Sleep disturbance in hospitalized medical patients: A review article

Trastornos del sueño en pacientes médicos hospitalizados: un artículo de revisión

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Abstract

Introduction and Background. Sleep disorder has side effects on health. Given the high prevalence of sleep disorders in hospitalized patients and since few studies have been conducted to investigate the effects of sleep improvement on the physical condition of hospitalized patients, the present study was conducted to examine the environmental and non-environmental factors and effective interventions in the sleep of hospitalized patients. Methods. This research was theoretical, and the research method was descriptive-analytical, and data were collected through the library method by referring to documents, books, and articles. Results. Several environmental factors such as sound, light, temperature, environmental conditions of wards and rooms affect patients' sleep conditions. Environmental factors affecting patients' sleep quality include underlying disease, pain, pharmacological and non-pharmacological interventions, age, and primary sleep disorders. Conclusion. It seems that the simplest and most effective intervention to improve the sleep quality of hospitalized patients is non-pharmacological interventions and modification of environmental factors, although medications can play a major role in improving the sleep quality of patients.

Keywords: Sleep disturbances, Sleep disorders, Insomnia, Hospitalized patients, Medical patients, Sleep quality.

Resumen

Introducción y antecedentes. El trastorno del sueño tiene efectos secundarios sobre la salud. Dada la alta prevalencia de trastornos del sueño en pacientes hospitalizados y dado que se han realizado pocos estudios para investigar los efectos de la mejora del sueño en la condición física de los pacientes hospitalizados, el presente estudio se realizó para examinar los factores ambientales y no ambientales y las intervenciones efectivas en el sueño de los pacientes hospitalizados. Métodos. Esta investigación fue teórica y el método de investigación fue descriptivo-analítico, y los datos se recolectaron a través del método de biblioteca haciendo referencia a documentos, libros y artículos. Resultados. Varios factores ambientales como el sonido, la luz, la temperatura, las condiciones ambientales de las salas y las habitaciones afectan las condiciones de sueño de los pacientes. Los factores ambientales que afectan la calidad del sueño de los pacientes incluyen enfermedades subyacentes, dolor, intervenciones farmacológicas y no farmacológicas, edad y trastornos primarios del sueño. Conclusión. Parece que la intervención más sencilla y eficaz para mejorar la calidad del sueño de los pacientes hospitalizados son las intervenciones no farmacológicas y la modificación de los factores ambientales, aunque los medicamentos pueden jugar un papel importante en la mejora de la calidad del sueño de los pacientes.

Palabras clave: Trastornos del sueño, Trastornos del sueño, Insomnio, Pacientes hospitalizados, Pacientes médicos, Calidad del sueño.

Introduction

Hospitalized patients often complain of sleep disorders for a variety of reasons, including environmental factors and underlying diseases. This study separately evaluates the effect of each of these internal and external factors on sleep quality and introduces some effective pharmacological and non-pharmacological interventions.

Sleep is a natural state contributing to the maintenance of mental and physical health and cognitive function[1].

Hospitalized patients usually suffer from sleep disturbances, including circadian rhythms disturbance, sleep-disordered breathing, poor sleep quality, low sleep effectiveness, problems in initiating or maintaining sleep, and early morning awakening[2]. In a study in a general hospital in Iran, it was estimated that about 60% of patients suffered from sleep problems[3]. In the study by Frighetto et al., the prevalence of sleep disturbances in hospitalized adult patients was about 50%. In the same way, Manian et al. reported ≥ 50% rates of a sleep problem in 1,238 hospitalized patients with infectious disease[4]. In a study conducted on 2005 patients in the Netherlands, all aspects of sleep quality were rated worse during hospitalization than at home[5]. In a brief report by An Ho et al., 36% of inpatients developed new-onset insomnia in the first days of their hospitalization[6]. Furthermore, a study concluded that new-onset insomnia could continue following hospitalization[7].

Sleep disturbances can cause or worsen medical conditions like diabetes, chronic obstructive pulmonary disease, asthma, arthritis, obesity, hypertension, delirium, neurocognitive disorders, and mood and anxiety disorders[8]. Some studies have linked sleep loss with alteration in the immune and neuroendocrine system[9]. Additionally, it has been reported that sleeping problems affect wounds healing, recovery from illness, pain perception, ordinary activities of patients, length of hospital stay, morbidity and mortality, patient satisfaction, and therefore healthcare resources[10].

Sleep disturbance in hospitalized patients is multifactorial, and many factors affect sleep quality in these patients, including current medical condition, pain, psychiatric disorders, medications, hospital environment, length of hospital stay, and even demographic factors[10]. Some previous studies concluded that sleep abnormalities are more common in some wards, such as intensive care units (ICUs); they are also more common in the surgical wards in comparison with the internal wards[11].

