TELE-REHABILITATION GUIDELINE
Sleep and Fatigue after Traumatic Brain Injury

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I. Define, Assessment, Diagnosis

A. Definition:

1. Post Traumatic Fatigue (PTF) (Zasler, Katz, & Zafonte, 2013; Zollman, 2016): Subjective complaint for which there is no universally accepted definition. Most descriptions involve a lack of interest in, failure to initiate, and/or decreased capacity for attentional tasks and physical activities requiring self-motivation (as opposed to external stimulation).
    a. Often under-reported with variable incidence in the literature, ranging from 2% to 98% of Traumatic Brain Injury (TBI) patients.
    b. Central Fatigue: result of cerebral dysfunction
    c. Peripheral Fatigue: origins are purely physical, metabolic or muscular in nature
    d. There is overlap in central and peripheral causes of fatigue in patients with brain injury. Brain trauma often causes injuries to cerebral pathways involved in sensory and motor function resulting in weakness, spasticity, ataxia, impaired proprioception etc. This central impairment translates into peripheral increases in energy requirements and reduction of efficiency.
2. Sleep disorders (Zasler, Katz, & Zafonte, 2013; Aoun, Rawal, Attarian, & Sahni, 2019; DiTommaso, 2016):
    a. Because of variability in severity, recovery, and reporting of TBI, there is inconsistent data on sleep disturbances after head injury. Estimated prevalence in TBI patients is up to 84%, compared to approximately 30% in the normal population.
    b. Severity of TBI does not correlate with the severity of sleep disorder (Draganich, et al., 2019; Grima, Ponsford, Rajaratnam, & Pase, 2016)
    c. Hospitalized, acute TBI patients more commonly suffer from disorders of initiating and maintaining sleep whereas post-acute TBI patients more commonly experience disorders of excessive somnolence.

d. TBI patients are more likely to experience problems with sleep efficiency, more restless sleep during the night, early awakenings, decreased total sleep time, and nightmares (Draganich, et al., 2019; Duclos, et al., 2020; Grima, Ponsford, Rajaratnam, & Pase, 2016; Mathias & Alvaro, 2012)
e. Types of Sleep Disorders (Mathias & Alvaro, 2012; Castriotta & Murthy, 2011)
    i. Insomnia: Disrupted sleep characterized by problems with falling asleep, maintenance, and/or frequent awakenings. Symptoms occur at least 3 nights per week and result in impaired daytime functioning. (Zollman, 2016)
    ii. Hypersomnia: Excessive sleep quantity and daytime sleepiness
    iii. Parasomnia: undesirable events occur during sleep (sleep walking, nocturnal bed-wetting, etc.)
    iv. Obstructive sleep apnea (OSA): Intermittent apnea and asphyxia from upper airway obstruction and/or collapse that occurs despite continued respiratory effort (Webster, Bell, Hussey, Natale, & Kakshminarayan, 2001)
        1. Most commonly associated in males with obesity, older age, and snoring. (Webster, Bell, Hussey, Natale, & Kakshminarayan, 2001)
    v. Central sleep apnea: Lack of respiratory effort resulting in lack of airflow. (Webster, Bell, Hussey, Natale, & Kakshminarayan, 2001)
        1. May occur more commonly with TBI due to dysregulation of the autonomic system and injury to the ascending reticular activating system in the brainstem, prefrontal cortices, anterior cingulate, hippocampus, and/or parietal cortices (Webster, Bell, Hussey, Natale, & Kakshminarayan, 2001; DiTommaso, 2016)
        2. Weight changes, mood disturbances, medications, pain, and premorbid sleep disorders can exacerbate central sleep disorders resulting from TBI
    vi. Periodic limb movement disorder (PLMD): Bilateral rhythmic jerking or twitching movements in the lower extremities more so than the upper extremities. Often this movement goes unnoticed by the patient but disturbs quality of sleep resulting in fatigue and/or daytime sleepiness.
    vii. Restless leg syndrome (RLS): unpleasant sensations in the legs or feet that are temporarily relieved by movement. Symptoms

are present during the day but are often worse at night resulting in impaired sleep onset.

viii. Circadian Rhythm Disorder

ix. Narcolepsy: excessive urge to sleep at inappropriate times. Impaired sleep latency and sleep-onset REM.

