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Review Article

Understanding Sleep Patterns and Sleep Disorders in ICU: Role of Respiratory Physiotherapy in Improving Sleep Quality for Critically Ill Patients

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ABSTRACT

Sleep and wakefulness schedules must be organized appropriately for the human body's adequate functioning. Within the sleep-wake cycle, sleep is an active process for promoting physical and mental health. Behavioral or respiratory sleep disorders increase the risk of body disorders, such as increased blood pressure, cardiovascular diseases, diabetes, depression, immune system deficits, and disruptions in neurophysiological organization. In the Intensive Care Unit (ICU), sleep disturbances can lead to delirium, prolonged intensive care stay, and increased mortality.

The presence of sleep disorders in critically ill patients is a severe problem. It is directly related to the exposure of these individuals to exogenous and endogenous factors that impair their sleep quality. Both pharmacological and nonpharmacological interventions may be employed to facilitate optimal sleep quality among patients in the Intensive Care Unit (ICU). Still, they require coordinated efforts and a change in the culture and behavior of ICU care structures. In this context, the respiratory physiotherapist plays a fundamental role, possessing the skills to develop and implement measures that contribute to better sleep quality for critically ill patients.

Keywords: Intensive Care Unit (ICU); Circadian rhythms; Non-Rapid Eye-Movement sleep (NREM); Insomnia; sleep-wake cycle

INTRODUCTION

The normal sleep

Circadian rhythms are self-sustaining temporal phenomena in physiology and behavior regulated by a central clock in the hypothalamus. They hold many physiological functions, such as central body temperature, hormone release, and sleep. The sleep-wake cycle is the most evident circadian rhythm in men and women, with its primary stimulus being ambient light. Sleep and wakefulness schedules must be organized appropriately for the human body's proper functioning. However, despite reports of sleep disturbances dating back to ancient times, this field has recently received more attention in the medical field.

Within the sleep-wake cycle, sleep can be defined as a complex, physiological state necessary for life, reversible and cyclical, characterized by loss of consciousness and relative immobility [1,2]. It is an active process with controlled duration and variation by specific structures in the central nervous system. During sleep, brain activity alternates between a synchronized state called Non-Rapid Eye-Movement sleep (NREM) and an activated state called REM sleep (also known as paradoxical sleep, as it is when our mind is most active and muscle tone is more relaxed) [1].

NREM and Rapid Eye-Movement (REM) sleep have distinct characteristics regarding endocrine, respiratory, cardiovascular, gastrointestinal, and genitourinary functions. In NREM sleep, there is a regular decrease in ventilation, maintenance of the effectiveness of proprioceptive reflexes, active intercostal muscles, maintenance of the muscle tone of the upper airways, rhythmic reduction in heart rate, and regular decrease in blood pressure and cardiac output. In REM sleep, there is variable ventilation, abolished proprioceptive reflexes, inactive intercostal muscles, reduced muscle tone of the upper airways, variable

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heart rate irregularities, and irregular oscillations in blood pressure and cardiac output [3].

The entirety of sleep in which all stages of NREM sleep are completed (N1: 2 to 5% of total sleep, N2: 45 to 50% of total sleep, and N3: 18 to 25% of total sleep) along with REM sleep (20 to 25% of total sleep) is called a cycle and in a normal individual lasts between 70-110 minutes, repeating 4 to 6 times during the night [2]. The distribution of sleep stages during the night can be altered by factors such as age, ambient temperature, drug intake, or certain diseases. Typically, NREM sleep is more concentrated in the first part of the night, while REM sleep predominates in the second part. Despite the exact function of different sleep stages still being unknown, REM and NREM N3 sleep stages are considered the most effective in the body's restorative processes [4].

