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CLINICAL REVIEW

Sleep of critically ill children in the pediatric intensive care unit: A systematic review

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SUMMARY

Critically ill children in the pediatric intensive care unit (PICU) are exposed to multiple physical, environmental and pharmacologic factors which increase the propensity for sleep disruption and loss and may, in turn, play a role in short-term recovery from critical illness and long-term neurocognitive outcomes. Mechanically ventilated children receive sedative and analgesic medications, often at high doses and for long durations, to improve comfort and synchrony with mechanical ventilation. Sedatives and analgesics can decrease slow wave sleep and rapid eye movement sleep. Paradoxically, sedative medication doses are often increased in critically ill children to improve the subjective assessment of sedation and sleep, leading to further agitation and deterioration of sleep quality. The heterogeneity in age and critical illness encountered in the PICU pose several challenges to research on sleep in this setting. The present article reviews the available evidence on sleep in critically ill children admitted to the PICU, with an emphasis on subjective and objective methods of sleep assessment used and special populations studied, including mechanically ventilated children and children with severe burns.

Introduction

Approximately 250,000 children are admitted to the pediatric intensive care unit (PICU) each year in the United States.[1] Critical illnesses in children encompass a range of medical and surgical diagnoses, such as multi-system organ failure requiring extracorporeal support, complex congenital heart disease, and severe trauma. The modern PICU admits all critically ill infants and children aged 0–18 y with the exception of critically ill neonates, who are admitted to the neonatal intensive care unit (NICU). As a result, the PICU provides care for a heterogeneous age range of patients at vastly different developmental stages and biological needs. Thus, during any given shift over a 24 h period, physicians and nurses in the PICU may be concurrently responsible for the care of a one month old infant and a 12-y old adolescent. Admission to the PICU is a stressful experience for children who are going through active neurocognitive development, and sleep disturbances are often an unavoidable result of the critical illness and associated management.

Although the importance of sleep in the intensive care unit (ICU) setting has become a topic of significant research interest in recent years, there is a paucity of scientific evidence investigating sleep as a modulator of outcomes in critically ill children.[2] Studies that have used polysomnography (PSG) in adults admitted to the ICU have demonstrated a decrease in sleep efficiency, an increase in arousal frequency, and a decrease or absence of slow wave sleep (SWS) and rapid eye movement (REM) sleep.[3–6] Furthermore, poor sleep quality and sleep onset and maintenance insomnia are the most frequent complaints noted by adult survivors of critical illness – impairments that persist even after discharge from the ICU.[7] When a child becomes critically ill, admission to the PICU brings with it a multitude of risk factors for disruption of the normal rhythm of the sleep–wake cycle, including a chaotic environment, administration of centrally acting medications, pain associated with the underlying illness, interruptions for nursing care, and invasive medical interventions (Fig. 1). The resulting disruption in sleep continuity and reduction in sleep duration can interfere with a myriad of fundamental physiologic processes that, in turn, can lead to delirium, impaired immunity, catabolism and respiratory compromise – undesirable effects when a child is critically ill and recovery and

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Abbreviations

BSA	body surface area
BSI	bispectral index
db (A)	A-weighted decibels
DHEA	dehydroepiandrosterone
EEG	electroencephalography
GH	growth hormone
ICU	intensive care unit
NICU	neonatal intensive care unit
NREM	non-REM
PICU	pediatric intensive care unit
PRISM	pediatric risk of mortality
PSBOT	patient sleep behavior observation tool
PSG	polysomnography
REM	rapid eye movement
SWS	slow wave sleep

healing are the goal.[2,8–10] Despite obvious similarities between the pediatric and adult ICU environments, key differences exist in the exposures experienced by the critically ill child and adult. Moreover, across the age spectrum, there is substantial biological variability in normal sleep–wake behavior which may modify the detrimental impact of the ICU environment.

It is well known that sleep needs are in a constant state of change as a child matures, reflecting neurologic maturation. Newborns typically sleep up to 18 h per day on an irregular schedule, with periods of wakefulness that are limited to one to three hours. A newborn's sleep cycle ranges from 50 to 60 min and is comprised of an equal proportion of REM and non-REM (NREM) sleep. Over the first twelve months of life, sleep becomes consolidated in infants, and by five years of age sleep patterns stabilize to one continuous period of sleep at night.[11–13] Healthy children between three and 12 y old sleep from nine to ten hours each night on average, and spend a greater proportion of the night in slow wave sleep than adults, from 20 to 38% of total sleep time.[12,14,15]

