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Applying the 2015 Clinical Practice Guideline for the treatment of Circadian Rhythm Sleep Disorders to a Real World Patient



PHYSICIAN PROFILE

Katherine M. Sharkey, MD, PhD, FAASM

Assistant Professor of Medicine and Psychiatry & Human Behavior

Alpert Medical School of Brown University

Dr. Sharkey is Medical Director of the University Medicine Sleep Center, where she maintains a busy clinical practice, and Associate Director of the Sleep for Science Research Laboratory. Dr. Sharkey's research focuses on sleep and circadian rhythms as they relate to mood regulation and women's health. This case study, inspired by a few different patients in her practice, exemplifies an approach to treating elderly patients with Irregular Sleep-Wake Rhythm Disorder.

HISTORY OF PRESENT ILLNESS

Mrs. C is an 82 year-old woman with multiple medical problems, including dementia and hypothyroidism, who is referred to Dr. Sharkey for evaluation of insomnia and hallucinations. The patient is accompanied by her husband, who states that Mrs. C began having memory difficulties about 3 years ago. Her decline in functioning was accompanied by daytime sleepiness, hallucinations, and confusion, as well as nocturnal behaviors that included waking from sleep and getting out of bed with the intention of performing activities that did not make sense, e.g., getting dressed and ready to go grocery shopping at 3 am.

Mr. C reported that his wife retires to the bedroom around 10 pm - most of the time she falls asleep without difficulty. He reported that she wakes 2 to 4 times per night, usually to use the bathroom, and most of the time she can quickly fall back to sleep. Mr. C reports that his wife snores, has fragmented sleep, and awakens at night with hallucinations and confusion. She does not complain of restless legs symptoms or kicking her legs at night. Mr. C wakes her at 7 am to take her thyroid medicine (though they both agree that she is often already awake at this time). She stays in bed until 8:00-8:30 am then they both get up and have breakfast. The patient states that she feels best in the early afternoon, but her husband reports that he thinks she dozes too much during the day. Mr. C states that some of the daytime hallucinations appear to emanate from sleep - in other words, she will

be napping and then reports that she sees her son or sister in the room. Both Mr. and Mrs. C are distressed by the hallucinations.

PRELIMINARY EVALUATION

Pertinent physical exam findings include BMI: 32.4 kg/m², Mallampati class 4 airway with crowded posterior oropharynx, no cogwheel rigidity on neurologic exam, oriented to self, place, and purpose, MMSE = 25/30. Differential diagnosis in this patient includes:

- Obstructive sleep apnea (OSA)
- Irregular sleep-wake rhythm disorder (ISWRD)
- REM behavior disorder (RBD)

INITIAL PLAN AND FOLLOW-UP

Laboratory polysomnography was scheduled for Mrs. C. and arrangements were made for Mr. C to accompany her. Mr. C also agreed to keep a diary of Mrs. C's sleep for the two weeks before her follow-up visit.

The sleep study showed a few apneas and hypopneas, but her AHI with 4% hypopneas was less than 5 events per hour, and her oxygen saturation minimum was 89%, with 98.3% of the recording showing an oxygen saturation greater than 90%. The patient did not have any REM sleep during the study, but her sleep was fragmented with an arousal index of 22.1 events per hour and a sleep efficiency of 71%. No periodic limb movements were observed.

CLINICAL ASSESSMENT & TREATMENT PLAN

Mrs. C's sleep diary shows sleep patterns consistent with irregular sleep-wake rhythm

disorder - she has sleep fragmentation at night and intrusion of sleep into the day – possibly including REM sleep, which may explain why she is experiencing hallucinations after daytime naps.

Dr. Sharkey discussed treatment recommendations for ISWRD with Mr. and Mrs. C – specifically bright light therapy and melatonin administration. The AASM 2015 Clinical Practice Guidelines for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders recommend that clinicians treat ISWRD in elderly patients with dementia with light therapy (versus no treatment). This recommendation is based mainly on two trials that tested light therapy for improving sleep, circadian rhythms, and problematic daytime behaviors in institutionalized elderly patients with dementia. Light levels in these studies were 2500-5000 lux and patients sat in front of the light boxes for 60-120 minutes each morning. Based on these trials and other studies of bright light that showed positive effects of morning bright light exposure, including more consolidated rest periods at night with more activity and fewer naps and problematic behaviors during the day, Dr. Sharkey recommended morning bright light to Mr. and Mrs. C. They were reluctant to get a bright light box at the time, but noted that the room where Mrs. C sits in the morning is well lit and has south-facing windows.