In this review article, we provide an overview of the factors that contribute to sleep disturbance in hospitalized patients. Furthermore, we discuss the recommended interventions and explore the challenges, limitations, and opportunities associated with this critical issue.

Materials and methods

This research is of theoretical type and the research method is descriptive-analytical and the method is based on a systematic review integrated into the literature obtained from different important scientific databases and has been done by referring to documents, books, and articles.

Results

Causes of Sleep Disturbances during Hospitalization

The factors influencing sleep can be divided into two categories: environmental and non-environmental factors:

Environmental Factors

Noise

In several studies, environmental factors were the main cause of insufficient sleep in hospitalized patients and the noise was the most common factor interrupting sleep[12-15]. According to the World Health Organization (WHO) guidelines on preventing the effects of noise on the health status of people in hospital wards, the maximum permitted noise levels are 30 to 45 dBA (less than 35 dBA during the daytime and less than 30 dBA at night)[16].

In a Korean study, the noise level was assessed in 29 rooms of a general hospital, and it was indicated that the noise level of rooms was 86.6 dBA, which was much higher than the recommended level by WHO. In this regard, a study found that noises above 77 A-weighted decibels (dBA) accounted for 66% of nocturnal awakenings in patients admitted to the ICU[17].

The resources of noise include other patients and their caregivers and visitors (people chatting, roommate snoring, toilet flushing), the noise of hospital staff, noise of telephone, cellphone, and TV, and noise of medical devices[18].

Light

Light is one of the most important factors in creating alignment between the circadian rhythms and the dark/light cycle[19]. Many hospitalized patients are not exposed to enough daylight (2000 to 5000 lux for 2-5 hours per day), and most hospital rooms often have very little light (50-300 lux). This can disrupt circadian rhythms and nocturnal sleep[20].

In a general hospital in the United States, light exposure, sleep quality, pain, and mood were assessed through 72 hours. It was found that daytime light intensity was about 104 lux, which was low. Pain perception and mood scores were inversely associated with light. On the other hand, Norton et al. declared that light stress at night was associated with circadian rhythm disruption and poor sleep quality. Conversely, in another study, light stressor was not associated with sleep disturbances. Thus, it could be concluded that enough light in the mornings and enough darkness at night would improve the sleep structure of hospitalized patients.

Other Environmental Factors

Uncomfortable bed or pillow, unfamiliar bed, loss of a normal routine, transfer between rooms and wards, inappropriate

room temperature, limited personal space, restricted privacy, and disturbance of drips and tubes are other environmental factors affecting sleep[21].

Medical Care Disruptions

The disruptions by staff, including physicians, nurses, nurses assistants, and housekeepers during night shifts to complete tasks are another preventable cause of sleep disruption in hospitalized patients. In a study, 35.8% of awakenings were due to disruptions by medical care staff. In another study, staff interruptions were reported by 68% of subjects as the main reason for insomnia. Examination, blood sampling, check of vital signs, checking continuous night-time drip, cleaning the room and toilets, and prescribing medication during the sleeping time are examples of medical care disruptions[22].

Non-Environmental Factors

Underlying diseases, disrupting symptoms, primary sleep disorders, and side effects of medications and medical equipment are the most important non-environmental factors that could affect sleep structure. In this section some of these factors will be described:

Medical Condition:

Pain

About half of all hospitalized patients experience pain, of whom 25% find it unbearable[23].

Pain is one of the factors that can affect the sleep quality of hospitalized patients. The hospitalized patients with acute or chronic pain are at risk of sleep impairments. Acute pain causes cortical arousal leading to prolonged sleep latency, inhibition of stage N3 sleep (Deep or Delta-wave sleep) and rapid eye movement (REM) sleep, and inability to maintain sleep. On the other hand, sleep deprivation caused by pain can increase pain sensitivity by inhibiting the synthesis of opioid proteins[24-26].

Severely ill ICU Patients

Poor sleep is a major concern in ICU patients due to its potential interaction with other mental and physical illnesses and the impact on patient rehabilitation. So most of the studies about sleep disorders in hospitalized patients have focused on inpatients of the Intensive Care Unit (ICU). It seems that the rate of sleep disturbances in ICU is significant and in some studies, up to 50% of sleep structure abnormalities were reported[27]. Severely ill ICU patients often develop sleep disorders and circadian rhythm sleep-wake disorder (CRSWD). According to the results of several studies, nearly all patients complained of sleep problems while being admitted to the ICU[28].

In severely ill patients, such as patients with sepsis, the following changes in sleep architecture are reported: decreased REM sleep decreased N3 stage, increased N1 and N2 stages, difficulty in falling asleep, and CRSWD. In these patients, circadian rhythm is often absent or delayed. Moreover, sleepiness during the day and short total sleep time are common in them[29,30].

