ORIGINAL ARTICLE

Comparison of Quantium Consciousness Index and Richmond Agitation Sedation Scale in Mechanically Ventilated Critically Ill Patients: An Observational Study

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Abstract

Background: The quantium consciousness index (qCON), an electroencephalography (EEG)-based modality, has no studies regarding intensive care unit (ICU) sedation, though very few studies describe its use for assessing depth of anesthesia in the operation theater. In this study, we evaluated qCON for assessing sedation compared with Richmond Agitation Sedation Scale (RASS) in patients on a mechanical ventilator in the ICU.

Materials and methods: Eighty-seven mechanically ventilated patients aged between 18 and 60 years were investigated over a 12-hour period. They were given a standardized dosage of sedation comprised of a bolus dose of propofol 0.5 mg/kg and fentanyl 1 µg/kg, and then infusions of propofol 2–5 mg/kg/hour and fentanyl 0.5–2 µg/kg/hour. These drug infusions were adjusted to achieve a RASS score between 0 and -3. Using the qCON monitor, the investigator recorded the qCON values and then assessed the RASS score.

Results: A total of 1,218 readings were obtained. After contrasting each qCON value correspondingly with time to each RASS value, we found their correlation to be statistically significant ($\rho = 0.288$, $p < 0.0001$). With the help of receiver operating characteristic (ROC) curves, we were able to differentiate appropriate from inappropriate levels of sedation. A qCON value of 80 had a sensitivity of 72.67% and a specificity of 67.42% (AUC 0.738 with SE 0.021).

Conclusion: qCON can be used for assessing sedation levels in mechanically ventilated critically ill patients.

Clinical trial registration: CTRI/2019/07/020064.

Keywords: Intensive care unit (ICU), Quantium consciousness index (qCON), Richmond agitation sedation scale (RASS), Sedation.

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Introduction

Patients admitted to the ICU are predisposed to experience pain, anxiety, and agitation. This can be due to many factors, such as the disease process itself, catheters and tubes inserted into them, their immobility, or disturbances in their circadian rhythm. The failure to manage agitation leads to immediate complications, such as increased oxygen consumption, patient–ventilator asynchrony, inadvertent removal of devices and catheters, delayed weaning from the ventilator, and long-term complications, like posttraumatic stress disorder.[1] Therefore, sedation and analgesia are a necessary part of managing ventilated patients.[2] There are much data collected from randomized controlled trials, which strongly advocate using sedative agents as minimally as possible.[3] Therefore, monitoring sedation level is crucial for optimizing the dose and duration of sedatives, thereby providing optimum patient care.

Over the years, various methods have been devised to measure the level of sedation. They can be classified as subjective and objective. Subjective methods include sedation scales that are widely used throughout the world. These have been used for the assessment of the adequacy of the level of sedation in ICU patients. Some of the most commonly used sedation scales are Ramsay Sedation Scale (RSS),[4] Sedation Agitation Scale (SAS),[5] RASS,[6] and others.

The sedation scales are challenged when visual effects disappear due to oversedation or muscle relaxation. In such circumstances, the practitioner needs to rely on other parameters to assess the sedation depth.[7] The unreliability of commonly used sedation scales in conditions where the patient is nonresponsive due to muscle relaxation leads to various objective methods of assessment. The objective methods of assessing sedation in mechanically ventilated patients are Bispectral Index (BIS),[8] Entropy,[9] Narcotrend,[10] and others.

The EEG is a direct interpretation and response related to the activities within the brain, and from its recorded data, one can interpret the hypnotic and the nociceptive effect. CONOX monitor (Quantium Medical, Spain/Fresenius Kabi, Germany) has been introduced recently, based on an EEG algorithm.[11] The development of qCON involves a mathematical model, a blend of artificial neural networks and fuzzy logic systems. This algorithm is based on

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combining the energy of four frequency ratios, which generates the qCON index. CONOX monitor shows the qCON index of hypnosis and the qNOX index of pain. Both these indices are grounded on the amalgamation of various bands of frequency that are put as an input in Adaptive Neuro-Fuzzy Inference System (ANFIS). CONOX's qCON index is based on an easily readable 0–99 scale, resulting from the processing of EEG readings. A qCON index between 40 and 60 points to an adequate anesthesia level, while 0 points to an isoelectric EEG.[12]

