

REVIEW ARTICLE

Sleep and delirium in the Intensive Care Unit

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ABSTRACT

Intensive Care Unit (ICU) patients almost uniformly suffer from sleep disruption. Even though the role of sleep disturbances is not still adequately understood, they may be related to metabolic, immune, neurological and respiratory dysfunction and could worsen the quality of life after discharge. A harsh ICU environment, underlying disease, mechanical ventilation, pain and drugs are the main reasons that underlie sleep disruption in the critically ill. Polysomnography is the gold standard in evaluating sleep, but it is not feasible in clinical practice; therefore, other objective (bispectral index score [BIS] and actigraphy) and subjective (nurse and patient assessment) methods have been proposed, but their adequacy in ICU patients is not clear. Frequent evaluation of neurological status with validated tools is necessary to avoid excessive or prolonged sedation in order to better titrate patient-focused therapy. Hypnotic agents like benzodiazepines can increase total sleep time, but they alter the physiological progression of sleep phases, and decrease the time spent in the most restorative phases compared to the phases normally mediated by melatonin; melatonin production is decreased in critically ill patients, and as such, exogenous melatonin supplementation may improve sleep quality. Sleep disruption and the development of delirium are frequently related, both because of sleep scarcity and inappropriate dosing with sedatives. Delirium is strongly related to increased ICU morbidity and mortality, thus the resolution of sleep disruption could significantly contribute to improved ICU outcomes. An early evaluation of delirium is strongly recommended because of the potential to resolve the underlying causes or to begin an appropriate therapy. Further studies are needed on the effects of strategies to promote sleep and on the evaluation of better sleep in clinical outcomes, particularly on the development of delirium.

Key words: Sleep - Delirium - Critical illness - Analgesia.

Sleep is an essential biological function contributing to physiologic and psychological homeostasis. However, ICU patients almost uniformly have sleep alterations.¹ Sleep disturbances in the ICU are still poorly understood, but they could worsen comorbidities or be the result of underlying disease. They have a role in the alteration of catecholamines and hormone secretion, in determining insulin resistance and immune dysfunction with impaired resistance to infections, in alterations of nitrogen balance, in wound healing and pulmonary mechanics, in psychopathol-

ogy and in worsening the quality of life after ICU discharge.^{2,3}

Quantity and quality of sleep in ICU

Sleep in ICU patients has been characterized by long sleep-onset, sleep fragmentation, poor sleep efficiency, frequent arousals, a predominance of stage 1 and 2 non-rapid-eye-movement (NREM) sleep, decreased or absent stage 3 NREM (the most restorative), and decreased or absent rapid-eye-movement sleep.⁴

The literature contains different conclusions as to whether critically ill patients are sleep deprived, with or without sedation, but even in the studies that found relatively adequate amounts of sleep (7-9 hours per day), the investigators noted altered sleep quality, large variations in total sleep time (from 1 to 19 hours/day),^{1, 5} daytime sleepiness and short naps; generally, there is an overall agreement about severe sleep disruption during recovery from critical illness.^{2, 4, 6, 7}

In addition, surveys of ICU patients indicate that sleep disturbances are one of the biggest complaints; this perception of poor sleep, which manifests during the acute illness, often persists for an extended period of time after ICU discharge.^{8, 9}

Reasons for ICU sleep disruption

Reasons for sleep deprivation in the ICU are multifactorial and include the type and the severity of the underlying illness, the pathophysiology of acute disease, the pain from surgical procedures and the ICU environment itself. Light, noise, nursing procedures, lab draws, vital signs, radiographs, and physician interventions all contribute to sleep deprivation, even though, in a controlled setting, some of these have been shown not to be extremely important (noise 21% and nursing 9% of awakenings).⁷

The sleep of mechanically ventilated patients may be worsened by dysynchronous breathing, the ventilation setting, discomfort from the endotracheal tube, and stress related to the increased difficulty in communicating.^{2, 10}

Several pharmacological agents, including sedatives and analgesics, cardiovascular pressors, antibiotics, chemical paralytic agents, antidepressants, anticonvulsants, gastric protectors and anti-asthma medications have been found to have a negative effect on patient sleep quality and architecture; withdrawal reactions should be considered as other possible triggers of sleep disruption.¹¹ Moreover, some of these drugs are associated with reduced secretion of melatonin, an endogenous regulator of circadian rhythms, and patients with septic shock have significantly lowered melatonin levels, both in nocturnal peaks and basal daytime levels.¹²

Methods of sleep evaluation

Polysomnography is the gold standard to objectively measure quality and quantity of sleep.¹³ However, it is difficult to undertake, particularly in high-risk¹⁴ critically ill patients, and it is presently used only for research. Therefore, other methods, both objective (actigraphy and bispectral index, BIS) and subjective (nurse or patient assessment), have been used in critical care studies.