LITERATURE REVIEW

Sleep disorders

Sleep disorders can be behavioral or respiratory. Within behavioral disorders, we have examples such as REM sleep behavioral disorder, restless legs syndrome, narcolepsy, nocturnal enuresis, sleepwalking, and night terrors, among many others. Insomnia is the most common behavioral sleep disorder characterized by difficulty initiating or maintaining sleep or early awakening, with repercussions on daytime activities. Insomnia appears in various circumstances, with increased brain alertness during the night. Some factors that can exacerbate the condition are anxiety, stress, depression, lack of a regular sleep schedule, and certain organic conditions (such as thyroid alterations).

Respiratory sleep disorders refer to difficulty maintaining an adequate respiratory, and often ventilatory, pattern during sleep. Among these disorders, we can mention primary snoring, congenital central hypoventilation syndrome, Cheyne-Stokes respiration, obesity hypoventilation, and neuromuscular-origin hypoventilation, among others. Obstructive Sleep Apnea (OSA) is the most frequent among respiratory sleep disorders. It is characterized by repetitive episodes of partial or complete obstruction of the Upper Airways (UA), followed by drops in oxygen hemoglobin saturation and sleep fragmentation. Cyclic apnea episodes throughout the night harm various organ systems, primarily increasing the risk of cardiovascular events. The main risk factors for OSA are obesity, advanced age (>65 years), male gender, and craniofacial anatomical alterations that narrow the upper airway and make it susceptible to collapse. The clinical manifestations include loud and frequent snoring, witnessed breathing pauses, recurrent awakenings, daytime sleepiness and fatigue, intellectual deterioration, and mood changes [5].

Diagnostic methods

The standard method for diagnosing sleep disorders is Polysomnography (PSG) conducted in a laboratory, which allows for identifying cardiorespiratory patterns, limb movements, sleep stages, and other vital signs to identify abnormalities during sleep. However, several other methods can assess physiological data during sleep and, knowing their respective limitations, can be used in an intensive care environment [6]. These methods include portable polysomnography (either supervised or unsupervised by a specialized technician) and peripheral arterial tonometry (both methods performed with portable equipment, allowing for the identification of sleep cycles in more or less detail, respectively), nocturnal polygraphy (which does not assess sleep stages but provides a good reading of cardiorespiratory patterns during sleep), and nocturnal oximetry (a more straightforward method that acts as a screening tool to check oxygen saturation variations during sleep) [7].

Despite actigraphy being a recognized objective method for measuring sleep disorders, it has significant limitations for use in the ICU. Actigraphy uses a small wristwatch-like device capable of sensing and storing data about an individual's movements during sleep, determining their sleep and wake periods. It is characterized by the limitation of not providing specific data about sleep stages and quality, and in the intensive care setting, its application is further limited by the patient's immobility and restricted movements, often related to the underlying disease they have [8].

Subjective methods for sleep assessment are questionnaires, which can be answered by the patient themselves, their caregiver, or the patient care team, for example, in an intensive care environment [4,9]. The advantages of subjective sleep assessment are simplicity, ease of application, and low cost. However, subjective assessment does not provide information about sleep architecture, and questionnaires cannot be used in specific situations in the intensive care unit (e.g., patients in a coma, delirium, or with significant cognitive impairment) [4].

Sleep in intensive care unit

Today, we know that getting good sleep is essential for our physical and mental health. When we sleep, there is a change in our state of consciousness, and we restore our balance while preserving various functions such as immunity, metabolism, cognition, cardiovascular activity, and mood, among many others. Several studies have shown that poor sleep quality increases the risk of disorders in the body, such as increased blood pressure, cardiovascular diseases, diabetes, depression, immune system deficits, and disruptions in neurophysiological organization [4].

Critically ill patients are typically exposed to a busy environment with many stimuli (therapeutic and mechanical procedures, high levels of noise and light, mechanical ventilation, medications, pain, and the disease weakening their bodies). All of these factors can, in one way or another, influence the development of behavioral sleep disorders such as sleep fragmentation and insomnia [10,11]. Respiratory sleep disorders can also arise or worsen in the Intensive Care Unit (ICU) due to factors such as a prevalence of supine positioning (which favors gravity's action on upper airway structures, leading to partial or complete collapse), or the action of medications that promote relaxation of the upper airway musculature (also favoring upper airway collapse, impairing functional breathing). In the ICU, sleep disorders and the previously mentioned risks can lead to

delirium, prolonged intensive care stay, and increased mortality [4].

