Sleeping Disorders and the Effects on Health of Patients with Spinal Cord Injury

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ABSTRACT

Introduction: Spinal cord injury (SCI) is recognized as a disability affecting every aspect of patients' lives. Compared to the able bodied population, sleep disturbances are more frequent in patients with SCI and can lead to dysfunction that negatively affects quality of life. However, many healthcare providers omit to determine the quality of sleep of SCI patients or are not aware of insomnia symptoms such as restless legs or sleep apnea. A review of the current literature was performed in order to highlight the association between SCI and sleep disturbances, the importance of awareness of sleep disturbance symptoms and how these affect the overall health and quality of life of SCI patients. By using the online Pubmed database and the PRISMA guidelines, studies regarding sleeping disorders and their effect on SCI patients were identified. Results: SCI patients often suffer from sleeping disturbances which can cause severe health problems. More specifically, these patients have increased risk of developing depression, obesity, cardiovascular diseases, hypertension and sleep related breathing problems. Patients are also in increased risk for experiencing pain, fatigue, daytime sleepiness and loss of communication. Conclusion: Sleep disturbances are associated with SCI in a great extend and can lead to multiple medical complications. The pivotal role that sleep is having in overall health and quality of life cannot be underestimated.

KEYWORDS: sleep disturbances, spinal cord injury, sleep breathing disorders, sleep movement disorders, sleep quality

Introduction

According to the World Health Organization the term 'spinal cord injury' refersto damage to the spinal cord resulting from trauma (e.g. car crash), disease or degeneration (e.g. cancer). Spinal Cord Injury (SCI) is recognized as a catastrophic disability affecting every

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VOLUME 73 | ISSUE 4 | OCTOBER - DECEMBER 2022

aspect of life. Most patients with traumatic SCI are between the second and fourth decade of life. Their life expectancy is reduced compared to the general population; however, much of this is due to peri-injury complications and if patients survive the first year past the injury then their life expectancy is impacted less. This means that many SCI patients have the potential to live a long life and for this reason it is important to prevent morbidity and mortality from secondary complications. [1]

Sleep disorders are common in patients with SCI. Indeed, patients with chronic SCI often report poor sleep quality as a consistent outcome. Sleep disordered breathing (SDB), particularly in patients with high thoracic and cervical level injuries, abnormal leg movements during wake and sleep and poor quality of sleep are some of the sleep disorders mentioned in the literature. Poor sleep may be due to pain, insomnia and/or sleep-wake circadian rhythm disturbances. Patients often report daytime symptoms as fatigue, sleepiness, difficulty in concentration and impaired quality of life. Fatigue and excessive daytime sleepiness are also associated with pain, depression, side effects of medications, spasticity and autonomic dysfunction in SCI patients. This likely contributes to reduced social participation and quality of life or in some circumstances leads to premature death. [1,2,3]

SDB is highly prevalent after SCI. There are several factors that may influence the prevalence of SDB in patients with SCI. First, the level of spinal injury affects the occurrence and manifestations of SDB and patients with tetraplegia are more likely to have SDB than patients with paraplegia. Patients with cervical SCI suffer from the full continuum of derangements that impair the ability of the ventilatory system to compensate for physiologicchallenges, including neuromuscular weakness, decreased lung volumes, abnormal chest wall mechanics, frequent use of CNS suppressants, and unopposedparasympathetic system promoting airway narrowing. [2]

The most commonly reported objectively diagnosed sleep disorder in patients with SCI, particularly in those with cervical lesions but also present in thoracic-level injuries, is obstructive sleep apnea (OSA) with an estimated prevalence of 50% to 80%. Reported estimates vary depending on the level of injury and the methodology used to measure OSA. Regardless, the prevalence of OSA in individuals with SCI far exceeds what is reported in the general population. In the general population sleep apnea has been associated with cardiovascular morbidity, and individuals with chronic SCI are also at increased risk for accelerated onset of cardiovascular disease. It is plausible that the combination of SCI and OSA may indeed increase cardiovascular morbidity and mortality. [3]