Only a few published studies show its utility during the intraoperative period,[11,13,14] but no study has investigated it for the depth of sedation or correlated with clinical sedation scales in ICU patients on mechanical ventilation. The primary objective of this study was to correlate the sedation objectively with processed EEG (qCON) using the CONOX module to the subjective scoring system, RASS, in patients on propofol–fentanyl sedation, requiring mechanical ventilation in the ICU. The secondary objective was to assess the feasibility of qCON for monitoring ICU sedation.

Materials and Methods

This prospective observational study was carried out in the ICU of a teaching hospital. The study was approved by the Institutional Review Board (IEC No./810). Written informed consent was obtained from a legal surrogate of all the subjects.

A total of 87 male and female patients, aged between 18 and 60 years, admitted to the ICU from July 2019 to December 2020 were recruited in this study. We excluded patients with hemodynamic disturbance (mean blood pressure <65 mm Hg), hypothermia (core temperature <36°C), dyslipidemia, pancreatitis, and patients getting neuromuscular blockade or sedative medication other than those prescribed.

The monitoring of the patients included standard equipment, including continuous EEG, pulse oximetry, invasive/noninvasive arterial blood pressure, temperature, and the additional use of noninvasive qCON monitoring.

After being included in the study, all patients received a standard regimen as per ICU protocol, which begins with the administration of a bolus dose of propofol 0.5 mg/kg and fentanyl 1 µg/kg, and then infusions of propofol 2–5 mg/kg/hour and fentanyl 0.5–2 µg/kg/hour. These drug infusions were adjusted to achieve a RASS score between 0 and -3. The rate of infusion was increased by 10% whenever the RASS was more than 0 and similarly decreased by 10% whenever the RASS was less than -3 and re-evaluating RASS in 10 minutes in either case.

The CONOX electrodes were placed on specified places, above the nose bridge, over the temple, and between the lateral side of the eye and medial part of the hairline, after skin cleaning with chlorhexidine swab according to the directive of the manufacturer. The connections were readjusted if an inadequate signal was sensed. After the signal quality index (SQI) was seen >50%, qCON readings were noted. The investigator recorded three consecutive qCON values, observed every 5 seconds for 15 seconds, and their average was noted down as the qCON value. All the measurements were registered in the absence of any physical stimulus.

At a single point of time, values of RASS and qCON were recorded, first on the admission of the patient in ICU (0 hours), then every 15 minutes for the first 2 hours, and after every 2 hours for a total duration of 12 hours. The values of qCON were taken before noting down the RASS values. This was done because any stimulation during the assessment of sedation or during stimulation could have increased the values of qCON and resulted in spurious results. Other stimulations, like endotracheal suctioning or positioning, were avoided before taking the readings. In the ICU, as per standard practice, optimum sedation levels were maintained as per RASS score by altering doses of sedatives. The same was done for all patients in the study. The rate of infusions of propofol and fentanyl during the study period was noted down. All patients were ventilated for 12 hours. Individual ventilatory modes and other parameters were decided as per the specific necessities of the patient.

To check whether qCON would differentiate between various sedation grades, RASS was divided into two groups. The first group was for a RASS score of 0 to -1, which was taken to be as minimal sedation; and the second group was for a RASS score of -2 and -3, which was taken as moderate sedation.

For descriptive purposes, values were described using mean and standard deviation wherever the data were uniformly distributed or median and interquartile range where data were skewed. A correlation was calculated with the help of Spearman (Spearman's rho). Statistical analysis was done using Statistical Package for Social Sciences (SPSS Inc., Chicago, Illinois, version 21.0, for Windows). The result was perceived to be statistically significant only when the "*p*" value was less than 0.05.

Results

A total of 87 patients were included in the study after it was ascertained that they met the inclusion criteria. The patients comprised 32 females and 55 males. The mean age of patients was 42.56 ± 15.27 years, and the mean weight 62.07 ± 9.40 kg. Out of the 87 patients, 78 patients were postoperative patients who had undergone abdominal, thoracic, orthopedic, urological, or gynecological surgeries, and the rest of the nine patients were suffering from medical disorders, such as interstitial lung disease requiring mechanical ventilation as part of their treatment regimen (Table 1). A total of 1,218 readings were collected.

