

Bright times for patients with cirrhosis and delayed sleep habits: a case report on the
beneficial effect of light therapy

Light therapy for sleep disturbance in cirrhosis

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To the Editor: In February 2011, an 82-year-old female was admitted into hospital for a chest infection. She had a history of viral cirrhosis, with a previous, minor episode of hepatic encephalopathy, a tendency to sleep-wake inversion, systemic hypertension, mood disorder, remote quadrantectomy for carcinoma breast, and accidental femur/fibula fractures. She had been bed-ridden for periods of time. At home, she was on treatment with benzodiazepines, evening melatonin, pregabalin, olanzapine, ursodeoxycholic acid, and lactitol. On admission, she was started on ceftriaxone. As response was incomplete, on day five she was swapped to piperacillin-tazobactam, with almost immediate benefit. Whilst in hospital, a marked alteration of the sleep-wake cycle was confirmed, with delayed sleep onset/offset times, numerous night awakenings, and excessive sleepiness in the morning. An electroencephalogram (EEG) recorded at 11:00 on day two

showed a slowed background rhythm at 7 Hz, interspersed with sequences of slower activity at 2-3 Hz, compatible with difficulties maintaining wakefulness (slow/fast EEG activity ratio: 7.3). Sleep timing/quality monitoring was started on day two, to include sleep diaries and repeat day-time assessments of subjective sleepiness (Karolinska Sleepiness Scale¹). On day three, the patient was moved to a room with controlled lighting (Amadea wall-mounted lamp, with variable light intensity/spectrum; Derungs-Waldmann Illuminotecnica, Italy). In order to advance her sleep-wake cycle, the lamp was set to automatically switch on at 06:30 and off at 22:30. In addition, light was more intense and blue-enriched in the morning, while it became less intense and red-enriched during the afternoon/evening hours. Sleep-wake rhythms progressively improved, with reduced daytime sleepiness and fewer night awakenings (Figure 1). An EEG recorded at 11:00 on day nine confirmed significant improvement (slow/fast activity ratio: 3.1). The patient was discharged on day 15 on ursodeoxycholic acid, lactitol, and a reduced dose of olanzapine. Advice was provided on sleep and light hygiene at home. At four weeks, she remained well, with a residual tendency to delayed sleep habits but considerably improved morning vigilance and night sleep quality, not taking benzodiazepines or melatonin.

Night sleep disturbance and delayed sleep habits are common in patients with cirrhosis, regardless of their neuropsychiatric status.^{2,3} Excessive daytime sleepiness/napping are also common, and generally associated with hepatic encephalopathy.³ The pathophysiology of these alterations is largely unknown. Delayed sleep habits have been ascribed to delayed melatonin rhythms, particularly in patients with decompensated cirrhosis.⁴ The combination of delayed sleep habits, impaired sleep quality and delayed melatonin rhythms is reminiscent of 'delayed sleep phase syndrome' (DSPS), a circadian disorder characterised by considerable delays in sleep onset/wake-up times compared to the healthy population. The goal of DSPS treatment is to re-synchronise the circadian clock with the 24-hour light/dark cycle: structured sleep-wake schedules and avoidance of exposure to bright light in the evening are advised. In addition, exposure to bright light shortly after morning awakening has been shown to advance sleep timing.⁵ Recent data suggest that bright blue

light may be particularly efficacious in favouring wakefulness and phase advancing the melatonin rhythm.⁶ In patients with cirrhosis, naturally occurring DSPS might be exacerbated by delayed hepatic melatonin metabolism and impaired sensitivity of the retinal-hypothalamic tract to light cues,⁷ increasing its prevalence and/or modulating its features.

In the patient presented, the observed, extreme delay in sleep-habits, bordering sleep-wake inversion, was probably the result of cirrhosis plus a combination of other factors, to include poor sleep/light hygiene, chronic use of benzodiazepines and inappropriate use of melatonin. Advance of the sleep-wake rhythm and amelioration of sleep was obtained by removal of the precipitants, enforced wake-up schedules, and appropriately timed light administration.

The treatment of sleep-wake disturbance in cirrhosis remains a challenge. Should the observed, beneficial effect of light therapy be confirmed by formal trials, a rational, non-pharmacological and side-effect free treatment might become available.

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Legends to Figures

Figure 1. Karolinska Sleepiness Scale scores (left axis, blue line) and number of night awakenings (right axis, pink line) prior to (based on reports from patient/carers), during (formal measurement) and after the inpatient stay (based on reports from patient/carers). Treatment regimes, including light therapy, light hygiene and sleep-wake schedules are also indicated. A progressive decrease in subjective daytime sleepiness and in the average number of night awakenings can be observed during and after the inpatient stay, most likely in relation to light treatment and the removal of potential precipitating factors, including treatment with melatonin and benzodiazepines and inadequate sleep-wake and light hygiene.

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