Periodic leg movements (PLM) are characterized by periodic episodes of repetitive and highly stereotyped limb movements, typically big toe and ankle dorsiflexion which are often accompanied by knee and hip flexion. The prevalence of PLM disorder appears to be markedly elevated in people with SCI, especially in tetraplegic patients. This can result in considerable disruption of sleep quality and is typically associated with excessive daytime sleepiness. Although SDB and PLM are highly prevalent in tetraplegia and can co-exist, there are many studies which strongly suggest that they are independent phenomena in tetraplegia. [4,5]

Moreover, there is evidence that the circadian rhythmicity of melatonin is disrupted in tetraplegia. It appears that complete cervical SCI, which cuts the suprachiasmatic nuclei to superior cervical ganglion pathway, is associated with near abolition of circadian melatonin rhythmicity and a markedly reduced circulating melatonin level. Other endocrine rhythms similarly modified by circadian influences, such as cortisol and thyroid-stimulating hormone, do not appear markedly affected by cervical SCI, however, the temperature is affected. The temperature phase advance observed in tetraplegia may be yet another contributor to the poor sleep quality. [2,3]

Insomnia is highly prevalent in the general population with estimates ranging from 15-30%. Women have a 1.4 times higher risk than men for developing insomnia. This disorder, defined as difficulty falling or staying asleep that persists for at least three nights per week and is accompanied by daytime consequences, is likely less common, but estimates still suggest rates of 10-20% in the population. In a recent study, most SCI patients had insomnia symptoms, although it is not clear that these patients would meet criteria for insomnia disorder as they also had significantly higher risk for SDB and had greater differences in weekday/

VOLUME 73 | ISSUE 4 | OCTOBER - DECEMBER 2022

weekend sleep which may be associated with insufficient sleep rather than insomnia disorder. This does suggest that evaluation for insomnia disorder is useful in understanding the effect of other sleep disorders experienced by individuals with SCI and can affect the choice of treatment. [2,6]

Treatment of SDB in SCI patients is challenging, although symptomatic improvements may be observed in many patients. The most commonly used treatment for SDB is continuous positive airway pressure (CPAP) which consists of a mask attached to the nose/face that gives a positive pressure to the upper airway preventing its collapse during sleep. CPAP is effective in eliminating obstructive events during sleep and improving oxygenation. There are challenges related to arm strength/mobility in tetraplegia and additional factors such as increased nasal congestion. This may be the reason that only 20-50% of patients with chronic SCI and SDB reported adherence to CPAP. [3,7,8]

There are multiple challenges in treating insomnia disorder in SCI patients. Pharmacological agents have multiple effects that may be even more significant among individuals with SCI. In ambulatory patients they may further increase the risk of fall and impaired cognition may be exacerbated. For this reason, pharmacological therapy is recommended only after cognitive-behavioral therapy for insomnia (CBT-I) has been attempted. CBT-I is a multi-component psychological treatment that includes behavioral techniques (stimulus control, sleep restriction therapy, sleep hygiene and relaxation/arousal reduction strategies) plus cognitive therapy to address sleep-related thoughts and beliefs. Mehta S et al, in their systematic review found evidence that cognitive-behavioral therapies, in general, are helpful for anxiety, depression, adjustment and coping problems. [9]

The aim of this study was to identify the association between SCI and sleeping disorders and to examine the consequences that sleeping disorders have on patients' overall health and quality of life. For this reason, a review of the current literature was conducted by using the online Pubmed database and following the PRISMA guidelines. Article titles were searched by using the following keywords: "sleep disturbances", "spinal cord injury", "sleep breathing disorders", "sleep moving disorders'', "sleep quality". Studies in non-English language, studies published before 2010, studies in children and adolescents, case reports and study protocols were excluded from this review. Primary search results included 256 articles. After screening of titles and abstracts, 166 articles were excluded as inappropriate. From the remaining 90 studies, 69 were rejected for various reasons (Table 1). Finally, 21 studies were included in this review.