The qCON values at baseline varied from 47 to 99, and the RASS values at baseline ranged from -3 to 0. The median qCON value was 76 with an interquartile range from 65 to 83. The mean qCON value was 74.22, with a standard deviation of 12.76. Figure 1 depicts mean qCON numbers noted correspondingly with different periods. The median RASS was -3; as brought up previously, the sedation was adjusted to maintain RASS values within the range of 0 to -3.

Table 1: Disease distribution in patients

	Patient number (n)	*Percent*
Surgery cases	78	89.65
Gastrosurgical	16	18.39
ENT	11	12.64
Peripheral	16	18.39
Urological	4	4.59
Neurosurgical	24	27.58
Gynecological	2	2.29
Thoracic	5	5.74
Medical cases	9	10.34
Cardiac	3	3.44
Aspiration pneumonia	2	2.29
COPD	1	1.14
ILD	3	3.44

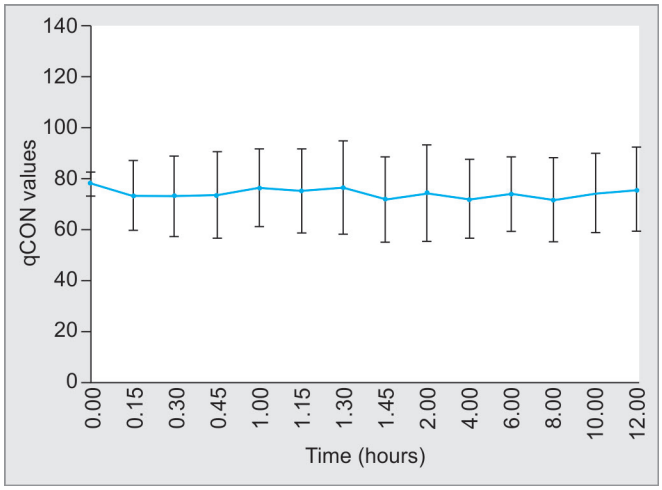

Fig. 1: Mean qCON values at different time intervals

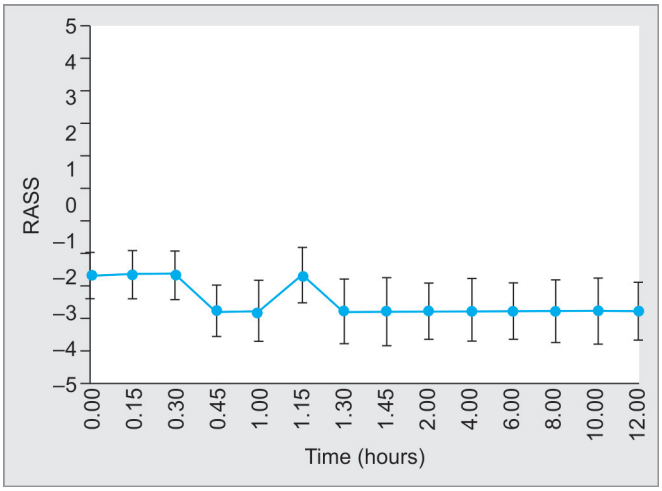

Fig. 2: Median RASS score at different time intervals

Figure 2 depicts median RASS numbers noted correspondingly with different periods. The mean rate for propofol infusion was 1.44 ± 0.49 mg/kg/hour and for fentanyl 0.7 µg/kg/hour.

After contrasting each qCON value correspondingly with time to each RASS value, we found their correlation to be statistically significant ($\rho = 0.288$, $p < 0.0001$). As depicted in box and whisker plots between qCON and RASS (Table 2 and Fig. 3), for the RASS value of -3, we obtained 43 qCON values. The median qCON value for a RASS score of -3 was 73, and the interquartile qCON values ranged from 62 to 80. For the RASS value of -2, we obtained 132 qCON values. The median qCON value for a RASS score of -2 was 77, and the interquartile qCON values ranged from 67 to 83. For the RASS value of -1, we obtained 405 qCON values. The median qCON value for a RASS score of -1 was 84, and the interquartile qCON values ranged from 77 to 90. For the RASS value of 0, we obtained 638 qCON values. The median qCON value for a RASS score of 0 was 85, and the interquartile qCON values ranged from 79 to 92.