Circadian rhythms in patients with sepsis can activate inflammation by increasing circulating inflammatory cytokines. The acute and massive release of pro-inflammatory cytokines in response to infections increases the risk of a cytokine storm and such as tumor necrosis factor and interleukin-1 are increased[31].

Most of these patients complain about noise from mechanical ventilators and alarms and a crowded ICU environment that prevents them from getting enough sleep. In this regard, a study found that noises above 77 A-weighted decibels (dBA) accounted for 66% of nocturnal awakenings in patients admitted to the ICU. Altered metabolic function, pain, drug complications, ambient light, stress, and high temperature are some of the factors affecting the sleep quality of ICU patients[32,33].

Postsurgical Patients

Some researches indicated that sleep abnormalities are more prevalent in surgical wards in comparison with medical wards[34]. It has emerged that more pain, more invasive interventions, and less analgesic and sedative medication prescription might be the causes of this variance[35].

In post-surgical patients, the pain remains a common cause of impairment in sleep. In patients undergoing major surgeries, REM sleep is suppressed for a variety of reasons, including elevated levels of catecholamines, cortisol, and prescription of opioid compounds to control pain. However, REM sleep suppression often occurs in the first days after surgery, REM rebound is observed during days 3 to 6 after surgery and can result in oxygen desaturation during the night, affecting the lung function[36].

Asthma and Chronic Obstructive Pulmonary Disease (COPD):

Poor sleep quality and sleep disturbance are common in patients with asthma, especially severe asthma. Sleep quality affects the quality of life (QOL) and disease control. Obstructive sleep apnea (OSA) is more common in patients with asthma than in non-asthmatic patients, and treating these patients with continuous positive airway pressure can help improve their QOL.

In patients with asthma, multiple arousals occur due to nocturnal exacerbation. Sleep deprivation reduces the response of the respiratory system to hypoxemia and hypercapnia. Corticosteroids and inhaled bronchodilators are used to treat these patients. Using corticosteroids can result in a decrease in total sleep time and sleep efficiency, as well as inhibition of N3 stage and REM sleep[37,38]. In addition, prescribing beta-agonists and theophylline can cause insomnia by prolonging sleep latency. Using theophylline can result in the following issues: decreased sleep efficiency, decreased total sleep time, inhibition of N3 stage, and increased N2 stage[39,40].

Patients with COPD often suffer from nocturnal hypoxemia and corpulmonale. In these patients, we often witness an increase in arousals during sleep, an increase in sleep latency, and a decrease in total sleep time. When these patients are hospitalized, the risk of sleep deprivation increases.

These patients complain more when they sleep in the supine position due to a decrease in Functional Reserve Capacity (FRC).

About 10-12% of people with COPD also have OSA which is known as overlap syndrome. In these people, the possibility of sleep deprivation following hospitalization increases. People with overlap syndrome often have lower oxygen saturation levels and higher partial pressure of carbon dioxide ($PaCO_2$) com-

pared to people with only OSA. It is rational to hypothesize that prescribing sedative-hypnotics is not accepted in these patients because they cause suppression of the respiratory system[16], But the effect of sedative-hypnotics like benzodiazepines and Z-drugs on respiratory disease states is not yet clear. Some studies reported that benzodiazepines reduce respiratory function by diminishing airway smooth muscle tone in airway obstructed sleep states and increased the risk of adverse respiratory events in patients with COPD. In contrast, other studies observed that Z-drugs, unlike benzodiazepines, were absent of any notable effect on either ventilation or central nervous system (CNS) control of breathing in normal subjects and patients with mild to moderate COPD[41,42].

Congestive Heart Failure

Low-quality sleep, short total sleep time, and sleep apnea are common in patients with heart failure. About 33% of these patients experience insomnia, which might be due to drug complications, clinical manifestations of the disease, psychological stress, and mood disorders in the context of the disease. Sleep-related respiratory disorders such as OSA and central sleep apnea (CSA) are common in these patients and affect the prognosis of the disease. Many of these patients complain of orthopnea, paroxysmal nocturnal dyspnea, and nocturnal diuresis, which cause frequent awakenings. Nocturnal polysomnography (PSG) results show Cheyne-Stokes respiration in these patients.

Using continuous positive airway pressure (CPAP), which affects the left ventricular ejection fraction, can help in the treatment of OSA in these patients[43,44].

Gastroesophageal Reflux Disease (GERD)

Based on clinical evidence, there is a very strong and bidirectional association between gastroesophageal reflux disease (GERD) and sleep disturbances. Low-quality sleep, short total sleep time, sleep latency, frequent nocturnal arousals, and early morning awakenings are common in these patients. In addition, sleep disorders caused by GERD can exacerbate its severity by increasing the perception of intraesophageal stimuli.

