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CORRELATION BETWEEN BISPECTRAL INDEX AND TWO CLINICAL ASSESSMENT SCALES RAMSAY SEDATION SCALE AND RICHMOND AGITATION SEDATION SCALE IN CRITICALLY ILL ADULT PATIENTS IN THE ICU

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Abstract

Introduction: Sedation and analgesia are integral parts of patient care in intensive care units. These medications are routinely administered to mechanically ventilated patients to reduce pain, anxiety, improve patient comfort, to allow the patient to tolerate the physical environment and unpleasant procedures, avoiding awareness during ICU stay, reduce the requirement for the use of neuromuscular blocking agents and to contribute in maintaining metabolic and haemodynamic homeostasis.

Materials and Methods: After approval by the Institutional ethical committee the study was conducted in the Main ICU of Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh. All the patients who were admitted in the main ICU were eligible for the study. After taking informed written consent, 70 adult patients who were haemodynamically stable and require sedation were studied. Patients were stabilized after admitting in the ICU. The demographic data including the admission diagnosis, admitting unit were collected. APACHE II score was calculated in first 24 hours. BIS electrodes were applied to the forehead of each patient after skin preparation to ensure low impedance and a good quality of signal. BIS offers continuous monitoring of sedation for 24 hours. Baseline BIS score and RSS, RASS scores were collected.

Results: Seventy critically ill sedated patients were studied prospectively in MICU, PGIMER, Chandigarh. From January to December 2014. The mean patient age was 38.8 ± 16.5 years (range: 18-92 years). 35 (50%) patients were male and 35 (50%) were female patients. The median APACHE score of the 70 patients was 11 with IQR of 8-13. Parameters like SBP, DBP, HR, SpO_2, temperature; blood gases and electrolytes were assessed for normality by Shapiro Francia test. However, none of them showed normal distribution. The BIS, RSS, RASS of the patients during the study period are given in the table 1, and figures 1, 2, 3.

Conclusion: We found significantly better correlation between RSS & RASS compared to RSS & BIS and RASS & BIS. This concludes that RSS and RASS are not a good substitute for BIS. Whereas RSS and RASS can be substituted each other. We found negligible correlation between BIS and clinical scores to APACHE. Hence we can conclude no influence of change in APACHE on BIS and clinical sedation scores (RSS and RASS).

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Key Words: Sedation, analgesia, haemodynamic homeostasis, SpO_2.

INTRODUCTION

Sedation and analgesia are integral parts of patient care in intensive care units. These medications are routinely administered to mechanically ventilated patients to reduce pain, anxiety, improve patient comfort, to allow the patient to tolerate the physical environment and unpleasant procedures, avoiding awareness during ICU stay, reduce the requirement for the use of neuromuscular blocking agents and to contribute in maintaining metabolic and haemodynamic homeostasis.[1,2]

Optimal sedation is one of the goals of ICU care. Over- and under-sedation must be avoided due to their dangerous effects. Inadequate analgesia and sedation can induce many important pathophysiologic alterations (e.g. hypercatabolism, immunosupression, hypercoagulability, increased sympathetic activity) that are associated with a significant outcome impairment.[3,4] Increased production of endogenous catecholamines because of inadequate sedation results in an increase in blood pressure, heart rate and myocardial oxygen consumption, self-extubation and post-traumatic stress disorder[5] that may require prolonged therapy after discharge. Patients who receive neuromuscular blocking agents are most at risk for inadequate sedation as they are unresponsive.[5] On the other hand, over-sedation can increase time on mechanical ventilator support, risk of pulmonary complications and neuromuscular alteration and duration of ICU stay.[6] Therefore continuous monitoring of sedation is needed.