Discussion

Periodic Leg Movement-Restless Leg Syndrome

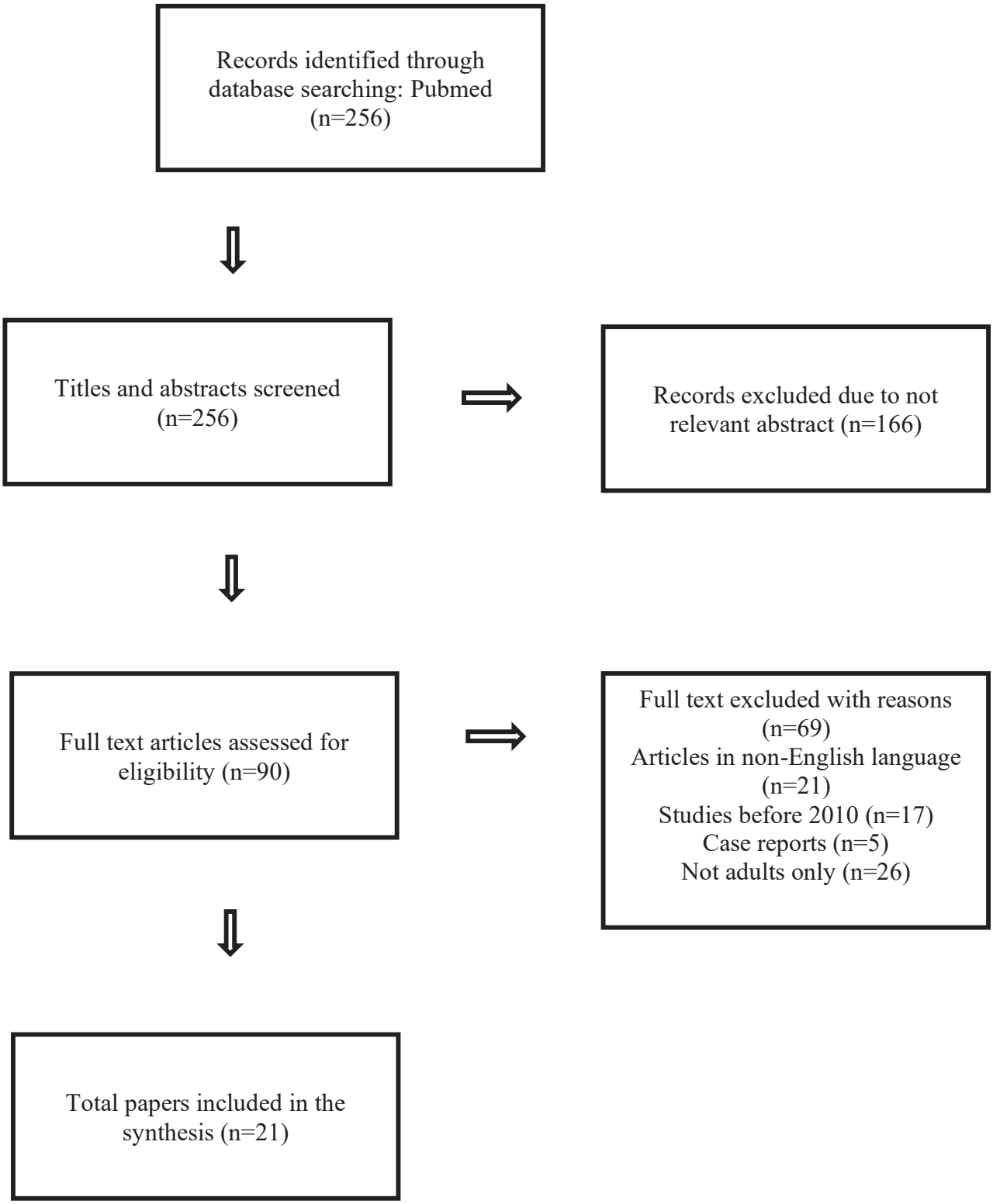
In 2010, a study established the occurrence of PLM and Restless Legs Syndrome (RLS) in SCI patients. In this study, Telles et al, compared 24 patients: the control group was composed of 16 patients and the SCI group of 8 patients. As a result they found a 100% relevance of RLS in SCI patients. Most of the patients with RLS also suffered from PLM. These situations led to decreased quality of sleep and were associated with daytime sleepiness. [4]

