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Sleep and Sleep Impairment in Victims of Traumatic Brain Injury

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Abstract

Context: Sleep impairment after Traumatic Brain Injury (TBI) is a common consequence of the injury and frequently complicates recovery. To review in brief the current knowledge in regard to sleep impairment following traumatic brain injury.
Evidence Acquisition: The relevant literature was reviewed.
Results: Practical issues in regard to epidemiology, clinical presentation, medical workup, as well as pathophysiology and treatment modes were addressed.
Conclusion: As the spectrum of civil head and brain trauma is quickly expanding, it is important to increase our knowledge of sleep impairment characteristics in victims of TBI and look for more efficient treatment modes for those impairments than those used today.

Keywords: TBI, Secondary Insomnia, Secondary Hypersomnolence Disorder, Circadian Rhythm, Cognitive Behavior Therapy, Sedatives and Hypnotics

1. Context

At present, non-military traumatic brain injury (TBI) is a major cause of morbidity and mortality. In the USA, with a highly mechanized society, the annual rate of TBI between the years 2002 - 2006 was 500 - 600 per 100000. Out of those, 16.3% had to be admitted to the hospital (1). In 2013, approximately 2.8 million TBI related emergency room visits were reported in the USA (1). After the acute phase, many of those patients will continue to suffer from a variety of physical, cognitive, behavioral, and emotional sequelae, which will frequently also affect family members, friends, and the patient's community. Indeed, about 68% of such patients will complain of disturbed sleep during their stay in rehabilitation units (2). Abnormal polysomnography (PSG) is reported in 46% of such patients during the subacute post injury phase and 25% will suffer from daytime hypersomnia as assessed by the multiple sleep latency test (MSLT) (3). About 25% of the patients will subsequently suffer from chronic sleep impairment (4). New sleep difficulties or aggravation of past sleep-wake problems are often experienced by the patients and observed by bed-partners and family members.

In this paper, the scope of post TBI sleep disturbances will be reviewed and the clinical features, pathophysiology, and treatment modes will be described.

1.1. The Impact of TBI on the Structure of Sleep

Polysomnography, the gold standard tool for studying sleep structure is very informative in TBI. It also provides distinct clues to the severity and recovery process from TBI. Sleep spindles, the hallmark of sleep stage 2, tend to disappear during the acute phase of severe TBI. Their disappearance is directly related to low Glasgow coma scale scores and their reappearance herald the process of recovery (5). In those patients who are in coma, the particular sleep stages (wake, rapid eye movement (REM) and Non-REM sleep) are difficult to distinguish. The presence of EEG patterns which indicate sleep is considered as a favorable sign. With the ongoing process of rehabilitation, those sleep stages become more distinct. During the months following the regain of consciousness, the percentage of stage 3 - 4 i.e. slow wave sleep as well as REM sleep is decreased and the total sleep time is shortened (6).

1.2. The clinical features of disturbed sleep in TBI

Sleep impairment is quite common after TBI affecting about half of the patients in the form of insomnia and or daytime sleepiness (7), which are the 2 opposite ends of the spectrum of sleep- wake disorders present in victims of TBI, regardless of the severity of the trauma. Disturbed sleep may appear shortly following the traumatic event or somewhat later. The symptoms can be transient or last

many years. Impaired sleep may aggravate the cognitive and emotional outcome of the injury as well as increasing pain perception and intensifying the feeling of easy fatigability. Indeed, fatigue assessed by validated scales is quite common. In a cohort of mild TBI patients, a 3rd still suffered from fatigue 6 months after the traumatic event, which affected negatively their life quality (8). It should be remembered that estimates of frequency, severity, and timing of those symptoms are influenced by issues such as compensation claims, changes in daily habits and occupational status of the patients following the traumatic event. Moreover, the extent and severity of neurotrauma may also influence those estimates. For example, insomnia is reported more frequently with mild TBI. A possible explanation can be the fact that the general awareness of those patients compared to moderate-severe TBI is much better. They tend to complain more of their difficulties as well as of impaired sleep.