Many clinical and instrumental tools have been used to titrate ICU sedation.[7] The clinical tools are subjective sedation scales in which the patient is assigned a score depending on his or her response to standard stimuli. The most widely used clinical assessment scales are Ramsay Sedation Scale (RSS), Richmond Agitation-Sedation Scale (RASS), Glasgow Coma Scale (GCS), Sedation Agitation Scale (SAS) and Adaptation to Intensive Care Environment Scale (AICE). The main advantages of such scales are low cost and easy clinical applicability. Among the clinical scales, the Ramsay scale[8] and Richmond Agitation-Sedation scale are frequently employed. Ramsay score is most commonly used in postoperative intensive care patients and RASS is routinely used in intensive care units.

Many instrumental tools of sedation have been proposed to assess the level of sedation objectively, in particular electroencephalograph (EEG). However, acquisition and interpretation of EEG signals are very difficult for untrained personnel; therefore many derived parameters have been introduced in order to simplify EEG pattern analysis.[7] Among EEG-derived parameters, Bispectral Index (BIS) is widely accepted as a tool for the evaluation of CNS sedative drug effects. It has been employed to monitor ICU sedation[9] and surgical anaesthesia.[10]

Several problems affect the interpretation of BIS scores in patients in the ICU. Numerous authors have noted that electrical activity of muscles as measured by electromyography (EMG) interferes with BIS measures of sedation. BIS XP was designed to overcome EMG interference. Other confounding factors that may influence BIS scores include hypoglycemia, sleep, temperature, age and drugs such as aminophylline, epinephrine, and ketamine.

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Though BIS is reliable and validated in ICUs, it increases ICU costs. Due to the cost and time limitation of the sensors, accurate clinical scores will be a cheaper substitute for BIS. Therefore our study was designed to assess the correlation between clinical scales and BIS.

AIMS AND OBJECTIVES

To correlate the Bispectral Index (BIS) with two clinical sedation scales Ramsay Sedation Scale (RSS) and Richmond Agitation- Sedation scale (RASS) in critically ill adult patients.

MATERIAL AND METHODS

Study setting: Main ICU, Post Graduate Institute of Medical Education and Research, Chandigarh.

Study period: 1year from Jan 2014 to Dec 2014.

Study design: A prospective observational study.

Study group: The study was conducted in 100 critically ill patients receiving sedation in Main ICU, Post Graduate Institute of Medical Education and Research, Chandigarh from Jan 2014 to Dec 2014.

Inclusion criteria:

1. Age 18 years or older.
2. Haemodynamically stable patients requiring sedation.

Exclusion criteria:

1. Patients with altered level of consciousness including those with haemodynamic instability, encephalitis and severe hypoxemia.
2. Patients receiving neuromuscular blocking drugs.
3. Conditions that affect BIS monitoring such as seizures, increased neuromuscular activity (e.g. tetanus, encephalopathy).

Methodology:

After approval by the Institutional ethical committee the study was conducted in the Main ICU of Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh.

All the patients who were admitted in the main ICU were eligible for the study. After taking informed written consent, 70 adult patients who were haemodynamically stable and require sedation were studied.

Patients were stabilized after admitting in the ICU. The demographic data including the admission diagnosis, admitting unit were collected. APACHE II score was calculated in first 24 hours. BIS electrodes were applied to the forehead of each patient after skin preparation to ensure low impedance and a good quality of signal. BIS offers continuous monitoring of sedation for 24 hours. Baseline BIS score and RSS, RASS scores were collected. Patients were sedated with standard sedation protocol of Main ICU with either midazolam, morphine or combination of both and propofol. The level of sedation was assessed by using BIS and two clinical assessment scales (RSS and RASS)

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simultaneously at the starting of sedation and every 4 hours thereafter. A total of 490 measurements were performed among 70 patients. All the assessments were done by chief investigator after stabilizing the patient after admitting in the ICU.

The following data was collected at the time of assessment,

- Use of sedative drug and its dosage
- Hemodynamic parameters such as blood pressure, heart rate
- Temperature
- Oxygen saturation (SpO_2)
- Mode of ventilation at the time of assessment
- Any use of medication which alter the level of consciousness
- Partial pressure of oxygen (po_2)
- Partial pressure of carbon dioxide (pco_2)
- ph
- Sodium (sod)
- Potassium (pot)
- Calcium (ca)

STATISTICAL ANALYSIS: Correlation analysis was done between BIS and RSS, between BIS and RASS and between RSS and RASS. Also correlation analysis was done between APACHE II score and BIS, APACHE II and RSS, APACHE II and RASS.