According to some researchers, GERD is associated with OSA and there may be a potential causal link between the two diseases. However, no association has been found between the severity of OSA and the likelihood of GERD symptoms.

These patients often experience more severe complications when they sleep in the supine position; hence, it is recommended that they avoid eating foods four hours before going to bed. The use of proton pump inhibitors (PPIs) improves nocturnal symptoms and subjective sleep parameters[45,46].

Stroke

Assessment and treatment of sleep disorders should be a part of stroke prevention. Sleep disorders, including insomnia, sleep-disordered breathing, sleep-related movement disorders, parasomnias, and hypersomnia can be co-morbid with cardiovascular diseases and increase stroke risk[47].

In stroke patients, there is the possibility of hypersomnia or insomnia depending on the damaged area of the brain. Approximately, 60-96% of hospitalized patients with cerebrovascular accidents (CVA) simultaneously suffer from sleep-disordered breathing (SDB); and many of them are at risk of OSA. The location and severity of cerebral ischemia, neurological function after CVA, and medications are some of the factors influencing the severity of SDB after CVA[16].

Cardiovascular Disease

It was demonstrated by previous studies that there is an association between sleep disturbances and the incidence of coronary heart disease and hypertension. The probable mechanisms of this association are dysregulation of the hypothalamic-pituitary axis and autonomic system and release of inflammatory factors[48]. On the other hand, insomnia has been reported as the most common sleep complaint in this population. It seems that factors such as psychological distress, underlying symptoms, and side effects of medication contribute to sleep disturbances in these patients[49].

Coronavirus Disease 2019 (COVID-19)

Sleep is a biological process that can play an important role in immune systems and the health of the population[50]. Howsoever, the role of sleep quality during hospitalization of patients for COVID-19 is still unclear. In a study conducted in 2020, it was found that poor sleep is associated with the increased requirement of ICU care, prolonged length of hospital stay, and slow recovery from lymphopenia in hospitalized COVID-19 patients[51].

About 15% of hospitalized COVID-19 patients have impaired consciousness including somnolence, confusion, and delirium. In these patients sleep deprivation and circadian disruption by sleep loss are risk factors and consequences of delirium. Administration of Melatonin or Melatonin Receptor Agonists (MRA) has been strongly associated with a shortened Intensive Care Unit (ICU) stay reduced prevalence of delirium and improved sleep quality[52, 53].

The number of medical diseases related to sleep disturbances is high and in addition to the conditions mentioned above, in other diseases such as skin diseases[54], renal failure[55], metabolic and endocrine diseases[56] arrhythmia[57], etc., the prevalence of sleep disorders is significant.

Ventilators and Other Medical Equipment

Mechanical interventions such as using mechanical ventilators (MV), endotracheal tubes, nasogastric tubes, and urinary catheters can all affect the quality and quantity of sleep in hospitalized patients[22]. Patients receiving mechanical ventilation may be more susceptible to sleep disruption. Overventilation followed by apnea, arousal, and patient-ventilator asynchrony cause sleep impairments in patients treated with MV. increased N1 and N2 stages, inability to maintain sleep and inhibit REM sleep, increased daytime sleepiness, and CRSWD is common in patients on ventilators[16].

Medications

Many medications prescribed to patients admitted to the ICU and other medical wards can alter the sleep structure in terms of quantity and quality[58].

Antipsychotics, antihistamines, and benzodiazepines are drugs that are often used to promote sleep in hospitalized patients;

but they have serious side effects, including the inhibition of stage N3 and REM sleep and increasing the likelihood of delirium.

Antihistamines, such as diphenhydramine and hydroxyzine, are widely used to promote sleep[16], in outpatients. However, they are not recommended for hospitalized patients due to increasing the risk of daytime sleepiness, delirium, orthostatic hypotension, urinary retention, long QT syndrome (LQTS), and blurred vision, which can increase the risk of falls, cardiac arrhythmias, and urinary tract infections in hospitalized patients[59].

Although benzodiazepines can reduce sleep latency and promote sleep by increasing total sleep time and sleep efficiency, they may alter sleep structure by inhibiting stage N3 and REM sleep and increasing stage N2 and the presence of sleep spindles; in addition, they have several side effects, including increased risk of daytime sleepiness, delirium, exacerbation of OSA, as well as the risk of developing drug dependence[60].

Narcotic drugs, which are prescribed abundantly in hospitalized patients, are associated with an increase in the development of CSA, inhibition of stage N3 and REM sleep, and increased nocturnal awakenings and stage N2[59].