Dr. Sharkey also discussed treating Mrs. C's ISWRD with melatonin. The AASM 2015 Clinical Practice Guidelines for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders suggest that clinicians avoid the use of melatonin as a treatment for ISWRD in older people with dementia (versus no treatment). This recommendation (which was noted to

be “weak” based on available evidence) is based mainly on a study of 25 elderly patients with dementia and ISWRD who took 6 mg slow-release melatonin and placebo for two weeks in a crossover design that included a 2 week baseline and 1 week washout period between treatments. Mean total sleep time (TST) estimated with actigraphy did not differ between the two treatments. Another trial comparing 2.5 mg slow-release melatonin, 10 mg immediate-release melatonin, and placebo in patients with Alzheimer's disease and sleep disturbance (but no formal diagnosis of ISWRD) also failed to show an increase in TST with either dose of melatonin compared to placebo. On the other hand, a study of 2.5 mg immediate-release melatonin in dementia patients in assisted living (but in whom ISWRD was not specifically diagnosed) showed an improvement in actigraphic sleep latency and increased TST compared to placebo. Importantly, this study also showed decreased positive affect, increased negative affect, and an increase in withdrawn behaviors with melatonin. Patients did not exhibit the withdrawal symptoms when melatonin was used in combination with increased all-day light exposure provided by increasing overhead lighting in the assisted living facility. Mr. and Mrs. C were interested in trying melatonin in combination with increasing her daytime light exposure, so melatonin, 3 mg immediate release, 1 tablet at bedtime was prescribed. All agreed that Mrs. C would need to be followed closely for depressive symptoms because of the increased risk described above.

The possibility of RBD cannot be excluded based on the patient's sleep study because no REM was recorded, however Mrs. C's symptoms do not justify the use of clonazepam at this time because a diagnosis of ISWRD

better explains her symptoms. In addition, the 2015 AASM Clinical Practice Guideline for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders recommends that clinicians avoid the use of sedative hypnotics sleep to treat elderly patients with dementia with ISWRD (versus no treatment) due to increased risk of falls and daytime sedation.

SECOND FOLLOW-UP

Mrs. C started taking melatonin since her last visit, and Mr. C has made a conscious effort to ensure that the drapes are open and that the room is bright when Mrs. C is sitting and watching TV in the morning. Mr. C states that he thinks it is helping her sleep at night. In addition, he says the hallucinations have improved.

When Mrs. C first started the melatonin, she would doze on and off in front of the TV until

around noon. Thus, Mr. C cut the melatonin in half and she is now taking 1.5 mg of immediate release melatonin. He notes that Mrs. C's sleep was still good at night even with the lower dose. Mrs. C also thinks that her sleep is better. She also reports that "various aches and pains in her body are not as bad and that she has not had as much trouble settling down at night." Neither the patient, nor her husband, has noted an increase in depressive symptoms; specifically, she has not had excessive sadness or crying, emotional lability, decreased interaction with others, or suicidal ideation since starting the melatonin.

Mrs. C should continue taking melatonin 1.5 mg at bedtime and consider a bright light box in the winter months. The patient will be seen by Dr. Sharkey again in 6-to 9 months but is encouraged to return sooner if symptoms worsen.

The recommendations and tactics described in the case studies reflect the best practices of AASM members and are not the official position or policy of the AASM.

KEY TAKEAWAYS:

- Bright light therapy in the morning is recommended for patients with dementia and ISWRD. If acquiring a bright light box is not feasible, teaching patients and their families about outdoor light exposure and increasing the brightness of ambient lighting may be effective.
- The 2015 AASM Clinical Practice Guideline for the Treatment of Intrinsic Circadian Rhythm Sleep-Wake Disorders suggests that clinicians avoid use of melatonin in elderly patients with dementia for the treatment of ISWRD, based on a small number of studies that failed to show an improvement in total sleep time and one study that showed adverse effects on mood when melatonin was used alone. If clinicians and patients want to do a trial of melatonin, patients should be monitored closely for sedation and mood symptoms. Melatonin in combination with bright light may be effective, however, and more studies are needed in this area.