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CORRELATION BETWEEN THE SEDATION AGITATION SCALE AND BISPECTRAL INDEX FOR SEDATION IN THE MECHANICALLY VENTILATED PATIENTS IN INTENSIVE CARE UNIT

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Abstract

Background: Adequate sedation is required for smooth ventilation of patients on invasive mechanical ventilation. Under sedation may result in prolonged stress mobilization and patient harm, whereas over sedation obscures neurologic abnormalities and increases mortality and morbidity. In instances such as deep sedation/analgesia, the Bispectral Index (BIS) may be used as an auxiliary to clinical assessment of sedation to assist in determining depth of sedation. Determining the correlation between clinical and BIS measurements of sedation will assist in determining the appropriate role of BIS in intensive care unit (ICU). The aim of the present study to monitor depth of sedation of patients in ICU using Riker Sedation Agitation Scale (RSAS) and to assess the correlation between RSAS & BIS.

Methods: The present observational study was conducted from May 2022 to April 2023. 47 cases that required mechanical ventilation and sedation with a baseline intact brain function were enrolled as per inclusion-exclusion criteria. Patients of either of 18 years or older who required mechanical ventilation and sedation with a baseline intact brain function and willing to participate were included in the study. Patients with age less than 18 years, diagnosed or suspected condition that resulted in a decreased level of consciousness or reduced blood flow/oxygen supply of the brain, i.e., prolong seizure activity, encephalopathic state, hypoxemia with PaO2 less than 55 mm Hg, altering level of consciousness, and severe ischemic or hemorrhagic stroke were excluded from study. Patients with clinical states such as drug overdose producing alterations in level of consciousness, severe anemia impairing consciousness, and severe alkalotic/ acidotic states, patients with birth injuries impairing neurologic function such as cerebral palsy were not included in study. The BIS and RSAS measurement was done before initiation of sedation & in 4-hour intervals after initiation of sedation

up to 24 hours.

Results: At all the periods of observation correlation between BIS and RSAS were highly significant and level of correlation was strong to very strong/perfect.

Conclusion: BIS monitoring may play an additional function in sedation assessment in cases where the clinical assessment is ambiguous. BIS results must be taken with caution, however, because electromyography activity and other variables appear to confuse BIS scores. Additional research is required to determine the clinical utility of BIS monitoring in ICU practice.

Keywords: electrophysiological monitoring, mechanical ventilation, intensive care unit, sedation, bispectral index

Introduction

Adequate sedation is required for smooth ventilation of patients on invasive mechanical ventilation in ICU. These patients also need sedation to reduce their anxiety and pain perceptions, and stress responses. The titration of optimal sedation for patients on mechanical ventilation is a challenging task and many patients are at risk of being under or over-sedated. [1] Extreme care must be taken between the peaks of over sedation and under sedation in critically ill patients. Sedation monitoring can be done by using various sedation assessment scales available to assess the level of consciousness and reactivity to stimuli, among these, the Ramsay Scale, RSAS, or Motor Activity Assessment Scale are commonly used. [2] Patients with a decrease level of consciousness, on muscle relaxant, deep sedation/analgesia, or in state of encephalopathy are less accurate and receptive throughout this the evaluation. In these groups, subjective clinical evaluation determines the regulation and monitoring of sedation, which can result in under sedation or over sedation.

The BIS is a non-invasive electroencephalogram (EEG) device applied to the forehead through an adhesive electrode sensor strip. As the device's output, the BIS index is a dimensionless number ranging from 0 to 100, with 0 representing the absence of measurable brain activity and 100 signifying the awake state [3-5].

The aim of this study was to evaluate a correlation between the RSAS and the BIS in ventilated critical care unit patients.