Extra caution is advised with the potential co-administration of opioids and benzodiazepines due to the heightened respiratory depression risk[61].

Beta-blockers, such as metoprolol and propranolol, can cross the blood-brain barrier (BBB); some of the complications of these drugs include insomnia, nightmares, decreased sleep efficiency, and inhibition of REM sleep. In contrast, those beta-blockers that cannot cross the BBB, such as atenolol, are less likely to cause sleep disorders.

Some of the side effects of antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and tricyclic antidepressants (TCAs), include inhibition of REM sleep, reduction of total sleep time, and increase of periodic limb movements during sleep (PLMS), and daytime sleepiness.

Trazodone is an antidepressant of the serotonin (5-HT2) antagonist and reuptake inhibitor class which reduces sleep latency and increases stage N3; but it can increase the risk of cardiac arrhythmias and lead to drug interactions. Dry mouth, headache, nausea, and orthostatic hypotension are the major complications of this drug[49].

Prescribing propofol results in reduced sleep latency, increased total sleep time, REM sleep inhibition, and exacerbation of sleep efficiency[62].

Dexmedetomidine is an α2-adrenoreceptor agonist that is approved for sedation. It can inhibit REM sleep and increase stage N2 sleep[63]. Dexmedetomidine has benefits reducing the risk of development of delirium when compared to benzodiazepines[61].

Underlying Sleep Disorders

Primary sleep disorders, such as sleep apnea, restless legs syndrome (RLS), and chronic insomnia disorder, can affect the sleep of hospitalized patients. Diagnosing these disorders through examining their existence in high-risk patients and taking appropriate interventions can help to promote sleep in these patients.

Patients with SDB are often at risk of chronic sleep deprivation, and OSA is one of the most common SDB. Moreover, patients with OSA are more likely to have comorbidities such as diabetes mellitus (DM), heart failure, hypertension, cardiovascular disease, and stroke. According to epidemiological studies, the prevalence of moderate OSA is about 2-7% in females and 7-14% among males. In addition, among the patients undergoing surgery, OSA is an independent factor in the development of respiratory failure and cardiac events after surgery; and it might increase the possibility of transferring the patient to the ICU[64].

All hospitalized patients suspected of having sleep-related breathing disorders should be referred for the assessment of sleep status.

Diagnosing sleep apnea and its screening is important, especially in patients undergoing surgery. In this respect, the Snoring, Tiredness, Observed apnea, Blood Pressure, Body mass index, Age, Neck circumference, and Gender (STOP-BANG) questionnaire has been designed as a screening tool for OSA in patients before surgery and to predict the possibility of respiratory problems after surgery[36].

The RLS occurs in 5-15% of the general adult populations. The prevalence of the disease increases with age, especially in women over 35 years of age. In some conditions and underlying diseases, such as pregnancy, chronic kidney disease (especially people undergoing hemodialysis), iron deficiency anemia, DM, and Parkinson's disease, it is essential to assess the patient for this syndrome.

Decreased sleep quality, difficulty falling asleep, and difficulty in maintaining sleep are seen in these patients. In this regard, interviewing the patient and obtaining a good past medical history could be helpful. In patients with chronic kidney disease and DM, many RLS-related sleep disorders can be managed by controlling hyperphosphatemia, uremia, and blood sugar[65].

Insomnia disorder is one of the most common sleep disorders in the world. According to a study, 36% of hospitalized patients show short-term symptoms of insomnia for the first time, which are mainly due to the disease symptoms and environmental factors[58].

However, many patients have a history of chronic insomnia disorder. Although the existing evidence is very limited, it seems that patients with a previous history of insomnia are more likely to have more sleep disorders during and after hospitalization. In addition, elderly patients and those with a history of psychiatric problems are at a higher risk[66].

In addition to factors that have been discussed above, demographic factors might have an association with sleep disturbances. Accordingly, age has been considered as one of these factors, so sleep in the elderly will be reviewed.

Sleep in Hospitalized Elderly Patients

The percentage of the old adult population is rising due to more extended lifespans and improved health care services and socioeconomic status. By 2050, the global elderly population would

be more than 25% of the population in developed countries and will increase from nearly 800 million in 2019 to more than 2 billion in 2050[67].

Aging is typically associated with alterations in sleep patterns. In the elderly frequent awakening increases and arousal thresholds, duration of slow-wave sleep (SWS), and total REM sleep reduces, and consequently, total sleep duration decreases. However, it seems that the relationship between insomnia and age might not be linear and it was reported that peak incidence of insomnia occurs in the middle age people which decreases in young-old and increases in old-old.

