Shift work disorders: implications and proposed management

Trabalho em turnos: consequências e propostas de gerenciamento

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ABSTRACT
Economic demand has modified the temporal organization of work and established the system of shift work. The inability of the individual worker to maintain an adequate quantity and quality of sleep after a day of shift work is damaging to the physical, psychological and socio-familiar aspects of worker health. It may cause chronic fatigue and stress and increase the risk for cardiovascular and gastrointestinal diseases. The sleep disorders most often developed by routine shift work are insomnia and excessive sleepiness. These disorders have the potential to generate errors at work due to a loss of attention and promptitude during the performance of tasks, harm the productivity and quality of services and contribute to accidents and fatalities. In this short review, the main consequences of shift work as they relate to worker health and welfare and some management proposals currently being discussed in the literature are presented.

Keywords: circadian rhythm, disorders of excessive somnolence, health risk, insomnia, shift work, sleep.

INTRODUCTION

In 2004, it was estimated that more than 20 million American workers, approximately 17.7% of the workforce, routinely worked alternate shifts that fell at least partially outside the 6 a.m. to 6 p.m. schedule.¹ According to an extensive survey conducted in 2005 of European countries, evening and night work schedules were quite rare in most countries except in those in eastern Europe, including Romania, Bulgaria and the Czech Republic, where 25% of the working population was affected. The sectors in which there is consistently more work at atypical hours are agriculture, restaurants and hotels and communication and transport.² There is no reliable data, to the best of our knowledge, regarding the prevalence of shift work in Latin American countries. Shift work can have negative consequences that are relatively common but not always recognized and often overlooked.

These patients may suffer social, economic and health damage and a reduction in quality of life. There is an increased risk of psychological, cardiovascular and gastrointestinal disorders and complaints of insomnia and excessive sleepiness, comorbidities related to shift work that can potentially be prevented or treated.

The circadian rhythm disorder related to shift work is dependent on the work shift and is characterized by insomnia or excessive sleepiness. The night, rotation and morning shifts are most associated with this morbidity.³,⁴ The prevalence of shift work sleep disorder is approximately 10% in the night and rotating shift work population.⁵

In this short review, the main consequences of shift work as they relate to worker health and welfare and some management proposals currently being discussed in the literature are presented.

HEALTH CONSEQUENCES

Stevens et al.⁶ (2009) discussed the relationship between the incidence of breast cancer and the industrialization of societies. Changes during the process of industrialization, especially after the advent of electricity and lighting at night, were highlighted, which could suppress melatonin production and disrupt the circadian rhythm. It was proposed that the advance in the use of electricity for lighting at night could be related to the increased risk of breast cancer.

It is known that the circadian genes directly control other genes, such as cell cycle regulators. Both the methylation of circadian genes and their polymorphisms may cause changes in their function, increasing the risk of cancer development.⁷,⁸

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The variant 5-VNTR polymorphism of the Per3 gene, in particular, was associated with an increased risk of breast cancer in young women compared with the variant 4-VNTR. Thus, identifying an environmental factor that changes the methylation state of the circadian genes could become a promising area of research for the treatment of cancer.

There is evidence for an association between sleep, sleep-wake rhythm and metabolism. Light exposure, sleep and consumption of nutrients serve as signals to the suprachiasmatic nucleus, the biological clock, to synchronize daily activities, the burning of calories and rest with the circadian cycle. Lifestyles have changed over time, and the circadian and metabolic regulatory systems have not been able to evolve and adapt to the consumption of food high in sugar and fats throughout the year. Previously, this consumption was seasonal. Deregulation of the circadian system may lead to an imbalance of the autonomic system and result in health problems such as obesity, diabetes and hypertension.

Short-duration sleep, for example, can lead to insulin resistance by reducing the use of brain glucose and increasing sympathetic nervous system activity and evening cortisol levels, which in turn can compromise the function of pancreatic beta cells and lead to diabetes. Additionally, sleep deprivation decreases leptin and increases ghrelin and appetite, impairing insulin sensitivity and raising blood pressure.

Epidemiological studies led to the hypothesis that changes in circadian and sleep systems could also contribute to the pathogenesis of the metabolic syndrome. Maury et al. (2010) note in a review that disturbances in the system’s internal clock and sleep are risk factors for cardiovascular disease, obesity, diabetes mellitus, thrombosis and inflammation. An association between cellular/molecular alterations and disturbances in circadian rhythms and sleep, as well as the connection between those disturbances and the metabolic syndrome, were observed.