ETHICAL JUSTIFICATION: Patients were included in the study only after fully explaining the aim of the study and its possible outcomes to them or their guardians, in an appropriate language. They were also be told that it is their decision to take part in study and that any personal data were kept confidential. This study is observational in nature with no modification of treatment strategies. Hence no increased morbidity is anticipated due to the study. This study gave us the data regarding the validity, reliability and applicability of BIS and clinical scales of sedation, which will help to implement the good sedation protocols in ICU to improve patient outcome. The modified guidelines set by ICMR in the year 2000 and the Helsinki declaration will be strictly adhered to.

RESULTS

Seventy critically ill sedated patients were studied prospectively in MICU, PGIMER, Chandigarh. From January to December 2014. The mean patient age was 38.8 ± 16.5 years (range: 18-92 years). 35 (50%) patients were male and 35 (50%) were female patients. The median APACHE score of the 70 patients was 11 with IQR of 8-13. Parameters like SBP, DBP, HR, SpO_2, temperature; blood gases and electrolytes were assessed for normality by Shapiro Francia test. However, none of them showed normal distribution. The BIS, RSS, RASS of the patients during the study period are given in the table 1, and figures 1, 2, 3.

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Table 1: BIS, RSS, RASS of patients during the study period (median [IQR])

		4 hrs	8 hrs	12 hrs	16 hrs	20 hrs	24 hrs
BIS	62.5[48.3-79.8]	64.5[52-79.8]	62 [50-80.8]	68 [50.3-80]	68 [54-80.8]	72 [52.5-82]	70 [51.3-80]
RSS	3 [2-5]	4 [2-5]	4 [2-5]	4 [2-5]	3 [2-5]	3.5 [2-5]	4 [2-5]
RASS	-2 [-3.8-0]	-2 [-3-0]	-2 [-3.8-0]	-2 [-3.8-0]	-2 [-3-0]	-2 [-3-0]	-2 [-3-0]