BIS is simpler than polysomnography, but it is subject to electrical interference; it is capable of detecting sleep, but the current spread of the BIS overlap for a given stage of sleep prevents its use as a depth-of-sleep monitor.

Actigraphy (a small wristwatch device capable of sensing and storing information regarding patient movements) provides evaluations of total sleep time, the number and frequency of awakenings, and sleep efficiency, with a good correlation with polysomnography in healthy volunteers. In the ICU, actigraphy usually overestimates total sleep time, with a high sensitivity for detecting sleep, but is barely reliable in detecting wakefulness.

Judgements based on inspection consistently overestimate sleep time and do not detect sleep disruption.^{2, 6}

Sleep and sedation

Analgo-sedation is commonly used in ICU patients to provide comfort, to minimize anxiety and pain, to decrease stress reactions, to control agitation, to make the harsh ICU environment acceptable, and to facilitate sleep. Sedatives may have both negative effects on sleep, by altering the patients' naturally occurring circadian rhythms and sleep phases, and positive effects, by increasing total sleep time and sleep continuity; propofol, barbiturates, dexmedetomidine, benzodiazepines and opiates affect neurophysiologic pathways involved in sleep.¹¹

Frequently, a combination of a benzodiazepine and an opioid is used to address pain and anxiety and facilitate mechanical ventilation or tolerance of other uncomfortable critical needs. The intensive care provider must recognize that although patients may appear to be sleeping, benzodiazepines and opioids significantly alter the nor-

mal sleep pattern.² In addition, paradoxical effects such as insomnia, hallucinations, and agitation can occur.

Sleep and sedation share similar neurobiological and phenotypic properties, but are different in many characteristics: the biologic need for sleep and the therapeutic need for sedation almost universally coexist in critically ill patients. Because the side effects of sedation are noteworthy, it is important to further study the possibility of keeping critically ill patients at a sedation level that leaves them as “conscious” as possible during the whole ICU stay,¹⁵ daily challenging the clinical condition and its compatibility with the lowest acceptable level of sedation with consciousness.¹⁶

Based on evidence that disturbed melatonin secretion is associated with sleep disturbances in both postoperative and longer term ICU patients, melatonin may be another option for correcting insomnias in critical patients. Since melatonin acts by promoting sleep without inducing significant sedation, it could also be useful in patients in whom sedation and reduced respiratory effort are undesirable. Unlike benzodiazepines, melatonin maintains the normal sleep architecture.¹¹

Methods of neurological status evaluation

Patient-focused analgo-sedation in the ICU involves a strategy of comprehensive structured management that combines initial evaluation, continuous monitoring, drug selection, protocol use, and the careful consideration of patient characteristics and needs.

After the early evaluation of potential predisposing and precipitating factors, frequent monitoring with validated tools¹⁷ improves communication among critical care providers and plays an important role in detecting and treating pain and agitation while avoiding excessive or prolonged sedation. Bedside evaluation of the level of consciousness or arousability, cognitive function, presence and intensity of pain, and presence and intensity of agitation is an integral component of daily patient care.^{18, 19}

The utilization of tools such as sedation scales and pain evaluation instruments is important for patient-focused therapy, typically by minimizing

pain and establishing a target level of sedation to which medications are titrated to achieve.

