Practice Parameters for the Clinical Evaluation and Treatment of Circadian Rhythm Sleep Disorders

An American Academy of Sleep Medicine Report

The expanding science of circadian rhythm biology and a growing literature in human clinical research on circadian rhythm sleep disorders (CRSDs) prompted the American Academy of Sleep Medicine (AASM) to convene a task force of experts to write a review of this important topic. Due to the extensive nature of the disorders covered, the review was written in two sections. The first review paper, in addition to providing a general introduction to circadian biology, addresses "exogenous" circadian rhythm sleep disorders, including shift work disorder (SWD) and jet lag disorder (JLD). The second review paper addresses the "endogenous" circadian rhythm sleep disorders, including advanced sleep phase disorder (ASPD), delayed sleep phase disorder (DSPD), irregular sleep-wake rhythm (ISWR), and the non-24-hour sleep-wake syndrome (nonentrained type) or free-running disorder (FRD). These practice parameters were developed by the Standards of Practice Committee and reviewed and approved by the Board of Directors of the AASM to present recommendations for the assessment and treatment of CRSDs based on the two accompanying comprehensive reviews. The main diagnostic tools considered include sleep logs, actigraphy, the Morningness-Eveningness Questionnaire (MEQ), circadian phase markers, and polysomnography. Use of a sleep log or diary is indicated in the assessment of patients with a suspected circadian rhythm sleep disorder (Guideline). Actigraphy is indicated to assist in evaluation of patients suspected of circadian rhythm disorders (strength of recommendation varies from "Option" to "Guideline," depending on the suspected CRSD). Polysomnography is not routinely indicated for the diagnosis of CRSDs, but may be indicated to rule out another primary sleep disorder (Standard). There is insufficient evidence to justify the use of MEQ for the routine clinical evaluation of CRSDs (Option). Circadian phase markers are useful to determine circadian phase and confirm the diagnosis of FRD in sighted and unsighted patients but there is insufficient evidence to recommend their routine use in the diagnosis of SWD, JLD, ASPD, DSPD, or ISWR (Option). Additionally, actigraphy is useful as an outcome measure in evaluating the response to treatment for CRSDs (Guideline). A range of therapeutic interventions were considered including planned sleep schedules, timed light exposure, timed melatonin doses, hypnotics, stimulants, and alerting agents. Planned or prescribed sleep schedules are indicated in SWD (Standard) and in JLD, DSPD, ASPD, ISWR (excluding elderly-demented/nursing home residents), and FRD (Option). Specifically dosed and timed light exposure is indicated for each of the circadian disorders with variable success (Option). Timed melatonin administration is indicated for JLD (Standard); SWD, DSPD, and FRD in unsighted persons (Guideline); and for ASPD, FRD in sighted individuals, and for ISWR in children with moderate to severe psychomotor retardation (Option). Hypnotic medications may be indicated to promote or improve daytime sleep among night shift workers (Guideline) and to treat jet lag-induced insomnia (Option). Stimulants may be indicated to improve alertness in JLD and SWD (Option) but may have risks that must be weighed prior to use. Modafinil may be indicated to improve alertness during the night shift for patients with SWD (Guideline).

Keywords: Circadian, light therapy, melatonin, naps, jet lag, shift work

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Circadian Rhythm Sleep Disorders: Part I, Basic Principles, Shift Work and Jet Lag Disorders

An American Academy of Sleep Medicine Review

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Objective: This the first of two articles reviewing the scientific literature on the evaluation and treatment of circadian rhythm sleep disorders (CRSDs), employing the methodology of evidence-based medicine. In this first part of this paper, the general principles of circadian biology that underlie clinical evaluation and treatment are reviewed. We then report on the accumulated evidence regarding the evaluation and treatment of shift work disorder (SWD) and jet lag disorder (JLD).

Methods: A set of specific questions relevant to clinical practice were formulated, a systematic literature search was performed, and relevant articles were abstracted and graded.

Results: A substantial body of literature has accumulated that provides a rational basis the evaluation and treatment of SWD and JLD. Physiological assessment has involved determination of circadian phase using core body temperature and the timing of melatonin secretion. Behavioral assessment has involved sleep logs, actigraphy and the Morningness-Eveningness Questionnaire (MEQ). Treatment interventions fall into three broad categories: 1) prescribed sleep scheduling, 2) circadian phase shifting (“resetting the clock”), and 3) symptomatic treatment using hypnotic and stimulant medications.

