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CLINICAL REVIEW

Sleep disorders in patients with spinal cord injury

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SUMMARY

Sleep disturbances are globally more frequent in patients with spinal cord injury (SCI) than in the able-bodied population, and could contribute to dysfunction and poor quality of life in these patients. Specific sleep disorders may also contribute to negative health outcomes enhancing cardiovascular risk in a condition that *per se* increases heart disease related mortality. This review focuses on prevalence, features and treatment of sleep disorders in SCI. Although data on these subjects have been produced, reports on pathophysiology, consequences and treatment of sleep disorders are scarce or contradictory and more studies are required.

Introduction

Traumatic spinal cord injury (SCI) is a significant cause of mortality and morbidity worldwide. As incidence rates are higher for people in the second to fourth decades of life and improvements in acute management and long-term supportive care provide a longer life expectancy, the prevalence of SCI is destined to grow in the coming years.[1] This requires us to address conditions secondary to SCI that have a significant long-term impact on the survival and quality of life of SCI patients. Sleep disorders, given the relative high prevalence of co-shared risk factors and their significant impact on quality of life and mortality in the general population, are certainly among these conditions.

Sleep disorders are common in patients with SCI.[2–4] A growing number of studies have found that poor or decreased sleep, mainly related to obstructive sleep apnoea (OSA), may have long-term health consequences and may lead to premature death,[5] an increased risk for cardiovascular disease, and the development of metabolic disorders including diabetes.[6–10] Sleep deprivation may also worsen cognitive performances and mood, that are often compromised in SCI patients.[7,11]

The aim of this review is to present data on the prevalence, pathophysiology, clinical features and treatment options for sleep disturbances in SCI patients.

Methods

We systematically searched the online database PubMed for relevant publications up to October 2012. The following search terms were used; “spinal cord injury” combined with “sleep”, “sleep disorder”, “insomnia”, “sleep apnoea”, and “sleep movement”. We included only studies published in English. Based solely on title and abstract, and eventually on the full reading of the article if more information was required for a decision, two of the authors (MPG, KKM), MPG for general information on sleep disturbances and sleep breathing disorders and KKM for sleep movement disorders, independently classified each publication as being eligible or not. The database search yielded a total of 221 publications, 182 of which were excluded. 61 additional references allocated to the review were derived from the reference lists of the included publications. 13 references were added after the first revision on the basis of reviewers’ advice.

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Abbreviations

AHI	apnoea-hypopnoea index
AIS	ASIA impairment score
ARAS	ascending reticular activating system
ASIA	American Spinal Injury Association
BiPAP	bilevel positive airway pressure
BMI	body mass index
CPAP	continuous positive airway pressure
EDS	excessive daytime sleepiness
EEG	electroencephalographic
ESS	Epworth sleepiness scale
GABA	gamma-aminobutyric acid
IRLS	restless legs syndrome rating scale
MAPI	multivariate apnoea prediction index
MOSS	medical outcomes study sleep
NIPPV	noninvasive positive pressure ventilation
NSQ	nordic sleep questionnaire
ODI	oxygen desaturation index
OSA	obstructive sleep apnoea
PLMi	periodic legs movements index
PLMS	periodic limb movements
PSG	polysomnography
PSQI	Pittsburgh sleep quality index
RDI	respiratory distress index
RF	reticular formation
RIMT	resistive inspiratory muscle training
RLS	restless legs syndrome
SBD	sleep breathing disorder
SCI	spinal cord injury
SCN	suprachiasmatic nucleus
SMD	sleep movement disorder

Prevalence and features of sleep disorders in SCI

Questionnaire-based studies

Several studies compared self-reported sleep complaints in large populations of chronic SCI patients versus healthy control groups by means of questionnaire assessments focused on sleep quality.