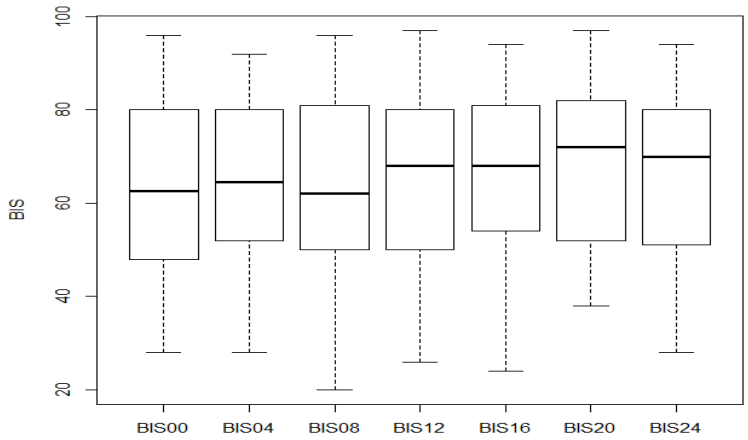

Fig 1: BIS during the study period

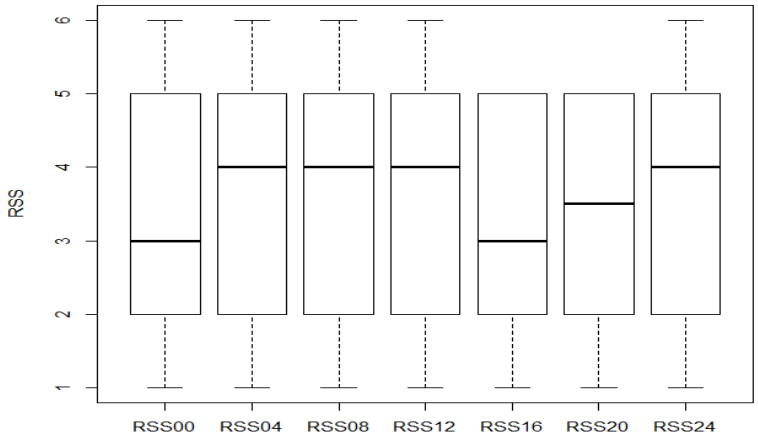

Fig 2: RSS during the study period

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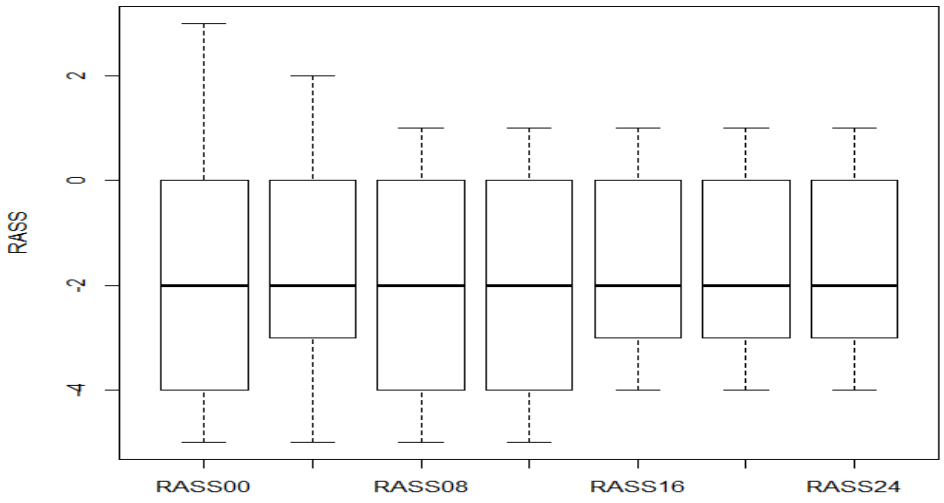

Fig 3: RASS during the study period

The haemodynamics, blood gases and electrolytes of the patients during the study period was given in the tables 2, 3.

Table 2: The haemodynamics of the patients during the study period (median [IQR]).

	Baseline	4 hrs	8 hrs	12 hrs	16 hrs	20 hrs	24 hrs
SBP	123 [116-134]	123.5 [112.3-136]	121 [115-130]	117 [110-132]	122 [114-130]	120 [114-131.5]	124 [116-134]
DBP	68.5 [64-76.8]	68 [62-76.3]	68 [62-77]	68.5 [62-74]	70 [63-76]	68 [62-74.8]	70 [65-77.5]
HR	103.5 [84-116]	98 [87-112.8]	99 [88.5-114]	105 [90-114.8]	101.5 [89-112.8]	102.5 [92-116]	103 [92.5-114.8]
SpO2	98 [96-99]	98 [96-99]	98 [96-99]	98 [96-99]	98 [96-99]	98 [96-99]	98 [96.3-99]
Temperature	37.2 [37-37.6]	37.4 [37-37.8]	37.3 [36.9-37.8]	37.3 [37-37.6]	37.4 [37-37.8]	37.2 [37-37.6]	37.2 [37-37.5]

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Table 3: Blood gases and electrolytes during the study period (median [IQR])