Materials and Methods

This observational study was conducted in a tertiary level ICU. The study duration was one year from May 2022 to April 2023 (IRB no. 363/Ethics/2022). Patient were enrolled in the study after satisfying inclusion and exclusion criteria, total 47 patients were enrolled. Sample size calculated based on the previous study. [6]

Patients of either of 18 years or older who required mechanical ventilation and sedation with a baseline intact brain function and willing to participate were included in the study. Patients with age less than 18 years, diagnosed or suspected condition that resulted in a decreased level of consciousness or reduced blood flow/oxygen supply of the brain, i.e., prolong seizure activity, encephalopathic state, hypoxemia with PaO2 less than 55 mm Hg on room air, altering level of consciousness, and severe ischemic or hemorrhagic stroke were excluded from study. Patients with clinical states such as drug overdose producing alterations in level of consciousness, severe anemia impairing consciousness, and severe alkalotic/ acidotic states, patients with birth injuries impairing neurologic function such as cerebral palsy were not included in study. Patients were given continous intravenous sedation (fentanyl and midazolam) after initial bolus.

The RSAS is used for assessing the level of sedation in intensive care unit. RSAS is a reliable and valid subjective tool. In this study, Drager BIS monitor the infinity® BISx® SmartPod® was used. The RSAS scale ranges from 1-7 in which score 1 indicate unarousable patient at one extreme and score 7 is for dangerously agitated. In BIS scale reading of zero indicated no brain activity, and a reading of 100 indicated a fully awake state. The single channel of EEG data obtained from frontal-temporal montage electrode placement (4 electrode) is digitized and then subjected to multiple processing steps, ultimately producing the BIS value on a linear scale (0 -100). [7]

Results

All the ventilated patients admitted in ICU of institution screened, of those 47 patients fulfilling the inclusion criteria were enrolled in the study after obtaining consent from the caregiver/legal guardian.

Age of patients enrolled in the study ranged from 18 to 60 years, median age was 38 years, mean age was 39.81±12.70 years. Most common age group was 31-50 years, only 13 (27.7%) patients were aged 18-30 years rest 23.4% patients were aged ≥50 years. (Table-1) Out of 47 patients enrolled in the study, 27 (57.4%) were male and 20 (42.6%) were females.

Demographic characteristics	No.	%
Age Group (years)		
18-30 yrs	13	**27.7**
31-50 yrs	23	**48.9**
≥50 yrs	**11**	**23.4**
Mean age ± SD (Range; Median)	**39.81±12.70 (18-60; Median 38)**	
Gender		
Female	20	**42.6**
Male	**27**	**57.4**

TABLE 1: Demographic Profile of Study Population (N=47)

Bispectral Index and Sedation Agitation Scale of all the patients were assessed at baseline (0), thereafter at 4 hourly interval up to 24 hours (Table-2). Minimum sedation score were recorded when bolus sedation was given.

Time period in hours	Min.	Max.	Mean	SD
0	10.00	90.00	33.21	**22.16**
4	12.00	89.00	46.55	**25.29**
8	11.00	92.00	50.85	**23.41**
12	11.00	96.00	58.77	**24.34**
16	10.00	94.00	58.02	**27.69**
20	11.00	94.00	56.66	**25.08**
24	**10.00**	**92.00**	**60.40**	**27.70**

TABLE 2: Assessment of Bispectral Index at different time intervals (N=47)

During the overall period of assessment of BIS, minimum score recorded was 10.0 and maximum 96.00. Mean BIS was minimum at 0h (33.21±22.16) followed by at 4h (46.55±25.29) while mean BSI was maximum at 24h (60.40±27.70) followed by at 12h (58.77±24.34). A sequential increment in the BSI was observed till 12h. Range of RSAS during the period of study was 1 to 4 at all the periods except at 20 h where it was 1 to 5. Median SAS was 2.0 majority of the periods of observation except at 12h, 16h and 24h where median RSAS was 3.0. Mean RSAS was minimum at 0h (1.74±0.77) followed by at 4h (2.19±0.95) while maximum RSAS was observed at 24h (2.70±1.04) followed by at 12h (2.51±0.98) (Table-3). Minimum sedation score were recorded when

bolus sedation was given.