To understand key factors that disrupt the normal sleep–wake cycle in children admitted to the PICU, it is imperative to recognize that there are several features of critical care in children that are distinct from adults. Perhaps one of the most challenging components of pediatric critical care is sedation of mechanically ventilated children. Mechanically ventilated children universally receive sedative and analgesic drugs for pain and anxiety associated with invasive instrumentation, the most common being the endotracheal tube. The inability to communicate and the developmental limitations in understanding the need for ICU interventions compounds the challenges involved in adequately sedating children to maintain safety and prevent inadvertent extubation or decannulation of catheters.[16–18] Common medications used for sedation include opioids, benzodiazepines, ketamine, barbiturates and alpha-agonists such as dexmedetomidine and clonidine. Often these medications are used in combinations of two or more classes, the most common combination consisting of an opioid and a benzodiazepine after the initiation of mechanical ventilation. Opioids and benzodiazepines have been shown to decrease slow wave and REM sleep in adults.[19,20] Paradoxically, sedative and hypnotic medications doses are often increased in critically ill children to improve the subjective assessment of sedation and sleep, leading to further agitation and deterioration of sleep quality. In a study of "difficult to sedate", mechanically ventilated children in a tertiary care PICU ($n = 47$), over 50% of these children received four or more distinct sedative or analgesic agents simultaneously highlighting the challenge of balancing patient comfort and medication side effects.[21] Indeed, excessive sedation is a risk in the critically ill child given the efforts that are usually made to help the patient "sleep" and maintain comfort and safety. Part of the difficulty in optimizing the use of centrally acting medications in critically ill children is the use of subjective measures to assess sedation such as the COMFORT scale, the state behavioral scale (SBS), and the Richmond agitation and sedation scale (RASS). While helpful to some degree, these scoring systems are subjective and rely on the nurse's assessment of patient comfort and sedation. Negative consequences of the escalating doses of sedative medications include lengthened time to extubation, withdrawal syndromes, and need for detoxification from sedatives due to pharmacological dependence. The addition of neuromuscular blockade as an adjunct to the sedation regimen adds an additional layer of complexity to the assessment of sedation and potentially compounds the problem of achieving adequate sleep quality in the ICU. Neuromuscular blockade diminishes the ability of care providers to use physical movement as an indicator of sleep state, and may lead to oversedation in an effort to ensure that the child is amnestic while receiving muscle relaxant. The role of impaired sleep quantity and quality in escalating sedative needs requires further evaluation in the PICU.

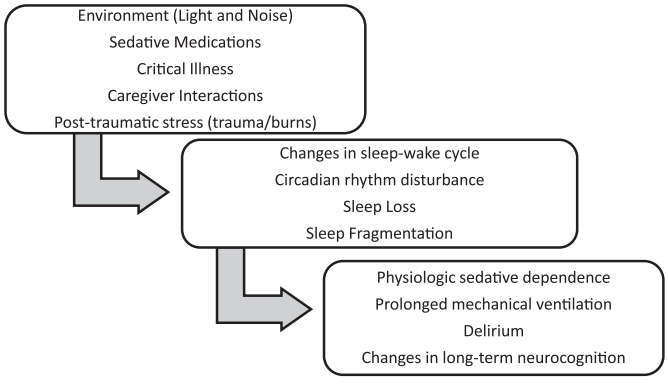

Fig. 1. Proposed causal pathway for changes in sleep behavior as a modulator of outcomes in critically ill children.

Previous research on sleep in the PICU has relied predominantly upon subjective assessments. As a result, assessment of sleep quality and quantity in the PICU remains an area for much needed research. An obvious challenge in characterizing sleep in the ICU results from the need to provide life-saving interventions and care for the critical illness that can interfere and confound the assessment of sleep. Interestingly, recommendations by the Society for Critical Care Medicine guidelines on sedation monitoring suggest that sleep assessment be a part of routine care.[4] Both subjective and objective sleep assessment tools are available for use in the ICU. Techniques for objectively characterizing sleep in the ICU include polysomnography, actigraphy, and bispectral index (BIS) monitoring. There are also subjective methods that are based on observations of patient's behavioral state.

Due to a lack of general awareness about the physical and psychological significance of sleep, hospital routines have been in place for decades that disrupt sleep continuity in the adult and pediatric ICU. Interestingly, many neonatal intensive care units nationally have adopted protocols to minimize sleep disruption, but neonates have distinct sleep physiology compared to children and adults, and many neonates do not require sedatives while mechanically ventilated. Lack of adequate sleep duration and quality has a known association with delirium, and the vast majority of PICUs internationally do not have protocols in place for sleep promotion and optimization. Given the limited information on sleep in critically ill children, the objective of the current study was to: a) summarize the current evidence base; b) highlight the challenges of sleep