < 0.0004$. The relation between BIS and PCS was weaker than for RASS with a correlation coefficient of 0.30 but was also highly significant, $P = 0.003$. As expected, the relation between the two validated clinical observation scores was also highly significant (RASS vs. PCS, correlation coefficient 0.57, $P < 0.0004$).

Discussion

In this study, a strong correlation was found to exist between BIS and RASS ($P < 0.0004$) and BIS and PCS ($P = 0.003$), suggesting that both scales are valid instruments for estimating the level of sedation and comfort, respectively, in unconscious palliative care patients. The scatter plots for RASS and PCS (Figs. 3a and 3b) show most scores are concentrated at the lower end of each scale. With RASS, this indicates an absent patient response to vocal and physical stimulation, and for PCS, it designates complete patient comfort. Given the context of the study, this finding is not unexpected. Corresponding BISs, however, are widely scattered ranging from a high of 95 to a low that approaches zero (Figs. 3a and 3b). Similar fluctuations have been noted in a recent publication by Masman et al., leading them to question the reliability and usefulness of the monitor in routine clinical practice.[20]

Signal pollution from high EMG activity has been identified as one of the most frequent sources of spurious BIS readings[24,26,27] and has led several authors other than Masman to advise caution in interpreting BISs.[11–13] Efforts have been made in the present study to exclude spurious BISs by not including data when EMG levels exceeded 50 dB and SQ fell less than 80%. Although this does not guarantee the validity of our data, it reduces the likelihood of misleading BISs and invites alternative explanations for the observed fluctuations other than the reliability of the monitor. The heterogenous patient population and the role of the many and varied medications used need to be considered. A more promising line of inquiry, however, would be to look at our limited understanding of unconsciousness and what observational scales and the Bispectral Index monitor actually measure. A better appreciation of unconsciousness could help to explain the discrepancy between the observational and objective measures which until now have been attributed to fundamental limitations of the monitor and/or the observational scales.[7]

When assessing unconscious patients, a distinction is generally made between the level of consciousness and the subjective experience of the patient.[28–30] The former is a measure of contact the unconscious person appears to have with the outside world and is quantifiable by means of observational scales, such as the RASS and PCS. The subjective experience is the patient's own experience of unconsciousness and has little relation to the level of consciousness.[28] An unconscious patient may, therefore, experience pain, fear, so forth, and not manifest visible clinical markers, such as restlessness or grimacing. The patient's

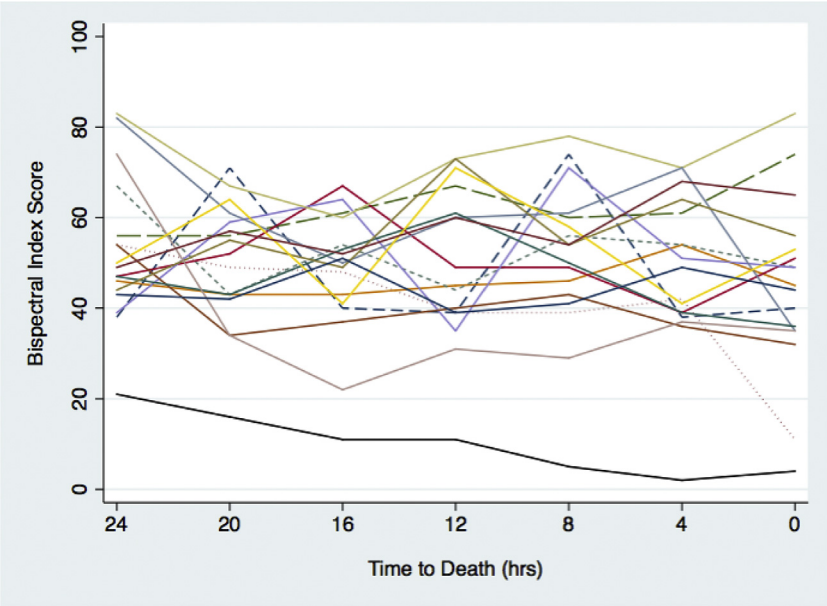


Fig. 2. The time course of the Bispectral Index Score recordings in 17 patients with 24 hours of observations before death. Note: Time 0 does not coincide with death. It represents the closest four-hourly reading to the moment of death.

experience of unconsciousness is much harder to measure. The Bispectral Index monitor is principally a measure of sedation, but as BISs can be influenced by alterations in a patient's subjective experience,[21] trend changes in BISs offer an opaque window into the patient's inner world. The extent to which BISs change depends on the intensity and nature of the subjective experience.

An important consideration then, when comparing observational scales and BISs, is to understand they do not measure the same thing.[7,28] A significant disconnect can exist between the two when a patient experiences discomfort or distress sufficient to arouse them while not altering their perceived level of consciousness. An example of this "covert consciousness"[30] is found in several anecdotal reports.[19,p.106] One describes a patient in whom the only clue she was in pain came from a raised BIS while in another patient the BIS was seen to rise when the bedside phone rang. This same disconnect could explain the discrepancy between BIS and observational scores as seen in Figures 3a and 3b and may account for some of the fluctuations in BISs noted in Figure 2.