Furthermore, in 2018 Peters et al, conducted a retrospective study to establish the prevalence of PLM during sleep in patients with tetraplegia, controlling for OSA. 173 participants with acute and 92 with chronic tetraplegia were included in the study. A randomly selected group of 21 patients was assessed for PLM during wakefulness. Of the participants, 41.6 % had a complete motor and sensory lesion. Sleep was poor with both OSA and PLM. There was no difference in the PLM between those with or without OSA. All 21 participants in the subgroup analyzed for PLM during quiet wakefulness, exhibited limb movements. This study confirms the high prevalence of PLM in tetraplegia and the prevalence of leg movements in non REM and REM sleep along with wakefulness after controlling for OSA. No associations between PLM and patient characteristics or injury specific aspects were found. [5]

Shafazand et al, in 2019, made a web based survey to determine sleep quality and presence of sleep disorders in participants with SCI. The study population included 304 male participants with chronic SCI. Symptoms suggestive of sleep apnea were reported by one-third of the study participants. 27% of the respondents reported daily uncomfortable leg sensation

VOLUME 73 | ISSUE 4 | OCTOBER - DECEMBER 2022

TABLE 1: CURRENT REVIEW FLOWCHART



VOLUME 73 | ISSUE 4 | OCTOBER - DECEMBER 2022

and 28% found leg symptoms ''moderately to extremely distressing''. Compared to those without insomnia, participants with insomnia were more likely to report nighttime unpleasant leg sensations and 'urge to move legs'. Insomnia symptoms were reported by more than half of the participants, with most complaints being restless sleep or difficulty maintaining sleep. An important finding of this study was that insomnia symptoms coexisted with other sleep disorders including sleep apnea symptoms and symptoms of restless legs. This highlights the need for a comprehensive approach to the management of insomnia complaints in SCI patients, including evaluation for other sleep disorders (sleep apnea, restless legs) and conditions that interfere with sleep quality. It is mentioned that restless legs symptoms coexist with insomnia symptoms. Symptoms of insomnia influence patients' participation in meaningful life tasks and roles. These people are not able to complete daily tasks of living due to lack of energy and can also miss healthcare appointments or work obligations because of fatigue or sleepiness as a result of poor sleep. [6]

Sleep Disordered Breathing-Obstructive Sleep Apnea

Sankari et al, studied 26 chronic SCI patients [15 patients with cervical (C4-C7) and 11 with thoracic (T2-T6) level injury] who had similar demographics. The major findings were that 77% of patients had symptomatic SDB and poor sleep quality. The level of SCI affected the prevalence of SDB and type of respiratory events (more central SDB noted in cervical SCI). Ventilation decreased significantly more in those with cervical SCI than those with thoracic SCI, as evidenced by the greater drop in tidal volumes and the rise in end-tidal CO2 seen in cervical versus thoracic SCI cases indicating the occurrence of alveolar hypoventilation during sleep. It was also noted that quality of sleep was very poor in the majority of subjects regardless of their level of injury or severity of SDB. [7]

In another study, Bascom et al, studied 18 SCI patients (10 with cervical and 8 with thoracic SCI) and 17 able-bodied participants. The aim of this study was to identify the ventilatory changes at sleep onset. They used overnight polysomnography (PSG) and if the subject had a concern about sleep difficulties Zolpidem was administered orally. Zolpidem dose was selected based on the subject's age. The number of subjects administered Zolpidem was similar for both groups. It was found that chronic SCI patients have hypoventilation on sleep onset compared to able-bodied participants. In addition, sleep onset hypoventilation predominantly presented in participants with cervical but not thoracic SCI and there was no change in upper airway resistance in either group. The study showed the occurrence of significant sleep onset hypoventilation in patients with chronic SCI compared to able-bodied subjects. The magnitude of sleep onset hypoventilation was not associated with increased upper airway resistance and was related to the level of SCI. [8]