Conclusion: Circadian rhythm science has also pointed the way to rational interventions for the SWD and JLD, and these treatments have been introduced into the practice of sleep medicine with varying degrees of success. More translational research is needed using subjects who meet current diagnostic criteria.

Keywords: Circadian rhythm sleep disorders

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Circadian Rhythm Sleep Disorders: Part II, Advanced Sleep Phase Disorder, Delayed Sleep Phase Disorder, Free-Running Disorder, and Irregular Sleep-Wake Rhythm

An American Academy of Sleep Medicine Review

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Objective: This the second of two articles reviewing the scientific literature on the evaluation and treatment of circadian rhythm sleep disorders (CRSDs), employing the methodology of evidence-based medicine. We herein report on the accumulated evidence regarding the evaluation and treatment of Advanced Sleep Phase Disorder (ASPD), Delayed Sleep Phase Disorder (DSPD), Free-Running Disorder (FRD) and Irregular Sleep-Wake Rhythm (ISWR).

Methods: A set of specific questions relevant to clinical practice were formulated, a systematic literature search was performed, and relevant articles were abstracted and graded.

Results: A substantial body of literature has accumulated that provides a rational basis the evaluation and treatment of CRSDs. Physiological assessment has involved determination of circadian phase using core body temperature and the timing of melatonin secretion. Behavioral assessment has involved sleep logs, actigraphy and the Morningness-Eveningness Questionnaire (MEQ). Treatment interventions fall into three broad categories: 1) prescribed sleep scheduling, 2) circadian phase shifting (“resetting the clock”), and 3) symptomatic treatment using hypnotic and stimulant medications.

Conclusion: Circadian rhythm science has also pointed the way to rational interventions for CRSDs and these treatments have been introduced into the practice of sleep medicine with varying degrees of success. More translational research is needed using subjects who meet current diagnostic criteria.

Keywords: Circadian rhythm sleep disorders

Citation: Sack R; Auckley D; Auger RR; Carskadon MA; Wright KP; Vitiello MV; Zhdanova IV. Circadian rhythm sleep disorders: Part II, advanced sleep phase disorder, delayed sleep phase disorder, free-running disorder, and irregular sleep-wake rhythm. SLEEP 2007;30(11):1484-1501.
Efficacy and Safety of Doxepin 1 mg, 3 mg, and 6 mg in Adults with Primary Insomnia

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Study Objectives: To evaluate the efficacy and safety of doxepin 1, 3, and 6 mg in insomnia patients.

Design: Adults (18-64 y) with chronic primary insomnia (DSM-IV) were randomly assigned to one of four sequences of 1 mg, 3 mg, and 6 mg of doxepin, and placebo in a crossover study. Treatment periods consisted of 2 polysomnographic assessment nights with a 5-day or 12-day drug-free interval between periods. Efficacy was assessed using polysomnography (PSG) and patient-reported measures. Safety analyses included measures of residual sedation and adverse events.

Measurements and Results: Sixty-seven patients were randomized. Wake time during sleep, the a priori defined primary endpoint, was statistically significantly improved at the doxepin 3 mg and 6 mg doses versus placebo. All three doses had statistically significant improvements versus placebo for PSG-defined wake after sleep onset, total sleep time, and overall sleep efficiency (SE). SE in the final third-of-the-night also demonstrated statistically significant improvement at all doses. The doxepin 6 mg dose significantly reduced subjective latency to sleep onset. All three doxepin doses had a safety profile comparable to placebo. There were no statistically significant differences in next-day residual sedation, and sleep architecture was generally clinically preserved.

Conclusions: In adults with primary insomnia, doxepin 1 mg, 3 mg, and 6 mg was well-tolerated and produced improvement in objective and subjective sleep maintenance and duration endpoints that persisted into the final hour of the night. The side-effect profile was comparable to placebo, with no reported anticholinergic effects, no memory impairment, and no significant hangover./next-day residual effects. These data demonstrate that doxepin 1 mg, 3 mg, and 6 mg is efficacious in improving the sleep of patients with chronic primary insomnia.