In addition to sleep structure changes that occur with aging, sleep disorders such as obstructive sleep apnea, REM sleep behavior disorder, nocturnal myoclonus, and RLS have been reported more in individuals greater than 60 years old. The prevalence of sleep disorders in the aged population was reported from 6 to 60%[68].

As mentioned before sleep disturbances negatively affect mental and physical health. This effect is even more significant in aged adults. Sleep disturbances are associated with cardiovascular diseases, obesity, hypertension, diabetes mellitus, headaches, immune diseases, gastroesophageal reflux disease, delirium, psychiatric disorders, declined cognitive performance, increased falling, frailty, and disability in the elderly[69]. This negative effect is more crucial in hospitalized medically ill patients. Besides, the rate of hospitalization significantly increases with aging[70]. In a study using the U.S. Nationwide Inpatient Sample database, it was indicated that sleep disturbances were associated with increased mortality risk, length of stay, and total charges in old inpatients[71]. In a study on 101 geriatric inpatients of a general hospital, it was suggested that the experience of hospitalization had a negative effect on sleep duration. Moreover, poor sleep quality was associated with pain, delirium, and decreased scores of and Mini-Nutritional Assessment-Short Form and The Katz Index of Independence in Activities of Daily Living[72].

Comparably, in a study on 280 old inpatients, it was demonstrated that 36.7% of subjects were suffering from sleep disorders and sleep disturbances were correlated with a worse clinical burden of medical problems and poorer activities of daily living[73].

It seems that comorbid medical and psychiatric conditions, polypharmacy, medical care interventions, pain, staff interruptions, and environmental factors are related to the development of sleep disorders in geriatric inpatients[74].

Recommended Strategies

In the elderly, most traditional medications for treating insomnia like benzodiazepines and sedative-hypnotics are associated with numerous side effects, including cognitive impairment, delirium, increased rate of falls, and disability[75].

Prescription of medication that causes insomnia such as sympathomimetic, antidepressant, amphetamines, phenytoin, bupropion, selective serotonin reuptake inhibitors, anti-parkinsonian agents, bronchodilators, laxative, and diuretics, at least six hours before bedtime could decrease sleep complaints[76].

In American Geriatrics Society Beers Criteria benzodiazepines, Z drugs, first-generation antihistamines, antipsychotics, and tri-tetra cyclic antidepressants have been considered as potentially inappropriate medication in older adults[77]. In a Single-center retrospective observational study in Canada, of 1308 patients, 208 (15.9%) received a potentially inappropriate prescription (benzodiazepine or zopiclone) for insomnia.

Maybe prescribing medications with a safer profile and good enough efficacy such as trazodone, melatonin, and melatonin receptor agonists would be a more sensible decision in treating older adults insomnia, however, it does not mean that this medication should be avoided in all of the old patients without application of clinical judgment and assessment of cost-benefits of the medication[78,79]. Alternately, the treatment should be tailored to the patients' needs and situations. The essential principles that should be considered in prescribing medications are adjustment of the dose according to renal and hepatic function, starting lower doses and going slow, and preferring benzodiazepines with a shorter half-life and inactive metabolites such as lorazepam, temazepam, and oxazepam[76]. In addition, Z drugs such as zopiclone appeared to cause lesser cognitive impairment and daytime sleepiness in comparison with BZDs[80].

Treatment of Sleep Disorders in Hospitalized Patients

There is no single intervention to promote sleep in hospitalized patients. Performing numerous small interventions on environmental factors of hospitals, as well as internal and underlying medical factors of the patients can promote sleep in them.

Non-Pharmacological Strategies

Some feasible strategies have been suggested in previous studies to decrease sleep disturbances and improve the quality and quantity of sleep in hospitalized patients due to environmental factors and staff interruptions[81].

The following interventions should be considered as the first-line treatments to promote sleep:

- Noise Reduction

Several studies have found a direct association between noise and sleep problems in patients, so that noise is one of the most common and important causes of sleep complaints.

Various methods, such as using earplugs or earmuffs in patients, sound masking (white noise), and soundproof acoustic materials can be helpful in this respect.

We may define a "quiet time" period and avoid making any noise during this time. In addition, the following measures can be taken: adjusting the volume of electronic devices (phones and TV) and reducing the noises from nurses, staff, patients, and visitor[82].

Some other studies advocated structural interventions such as placing noise-sensitive traffic lights and installing silent footwear. In addition, it is recommended to replace face-to-face care with remote care such as remote evaluation of vital signs and nocturnal checkups through CCTV, as far as possible[81].

The results of this intervention on patients' sleep were different. However, it seems that even a slight reduction in ambient noise

can have a significant effect on the quantity and quality of sleep in patients[82].

Light Therapy

Some studies have shown that using eye masks along with earplugs during the night can help promote sleep in patients admitted to the ICU[83-85].