Tran et al, conducted a prospective longitudinal observational study to determine the prevalence of SDB in acute SCI and to document the change in SDB over time during the rehabilitation period and to correlate the degree of SDB with ventilatory parameters. 16 patients with acute SCI in T12 level and above with complete motor impairment were recruited. The results showed that 11 of 16 subjects had evidence of sleep apnea and in five of them apnea was moderate to severe. This high incidence persisted during the acute admission, with 9 of 12 subjects (75%) having sleep apnea on PSG 20 weeks following injury. There was no correlation between the severity of SDB and other measures, such as level or completeness of injury, respiratory function tests or measures of ventilatory responses. This study demonstrated a high incidence of sleep apnea in the acute phase of SCI that persisted during the subacute phase of SCI. Despite the high incidence of sleep apnea, patients were relatively asymptomatic. [10]

Berlowitz et al, in 2012, examined the relationships between injury severity, quality of life, sleep symptoms, objectively measured sleep, and sleep disorders in chronic tetraplegia. They used a sample of 79 patients (39 with motor and sensory complete tetraplegia) who were not treated for sleep disorders. They observed that quality of life was worse in the complete lesions group compared with incomplete lesions. In addition, 91% of those who had complete lesions had OSA versus 55.8% of those with incomplete tetraplegia. Multiple regression analyses showed substantially stronger relationships between daytime sleep complaints and abnormalities observed in the sleep study

VOLUME 73 | ISSUE 4 | OCTOBER - DECEMBER 2022

in those with complete lesions. The authors concluded that OSA is a major problem, particularly in those with complete tetraplegia, and this single comorbidity is associated with reduced quality of life. In those with incomplete cervical lesions, the relationships between sleepiness, other sleep symptoms, and PSG indices were less precise. [11]

Moreover, Bauman et al, in 2016 also reached the conclusion that there is a high prevalence of OSA and nocturnal hypercapnia in individuals with SCI. 81 adults with C1-T6 SCI were included in the study; however, 10 of them did not complete the study. The authors concluded that unsupervised home sleep apnea testing with transcutaneous capnography effectively identifies sleep-disordered breathing and nocturnal hypercapnia in individuals with SCI. [12]

A prospective study by Brown et al, in 2018 included 91 patients with C1-T6 SCI; however, only 74 patients remained in the study and were evaluated for SDB. Specifically, the authors evaluated bi-level PAP for treatment of SDB in individuals with SCI. They found that PAP therapy was effective at improving OSA and hypercapnia. There was also reduction in symptoms of autonomic dysreflexia and orthostatic hypotension as well as some improved indices of quality of life. [13]

Berlowitz et al, recently assessed the effectiveness of CPAP in patients with SCI. One hundred and sixty patients were randomized to CPAP and no CPAP groups and followed up for three months. Sleepiness was significantly improved with CPAP (p=0.01) though other cognitive parameters were unchanged. One issue was that CPAP adherence was relatively low in the study (2.9 hrs/night, with 21% achieving >4 hrs per night) despite only randomizing patients who were able to tolerate a three-day CPAP run-in period. The fact that sleepiness was improved with CPAP despite only partial adherence is encouraging and suggests that if adherence could be improved, more substantial benefits could be achieved.[14]

Factors affecting Quality Of Sleep

In 2011, Wijesuriya et al, included a sample of 82 individuals in their study. 41 participants had chronic SCI and 41 were able-bodied. The aim of this study was to determine the impact of fatigue on health-related quality of life (HR-QOL) associated with SCI. As expected, persons with SCI were found to have significantly lower HR-QOL. Fatigue was found to be more prevalent in the SCI group, and was associated with lower HR-QOL in both groups. Factorial analysis of variance indicated significant interactions in which persons with SCI with low fatigue levels had similar HR-QOL to the able-bodied controls regardless of their fatigue level, while persons with SCI with elevated fatigue had significantly reduced HR-QOL. Factors such as age, education, completeness and level of lesion, and community integration were not associated with increased fatigue levels. However, a shorter time since injury was found to be significantly associated with higher levels of fatigue. [15]