Non-refreshing sleep, increased urge for sleep, sleep related breathing disorder, and impaired circadian rhythm of sleep - wake state are the main clinical features of sleep impairment following TBI. Half of the patients suffer from insomnia and sleep apnea, 28% from hypersomnia, and about 4% suffer from narcolepsy. The frequency of circadian rhythm abnormality is not well documented (7). In addition to insomnia, daytime hypersomnia seems to be a frequent complaint with a wide range of occurrence (14% - 57%). Delayed sleep phase disorder is the most frequent clinical form of circadian rhythm sleep disorder following TBI. Some victims experience and report significant irregularities of sleep-wake habits, poor sleep maintenance and efficiency, delayed sleep onset, early morning awakenings, and nightmares.

1.3. The Interrelationship Between TBI, Sleep Impairment and Recovery

It seems logical to assume that impaired sleep, in particular insomnia, has a deleterious effect on cognitive and emotional deficiencies already caused by TBI.

However, it is quite surprising that there are only scarce studies dedicated to this important issue. In a single study by Wilde et al. (9), a small sample of obstructive sleep apnea (OSA) patients were divided into those without TBI and those who had sustained TBI. Both groups were assessed for a verity of cognitive functions. The OSA + TBI group was found to suffer from increased impairment of sustained attention and memory as compared to the OSA group without previous TBI.

1.4. Neuroanatomical Correlations

Blunt head trauma is frequently associated with diffuse or focal brain damage in the form of intraparenchymal as well meningeal bleeding, brain laceration with local mass effect, and transient increased intracranial pressure. There are unfortunately only scarce data which point to distinct locations of injury, which are followed by a specific sleep impairment. The tight link between brain trauma and sleep abnormalities is supported by the observation that intracranial bleed and wide speared brain injury are both associated with increase sleep need (10). In a military setting, blunt head injury was found as a risk factor for OSA in a cohort of mild -moderate TBI (11).

Hypothalamic injury may be responsible for certain patterns of abnormal sleep after TBI. It is well established that the hypothalamic neuropeptide hypocretin- 1 (orexin), regulates sleep-wake cycles as well as appetite. A decreased level of hypocretin -1 is the hallmark of narcolepsy causing the typical brief sleep attacks of this devastating disorder. In several single case reports, the level of hypcretin -1 was acutely reduced after TBI. Baumann et al., (12) measured the hypocretin-1 level in the CSF of 27 out of 96 soldiers, 4 days after sustaining TBI during combat. Hypocretin-1 was undetectable in 13, low in 12, and normal in only 2 subjects. After 6 months, CSF hypoecretin-1 was measured in 21 subjects and was found normal in 17 and low in 4. Unfortunately, the authors did not mention how many of the initial patients in whom hypocretin-1 was measured had a repeated test and did not describe in detail the sleep characteristics of the tested patients at the time of the first CSF sample, during the interval between the 2 samples or at the time of obtaining the 2nd sample. However, the authors have noted that during the 6-month interval between the 2 samples, hypersomnia slowly resolved in the majority of the patients. Those results should be interpreted with caution since this group of soldiers had a better outcome than expected from published data. Moreover, it is not possible to determine from the data presented if the recovery from hypersomnia in a specific patient in this study can be correlated either with his acute and / or late CSF hypocretin-1 level.

The postulated vulnerability of the hypothalamus in TBI is reflected by quite an old report of 106 autopsies of fatal TBI. In 42.5% of the autopsies, ischemic or hemorrhagic lesions were found in the anterior hypothalamus (13).

1.5. Medical Workup

When assessing the sleep quality of patients with TBI, one should take into account the presence of circadian rhythm alteration in the form of altered sleep hygiene, medications used pre-and- post trauma, extent and severity of additional systemic trauma besides neurotrauma, psychological - psychiatric features, and sleep quality prior to trauma. To semi-quantitate sleep quality, there are a number of questionnaires, which may be used such as

the STOP- BANG (snoring, tired, observed, pressure, body mass, age, neck size, gender) (14), Epworth sleepiness scale (15), Berlin questionnaire, which is intended to screen for OSA (16), and the Pittsburgh Sleep quality index (17). Polysomnography is of course required and wrist actigraph can provide information on daytime and nocturnal sleep-wake activity. This important information is necessary for correlation with the subjective complains of insomnia and circadian rhythm disorder.