B. Assessment:

1. Sleep and fatigue disorders may be overlooked by medical professionals and often patients will not mention problems with sleep and/or fatigue despite high prevalence noted in the literature.
2. Poor sleep can increase risk for hypertension, heart disease, diabetes, and stroke. Furthermore, disrupted sleep can also lead to behavioral and cognitive issues in patients with TBI, both in the acute and chronic phases, thus identification of fatigue and sleep impairments is critical. (Draganich, et al., 2019; DiTommaso, 2016; Webster, Bell, Hussey, Natale, & Kakshminarayan, 2001)
3. History:
    a. Characterize patient's symptoms including onset, duration, evolution, and nature of complaint (problems falling asleep, staying asleep, early wakening, daytime sleepiness, fatigue, etc.)
    b. Detailed sleep-wake schedule: Sleep and wake times, Frequent napping
    c. Sleep hygiene: caffeine and alcohol intake, sleep environment, electronic devices
    d. How physical activity, cognitive load, and rest impact symptoms
    e. Mood impairments and/or agitation
    f. Cognitive impairments (i.e., memory difficulties, slow processing speed, impaired attention)
    g. Snoring or breathing interruptions
    h. Morning headaches
    i. Presence of dreams/nightmares, vocalizations during sleep.
    j. Review of daily function: work, activities of daily living, etc.
    k. Past medical history of sleep disorder, TBI, stroke, other neurological disorder, psychiatric disorders, obesity, endocrine disease
4. Physical exam:
    a. Vital signs
    b. General appearance/level of alertness
    c. Head and neck exam for structural causes of OSA and palpation of thyroid
    d. Neurological Exam
        i. Cranial nerve exam including light/dark differentiation
        ii. Assess for cognitive deficits
        iii. Motor exam can help delineate peripheral causes of fatigue
    e. Cardiovascular exam

f. Integumentary exam

5. Self-Report Assessments (Zasler, Katz, & Zafonte, 2013; DiTommaso, 2016): Help quantify and evaluate effects of fatigue/sleep impairments, not used for confirmatory diagnosis.
    a. Fatigue: No validated measurement for PTF.
        i. Fatigue Severity Scale (FSS)
        ii. Fatigue Impact Scale (FIS)
        iii. Modified Fatigue Impact Scale (MFIS)
        iv. TBI patients demonstrate significantly greater fatigue scores on the FSS and FIS compared to non-TBI controls. (LaChapelle & Finlayson, 1998)
    b. Sleep disorders:
        i. Epworth Sleepiness Scale
        ii. Pittsburgh Sleep Quality Index
        iii. Snoring, Tired, Observed, Blood Pressure, Body Mass Index, Age, Neck Circumference, and Gender (STOPBANG) Questionnaire (Nakase-Richardson, et al., 2020)
    c. Sleep Diary

C. Diagnosis

1. Significant overlap between symptoms of fatigue, sleep disorders, and/or other underlying medical conditions makes accurate diagnosis challenging.
2. Fatigue related to TBI is a diagnosis of exclusion after other conditions have been ruled out.
3. Differential diagnosis:
    a. Central fatigue or sleep disorder
    b. Obstructive sleep apnea
    c. Periodic limb movement disorder (PLMD)
    d. Restless leg syndrome (RLS)
    e. Circadian Rhythm Disorder
    f. Dyssomnias – insomnia, parasomnia, Hypersomnia
    g. Nutritional deficiency (Vitamin D, iron deficiency, etc.)
    h. Endocrine disorder (Hypothyroidism, diabetes mellitus, growth hormone deficiency, etc.)
    i. Anemia
    j. Cardiovascular disease
    k. Dehydration
    l. Infection
    m. Hydrocephalus
    n. Recurrent hemorrhage

o. Psychiatric disorder (depression, anxiety, drug/alcohol dependency, etc.)
p. Medication side effect
    i. Many drugs exacerbate fatigue and sleep impairments including but not limited to: antiepileptics, antihistamines, antipsychotics, corticosteroids, antiarrhythmics, antidepressants, antiemetics, antihypertensives, muscle relaxants, pain medications

4. Laboratory studies:
    a. Complete blood count
    b. Basic metabolic panel
    c. Thyroid function panel
    d. Iron panel
    e. Growth hormone & Insulin-like growth factor
    f. Testosterone level
5. Supplemental Tools (Zasler, Katz, & Zafonte, 2013; Draganich, et al., 2019; Aoun, Rawal, Attarian, & Sahni, 2019; DiTommaso, 2016; Castriotta & Murthy, 2011):

    a. Overnight pulse oximetry
    b. Polysomnography (PSG): Gold standard for measurement of sleep. Assesses sleep architecture and efficiency. Evaluates for OSA, central sleep apnea, & restless leg syndrome.
    c. Multiple Sleep Latency test: Validated, objective measure of daytime sleepiness. Utilizes daytime PSG recordings. Helps to differentiate pathological sleep abnormalities from subjective sleepiness and fatigue.
    d. Electroencephalography (EEG): Used to evaluate for seizure activity.
    e. Actigraphy: Lower cost alternative to PSG in which patient wears watch-like device on a limb. Evaluates for circadian rhythm impairments or poor sleep hygiene.