Research conducted over the past 10 years has shown that even a small reduction in sleep duration may hinder the availability of glucose. Stamatakis & Punjabi (2010) studied whether experimental sleep fragmentation in all phases could alter glucose metabolism, adrenocortical function and sympathetic-vagal balance. In their study, insulin sensitivity and the ability of glucose to be mobilized independent of the response to insulin decreased significantly. There was an increased activity of the sympathetic nervous system and a higher level of cortisol in the morning. They concluded that, possibly through increased sympathetic tone and adrenocortical activity, sleep fragmentation is associated with a change in glucose metabolism.

A higher incidence of gastrointestinal and appetite disorders is observed in shift workers, particularly night shift workers. This association can be explained by the change of usual meal-times, the difficulty of obtaining hot and nutritive food in this period and the inability to have social contact during meals.

There is a misalignment between the endogenous circadian clock and the external environment during the 24-hour day in these workers. Nojkov et al. (2010) investigated the prevalence of irritable bowel syndrome (IBS), constipation, functional diarrhea and other gastrointestinal symptoms among workers from different shifts (day, night and rotating). The rotating shift workers had a significantly higher prevalence of IBS compared with the day shift workers. The former group also had a higher prevalence of abdominal pain than the other two shift worker groups. Thus, it was realized that shift work, especially rotating shifts, is associated with the development of IBS and abdominal pain, regardless of the quality of sleep.

In addition, recent studies have shown that circadian genes are expressed in epithelial cells and in cells of the myenteric plexus of rats, suggesting a potential role of these genes in colonic physiology. In this manner, changes in these genes may lead to gastrointestinal symptoms.

Another potential long-term consequence of shift work is vascular disease and an increased secretion of catecholamines. Coronary artery involvement is related to this type of work, but its relationship to cerebrovascular accident (CVA) is uncertain. Brown et al. (2009) conducted a study with a cohort of nurses to examine the relationship between the duration of rotating night shift work and the occurrence of stroke. Rotating night shift work was associated with a 4% increase in the risk of stroke for every 5 years worked. This increased risk was significant in women with a history of 15 or more years of work in rotating shifts.

Endothelial dysfunction and alterations in heart rate variability (HRV) as well as sleep deprivation and shift work have been shown to be associated with cardiovascular disease.

Eleven experienced male shift workers and 14 non-shift workers were studied to compare HRV and endothelial function in response to total sleep deprivation and recovery sleep under identical laboratory settings. Despite similar demographics, circadian phases, postures and levels of food intake, differences in endothelial function and HRV were observed in the two groups, which may reflect higher sympathetic and/or lower parasympathetic activity, contributing to an increased cardiovascular risk among shift workers.

Few studies have reported an association between sleep duration and chronic kidney disease. Yamamoto et al. (2011), in a retrospective cohort study, assessed 6,834 employees of Osaka University who did not have proteinuria or undergo treatment for self-reported kidney disease. Self-reported questionnaires regarding lifestyle, including sleep duration, were used along with blood and urine testing. It was observed that short sleep duration, especially 5 or fewer hours, was a predictor of proteinuria. Thus, kidney disease is one of the many chronic problems that may affect shift workers.

Shift work is associated with significant neurocognitive deficits. A recent study of emergency physicians conducted before and after day and overnight shifts indicated that short-term memory appears to decline after both types of shifts. As shown by Wright (2012), cognitive processes vary over the course of the 24h day, and when wakefulness occurs at inappropriate biological times because of environmental pressures, such as shift work, the resulting misalignment between circadian and wakefulness-sleep physiology leads to impairments in cognitive performance, learning and emotion.

EFFECTS ON SLEEP AND WAKEFULNESS

Sleep disorders are common and observed worldwide. Their consequences include an impairment in social and recreational activities, an increase in human errors, a loss of productiv-
ity and a high risk of accidents. Most humans are active during the light phase and are prone to sleep in the dark phase. Therefore, alterations in this pattern can lead to behavioral changes in relation to sleep and can represent a risk factor for increased accidents and adverse worker health. Alterations in the sleep pattern can contribute to the complaint of excessive sleepiness in shift workers, sleep apnea, periodic limb movements, insomnia and narcolepsy.

Excessive sleepiness (ES) is a major complaint of individuals with sleep disorders and may be evidenced by mood changes and loss of normal behavior. A reduction in performance can become a public concern when individuals with ES are involved in potentially dangerous daily activities, such as driving a car.

Another problem relates to how much the next-day sleep may revitalize an individual, particularly for morning-type individuals who work in night shifts. Sleeping during non-physiological times of the day and in inadequate environments may aggravate the drowsiness of such workers.