In another study, Thijssen et al, recruited eight healthy recreationally active men and 15 recreationally active male patients with SCI. Eight of the SCI subjects presented with a complete cervical spinal cord lesion (tetraplegics), whereas seven subjects had a complete thoracic spinal lesion (paraplegics). All SCI subjects had a complete spinal cord lesion (ASIA A), varying between C5 and T12 that had existed for at least 5 years. The authors assessed the circadian variation of Tcore in SCI individuals and able-bodied controls matched for the timing of the sleep-wake cycle. Intestinal Tcore (telemetry system) and physical activity (ambulatory activity monitor) levels were measured continuously and simultaneously in 8 tetraplegics, 7 paraplegics, and 8 able-bodied controls during one 24-h period of "normal" living. The three study groups did not differ significantly in terms of the timing of the sleep-wake cycle and sleep length, both during the data collection period and via self-reports of their typical living. However, dependent on lesion level, SCI subjects demonstrated a marked difference in the circadian variation of Tcore. Tetraplegics showed a shorter time period during which the biphasic variation in Tcore was completed and an earlier nocturnal phasing of the Tcore value. The authors concluded that SCI individuals demonstrate a significant disturbance in the circadian variation of Tcore, which is unlikely explained by differences in physical activity levels. Interestingly, the circadian variation of Tcore is altered in tetraplegics, but largely preserved in paraplegics, compared to able-bodied controls. Furthermore, the disturbance in circadian variation of Tcore may contribute

VOLUME 73 | ISSUE 4 | OCTOBER - DECEMBER 2022

to the pathophysiologic mechanism that explains the frequently reported poor sleep quality in subjects with cervical SCI.[16]

A small size pilot study by Spong et al, demonstrated the safety of exogenous melatonin in tetraplegia. Exogenous melatonin may offer unique opportunities for sleep-onset insomnia and sleep phase entertainment. For this reason, they gave to 5 participants with complete tetraplegia 3 mg of melatonin two hours prior to usual sleep time for two weeks. The results showed that 3 mg of melatonin increased salivary melatonin from near zero levels at baseline in all but one participant. A delay in time to REM sleep, and an increase in stage 2 sleep were observed along with improved subjective sleep experience with a reduction in time to fall asleep, improved quality of sleep and fewer awakenings during the night. However, daytime sleepiness increased. [17]

Another cross-sectional survey by LaVela SL et al, observed a significant association of sleep dysfunction with weight gain, smoking, alcohol misuse and select chronic conditions as asthma and chronic obstructive pulmonary disease. According to the authors, sustained sleep dysfunction may contribute to health deterioration and mortality. These results highlight the need to address the high prevalence of sleep dysfunction (independent of sleep apnea) in SCI patients. [18]

A recent study by Clark et al, examined the relationships between self-reported demographics, mental health, physical health, and health behavior factors and subjective cognitive difficulties in a unique cohort of 553 SCI patients. The study conducted a cross-sectional analysis of self reported assessment data collection. Based on the results, greater subjective cognitive difficulties were associated with female gender, elevated anxiety, depression symptoms, sleep disturbance, cardiovascular disease, worse pain, polypharmacy, worse self-rated diet, and tobacco use. Depression, anxiety, pain, sleep disturbance, and injury level remained significant predictors of variance in subjective cognitive symptoms when considering all variables simultaneously. The authors concluded that improving mental health symptoms, pain experiences, and sleep difficulties may also improve subjective cognitive symptoms in individuals with SCI. [19]