Studies have shown that exposure to daylight (2000 to 5000 lux for 2-5 hours per day) can help improve circadian rhythms and improve nocturnal sleep[86-88].

The use of bright lights in the early evening can increase total sleep time in elderly people. One study found that patients whose beds were next to a window often had better sleep quality due to more exposure to sunlight[13,82].

Reduce Night–Time Interventions

Reducing night–time interventions (8 hours-overnight) in patients, which is defined as "quiet time", can reduce the need for sedatives. In this regard, the following measurements should not be taken as possible: prescribing night-time medications, checking vital signs, blood sampling, cleaning the rooms, and moving the equipment. To achieve this goal, educating nurses and staff on the importance of sleep for hospitalized patients and informing them about the high prevalence of sleep disorders in hospitalized patients is the first step and essential because the activity of nurses and staff at night is known as one of the main factors in patients' sleep problems[89-91].

Other interventions

It has been recommended to utilize a before-sleep checklist to implement simple necessary actions, such as alleviating pain, offering extra pillow, blanket, earplugs, and eye masks, adjustment of room temperature, reminding before-sleep toilet usage, drawing curtains, turning off lights, cellphones and television and closing the patient's room door[81]. According to the studies, the modifications mentioned above lead to 10 to 30 percent improvement in sleep quality and quantity which is considerable[81].

Relaxation Techniques

Some studies have used massage therapy, music therapy, guided imagery, and aromatherapy to improve the quality of sleep in patients. These studies have highlighted the positive effect of music on sleep. However, the existing evidence on the effectiveness of other techniques is not sufficient and requires further studies[82,84,86].

Finally, it should be noted that environmental factors (light, noise, and activity of nurses and staff) are common in hospitals, and especially in the ICUs, and limiting their potential impact on sleep quality is not always easy[60].

Discussion

Pharmacological Strategies

At present, there are no evidence-based guidelines on the type of sedatives to be used in hospitals, and different medications are prescribed. There is insufficient evidence to suggest that pharmacotherapy improves the quality or quantity of sleep in hospitalized patients suffering from poor sleep. According, no drug class or specific drug was identified as superior even when compared to placebo or no treatment[60]. In some studies, the rate of using sedative and hypnotic drugs in hospitalized patients has been reported up to about 88% and benzodiazepines are the most common drugs used[24,60].

Three classes of drugs have been accepted in treating insomnia, as follows:

- Benzodiazepine GABAA receptor agonists (BzRAs), such as estazolam, flurazepam, temazepam, and triazolam. Elderly patients and people prone to falls and delirium should not take these medications. Benzodiazepines such as flurazepam should not be used in hospitalized patients due to their long half-life. A study found that about 26% of hospitalized patients over the age of 65 received benzodiazepines or sedative-hypnotics for the first time during their hospitalization[92].

  Despite the increasing evidence on the side effects of sedatives, such as the risk of delirium or falls, they are still being increasingly used in hospitalized patients, especially the elderly. Although most of these patients do not have a history of using sedatives, they continue taking the medications after discharge from the hospital[93].

- Nonbenzodiazepine GABAA receptor agonists (NBzRAs), such as eszopiclone, zaleplon, and zolpidem. These drugs have fewer side effects than benzodiazepines, but they should be used with caution in elderly patients, as side effects such as delirium, cognitive impairment, and falls have been reported in hospitalized patients receiving these medications. Using these drugs in hospitalized patients with younger ages should also be monitored carefully[92-93].

- Melatonin and melatonin receptor agonists. Melatonin can be a good first-line treatment for insomnia in hospitalized patients due to its fewer side effects and drug interactions, as well as its ability to improve circadian rhythms.

In several studies, administration of 1 to 5 mg of melatonin per night improved sleep quality in patients[94]. Although there is no standard dose for melatonin, depending on the patient's usual bedtime, a dose of 1 to 3 mg (at 9 or 10 pm) can be used. Immediate-release melatonin and sustained-release melatonin can be prescribed 30-60 minutes and 1-2 hours before bedtime, respectively.

In this group, ramelteon has been approved by the FDA for the treatment of insomnia. Despite reducing sleep latency and increasing total sleep time, this drug is not associated with the risk of abuse, psychomotor impairment, and memory impairment. However, there are few studies regarding its effects on the sleep status of hospitalized patients[95].

Suvorexant, an orexin receptor antagonist (ORA), has a long half-life of about 13.5 hours and increases the risk of drowsiness the day after administration. Currently, there are not enough studies regarding the effect of this drug on improving sleep in hospitalized patients. Accordingly, the risk of drug interactions and drowsiness during the day should be considered before prescribing this drug[96].