**SOCIO-ECONOMIC IMPACT**

In 2009, a study on the economic consequences of excessive sleepiness of any etiology showed that ES was responsible for an annual cost of 53 to 69 billion dollars from traffic accidents and 18 to 24 billion dollars from work-related injuries.

The influence of shift work disorder (SWD) is of great importance in workers who provide emergency services or those who make critical decisions. The economic costs of untreated SWD, such as those related to accidents and decision errors, tend to be high.

Shift work involves public health risks because it may decrease the ability of daily performance and facilitate the occurrence of occupational and traffic accidents.

In his review article, Culpepper (2010) discussed the prevalence of SWD and its economic and social impact. In a study of flight controllers, it was shown that damage to the quality of life is significantly higher in shift workers when presenting SWD. In another study, it was found that individuals with SWD are more likely to be unable to attend social and family activities due to sleep problems.

An assessment of the social damage of SWD observed that workers suffering from such disturbances missed monthly social and family activities 5.7 times more when compared to workers without the disorder and that this rate was even higher in workers in rotating shifts, who had 10 times more incidents.

Shift workers have a greater likelihood of involvement in work-related injuries, especially when returning home after a night of shift work. For example, 40% of accidents involving American doctors in the first year of residency occurred under these conditions.

**CHARACTERIZING THE DISORDER**

**Predisposing factors**

It is known that there are individual differences in vulnerability to sleep loss and that this difference impairs the application of a single measure of regulation. Promising discoveries include genetic predictors of responsiveness to sleep deprivation, such as polymorphisms implicated in the regulation of neurotransmitters (catechol-O-methyltransferase), cerebral metabolism (adenosine receptor and adenosine deaminase) and circadian rhythmicity (Per3 gene).

A potentially important factor in the vulnerability to sleep disorders is aging. It has been shown that the severity and frequency of these disorders tend to increase with age and that the ability to make circadian adjustments tends to decrease in individuals who work in the night shift, leading to ES. In 2009, Pires et al. observed a significant effect of the time of sleep on the quality and quantity of sleep in 124 drivers who worked morning or night shifts; daytime sleep was less efficient and shorter compared to nocturnal sleep. No significant differences were observed with age with respect to the challenge of sleeping during the day.

**Diagnostic methods**

Methods would be useful to identify workers with an increased risk of errors and accidents related to sleep deprivation. A careful selection and monitoring of certain workers could improve performance and productivity, reduce errors and accidents, and prevent deaths.

**Particular groups**

Wilhelm et al. (2009) assessed sleepiness in physicians before and after night shift work by conducting the pupillographic sleepiness test (PST). The PST enables the recording and analysis of pupillary oscillations, which reflect the degree of sleepiness in the dark. Thirty-four subjects were evaluated by the PST and subjective scales. Data obtained during daytime work were compared to those obtained after the night shift, which was associated with an average of 4 hours of sleep. Considerable drowsiness was found in doctors after night duty, which can result in lower levels of safety for patients and physicians on duty.

The neurohormone melatonin is directly related to the wake-sleep schedule because the beginning of its secretion coincides with an increased propensity to sleep. A study of nurses working in fixed shifts (day, afternoon or evening) was conducted to evaluate how different types of shift work affect sleep and sleepiness. Subjective measures were analyzed, and urinary 6-sulfatoximelatonin (a melatonin metabolite) was measured. Mixed night-shift nurses had the worst quality of sleep after working at night. There was no correlation between urinary 6-sulfatoximelatonin and sleepiness in mixed night shifts, which may indicate that the influence of endogenous melatonin is limited. They also had longer durations of sleep during their day-off. This result may indicate that poor quality of sleep may be associated with the work schedule and is not a personality trait.

Few studies have evaluated the relationship between subjective complaints and objective evaluation of sleep disorders in shift workers. Workers at two nuclear power plants in Brazil were interviewed and those who reported sleep-related complaints were referred for polysomnography. With regard to the 327 volunteers initially evaluated by the sleep questionnaire, 113 (35%) reported complaints. These workers were significantly affected by sleepiness.
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older, had higher body mass index and performed their duties in shifts for more years than those without sleep complaints. Ninety out of the 113 individuals met the criteria for sleep disorders; of these, 30 (9%) showed obstructive sleep apnea, 18 (5.5%) showed periodic limb movements and 42 (13%) showed sleep abnormalities (higher proportion of arousals and stage 1 sleep compared to the 23 shift workers who had no sleep problems). Among the participants, 27.5% met the criteria for any type of polysomnographic sleep disorder. The authors suggested that this high percentage should be investigated in regard to other aspects such as time and number of hours worked, years of shift work, performance and access to health services.