	Baseline	4 hrs	8 hrs	12 hrs	16 hrs	20 hrs	24 hrs
Ph	7.4 [7.3-7.4]	7.4 [7.4-7.4]	7.4 [7.4-7.4]	7.4 [7.4-7.4]	7.4 [7.4-7.4]	7.4 [7.4-7.4]	7.4 [7.4-7.4]
Po_2	98.4 [83.8-120.9]	98.3 [81.2-120.4]	99.9 [82.6-117.7]	94.7 [80.1-113.9]	100.8 [83-136.4]	97.5 [80.4-119.6]	103.3 [83.8-121.2]
Pco_2	38.6 [34.8-43.5]	38.4 [34.6-43.8]	39 [35.5-44.9]	38.4 [34.6-44.2]	38.8 [35.4-45.6]	39.9 [35-46.2]	38 [34.7-44.5]
Na	140.3 [137-144.2]	140.4 [138.2-142.6]	139.4 [136.7-143.9]	140.3 [138.1-143]	138 [136.6-143.3]	139.7 [136.3-144]	140.3 [137.7-143.4]
K	3.4 [3.2-3.7]	3.5 [3.2-3.8]	3.6 [3.3-3.9]	3.5 [3.2-4]	3.7 [3.3-4]	3.7 [3.3-4]	3.5 [3.2-3.9]
Ca	0.9 [0.8-1]	0.9 [0.8-1]	0.9 [0.8-1]	0.9 [0.8-1]	0.9 [0.8-1]	0.9 [0.8-1]	0.9 [0.8-1]

Majority of the patients in our study were admitted for medical problems (41 patients). Followed by 11 post operative patients and 10 were trauma patients. Eighteen of the 70 patients had comorbidities. 10 patients had hypertension, 7 had associated diabetes, 2 also had associated chronic kidney disease and coronary artery disease. Whereas 1 patient each had tuberculosis, dilated cardiomyopathy, chronic kidney disease and depression.

In our study 53 patients were sedated with morphine and midazolam infusion, 15 with midazolam, 1 with morphine, and 1 with propofol infusion. One patient each was receiving haloperidol 0.25 mg, phenytoin 100 mg three times a day, lorazepam 2 mg/hr infusion.

We have done regression analysis to see the correlation between RSS and BIS, between RASS and BIS, between RSS and RASS. Three variables correlate well statistically. However Fifty one percent of variation in RSS was explained well by variation in BIS ($R^2 = 0.51$), 56 percent of variation in RASS was explained well by variation in BIS ($R^2 = 0.56$) and 82 percent of variation in RSS was explained by variation in RASS (R2 = 0.82).

We have done the regression analysis between baseline APACHE and baseline BIS, RSS, RASS shows good statistical correlation, but the r^2 values are (0.068, 0.108, 0.062) this shows variation in BIS, RSS and RASS values are explained poorly by variation in APACHE.

We have done correlation analysis between RSS and BIS, RASS and BIS, and RSS and RASS in males and females separately and observed negligible difference in correlation. The r^2 for RSS and BIS in males and females were 0.53 and 0.45 respectively. The r^2 for RASS and BIS in males and

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females were 0.58 and 0.48. The r^2 for RSS and RASS in males and females were 0.8 and 0.83 respectively.

We categorized the patients into 3 groups (medical, trauma, surgical) and we have done correlation analysis between RSS and BIS, between RASS and BIS and between RSS and RASS in each group of patients. The r^2 value for medical, surgical and trauma patients were 0.53, 0.48, 0.50 between RSS & BIS, 0.57, 0.63, 0.50 between RASS & BIS and 0.8, 0.9, 0.85 between RSS and RASS groups respectively.

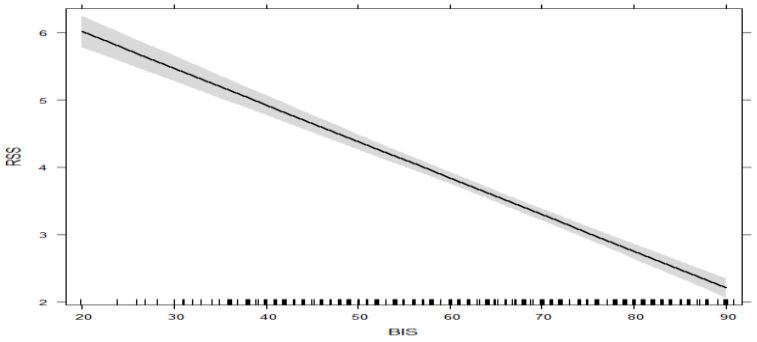

Figure 4: correlation of RSS on BIS [95% C.I]