In addition, sedative antidepressants and sedative antipsychotics that are not FDA-approved can use for the treatment of insomnia in hospitalized patients. Low-dose antidepressants such as mirtazapine, trazodone, and TCAs are among these drugs. Especially, patients simultaneously suffering from depression and insomnia can use sedative antidepressants. After considering the side effects and drug interactions, trazodone (50 mg) at bedtime can also be helpful.

Sedative antipsychotics such as quetiapine are useful in insomnia patients with comorbidity of psychiatric disorders. Especially, complications such as hyperlipidemia and hyperglycemia should be considered.

In a nutshell, to prescribe any medication to promote sleep in hospitalized patients, we should consider the following criteria: the patient's age, the severity of the sleep complaint, previous history of taking sedatives, and medical and psychiatric comorbidities. It is better to prescribe a drug with a short half-life, minimal drug-drug interactions, and with the minimum therapeutically effective dose for a short time. In addition to pharmacological treatments, it is better to use non-pharmacological interventions as well. The need to continue sedative-hypnotic drugs prescribed to patients during hospitalization should be evaluated before discharge[24].

Limitations

The limitations of this research can be assessed in terms of methodology and quality of articles included in the study, as well as the factors related to patients and the hospital environment. Accordingly, some of the most important limitations of the current study include:

- In most studies, the sleep habits of patients before hospitalization were not studied. The possibility of a "recall bias" was one of the main causes for this limitation[5].
- Physical problems and cognitive disorders in hospitalized patients impeded the data collection process[5].
- Since some studies had a small sample size and they had been conducted on specific patients, it was difficult to generalize the results to other patients[97,98].
- While some studies used objective methods, such as polysomnography and actigraphy in the data collection process, some others used subjective methods, such as questionnaires or interviews[5]. This methodological difference in the studies resulted in heterogeneous data. For example, in severely disabled patients or those with mobility problems, no accurate distinction can be made between sleep/wake states through using actigraphy. Although polysomnography provides more accurate data compared to actigraphy and subjective methods, it is a costly method and is not available in all medical centers. Moreover, polysomnography is not useful in the diagnosis or treatment of circadian rhythm sleep disorders, which are one of the most important sleep-related problems in hospitalized patients[99,100].
- In some studies, the treatment staff was trained to improve the sleep of patients. However, differences in the capabilities of staff, inconsistent training methods, and different facilities of medical centers to conduct training courses lead to some diverging results[101].
- There were only a limited number of eligible high-quality randomized controlled trials[81].
- It was not possible to control or eliminate most of the interfering and confounding factors, such as patients' physical condition, underlying disease, prescribed medications, and environmental factors of hospitals, all of which affect the quality of sleep in hospitalized patients[81].

Conclusion

The prevalence of sleep disorders in physically ill hospitalized patients is high. The effective causes for this issue can be divided into two categories: environmental and non-environmental factors. The most important environmental factors are sound, light, temperature, environmental conditions of wards and rooms, and medical care disruptions. On the other hand, the most important underlying factors include direct and indirect effects of physical illness on the structure of sleep, pain, pharmacological and non-pharmacological interventions, age, and early sleep disorders. It seems that the simplest and most effective interventions to improve the sleep quality in physically ill hospitalized patients are non-pharmacological interventions and adjustment of environmental factors. However, medications can also play an effective role in improving patients' sleep quality.

Recommendations for Future Studies

Given the importance of sleep on health, it is vital to evaluate sleep disorders in hospitalized patients. Hence, it is recommended that further high-quality randomized controlled trials with appropriate sample sizes be performed on the sleep status of hospitalized patients. In addition, objective methods such as polysomnography and actigraphy are preferred for data collection.

Since most studies used non-pharmacological interventions as the first-line treatment for sleep disorders in these patients, it seems that designing studies with non-pharmacological protocols can be practical and useful.

Furthermore, it is recommended to evaluate the impact of new drugs, such as Ramelteon and Suvorexant, on improving the sleep quality of patients. Future studies can also develop guidelines for using pharmacological and non-pharmacological interventions in the treatment of sleep disorders in hospitalized patients.

It seems that the importance of sleep quality in hospitalized patients has not been well explained to the medical staff, in-

cluding physicians and nurses, during their university and employment years; and this has led to a lack of attention to sleep quality of hospitalized patients among the staff. Accordingly, it is recommended that hospital managers develop standardized protocols for educating staff on the importance of sleep in hospitalized patients, as well as the ways to improve the quality and quantity of sleep. Meanwhile, raising awareness regarding the cost-effectiveness of eliminating environmental factors that affect the sleep quality of patients can be helpful.

Ethical Considerations

To organize this research, while observing the authenticity of the texts, honesty and fidelity have been observed.

Conflict of interest

The authors declare no conflict of interest for this article.

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