Mello et al. (29) (2000) found complaints related to sleep, depression and anxiety in 400 Brazilian bus drivers. A sleep questionnaire and the Beck (for depression) and state-trait (for anxiety) inventories were answered by the participants. At least one sleep-related complaint was reported by 60% of the respondents and 16% admitted to having fallen asleep at the wheel while in service. Other problems reported included physical fatigue in 59.8%, mental fatigue in 45.4%, somnolence in 25.8%, irritability in 20.6%, insomnia in 37.5%, respiratory disorders in 19.2% and snoring in 20.7%. It was shown that the bus drivers studied kept a lifestyle associated with an irregular work schedule without the possibility of adequate physical and mental recovery during sleep, making them highly dissatisfied.

In Brazil, truck drivers are likely to suffer serious injuries and death in accidents. Excessive daytime sleepiness is a major problem that leads to a loss of cognitive function, decreased vigilance and an increased risk of traffic accidents. De Pinho et al. (30) (2006) studied 300 male truck drivers to determine the prevalence and predictors of excessive sleepiness among these drivers. The average reported daily sleep duration was 5.6 ± 1.3 h and poor sleep quality was found in 46.3% of the individuals. Hypersomnia was found in 46% of drivers and was associated with a younger age, the presence of snoring and tirelessly working for more than 10 hours. ES and previous accidents were correlated. The study showed that sleep deprivation and ES are common among truck drivers. The authors mentioned the need for the treatment of sleep-disordered breathing and the implementation of educational programs directed primarily at younger drivers in an attempt to minimize damage and improve road safety.

INTERVENTIONS

Trying to adapt the circadian clock to the shift work schedule can be curative for SWD symptoms. To resynchronize the circadian clock, exposure to properly timed bright light and darkness is an alternative. Regarding the adjustment to night work, workers should be exposed to light at night and avoid sunlight in the morning (31-33). However, experience has shown that this intervention produces a partial circadian adaptation, and the associated improvement of the cognitive performance and alertness does not occur for all tasks assessed during the night (34,35). In an attempt to reduce sleepiness, the regular scheduling of naps during the night shift and before each work shift can be employed. A 40-min nap during a 12 h night shift was proven to improve reaction time, alertness and fatigue and to reduce the physiological signs of sleepiness (36,37). Drinking caffeinated beverages (300 mg) increased performance and alertness in a night shift setting by diminishing the influence of the homeostatic sleep drive (38). Nevertheless, subjective sleepiness was increased and some performance measures were unaffected using a low-dose strategy (39), and it was reported that shift workers may be at a greater risk of sleep disturbance with prior caffeine use (40). Interventions should be directed to the workers’ complaints and individualized case by case. If insomnia is the patient’s major complaint, improvements in sleep hygiene and hypnotics or melatonin should be employed. However, if excessive sleepiness is the major concern, prophylactic naps prior to the work shift or during the night shift and caffeine use are some options to be considered. In some cases, drugs that promote wakefulness may be used.

The pharmacological management of SWD can be diagnostically divided into 3 categories:

Wake-promoting agents

In January 2004, the wake-promoting agent modafinil was approved in the US by the FDA (Food and Drug Administration) for the treatment of ES associated with obstructive sleep apnea syndrome (OSAS) and shift work sleep disorder, representing an expansion of its labeling from the initial indication for ES associated with narcolepsy. Modafinil reduces the extreme sleepiness that is observed in patients with shift work disorder and results in a significant improvement in performance.

Laborers with SWD undergoing treatment with 200 mg of modafinil or placebo before the start of each shift were studied for 3 months. It was observed that with the use of modafinil there was a reduction in lapses of attention in tests, with no loss in daytime sleep compared to placebo (41). There was a decrease in extreme ES, despite the maintenance of residual sleepiness among the treatment group, showing the need to develop more effective interventions (42,43).

Many studies have evaluated the different types of interventions to enhance wakefulness and sleep in shift workers. Exposure to light, use of hypnotics, melatonin, stimulants, caffeine, and alertness promoters (armodafinil (44) and modafinil) were examined. Three randomized double-blind trials studied pharmacological treatments in patients with SWD and observed that modafinil and armodafinil significantly improved the ability to maintain wakefulness during activities and sustain attention and memory (45).