A significantly higher percentage of sleep complaints (35%, $p < 0.0001$) was reported by 326 SCI patients compared with a control population in the Stockholm spinal cord injury study.[2]

Another study using the Nordic sleep questionnaire (NSQ) found that SCI individuals had a poorer sleep quality, slept more hours and snored more and for more years than normal subjects and reported greater difficulty falling asleep and more frequent awakenings, slept subjectively less well, and were more often prescribed sleeping pills.[3]

A larger survey applied the medical outcomes study sleep (MOSS) scale to assess differences in sleep quality between an SCI group comprising 620 individuals and two normative reference groups including a chronically ill population and a general population.[4] As previously described, the SCI sample reported significantly greater overall sleep disturbances with fewer hours of sleep per night, poorer sleep adequacy and greater daytime sleepiness than both the chronically ill and general populations. The SCI group also reported more snoring than the other two populations, and significantly more nighttime respiratory difficulties than the general population ($p < 0.001$), but not the chronically ill population ($p > 0.05$).[4]

Instrumental studies

Few studies described the electroencephalographic (EEG) features of sleep in SCI.[12–15] In 1968 Adey et al.[12] investigated EEG sleep disturbances in 18 SCI patients and reported fragmented sleep architecture and reduced slow wave and REM sleep in tetraplegic patients. Conversely, in paraplegic patients all sleep stages were normally represented. However, lacking a full polysomnographic (PSG) study it was impossible to rule out their relationship with sleep disordered breathing (SDB) and/or sleep-related movement disorder (SMD).

Short et al.'s PSG study[13] of a group of 22 SCI patients found disrupted sleep with an increased amount of wake after sleep onset and a marked reduction of slow wave sleep, mainly unrelated to respiratory disturbances.

An increased percentage of stage 1 and a corresponding decrease in the percentages of stage 2 and REM sleep, compared with a control population, were reported in tetraplegic patients.[14,16] REM sleep appeared to be reduced both in minutes and as a percentage of total sleep time, whereas total sleep time was increased compared with normal values.[14]

Scheer et al.[15] reported increased REM sleep latency in tetraplegic patients compared to paraplegic and able-bodied controls, irrespective of SBD or SMD, although there were no statistical differences in sleep onset latency or proportions of the different sleep stages among groups. A similar observation was made in a larger cohort of tetraplegic patients by Berlowitz et al.[17] reporting a longer REM latency in those with complete lesions independently from the diagnosis of OSA.

Pathophysiological considerations on sleep disturbances in SCI

Animal studies

Few animal-model studies focused on sleep patterns in SCI. Esteves et al.[18] reported that after SCI rats presented an altered sleep pattern with increased arousals and paw movement during sleep. Another study by the same group[19] evaluated SCI-induced alterations in rat sleep architecture over a 15-day period. Compared with a sham group, SCI rats showed significant changes in sleep features characterized by reduced sleep efficiency, fragmented sleep, more arousals, and increased total wakefulness time in relation to baseline. SCI rats also showed disrupted circadian rhythms, increased total slow wave sleep time and decreased total paradoxical sleep time. In both studies,[18,19] paw movement during sleep emerged during the first week after SCI, possibly in relation to the activity of the gracilis and cuneate fascicles and of the spinal dopaminergic system.[19] The altered sleep architecture observed in SCI rats is in many aspects similar to that observed in SCI patients suggesting that spinal cord lesions *per se* disrupt sleep patterns.

Similarly to what was observed in humans, serum melatonin levels have been demonstrated to be reduced in tetraplegic rats compared with paraplegics,[20] although no correlation was made with sleep patterns in these two groups of animals.

Human studies

The reticular formation (RF) in the brain stem plays an important role in vital functions including sleep-wake regulation via projections to several brain areas including the thalamus, hypothalamus and most cortical regions.[21] Sleep and wake are regulated by a complex interaction between the hypothalamus extending from the suprachiasmatic nucleus (SCN), which regulates circadian rhythmicity, the hypocretinergic system involved in arousal promotion and state maintenance, and the ventrolateral preoptic nucleus promoting sleep, to the ascending reticular activating system (ARAS). The brain stem RF is connected to the spinal cord by ascending and descending pathways,[22] and cervical lesions, especially higher ones, may alter sleep regulation.[23]