A disconnect between level of consciousness and the patient's experience has been reported in the anesthetic and IC literature. In one review, a median 37% of anesthetized patients, which included patients receiving midazolam or propofol, were found to have "connected consciousness" or an awareness of what was happening despite being unresponsive.[31] A similar finding in IC studies led the authors to conclude that the absence of any physical response should not be interpreted as a lack of awareness.[32,33]

The concentration of RASS and PCS at the lower end of their respective scales has led us to conclude that both scales (and by extension other observational scales) are relatively blunt instruments particularly at their lower reaches, just where greater acumen is needed. Low scores should be interpreted cautiously even with instruments that have been validated. Despite its technologic limitations and palliative care's commitment to a noninterventionist approach to care, the Bispectral Index monitor may complement observational scales leading to a more comprehensive appraisal of unconscious patients and improved end-of-life care.[2,3] In some instances, it may also give the necessary assurance that a dying patient is not suffering in silence.

Although it would be premature to make a definitive statement about the reasons for the discrepancy between observational and BISs, the evidence suggests it could be related to our limited understanding of unconsciousness, uncertainty about what we are actually measuring and shortcomings with the instruments currently in use.

The major limitation of this study is the unproved reliability of the Bispectral Index monitor outside the anesthetic setting and the lack of data to confirm the validity of BISs as a measure of a person's subjective experiences. Further studies, particularly those that incorporate raw electroencephalographic data

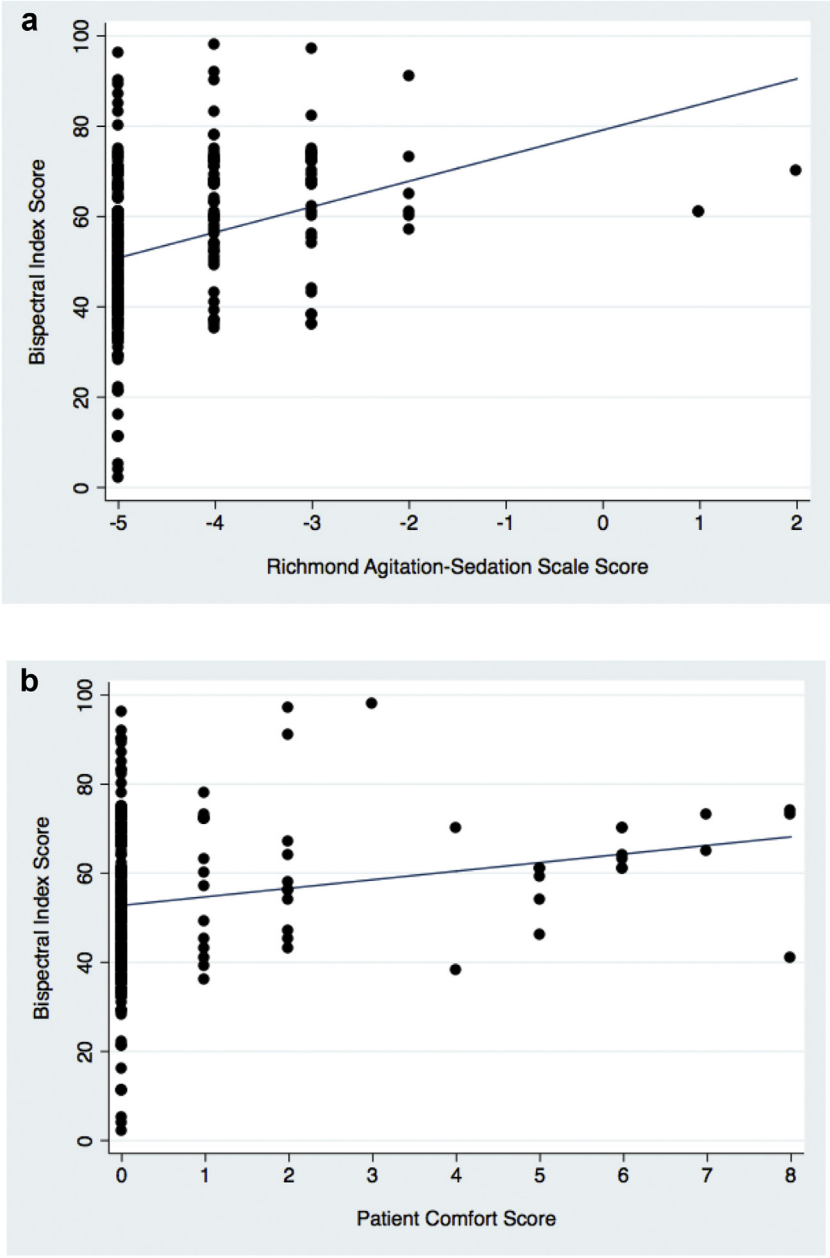


Fig. 3. (a) Relation between Bispectral Index Score and Richmond Agitation and Sedation Scale (correlation coefficient = 0.42; $P < 0.0004$). (b) Relation between Bispectral Index Score and Patient Comfort Score (correlation coefficient = 0.30; $P = 0.003$).

may help resolve these uncertainties. The other significant limitation is the relatively small sample size of 40, which was revised down from the original goal of 50 because of the time taken to recruit eligible and consenting patients.

Conclusion

This is one of a small number of studies to have looked at the role of the Bispectral Index monitor in the palliative care setting. Concerns raised in this and other studies about the validity of observational scales signal the need for additional research. Similarly, the reliability of Bispectral technology and the validity of BISs outside the controlled conditions of an operating theater requires further evaluation. Research of this nature is both ethically and methodologically challenging. Without it, however, there is little prospect of establishing an evidence base for observational measures currently used in palliative care. Until further data becomes available, the limitations of observational scales in reliably assessing unresponsive palliative care patients should be borne in

mind. Over-reliance on them is cautioned. The Bispectral Index monitor may be a useful addition to observational scales in assessing sedation, comfort, and the patient's own experience. In so doing, it may guide clinicians in preventing unwanted under-sedation and unnecessary over-sedation.

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