Time period in hours	Min.	Max.	Median	Mean	SD
0	1.00	4.00	2.00	1.74	**0.77**
4	1.00	4.00	2.00	2.19	**0.95**
8	1.00	4.00	2.00	2.28	**0.95**
12	1.00	4.00	3.00	2.51	**0.98**
16	1.00	4.00	3.00	2.49	**1.08**
20	1.00	5.00	2.00	2.47	**1.02**
24	**1.00**	**4.00**	**3.00**	**2.70**	**1.04**

TABLE 3: Assessment of Sedation Agitation Scale at different time intervals (N=47)

At all the periods of observation correlation between BIS and RSAS were highly significant and level of correlation was strong to very strong/perfect. (Figure *1-7*) (Table-4)

Time interval (hours)	'r'	Level of correlation	'p'	Level of significance
0	0.894	Strong	<0.001	**Highly significant**
4	0.930	Very strong/perfect	<0.001	**Highly significant**
8	0.887	Strong	<0.001	**Highly significant**
12	0.935	Very strong/perfect	<0.001	**Highly significant**
16	0.929	Very strong/perfect	<0.001	**Highly significant**
20	0.920	Very strong/perfect	<0.001	**Highly significant**
24	**0.926**	**Very strong/perfect**	**<0.001**	**Highly significant**

TABLE 4: Correlation of BIS and RSAS at different time intervals (N=47)