Delirium and sleep in ICU

Delirium, an acute reversible disorder of attention and cognition, is a common occurrence among critically ill ventilated patients (from 60% to 85%), and is a marker of poor outcomes, including increased incidence of post-traumatic stress disorder and increased long-term mortality.²⁰ It is a disturbance of the consciousness with inattention accompanied by a change in cognition or perceptual disturbance that develops over a short period (hours to days) and fluctuates over time. The current consensus is to consistently use the unifying term delirium and subcategorise it according to psychomotor symptoms (hyperactive, hypoactive, or mixed). Hyperactive delirium, in the past referred to as ICU psychosis, is rare in the pure form and is associated with a better overall prognosis. It is characterized by agitation, restlessness, attempting to remove catheters, and emotional lability. Hypoactive delirium, which is very common and more deleterious for the patient in the long term, often remains unrecognised; amid a busy emergency department ICU shift, patient hypoactivity does not seem like a problem and may be missed. This subtype is characterized by withdrawal, flat affect, apathy, lethargy and decreased responsiveness.

In particular, there is emerging evidence that many cases of hypoactive or mixed delirium in the ICU are related to the sedative effects of anxiolytic and analgesic drugs that ICU caregivers administer; thus, strategies that emphasize the use of the lowest effective sedative drug dose may help in avoiding delirium.¹⁶

On the other hand, sleep loss has been associated with irritability, memory loss, inattention, delusions, hallucinations, slurred speech, uncoordination and blurred vision. Even healthy subjects may be unable to complete simple repetitive tasks after a period of sleep loss. In short, all criteria for the diagnosis of delirium may be caused by sleep loss.² It is known that sleep deprivation is a common phenomenon in critically ill patients and that delirium occurs frequently (up to 85%) in groups at high risk, but the relationship between sleep dep-

rivation and delirium remains a subject of debate. It is not known whether sleep deprivation is a cause of delirium in the ICU, whether it contributes to ICU delirium by lowering patients' thresholds for developing delirium, or whether it has any relationship at all to delirium in the ICU. However, there is a growing body of evidence suggesting that the development of delirium in the ICU is an independent predictor of higher morbidity and mortality, increased length of stay, disposition to an institutional setting from the hospital, and cognitive impairment at hospital discharge.^{20, 21} Therefore, if a relationship between sleep deprivation and delirium were established, it would more closely link the poor sleep of the critically ill patient with the poor outcome of the delirious patient.

Evaluating delirium

Although routine screening for the presence of delirium is recommended in guidelines for sedative and analgesic therapy,^{18, 19} surveys indicate that delirium testing of ICU patients with a validated tool is rarely performed.

There are currently two validated tools for monitoring delirium in ICU patients: the Intensive Care Delirium Screening Checklist²² and the Confusion Assessment Method for the ICU (CAM-ICU).¹⁸

The Intensive Care Delirium Screening Checklist is an eight-item checklist (altered consciousness, inattention, disorientation, hallucinations, psychomotor symptoms, inappropriate speech, sleep disturbances and symptom fluctuation) with a sensitivity of 99% and specificity of 64% and inter-rater reliability of 0.94. Each of the eight items is scored as absent or present (1 or 0, respectively) and the score is summed. A score >4 indicates delirium.

The CAM-ICU was adapted for use in nonverbal ICU patients from the original Confusion Assessment Method, and includes a four-feature assessment (acute mental status changes, inattention, disorganized thinking and altered consciousness). Sensitivity and specificity values of the CAM-ICU are both >90%. The CAM-ICU is translated into over a dozen languages, easy to administer, takes, on average, less than one minute to complete, and requires minimal training. CAM-ICU

implementation projects within different types of hospitals have reported high compliance and accuracy. A complete description of the CAM-ICU and training materials including videos and translations can be found at the dedicated web site.²³

Conclusions

Critically ill patients consistently demonstrate sleep fragmentation and absence of subjective sleep restoration; they need a patient-focused use of sedatives and analgesics, in which the pharmacological interventions are carefully modulated. The use of guidelines, the frequent and personal assessment of the most "conscious" sedation level (comprehending the physiological sleep periods) consistent with clinical conditions, and the use of strategies to precisely target therapy to defined end points (goal-directed sedation) are three important tasks for ICU staff.

Objective monitoring of consciousness (BIS, actigraphy) could help ICU physicians in this arduous commission, but other clinical investigations are needed to assess reliability.

By now, all critical care providers are strongly invited to frequently evaluate sedation level and delirium, and to introduce validated tools to do so. In the daily discussion about monitoring and managing organ dysfunction, brain evaluations should always be present at the bedside of critically ill patients.

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