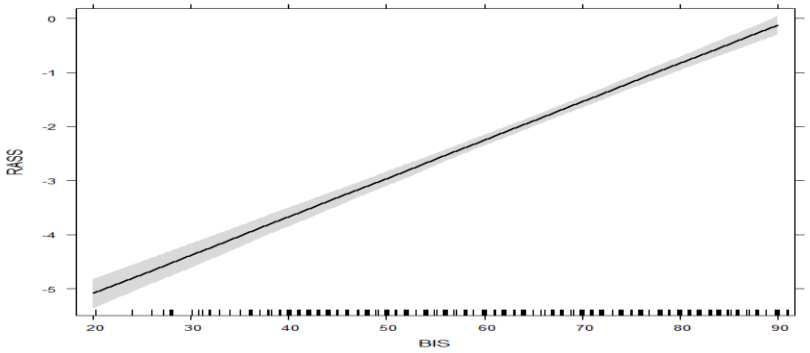

Figure 5: Correlation of RASS on BIS [95% C.I]

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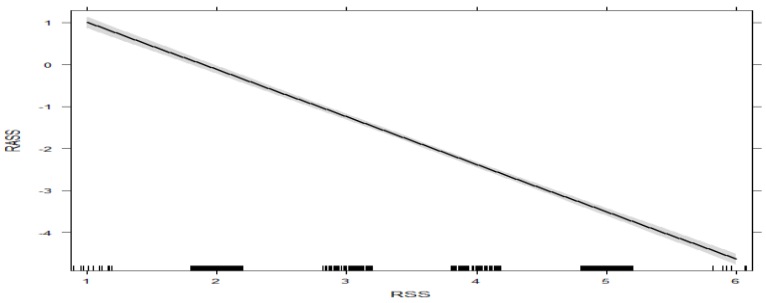

Figure 6: Correlation of RASS on RSS [95% C.I]

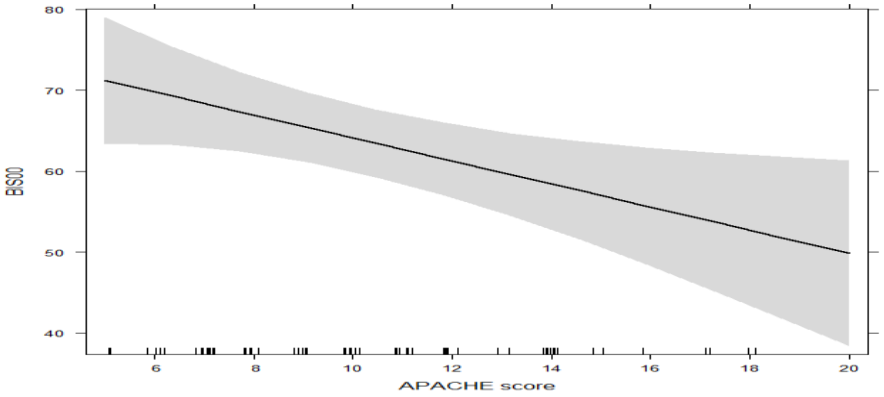

Figure 7: Correlation of baseline APACHE on baseline BIS [95% C.I]

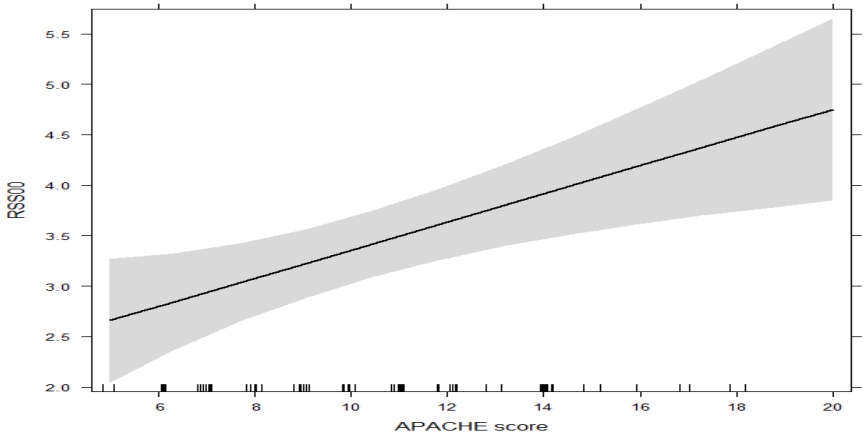

Figure 8: Correlation of baseline APACHE on baseline RSS [95% C.I]