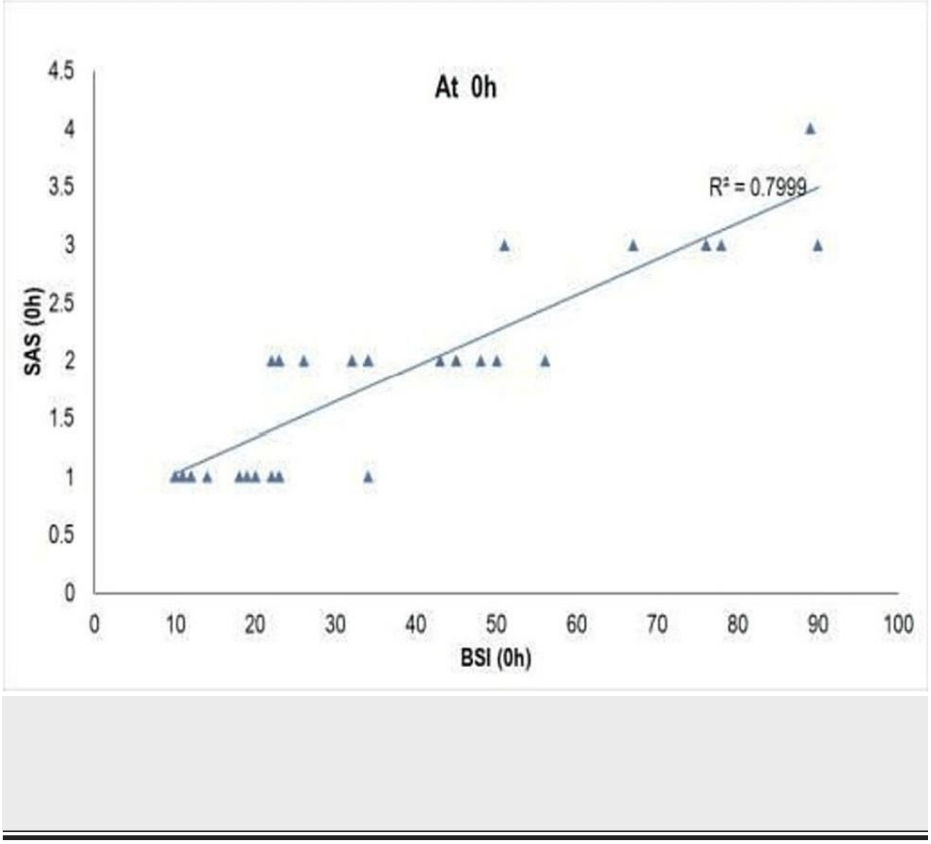

FIGURE 1: Figures showing correlation between BIS and RSAS at 0 hour

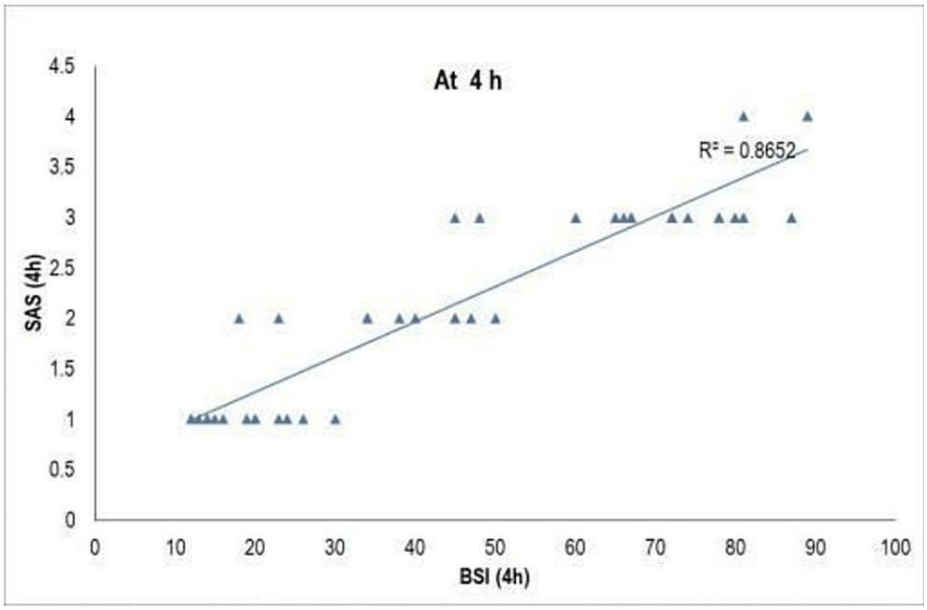

FIGURE 2: Figures showing correlation between BIS and RSAS at 4hour

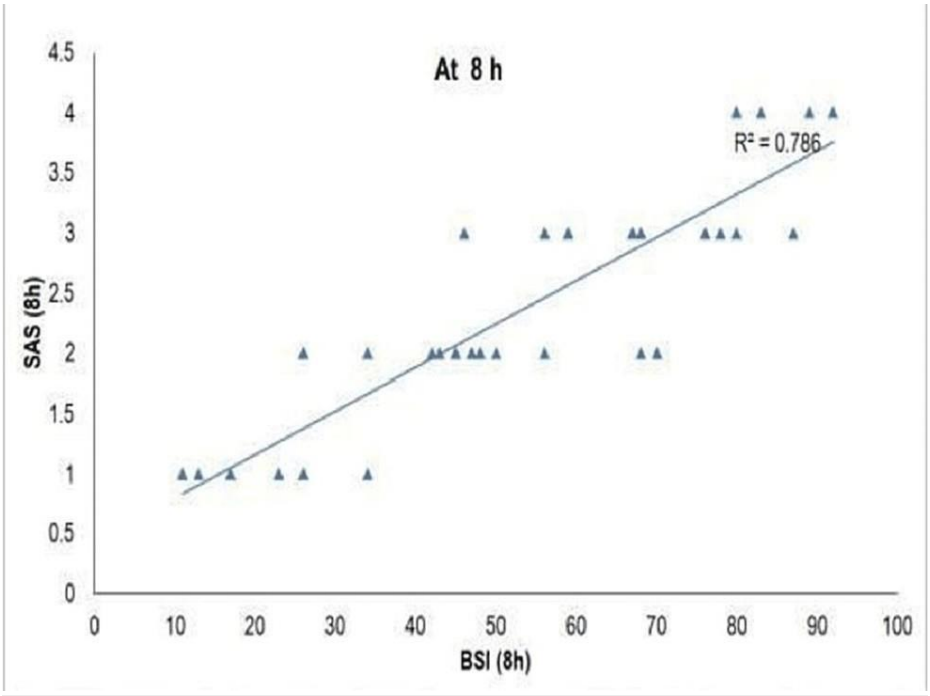

FIGURE 3: Figures showing correlation between BIS and RSAS at 8hour

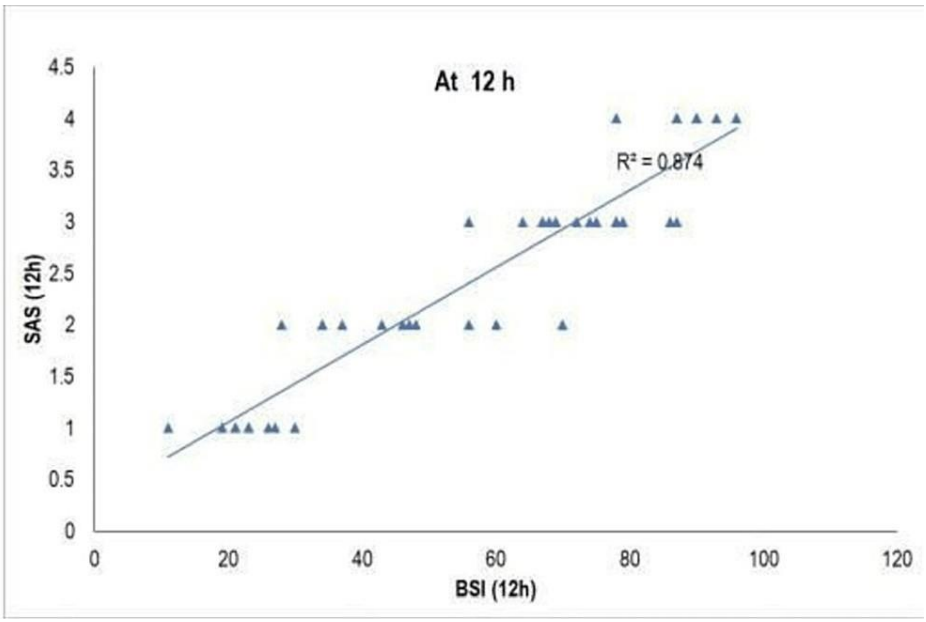

FIGURE 4: Figures showing correlation between BIS and RSAS at 12hour

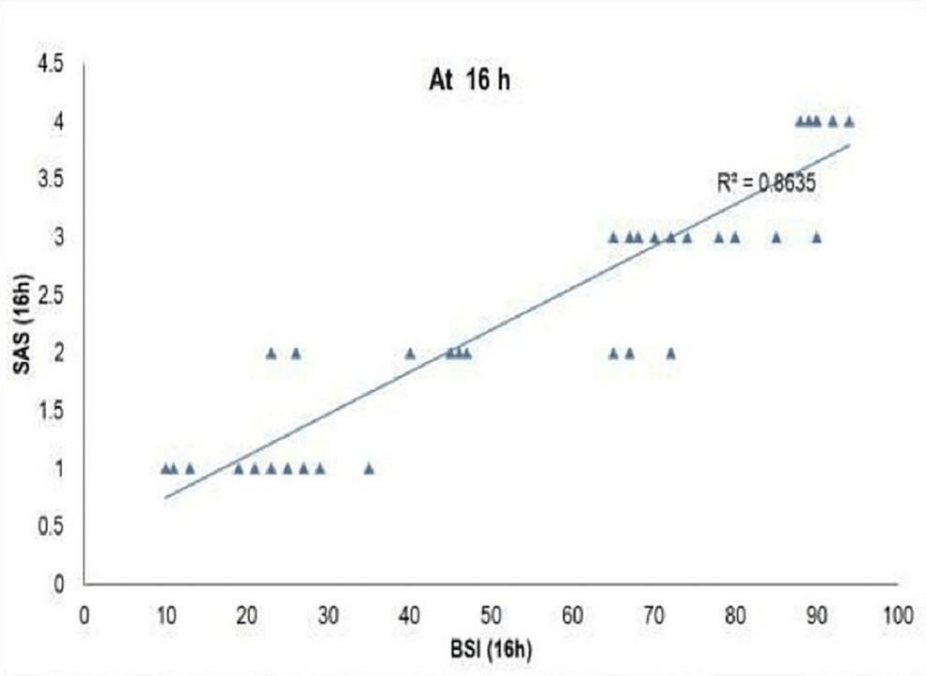

FIGURE 5: Figures showing correlation between BIS and RSAS at 16hour

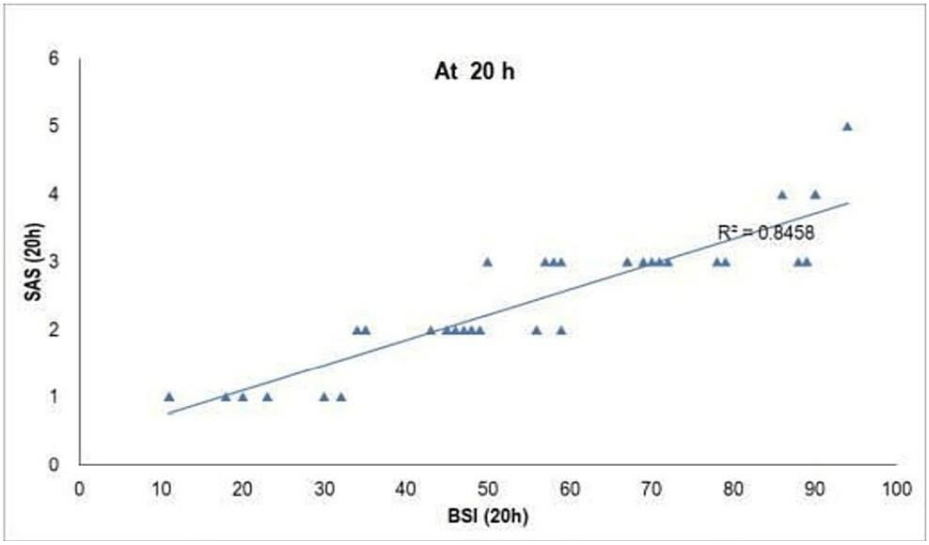

FIGURE 6: Figures showing correlation between BIS and RSAS at 20hour

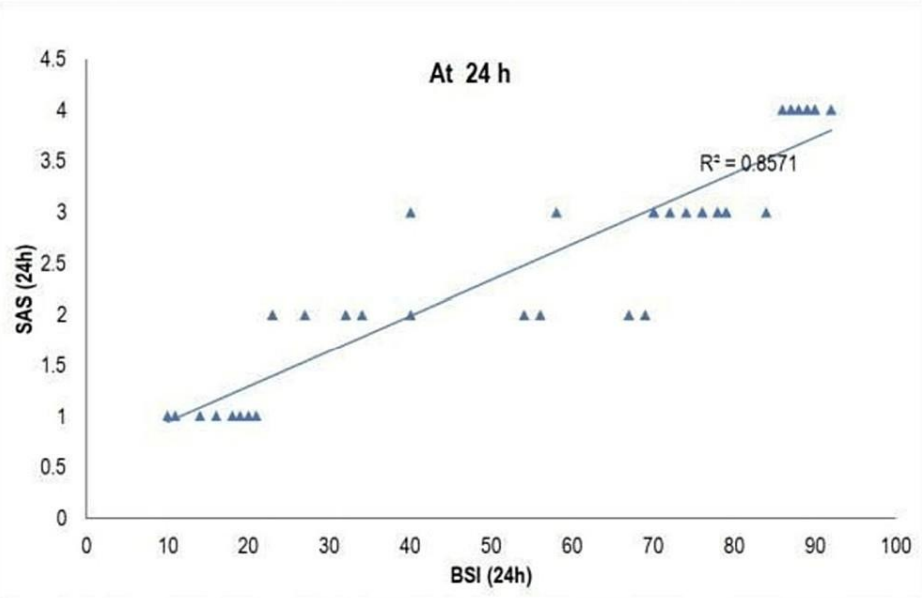

FIGURE 7: Figures showing correlation between BIS and RSAS at 24hour

Discussion

Optimal sedation monitoring is of paramount relevance in the field of critical care medicine. It is vital for maintaining a balance between over sedation and under sedation in patients with critical illness. Each level of sedation carries with it the risk of morbidity. Monitoring of consciousness level and response to physical stimulation can be done by using sedation scales such as the Ramsay Scale, RSAS, and Motor Activity Assessment Scale.