Primary risk factors for poor sleep quality in the ICU and their consequences

Environment: High noise levels (mainly due to conversations among healthcare professionals and equipment alarms) and patient manipulation during the night play a significant role in sleep fragmentation in the ICU, limiting the patient's duration of NREM N3 sleep, which is essential for recovery [4,10,12,13,14]. Loud noise alone can cause vasoconstriction reactions, changes in heart rate, increased adrenaline secretion, and other hormonal changes [10]. Studies have shown that noise levels in ICUs range from 60 to 84 dB (decibels), while the accepted noise level for quality sleep in a hospital environment should not exceed 35 dB, according to the recommendations of the World Health Organization (WHO) [15,16]. Additionally, 22% to 61% of ICU patients report sleep fragmentation due to excessive manipulation of procedures during the night [13]. The general pattern of nighttime work in the ICU allows for no more than three uninterrupted hours of sleep for the patient, which is insufficient for restorative sleep [17].

Medications: Medications can affect sleep in various ways, altering normal sleep physiology and architecture, whether during their initiation or maintenance of administration or when discontinued [18]. Sedation promotes a non-physiological state, disrupting the normal circadian sleep-wake rhythm, especially suppressing NREM N3 sleep and reducing REM sleep. Sedation also decreases sleep latency and increases NREM N2 sleep periods, which can be a causal factor for delirium in ICU patients. Additionally, sedation can reduce upper airway tone during sleep, contributing to airway obstruction and subsequent apnea. With repeated use, benzodiazepines can altogether abolish NREM N3 sleep. The administration of propofol to achieve the recommended level of sedation in critically ill patients further worsens the sleep quality of these patients. However, there are also controversies regarding the action of this drug on sleep, which will be discussed later in this text [19].

Analgesics suppress NREM N3 sleep and can increase wakefulness. Even non-steroidal anti-inflammatory drugs can adversely affect sleep by reducing sleep efficiency and increasing awakenings [16,18,20]. The use of blockers also affects sleep, depending on their lipid solubility. The more lipophilic ones (e.g., propranolol) tend to be associated with nightmares, insomnia, and REM sleep suppression. Amiodarone, a highly effective antiarrhythmic, has neurological side effects in up to 40% of patients at the therapeutic dose, including insomnia and nightmares. Norepinephrine, epinephrine, and dopamine are associated with insomnia and suppression of REM and NREM N3 sleep. The effects of corticosteroids on sleep depend on the type and dose of the medication. They have been associated with REM sleep suppression and increased nocturnal awakenings. Their adverse effects can also lead to insomnia.

In the ICU environment, antipsychotics have become one of the cornerstones for the care of agitated, critically ill patients. Single-dose haloperidol has been shown to increase sleep efficiency with little effect on slow-wave activity and REM sleep but reducing sleep latency [16,18].

Melatonin secretion suppression: Melatonin, a hormone secreted by the pineal gland, plays a important role in regulating sleep and the circadian sleep-wake rhythm [4]. Researchers have studied melatonin secretion in ICU patients and found that in these patients, the peak of melatonin secretion, which occurs at night in healthy individuals, is altered (especially in patients with sepsis) [20-23]. Recognizably, the light-dark cycle is one of the most potent factors in the human circadian sleep-wake cycle. Even with the traditional dimming of lights in the ICU, nighttime light levels in that environment can range from 5 to 1,400 lux. Research shows that light levels between 100 and 500 lux affect melatonin secretion, negatively affecting the circadian cycle. During the night, one chronic issue observed in the ICU is the patient's exposure to light for procedures such as collecting samples for laboratory tests [16].