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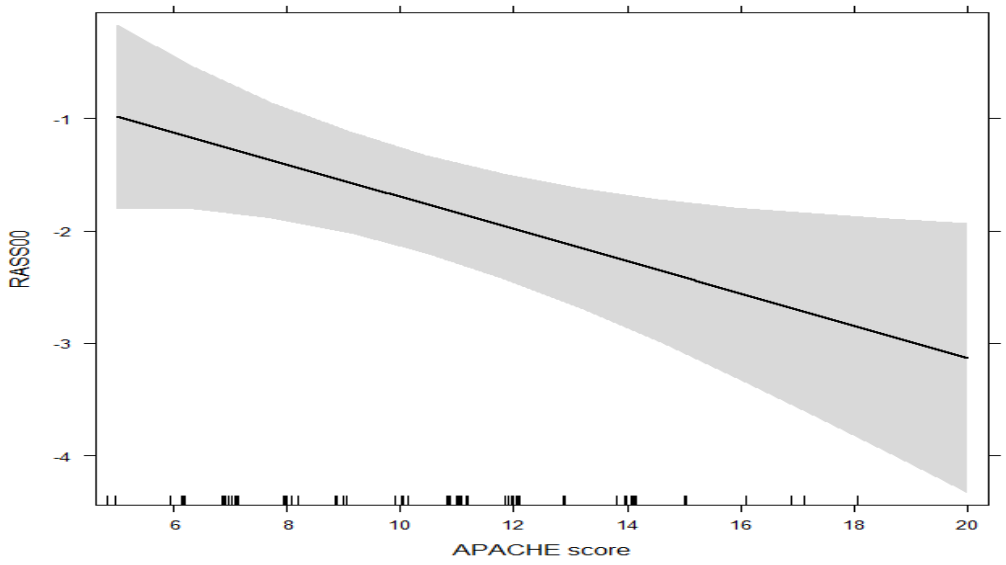

Figure 9: Regression of baseline APACHE on baseline RASS [95% C.I]

Sedation is used in the ICU to decrease the levels of anxiety and awareness of the patients who are mechanically ventilated. Continuous monitoring of the level of sedation is required in order to avoid over- or under-sedation because both cause detrimental effects to the patient. Level of the sedation can be assessed by instrumental tools or clinical scales.

This study was conducted to evaluate the correlation between instrumental tool-BIS and clinical sedation scores (RSS and RASS). Seventy critically ill, stable adult patients who were mechanically ventilated were assessed every 4 hourly for 24 hours in the ICU with total of 490 assessments.

In the current study, statistical correlation was observed between RSS & BIS values, between RASS & BIS values and between RSS & RASS values. These results are consistent with the previous studies in the literature. However only 51 and 56 percent of variations in RSS and RASS values respectively, were explained by variation in BIS values in our study.

There are variations in the degree of correlation between RASS and BIS were observed among the previously conducted studies. For example, Turkmen et al observed significantly higher degree of correlation between RASS and BIS (r^2=0.8) compared to our study. This higher degree of correlation might be due to very small sample size of 11 post-thyroidectomy patients. In another study Deogaonkar et al observed lesser degree of correlation between RASS and BIS (r^2 = 0.47) as compared to our study. This is because they did study in only brain injury patients in the ICU. Two different studies conducted by Ely et al demonstrated a variable correlation between RASS and BIS (r^2=0.5 and r^2=0.4). However, in their studies no standardized sedation protocol was followed and use of various sedation agents was done like morphine, fentanyl, midazolam, lorazepam. Karamchandini et al found a significant correlation between RASS and BIS values (Kendall's correlation coefficient = 0.562) in 24 critically ill patients in ICU. In contrast, Simmons et al observed poor correlation between

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RASS and BIS (r2 = 0.21) because they included patients in the analysis in whom muscle relaxants was administered intermittently might have contributed to this finding.