The present prospective observational study was performed in 20 bedded tertiary levels ICU. 47 patients were taken from critical care unit. The basic aim of the study was to monitor depth of sedation of patients in ICU using RSAS & to assess the correlation between RSAS & BIS.

The BIS monitor was created in the 1990s in order to monitor the impact of anaesthetics and other medicines on the brain during surgery [7]. Early studies of BIS monitoring in the operating room found that BIS identified patients at risk of awareness during surgery, improved drug management, reduced costs, and expedited recovery [8,9]. Comparing the percentage of time with optimal sedation, as defined by RSAS grade 4, between a BIS-guided remifentanil/propofol regimen and a clinically guided regimen in 54 randomised patients led Dahaba AA et al., 2006 [10] to the conclusion that BIS monitoring is an advantageous addition to conventional sedation monitoring. In contrast according to Manyam SC et al. [11] BIS monitoring is insufficient for measuring sedation levels in surgical patients, it has been determined.

In 2002, Mondello E. et al. [12] gathered data from 980 separate studies. A Ramsay Score could vary anywhere from 2 to 6. The values of BIS were between 34 and 98. Several statistically significant correlations were found after analysing the collected data, including one between the Ramsay Score and BIS ($p<0.01$) and another between the BIS and the dosage of propofol used ($p<0.01$).

Demographic data of our study showed that the majority of patients were between 31 and 50 years old, with the youngest being over 50 years old. In 47 patients participated in the study. Similarly, Riess ML et al., 2002 included 44 ventilated patients in their study and showed that the proportion of males was much higher than that of females. In contrast, Arbour, R., et al., 2009 [6] examined data from 40 subjects and found that the percentage of females was significantly higher than that of males.

BIS is an objective method for monitoring sedation that combines the frequency domain analysis of the electroencephalogram (EEG) with the determination of the degree of phase coupling between the EEG waves. Numerous EEG tracings were subjected to bispectral analysis, and the results were connected with different clinical levels of the utilized medications, permitting the development of a numerical scale [13]. In our study, the mean Bispectral Index (BIS) increased and stayed higher compared to baseline at all time interval. Sequential increment was observed till 12h. BSI of 12 h and 16 h was found to be approximately similar while there was slight decrease in BSI at 20 h as compared to 12 and 16 h while it increased again at 24 h.

According to Jacobi J et al., 2022 [14], sedation is a crucial concern for ICU patients, and selecting the dosage of sedatives to be administered necessitates assessing the level of unconsciousness of patients. The Sedation-Agitation Scale is a subjective but reliable instrument for assessing the level of sedation in sedated ICU patients, and it has been applied widely in both clinical and comparative sedation research. Our investigation found that the mean RSAS rose at each interval relative to the baseline. Up until 12 hours, the average RSAS increased sequentially, but at 16 and 20 hours, the average RSAS declined relative to 12 hours, and at 24 hours, the highest RSAS was recorded.