Ventilatory mode: Many patients in intensive care require ventilatory support. Mechanical ventilation is considered one of the factors contributing to worsened sleep quality in these patients, primarily due to patient-ventilator asynchrony, excessive ventilatory assistance resulting in central apneas, or increased ventilatory effort due to inadequate ventilator settings or unintentional air leakage in the mechanical ventilation system [4,16]. Research suggests that pressure support ventilatory mode causes more sleep fragmentation than assisted-controlled mode [24-27].Similarly, patients with hypercapnic respiratory failure requiring Non-Invasive ventilation (NIV) for longer than 24 hours show relevant sleep disturbances when evaluated by PSG. The level of sleep fragmentation found in patients receiving non-invasive mechanical ventilation in the ICU is similar to that observed in patients with obstructive sleep apnea who already have significant symptoms such as excessive daytime sleepiness and cognitive impairment [16].

Other factors: Factors such as pain, discomfort with the hospital bed, ambient temperature, physical activity restriction, anxiety, and concerns about family and their illness can influence the sleep quality of critically ill patients [10]. Since mealtimes trigger circadian cues for controlling the body's rest cycles, parenteral and enteral feeding can also disrupt these cues, altering circadian rhythm. Studies have shown that the disruption of these rhythms can lead to systemic inflammatory response syndrome, which can then progress to multiple organ dysfunction syndrome [28,29].

Another issue to consider is whether the critically ill patient has a pre-existing diagnosis of a sleep respiratory disorder (e.g., OSA) and whether the disease was taken into account when the patient was admitted to the ICU. Similarly, if the patient is already using a positive pressure device (CPAP or bi-level), and if they were allowed to continue their positive pressure therapy to treat sleep respiratory disorders in the ICU. The interruption of positive pressure therapy for patients with OSA, for example, triggers the recurrence of obstructive airway events during sleep, impairing sleep quality and the health of these individuals.

Interventions to improve sleep quality in the ICU

The evolution of ICU care, primarily aimed at reducing morbidity and mortality in critically ill patients, has been the subject of extensive research. Finding ways to improve these patients' situation includes practices promoting better sleep quality. However, the results of interventional measures to improve the sleep quality of ICU patients, including their repercussions on post-discharge recovery, are still not fully understood. Additionally, there is a challenge regarding healthcare professionals' perception of the importance of restorative sleep and the need to implement measures that promote sleep quality in critically ill patients.

In 2016, Kamdar and colleagues evaluated the perception of physicians and nurses regarding the sleep of critically ill patients. The study found that 75% of the respondents rated the patients' sleep as "poor" or "very poor," 81% believed that sleep was essential for these patients, and 88% reported that sleep deprivation could affect patient recovery. Despite healthcare professionals being aware of the impact of sleep quantity and quality in the ICU, only 32% of the respondents reported the implementation of sleep promotion protocols in their workplaces [30]. This study explains the need for a collective effort among professionals working in critical care environments to effectively implement measures for promoting sleep, whether pharmacological or non-pharmacological.

Pharmacological interventions

Melatonin: As mentioned earlier, in the ICU, artificial light during nighttime can affect the natural production of melatonin, leading to sleep disturbances in these patients. Exogenous melatonin is gaining increasing interest in the medical community as a strategy to improve the sleep of critically ill patients. Melatonin is a hormone synthesized by the pineal gland, crucial for the neuroendocrine regulation of the sleep-wake cycle. It is one of the primary circadian rhythm regulators responsible for promoting sleep. Exogenous melatonin, chemically an indolamine, readily crosses cell membranes by diffusion and has been proven safe and effective. Although extensively researched and presented consistent data on the subjective and objective improvement of sleep quality in ICU patients, the appropriate dosage for its use still lacks robust data [31,32].

Dexmedetomidine: Dexmedetomidine is a drug recently introduced in the sedation of critically ill patients, and its effects appear promising in reducing anxiety and promoting a more natural sleep pattern. Continuous low-dose nighttime infusion of dexmedetomidine has also been reported to increase total sleep time and efficiency while reducing the percentage of N1 (the shallowest stage of sleep) [33]. Studies have also shown that dexmedetomidine preserves sleep patterns and induces cooperative sedation, making patients more easily awakened with minimal impairment of cognitive function [16,18,20].