2. Treatment

2.1. Pharmacological Intervention

2.1.1. Insomnia

It is common practice, especially among family physicians, to prescribe a variety of sedatives and less frequently hypnotics for insomnia. Antidepressants, atypical antipsychotics, antihistamines, and anticonvulsant "mood stabilizers" are also used.

Unfortunately, many of those drugs, when given during the subacute and early rehabilitation phase post TBI, may exacerbate the already present cognitive impairment, fatigue, feeling of unsteadiness, and dizziness - giddiness in those patients. Those drugs may also have a negative effect on the limited ambulation and stance as well as leading to misuse of drugs already taken for ailments and conditions other than insomnia. Sedatives and hypnotics may also lower the epileptic threshold, an important issue in those patients who suffer from post-traumatic epilepsy. In general, sedative and hypnotics are recommended for a short duration only (about 2 weeks) since their long-term use carries a substantial risk of addiction. A short course of Benzodiazepines seems to be a good option due to its ability to reduce sleep onset latency and decrease the number and duration of awakenings. The end result is an increase in total sleep time and the proportion of Non-REM/ sleep stage 2 (N2), as well as a reduction in REM/ Non-REM slow wave (N3) proportion. The newer non-benzodiazepine sedatives, i.e. Z-drugs (Zolpidem, Zopiclone) seem to be effective. In spite of their hypnotic properties they are considered by many as safer than Benzodiazepines (18, 19). Few authors favor the Z-hypnotics mentioned above over benzodiazepines for TBI survivors, due to the fact that their negative affect on memory is lesser than Benzodiazepines (20). Those new observations have not, until now, changed the prescribing habits of the majority of general practitioners and family physicians who continue to recommend Benzodiazepines for insomnia in general and for TBI in particular. Both Benzodiazepines and Z-drugs are recommended for short-term use, however, the truth of the matter is that those drugs are used for long periods of time to combat insomnia by the general population as well as victims of TBI. In one study, 20% of the patients with TBI still used those drugs after an average of 9 years from the initial trauma (21). Melatonin, Amitriptyline, and Prazosin were found beneficial in only in small series of patients.

2.1.2. Daytime Hypersomnia

The drugs commonly used for this symptom such as the central psychostimulants methylphenidate (Ritalin ,Concerta) and Modafinil, were found generally not effective in reducing sleepiness during the day. However, in a placebo-controlled study on 117 mild-moderated TBI survivors, the efficacy of 3 doses (50, 150, 250 mg/day) of Armodafinil (Nuvigil, the most recent formulation of Modafinil) was studied. Only the 250 mg/day preparation given for 12 weeks resulted in a significant decrease of objective sleepiness without improving subjective sleepiness (22).

2.2. Non-Pharmacological Intervention

Cognitive Behavior Therapy (CBT) for insomnia in general, seems to provide short and long-term benefits. This mode of behavioral therapy was applied in a modified form in a small group of TBI survivors and showed similar efficacy to that found in non-TBI insomnia patients (23). Quite recently a group of 24 patients who sustained mild-severe TBI was assessed for efficacy of CBT as compared to the "classical" treatment modes (a combination of occupational and physiotherapy, pharmacotherapy, and mood psychotherapy). The assessment was performed after a mean of 3.81 years post TBI (range: 77 days - 20.7 years). Efficacy was assessed after 2 months of treatment and reassessed 2 months later. The 13 patients who received CBT reported better sleep quality, reduced daytime fatigue and improved mood as compared to the 11 patients who received the "classical" treatment (24).

CBT needs more scientific evidence of efficiency before it will be accepted as a leading mode of therapy for sleep abnormalities after TBI. Other forms of behavioral training/ adjustment of sleep habits (25) and blue light therapy (26) have shown preliminary encouraging results.

3. Conclusions

In spite of the technical advances in manufacturing safer motor cars and building better roads, the number of victims of motor vehicle accidents is constantly raising. Among them are millions with TBI and consequent impaired sleep. The data presented hereby indicate that there

is still an urgent need to expand the knowledge on this subject and to find better ways to manage the sleep abnormalities of the patients.

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