Instead of the Ramsay scale, Vivien, B. et al., 2003 [15] evaluated the sedation with RSAS. They have chosen to evaluate patients with a Sedation-Agitation Scale of 1 who are completely sedated. In reality, it should be emphasised that this was below the sensitive range of this score and may represent a substantial source of patient variability. Nevertheless, one of the possible applications of BIS monitoring in the ICU should be to detect over sedation. Therefore, they volunteered to investigate BIS monitoring in patients with a Sedation- Agitation Scale score of 1, i.e., those who were much more sensitive to over sedation than others.

The correlation between BIS and RSAS had been determined in a number of reports with different study designs. Results of these studies revealed statistically significant but fairly low correlation

coefficients ranging from 0.14 to 0.48. In some of these works, the correlation did not exist in some subgroups. With our study design the correlation between BSI and RSAS was strong to Very strong/Perfect at all time interval and highly significant at all the periods.

In contrast to our study Arbour, R. et al., 2008 [6] collected data from forty participants, yielding two hundred and nine paired readings. A Spearman Rank coefficient r value of.502 and a r2 value of.251 ($P<0.0001$) indicate a moderately favourable association between BIS and RSAS levels. Wide variances in BIS scores were seen, particularly in patients who were heavily sedated. With a r value of.749, a significant positive correlation was found between BIS and electromyography ($P < 0.0001$). Age and gender had a substantial effect on BIS/RSAS correlations. There were statistically significant variations in BIS scores between SAS levels 2 (extremely sedated), 3 (sedated), and 4 (not sedated). These discrepancies are of little practical significance, however, because four "extremely sedated" participants had BIS scores greater than 40, while three subjects (one as high as 94) had BIS scores greater than 80, indicating that they were just lightly sedated. Similarly, three of the "very sedated" individuals had BIS scores below 20, indicating they may have been over sedated. These variances may reflect the heterogeneity of the examined patient population. Frenzel et al. (2002) [16] observed that 42% of ICU patients had no link between the BIS and clinical sedation assessment scales, whereas 58% demonstrated moderate correlations. They were unable to discover criteria to distinguish patients with and without correlation; hence, the clinical utility of BIS scores remained limited. LeBlanc JM et al., 2012 [17] conducted a prospective open-label study of patients receiving mechanical ventilation in a surgical critical care unit and found a weak correlation between BIS and SAS score. Trouiller P et al., 2009 [18] determined that the correlation between the BIS and sedation measures was low.

Similarly to our study Riker RR et al., 2001 [19] did a prospective study comparing blinded evaluations of the RSAS, VAS, and BIS in 42 ICU-admitted patients and found a significant association between the BIS and the RSAS. Simmons LE, et al. [8] found stronger correlations between BIS and SAS scores; however, the R2 values were still less than 0.5, indicating that the RSAS score explains less than 50% of the variance in BIS. De Deyne, C., et al., (1998) [20] discovered a strong association between the BIS and the Ramsay sedation score. Riess, M. L. et al., 2002 [12] examined 44 ventilated patients and showed that the BIS linked with the Ramsay sedation score (-0.64; $P<0.01$) they found that temperature instability and electromyographic activity enhanced the BIS in profoundly sedated patients. BIS was substantially connected with electromyographic activity (0.80; P 0.01) and an increase in body temperature (0.55; $P<0.01$) not only in all patients, but also in clinically severely sedated individuals (0.57; $P <0.01$ and 0.46; $P< 0.05$).

Conclusions

The study contributes to the growing body of evidence that BIS scores are strongly linked with RSAS in ventilated ICU patients and that these data are highly significant. BIS monitoring may play an additional function in sedation assessment in cases where the clinical assessment is ambiguous. BIS results must be taken with caution, however, because electromyography activity and other variables appear to confuse BIS scores. Additional research is required to determine the function of BIS monitoring in ICU practice.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. King George's Medical University institutional ethics committee issued approval VIII-PGTSC-IIA/P3. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue.

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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