Regarding the degree of correlation between RSS and BIS, Mondello et al in his study on 20 COPD patients found good correlation between RSS and BIS. They have used propofol infusion and intermittent midazolam as sedative agents. In the study by Yaman et al, the correlation coefficient was slightly higher between RSS and BIS (r^2=0.57) when compared with RASS and BIS (r^2=0.56). Consales et al[2] observed good correlation between RSS and BIS in his study (r^2= 0.57). This is slightly higher than our study because they have studied only in postoperative cases, compared to our study group comprising mixed patients of medical, surgical and trauma with fewer postoperative cases. De deyne[9] et al observed good correlation between RSS and BIS. Because most of the patients in his study were having multy organ failure in whom metabolism of sedative drugs is known to be affected. We observed better correlation between RSS and RASS (r^2 = 0.82) as compared to correlation values of RSS and BIS, RASS and BIS. Similar results were observed by Mendes et al (r2 = 0.65) in 45 mechanically ventilated patients and Sessler et al (r^2 = 0.61). He has done the study in 192 patients from various ICUs.

Correlation analysis between BIS and APACHE, between RSS and APACHE, between RASS and APACHE also showed statistical correlation but variation in BIS, RSS, RASS were poorly explained by variation in APACHE (r^2 values are 0.07, 0.12, 0.06) respectively. Similar results were observed by Han liu et al found poor correlation between BIS and APACHE in a 33 critically ill patients with r^2=0.19.

There were only 3 patients in our study were above 65 years of age. So we have not done the correlation analysis between the age groups. Considering patient's age, Arbour et al observed that patients aged 50 years or less had better correlation between BIS and SAS (r^2 = 0.33) then age 50 to 65 years (r^2 = 0.25) and 65 years or more (r^2 = 0.12). He also showed that female patients had higher correlation (r^2= 0.32) than the males (r^2 =0.13). There were 21 females and 19 males in his study. In our study, correlation between BIS, RSS and RASS were comparable in both the gender and in different groups of patients (medical, surgical and trauma). However on comparing the study groups (medical, surgical and trauma patients), Simmons et al[19] found that the correlation was better for trauma patients (r^2 = 0.52) than for the general (r^2 = 0.26) or cardiac (r^2 = 0.25) surgical patients and the medical patients (r^2=0.10).

Haemodynamic parameters, blood gases, serum electrolytes and type of sedative agent administered were not related to change in BIS, RSS or RASS. Overall the degree of correlation between clinical sedation scores and BIS in our study was not homogenous with other studies in the literature this is because of different sample size, different sedation protocols and different group of patients.

We could not compare the correlation between geriatric and adult groups as only 3 of 70 patients were above 65 years age. We found negligible correlation among the different group of patients (medical,

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surgical, trauma) as the number of patients in each group are not comparable in our study. To see the actual correlation we need equal no of sample size. In our study we assessed patients for 24 hours similar to previous studies. This is because difficulty in using BIS electrodes more than 24 hours due to several factors like excessive sweating, oily skin, edema, frequent sponging and change in position. the BIS electrode once dislodged it is difficult to reapply. The need for improved quality of electrodes with longer-lasting and resistant adhesives needs to be considered.

CONCLUSION

We found significantly better correlation between RSS & RASS compared to RSS & BIS and RASS & BIS. This concludes that RSS and RASS are not a good substitute for BIS. Whereas RSS and RASS can be substituted each other. We found negligible correlation between BIS and clinical scores to APACHE. Hence we can conclude no influence of change in APACHE on BIS and clinical sedation scores (RSS and RASS).

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