Propofol: Propofol is an anesthetic agent that can be used in the ICU to maintain sedation in patients and seems to have beneficial effects on increasing slow-wave sleep quantity and subjective sleep quality, replicating normal sleep characteristics. Despite being commonly used, there is insufficient evidence to definitively conclude that the administration of propofol improves sleep quality in these patients. Some studies suggest that this drug may worsen sleep quality in ICU patients [19]. Its use should consider the increased risk of broncho aspiration and cardiovascular events.

Modafinil: Psychostimulants, particularly modafinil, have reduced symptoms such as depression, fatigue, and excessive daytime sleepiness. Especially after the critical phase of the illness, modafinil may be administered to facilitate rehabilitation, enabling more active participation in physical therapy, for example. Compared to other psychostimulants like amphetamines, modafinil does not appear to have the exact mechanism of action on the nervous system and has a much lower potential for abuse. It does not seem to disrupt normal sleep patterns [34].

Other medications: Studies have shown that atypical antipsychotics like olanzapine and risperidone increase total sleep time and NREM N3 sleep efficiency [16,18].

Non-pharmacological interventions

Environmental control (light therapy, white noise, and stimulus reduction): Based on the importance of light in the circadian rhythm, it is crucial to establish appropriate lighting levels in the environment throughout the day. Morning light exposure increases alertness and mood, which are essential for the recovery process of patients. Conversely, dimming the lights at night promotes sleep and regulates melatonin production [35]. Simple measures, such as opening curtains or blinds or using eye masks, can potentially improve the patient's sleep-wake cycle [36].

The use of earplugs and eye masks has been demonstrated as extremely effective strategies for promoting sleep and are economically accessible measures. Some studies have shown that the routine use of these devices improves subjective sleep quality and increases REM sleep duration and nighttime circulating melatonin levels [30,33,37,38]. These devices can also be considered for non-pharmacological prevention and treatment of delirium [8,38]. Adding white noise, a mixed-frequency environmental noise that raises the auditory threshold, can be an alternative to improve sleep in critically ill patients. White noise reduces the ability of intense auditory stimuli (such as alarms and ICU equipment sounds) to activate the cerebral cortex, significantly reducing awakenings. Consequently, it is possible to achieve an improvement in sleep architecture and consolidation [39]. Reducing other stimuli, such as the number of patient care interventions (e.g., hygiene, medication administration, lab tests), decreasing phone volume, controlling conversations among professionals in the units, and reducing external visits are important interventions that can improve the environment and positively impact the sleep of admitted patients.

Exercise: Critically ill patients spend most of their time inactive in bed, and this condition of inactivity is associated not only with cognitive, musculoskeletal, pulmonary, and cardiovascular complications but also interferes with sleep quality [40]. In contrast, peripheral and respiratory exercises break the cycle of immobility and, in addition to recognized health benefits in

many aspects, positively impact ICU patients' sleep patterns, increasing slow-wave sleep and total sleep time [41-43].

Integrative therapies: Complementary therapies such as therapeutic massage and aromatherapy (especially with lavender oil) have been studied in critically ill patients, and their effects have been reported as positive and effective in improving sleep quality [44,45]. When combined with aromatherapy (using valerian oil), acupressure, a technique from traditional Chinese medicine that applies pressure to specific points on the body's meridians to prevent and treat diseases, has also been shown to be effective in improving both the duration and quality of sleep in critically ill patients [46].