Keywords: Chronic insomnia, sleep maintenance insomnia, terminal insomnia, doxepin, wake time after sleep onset, total sleep time, wake time during sleep

Citation: Roth T; Rogowski R; Hull S; Schwartz H; Koshorek G; Corser B; Seiden D. Efficacy and safety of doxepin 1 mg, 3 mg, and 6 mg in adults with primary insomnia. SLEEP 2007;30(11):1555-1561.

Idiopathic Hypersomnia: A Study of 77 Cases

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Study Objectives: To review the clinical and polysomnographic characteristics of idiopathic hypersomnia as well as the long-term response to treatment.

Setting: The Respiratory Support and Sleep Centre at Papworth Hospital, Cambridge, UK.

Patients and Design: A large database of more than 6000 patients with sleep disorders was reviewed. A retrospective study of the clinical and polysomnographic characteristics of 77 patients with idiopathic hypersomnia was performed. Comparison with a similar group of patients with narcolepsy was performed. The response to drug treatment was assessed in 61 patients over a mean follow-up of 3.8 years.

Measurements and Results: Idiopathic hypersomnia was 60% as prevalent as narcolepsy. Comparison with a similar group of patients with narcolepsy showed that those with idiopathic hypersomnia were more likely to have prolonged unrefreshing daytime naps, a positive family history, increased slow-wave sleep, and a longer sleep latency on the Multiple Sleep Latency Test. The results of the Multiple Sleep Latency Test were not helpful in predicting disease severity or treatment response. The clinical features were heterogeneous and of variable severity. The majority of patients with idiopathic hypersomnia had symptoms that remained stable over many years, but 11% had spontaneous remission, which was never seen in narcolepsy. Two thirds of patients with idiopathic hypersomnolence had a sustained improvement in daytime somnolence with medication, although a third needed high doses or combinations of drugs.

Conclusions: Idiopathic hypersomnolence has characteristic clinical and polysomnographic features but the prolonged latency on the Multiple Sleep Latency Test raises doubt about the validity of this test within the current diagnostic criteria. The disease often responds well to treatment and a substantial minority of patients appear to spontaneously improve.

Keywords: Idiopathic hypersomnia, narcolepsy, polysomnography, treatment

Citation: Anderson KN; Pilsworth S; Sharples LD; Smith IE; Shneerson JM. Idiopathic hypersomnia: a study of 77 cases. SLEEP 2007;30(10):1274-1281.
Effects Of Moderate Sleep Deprivation and Low-Dose Alcohol On Driving Simulator Performance and Perception In Young Men

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Study Objective: To determine the combined effects of sleep restriction and low-dose alcohol on driving simulator performance, EEG, and subjective levels of sleepiness and performance in the mid-afternoon.

Design: Repeated measures with 4 experimental conditions. Normal sleep without alcohol, sleep restriction alone (4 hours) and sleep restriction in combination with 2 different low blood alcohol concentrations (0.025 g/dL and 0.035 g/dL).

Setting: Sleep Laboratory, Adelaide Institute for Sleep Health.

Participants: Twenty-one healthy young men, aged 18-30 years, mean (±SD) = 22.5(±3.7) years, BMI = 25(±6.7) kg/m²; all had normal sleep patterns and were free of sleep disorders.

Measurements: Participants completed a 70-minute simulated driving session, commencing at 14:00. Driving parameters included steering deviation, braking reaction time, and number of collisions. Alpha and theta EEG activity and subjective driving performance and sleepiness were also measured throughout the driving task.

Results: All measures were significantly affected by time. Steering deviation increased significantly when sleep restriction was combined with the higher dose alcohol. This combination also resulted in a significant increase in alpha/theta EEG activity throughout the drive, as well as greater subjective sleepiness and negative driving performance ratings compared to control or sleep restriction alone.

Discussion: These data indicate that combining low-dose alcohol with moderate sleep restriction results in significant decrements to subjective alertness and performance as well as to some driving performance and EEG parameters. This highlights the potential risks of driving after consumption of low and legal doses of alcohol when also sleep restricted.

Keywords: Sleep, driving, alcohol, performance, perception

Citation: Vakulin A; Baulk SD; Catcheside PG; Anderson R; van den Heuvel CJ; Banks S; McEvoy RD. Effects of moderate sleep deprivation and low-dose alcohol on driving simulator performance and perception in young men. SLEEP 2007;30(10):1327-1333.