Fogelberg et al, in 2016, examined self-reported sleep problems in SCI and Multiple Sclerosis (MS) patients in order to determine how common sleep problems are in these two distinct clinical populations. The study included 1.677 patients (SCI=581, MS=1096). SCI patients reported an average of 30 minutes fewer sleep per night and significantly greater difficulty initiating and maintaining sleep compared to the MS group. Although there were similar sleep problems in these groups, they exhibited different sleep problem profiles. As far as SCI patients are concerned, an additional focus on increasing sleep quantity and reducing sleep disruptions may be warranted. The same authors conducted a similar study in 2017, in order to examine the experience of sleep among SCI patients. The patient sample used was taken from an ethnographic study of community-dwelling adults with SCI. Twenty participants were included; 14 men and 6 women. Eighteen of these participants discussed sleep-related issues. Two participants did not mention sleep in any significant way. Three major categories were assessed: sleep difficulties following SCI, barriers to achieving sufficient amounts of high quality sleep and impact of sleep disturbances on daily function. Participants described diminished sleep duration and irregular sleep patterns. Several factors contributing to poor sleep were identified; including SCI related circumstances and sleep environment. Functional ability and quality of life were negatively influenced by several factors including pain, depression, obesity, and pressure ulcers, all of which can be exacerbated by poor sleep. SCI patients reported shorter sleep duration, more daytime sleepiness and greater difficulty in falling and staying asleep. Sleep disturbances led to feeling tired or fatigued during the day, and in some instances this sense of fatigue impacted patients' cognitive functioning. Some patients responded to daytime fatigue by skipping valued everyday activities while others attempted to complete them despite feeling tired, which often created safety concerns. [20,21]

Pain is a significant problem for many SCI patients. They describe pain as the most difficult medical condition to deal with; more so than the loss of motor or sensory function. Persistent pain associated with SCI, negatively affects functioning and physical health, including sleep, reducing quality of life. Avluk et al, in a cross-sectional study assessed the relationship be-

VOLUME 73 | ISSUE 4 | OCTOBER - DECEMBER 2022

tween chronic pain and functional status, depression and sleep quality in SCI patients. They observed that pain severity was positively correlated with impaired sleep. The quality of patients' sleep may be affected by the persistence and intensity of pain. In this study it was also noticed that patients who wake up have trouble maintaining sleep because of pain. [22]

Hassanisirdehi et al, conducted a cross sectional study to establish the relationship between pain and its effects in SCI patients. 58 male veterans suffering from SCI were admitted for a regular follow-up. To evaluate patients' pain quality and the effect of pain on daily life, a 3 part questionnaire concerning lumbar, cervical and shoulder pain was administered. Individuals with lumbar pain felt less recovered after sleep, had more problems going to sleep and reported a significant amount of pain affecting their daily life. Pain was higher in patients with lower General Health Questionnaire score or anxiety/depressive disorder. [23]

Another cross-sectional study by January et al, investigated the medical complications that increase the risk for poor sleep in adult patients with pediatric onset SCI and explored the relation between poor sleep and psychosocial outcomes. The study included 180 participants; 56% with tetraplegia and 74% with complete injuries. Poor sleep occurred with greater frequency in those with tetraplegia and the unemployed. Neck, shoulder, arm and lower extremity pain was associated with increased risk for poor sleep. Individuals suffering from poor sleep reported lower levels of mobility, perceived health and subjective happiness. Pain and secondary complications significantly increased the odds of poor sleep. Additionally, poor sleep was associated with decreased mobility and measures of well being. [24]

A recent study concerning SCI patients concluded that sleep problems, over and above other factors such as health and pain, adversely affect mental health. Patients with poor sleep reported lower levels of independence mobility in community activities and decreased perception of health and happiness. Another recent study showed that quality sleep is an important correlate of wellness in SCI patients. According to Alvaro et al, sleep disturbance and mental health exhibit a reciprocal relation such that mental distress disrupts sleep and poor sleep further exacerbates psychological symptoms. [25]

Conclusion

SCI is a severe condition that affects different aspects of patients' health and everyday life. Sleep disturbances are very common in this patient group. The aim of this study was to increase physicians' awareness of the pivotal role that sleep has in patients' overall health and quality of life and highlight the severe health problems following sleeping disorders. Physicians should always evaluate patients' quality of sleep and firmly address any problems. Further research is needed for finding promising solutions to sleeping disorders in this particular group of patients.

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