To check whether qCON could differentiate between various sedation grades, RASS was divided into two groups. The first group is for a RASS score of 0 and -1, which was taken to be as minimal sedation; and the second group is for a RASS score of -2 and -3, which was taken as moderate sedation. In the present study, we obtained

Table 2: RASS vs qCON

RASS	*0*	*−1*	*−2*	*−3*
Median qCON	85	84	77	73
Mode value qCON	87	83	73	78
qCON—interquartile range	79–92	77–90	67–83	62–80
Number of observations	638	405	132	43

RASS, Richmond Agitation Sedation Scale; qCON, quantium consciousness index

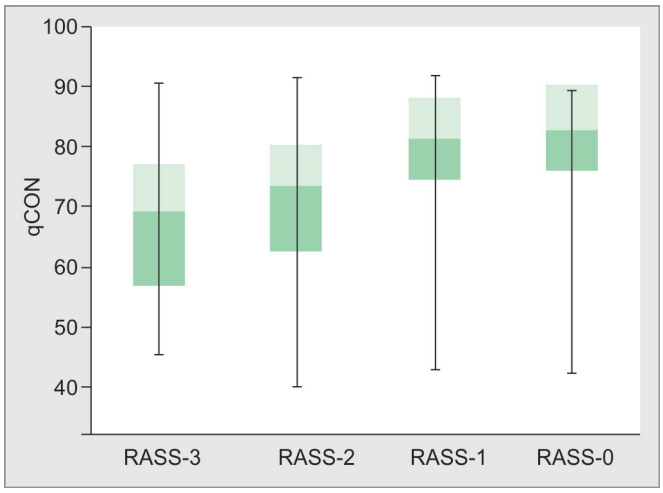

Fig. 3: Box and whisker plots showing qCON and RASS

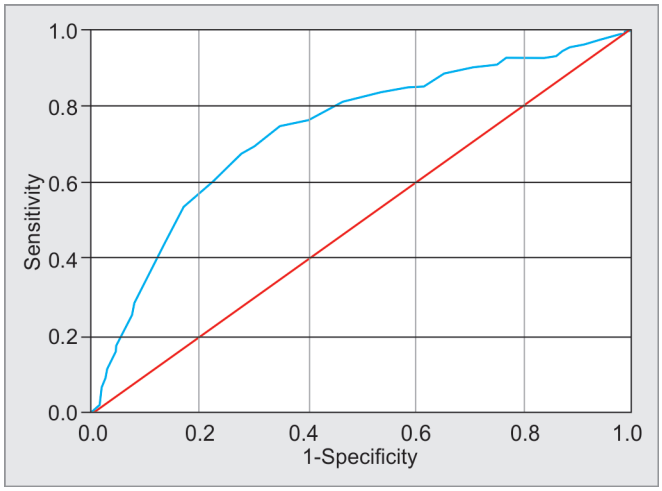

Fig. 4: ROC curve for qCON and RASS

1,043 values for the group RASS 0 and -1, the minimally acceptable sedation group, and 175 values for the group RASS -2 and -3, the moderately acceptable sedation group. With the help of ROC curves, we were able to differentiate appropriate from inappropriate levels of sedation. In this method, a qCON value of 80 had a sensitivity of 72.67% and a specificity of 67.42% (area under the ROC curve was 0.738 with standard error of 0.021) (Fig. 4). No significant adverse effects, i.e., skin allergy/rash, burn, blister, redness or irritation of area, were seen after prolonged placement of CONOX electrodes.