The role of the respiratory physiotherapist in improving sleep quality in the ICU

First and foremost, it is essential to remember that promoting sleep in critically ill patients requires coordinated and dedicated efforts and, most importantly, a change in the culture and behavior of the ICU care structure. In this context, respiratory physiotherapists play a crucial role, acting competently as an integral part of the healthcare team and working directly with patients and their families [47]. With the possibility of an educational promotion unit for the healthcare team in the ICU, with courses or scientific meetings, respiratory physiotherapists can raise the issue of measures to promote the sleep quality of patients in intensive care. They can also provide information on the subject to share with the team. Respiratory physiotherapists can work directly with patients, families, or caregivers, guiding the importance of sleep quality in health promotion and instructions on using devices that benefit sleep quality in the ICU, such as earplugs and eye masks during nighttime. Considering the importance of physical and respiratory exercise in promoting adequate sleep, respiratory physiotherapists should develop a comprehensive physical activity plan for ICU patients, exploring all possibilities for physical activity within the limitations of each patient [48]. Many conditions, such as excessive drowsiness due to medication or depression, can be identified by respiratory physiotherapists and referred to the ICU multidisciplinary team for actions that can minimize their effects and make patients more active for exercise in the ICU environment. Breaking the "inactivity-discomfort" cycle can have a positive impact on the sleep quality of ICU patients [46]. As mentioned earlier in this text, adjusting patient-ventilator synchrony and the ventilatory mode are crucial for the sleep quality of ICU patients. These topics require significant attention from respiratory physiotherapists. Precise adjustments of mechanical ventilation equipment and the choice of the most appropriate ventilatory mode during both day and night can be fundamental in promoting better sleep quality for the patient.

In cases where patients have been diagnosed with sleep-related breathing disorders before admission to the ICU, it is essential to maintain the recommended therapy. For patients with Obstructive Sleep Apnea (OSA), respiratory physiotherapists should request the patient's family to provide the home Positive Airway Pressure (PAP) device (CPAP or bilevel) and the interface (mask) as soon as possible and make the necessary adjustments to maintain the PAP therapy. For patients receiving treatment for primary snoring with a mandibular advancement device, the respiratory physiotherapist should consider the possibility of continuing to use this device during ICU admission. Maintaining these care measures reduces the potential negative impact on the patient's health caused by discontinuing treatment for sleep-related breathing disorders upon entry to the ICU. Respiratory physiotherapists can also work to implement nonpharmacological interventions to improve sleep in the ICU, such as the patient's use of earplugs or eye masks to minimize ambient stimulus [49]. Breathing exercises in routine respiratory physiotherapist interventions would have many positive effects, such as improving sleep quality, controlling many sleep disturbance factors, and reducing the occurrence of delirium [42,43,50]. Exercise training can also be considered as a non-pharmacological modality for modifying sleep quality and inflammation among elderly and obese subjects but, until now, there is no evidence supporting the use of the standard rehabilitation techniques (as active and passive movements, including limb exercising, moving or rolling in bed, sitting on the edge of the bed, walking with support, etc.) to improve ICU patients sleep [41,51,52]. Therefore, clinical trials that can investigate an exercise intervention's effects on ICU patients' sleep are needed.

In summary, respiratory physiotherapists in the ICU should be aware that the intensive care environment can negatively impact the sleep quality of critically ill patients. They should be able to identify potentially susceptible patients or those already experiencing behavioral or respiratory sleep disorders. Respiratory physiotherapists should develop and implement preventive, promotional, or recovery measures to improve ICU patients' sleep quality.

DISCUSSION AND CONCLUSION

We still do not fully understand the primary or secondary roles of exogenous factors or endogenous mechanisms in worsening sleep quality in ICU patients. We know that patients in intensive care have few opportunities for extended and adequate sleep. The ICU environment and various factors related to intensive care can lead to behavioral or respiratory sleep disturbances, directly affecting patient health and recovery. Sleep disorders in critically ill patients are a serious problem requiring a multidisciplinary intervention for resolution. Respiratory physiotherapists in the ICU have the skills to develop and implement measures to improve sleep quality in intensive care patients. Additionally, we recommend studies development to verify respiratory physiotherapist rehabilitation techniques' impact on critical illness patients' sleep.

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