Erman et al. (46) (2007) conducted a clinical trial with 278 adults with ES and chronic SWD in 31 centers in the U.S. for 12 weeks. The effects of modafinil on sleep, executive function and quality of life in relation to health in day and night periods were evaluated. Either modafinil (200 or 300 mg) or placebo was randomly administered 30 to 60 minutes before each night shift. It was observed that both doses of modafinil significantly improved the mental component of the quality of life questionnaire, despite the fact that it has not been validated for use in patients with SWD. The drug did not impair sleep when it was desired and was well tolerated. There were no clinically significant differences between modafinil and placebo with respect to vital
signs, physical examination parameters or electrocardiogram results. Modafinil significantly improved executive function and quality of life in patients with SWD(40). It was safe and had a very low potential for abuse(41).

In 2008, Kumar(47) reviewed the use of modafinil in randomized, double-blind and placebo-controlled studies. The author reported that the drug showed an improvement similar to that of caffeine on mood, fatigue, sleepiness and cognition in subjects deprived of sleep and maintained a longer duration of action. There was an improvement in ES and a reduction in the severity of SWD.

Schwartz(48) (2009) published a review of several aspects of modafinil, focusing on its use for ES in patients with SWD, narcolepsy and residual sleepiness in the syndrome of obstructive sleep apnea. With modafinil treatment, there was an objective reduction in sleepiness and an improvement in general clinical conditions related to the severity of sleepiness. The improvement in wakefulness was associated with an improvement in both behavioral alertness and functional status as well as in health and quality of life. In patients with SWD, there were decreases in the maximum level of sleepiness during night work, in the level of sleepiness during the travel to home and in the incidence of accidents. The medication was well tolerated with no impairment to sleep or cardiovascular parameters. Long-term studies suggest that the efficacy is maintained with little likelihood of tolerance and there were no adverse effects on scheduled sleep, demonstrating the beneficial effect of modafinil on daily life and well-being.

The R-isomer of racemic modafinil, armodafinil, has a longer half-life and is approved for the treatment of ES associated with SWD in Australia, Canada, Israel, New Zealand, Turkey and the United States(49). It has been shown that armodafinil improves alertness and performance among patients with SWD(50) in a 12-week double-blind, placebo-controlled trial and that its wakefulness-promoting properties are sustained throughout the night.

Melatonin and melatonin agonists

Melatonin has been used to treat some circadian rhythm disorders, including delayed or advanced sleep-phase disorder, the time zone change syndrome (jet lag) and SWD. It enables the modification of biological rhythms. The development of selective agents for melatonin receptors will help to clarify the actions of these receptors and provide new treatments for sleep disorders. Further studies are still needed to understand the mechanisms of action of melatonergic agonists, especially during insomnia. However, these drugs, such as ramelteon, agomelatine and tasimelteon, seem to be effective in treating circadian rhythm disorders and some types of insomnia. Melatonin can also improve the sleep of shift workers during their days off(53). The long-term effects of melatonin have yet to be evaluated on a larger scale(54).

Hypnotics

There are no controlled clinical trials of patients with SWD using sleep-promoting agents. However, the American Academy of Sleep Medicine task force’s practice parameters indicate the use of short-acting hypnotics, such as triazolam, temazepam and zolpidem, to improve daytime sleep(55). Because sleep maintenance problems are more common than sleep onset problems, these medications are most likely of little help to most night shift workers.

Finally, combined measures have been assessed and have been proven to be more successful than single treatments for improving nighttime alertness and performance. A study combining 300 mg of caffeine intake and a 2.5 h preshift nap resulted in an improvement of alertness and performance as measured by the maintenance of wakefulness test (MWT) and the psychomotor vigilance task, respectively(48).

Maintenance of alertness on the MWT and improvement of performance were also shown in a study where a combination of caffeine (200 mg at 20:00 h and 02:00 h) and bright light was used(56). The same results were obtained by the combination of modafinil and naps in a laboratory environment(57).

FINAL CONSIDERATIONS

Shift work disorder is a very common condition but is still poorly recognized and treated. Due to the strong association between sleep disorders and the occurrence of fatigue and sleepiness, the evaluation of sleep patterns and complaints of shift workers is essential and should be considered as a basic strategy for the prevention of accidents(20,26).

Periodic examinations should be performed routinely on shift workers. Early diagnosis and treatment of SWD will allow a reduction in costs related to this condition(22).

Physical exercise, setting the environment with intense light and the use of modafinil are recommended to improve alertness during night shifts and rotating work in individuals with SWD(55,56).

However, further studies are needed to be able to assess the different interventions for this disorder and their abilities to reduce its economic and health consequences.

REFERENCES


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