II. Management:

A. Fatigue & general sleep disorders (Zasler, Katz, & Zafonte, 2013; Zollman, 2016; Aoun, Rawal, Attarian, & Sahni, 2019; Grima, Ponsford, Rajaratnam, & Pase, 2016; Castriotta & Murthy, 2011):
    1. Compensatory techniques for energy efficiency
    2. Education of patient and caregiver
    3. Sleep hygiene:
        a. Routine sleep and wake times
        b. Daytime naps should be limited to less than 30 minutes, and should be taken before 3:00pm
        c. Limiting overall Caffeine intake, avoiding caffeine 4-6 hours before sleep
        d. Avoidance of nicotine and alcohol

e. No heavy eating before bedtime
f. Daily aerobic exercise late afternoon or early evening; at least 3 hours prior to bedtime
g. Appropriate sleep environment: comfortable bed, minimization of noise, minimizing light, avoiding extremes of temperature.
h. If unable to sleep, get out of bed.

4. Psychiatric care or psychological care including cognitive behavioral therapy, biofeedback, meditation, and relaxation therapies.
5. Medications:
    a. Melatonin: Decreases sleep onset latency. Regulates Circadian Rhythms. First line consideration for disrupted sleep due to favorable side effect profile.
    b. Neurostimulants: Increases wakefulness. Decreases REM sleep.
        i. Methylphenidate (Ritalin): Doses 5-60mg/day utilized
        ii. Dextroamphetamines (Adderall): doses 5-60mg/day utilized
        iii. Atomexitine
        iv. Modafinil (Provigil): recommended dosing 200mg/day
        v. Amantadine
    c. Antidepressants: Directly affects sleep by improving sleep architecture and efficiency. May reduce REM sleep percentage.
        i. Trazodone: Commonly used to treat insomnia after TBI
        ii. Selective Serotonin Reuptake Inhibitor (SSRI): Indirectly effects sleep by treating mood disorders resulting in impaired sleep.
        iii. TCAs typically avoided due to anticholinergic side effect
    d. Antihistamines (i.e. Diphenhydramine): Increase non-REM sleep. Adverse cognitive effects in TBI patients due to anticholinergic properties.
    e. Antiepileptics: Sleep disorders can be treated with antiepileptic medications by utilizing the sedating side effects of the medications.
    f. Sedatives/hypnotics: Decreases phasic interruption of sleep. Increased total sleep time. Can result in physical dependence, sedation, and physical/cognitive impairments.
        i. Benzodiazepines
        ii. Zolpidem (Ambien), Eszopiclone (Lunesta)
    g. Antipsychotics (i.e. Quetiapine, Risperidone, Olanzapine, etc.)
    h. Ginkgo Biloba

B. Specific sleep disorders (Zasler, Katz, & Zafonte, 2013; Aoun, Rawal, Attarian, & Sahni, 2019; DiTommaso, 2016):
    1. OSA: Dental devices, Oxygen supplementation via nasal cannula, CPAP or BiPAP, uvulopalatophyaryngoplasty, tracheostomy
    2. Central sleep Apnea: CPAP or BiPAP
    3. RLS:

a. Avoidance of exacerbating substances: caffeine, alcohol, & nicotine
b. Physical modalities: hot or cold baths, whirlpools, massage, vibratory or electrical stimulation
c. Vitamin supplementation, electrolyte replenishment, iron supplementation
d. TED hose for patients with varicose veins
e. Medications: dopaminergic agents are first line.
    i. Levadopa with carbidopa: Start 10/100mg PO TID-QID.
    ii. Pramipexole: Start 0.125mg QPM, 2-3 hours before bedtime. Increase by 0.125mg/day q4-7 days. Max dose 0.5mg/day.
    iii. Ropinirole hydrochloride: Start 0.25mg QPM x2 days then increase to 0.5mg x5 days, then 0.5mg/day qwk until optimal effect. Max 4mg/day.
    iv. Benzodiazepines: Clonazepam
    v. Opioids
    vi. Gabapentin indicated for patients with associated pain/neuropathy

b. Circadian Rhytham Disorders: Bright light therapy and Melatonin

This guideline was developed to improve health care access in Arkansas and to aid health care providers in making decisions about appropriate patient care. The needs of the individual patient, resources available, and limitations unique to the institution or type of practice may warrant variations.

Guideline Developers

Guideline developed by Dr. Lindsay Mohney, DO, in collaboration with the TRIUMPH team led by Thomas S. Kiser, MD, and Rani H Lindberg, MD.

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