Discussion

In the present study, correlating each qCON value for each RASS value for each patient correspondingly with time, we obtained a statistically

significant correlation between qCON and RASS ($\rho = 0.288$, $p < 0.0001$). In the study by Sharma et al., 27 critically ill patients of both sexes who were on mechanical ventilation and sedation with propofol and fentanyl were evaluated.[15] They compared entropy state entropy (SE) and response entropy (RE) to RASS during 24 hours, and out of a total of 507 readings, a significant correlation between SE and RASS ($\rho = 0.334$, $p < 0.0001$) and RE and RASS ($\rho = 0.341$, $p < 0.0001$) was found. In the present study, the sample size was much larger than in the study by Sharma et al. Therefore, it is expected to increase the reliability of the presented data.

Muller et al. examined the correlation between three different depth of anesthesia modalities, qCON, BIS, and SE, in 21 patients during flexible bronchoscopy with propofol sedation.[16] They found that all three indices enhanced significantly after bronchoscope insertion and coughing, and there was a good correlation of these three indices' trend throughout the procedure.[16] In their study, agreement of BIS/SE was 68 and 50% for BIS/qCON and qCON/SE. In the present study, qCON was evaluated for the depth of sedation for a longer duration, i.e., 12 hours. Further comparison of other modalities of the depth of sedation with qCON is needed for a prolonged period.

The 2013 PAD guidelines describe that if a lighter level of sedation is maintained, it will decrease the time required for weaning or extubation and reduce ICU length of stay.[17] Previously, the guidelines published before 2013 quoted light sedation to be considered when the RASS is > or = -2, and there is sustained eye-opening of at least 10 minutes.[18] This sedation level so mentioned could probably be more profound than necessary for treating and caring for the patients on mechanical ventilation in the ICU.

There might be various sedation assessment scales, but their functionality is similar. It is to differentiate between low, adequate, and high sedation. So, when we compare qCON with the sedation scales, its outcome also depends on those particular criteria used to define different variables or groups. When RASS score is maintained between 0 and -3, it is linked to sedation depth which is light or moderate, which is well suited for ICU patients who require sedation. A RASS value between -4 and -5 is linked to oversedation, and a RASS value >0 is related to deficient sedation. In the present study, RASS was maintained between 0 and -3 by adjusting the IV sedative agents accordingly. Therefore, it is not surprising in our research to find out that the median value of RASS came to be -3. For appropriate sedation, a RASS value between 0 and -3 had a mean qCON value of 74.22 ± 12.76.

The reference range of qCON for sedation in ICU patients has not been described in the literature. To differentiate appropriate from inappropriate levels of sedation in this study, a qCON value of 80 had a sensitivity of 72.67% and a specificity of 67.42%. This infers that a qCON value of 80 or less stipulates sufficient sedation in this patient subclass. The values obtained were close to the manufacturer's endorsed values for qCON (60–80) for adequate balanced anesthesia.[12]

There is no standardization in ICU sedation protocols, so there is considerable variability in the designs of studies. It is better if we have well-defined components and pathways as it could mitigate poor quality of studies, including, but not limited to, defining the best approach in managing issues, like level of sedation, stimulation during the evaluation of sedation, the influence of various disease factors on the accuracy of these objective instruments. It is also noteworthy to consider promoting such studies to confirm whether these instruments/devices can significantly contribute to patient improvement or can decrease hospital costs in the long run compared with the conventional method of assessing subjectively.

The various clinical effects of multiple drugs on the EEG and its derived parameters are mentioned in studies.[19] So, the impact of these different drug varieties on the EEG-derived qCON has been considered. In this study, standardization of sedation with a regimen comprising of propofol and fentanyl was used, which was the protocol of the ICU setting for sedation. This was done to prevent bias. The use of fentanyl decreases the pain and also has a synergistic effect with propofol for sedation.

The following are some of the study's limitations: qCON was not correlated to sedation scales apart from RASS, which might have provided our results more strength. Since we did not evaluate the use of qCON in differentiating oversedation (RASS value -4 and -5) from appropriate sedation, this aspect has to be dealt with before labeling qCON monitoring as an "ideal method" for assessment of sedation in the ICU. Further studies are required to support the effect of qCON on the maintenance of ICU sedation in the future.

Conclusion

The qCON monitoring can objectively help in assessing the depth of sedation in ICU patients on mechanical ventilation. It can reliably differentiate appropriate from the inappropriate levels of sedation and help prevent inadequate sedation hazards.

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