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BOARD REVIEW CORNER

I Couldn't Sleep at all Last Night

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Question 1

A 54-year-old female was diagnosed with Restless Legs Syndrome (RLS) two months ago by her primary care physician and had been started on levodopa-carbidopa at 25/100 mg one hour before her bedtime at 10 PM. She had not had polysomnography performed or any laboratory evaluation. She has had an improvement in her sleep with better subjective sleep and a lessening of her urge to move her legs before sleep. She is now referred to you complaining of problems of restless legs when she is relaxing in the afternoon around 3 PM. She also relates that her husband is noticing arm movements in her sleep. You advise her to:

a. begin oral ferrous sulfate 325 mg three times a day
b. change to carbamazepine 200 mg at bedtime
c. change to ropinirole .25 mg at bedtime
d. increase her dose of levodopa-carbidopa to 50/200 at bedtime
e. take additional levodopa-carbidopa at 3 PM

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A Case of Insomnia with Incontinence of Emotion

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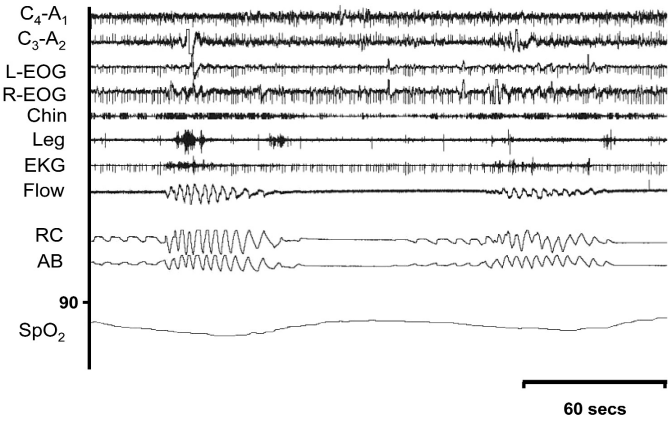
Question 2

A 58 year-old lady with Amyotrophic Lateral Sclerosis presents with difficulty falling asleep and 'mood swings'. Her daughter reports recent worsening muscle weakness that has confined her mother to her wheelchair. On examination, the patient has significant lower extremity weakness, and although she is able to lift her arms she is unable to hold a comb. She reports being depressed, anxious, and bursts into tears during the office visit. Additionally, her daughter reports that lately her mother 'drools' saliva and that her speech is slurred. Laboratory examination was normal except for elevated serum bicarbonate of 38 mEq/L (normal range, 21-28 mEq/L). Overnight polysomnography was performed and revealed a prolonged sleep latency (3 hours) following which she fell asleep for just 2 hours (sleep efficiency of 25%). A representative segment of her polysomnogram is shown below.



Which of the following would be the most likely to worsen her insomnia?:

a. Prescription of a sedative hypnotic medication.
b. Bilevel positive airway pressure therapy with or without oxygen.
c. Prescription of a sedating serotonin reuptake inhibitor antidepressant.
d. Performance of a tracheostomy.
e. Prescription of a medication with anti-cholinergic properties.

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ANSWER 1: C

DISCUSSION

This is an example of augmentation; a side effect of dopaminergic medications used for RLS and is especially seen with levodopa-carbidopa as opposed to ropinirole, pergolide or pramipexole. Of the choices given, changing her to ropinirole would be the safest and easiest choice for this patient. The incidence of augmentation is much less with this medication and there is now good evidence supporting its efficacy in RLS.

Adding oral iron is still somewhat controversial. However, ferritin levels and iron studies should be done before beginning this therapy, because there has been case report literature on the occurrence of hemochromatosis and RLS. Hemochromatosis is uncommon but not rare, and adding iron would be contraindicated. While there have been isolated reports of RLS improving with carbamazepine, there are clearly more efficacious and safer medications. Increasing the dose of the levodopa-carbidopa may make the symptoms of augmentation worse. Adding an additional dose of the levodopa-carbidopa in the afternoon would help with the afternoon symptoms but a clearer alternative would be to use a medication that would have a less chance of causing the augmentation and eliminating the need for additional medication.

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ANSWER 2: A

DISCUSSION

This patient has alveolar hypoventilation and obstructive sleep apnea secondary to neuromuscular weakness manifesting as insomnia. Thus, measures directed at treating sleep-disordered breathing should improve this patient's insomnia. Correction of the ventilatory insufficiency by the administration of positive airway pressure therapy with or without oxygen has been shown to prolong life in these individuals (response B).[1] Such ventilatory assistance may be administered using a non-invasive mask or in some individuals may require tracheostomy (response D).[2]

Slurred speech, incontinence of emotion (*pseudobulbar palsy*), and 'drooling' of saliva signify bulbar involvement due to Amyotrophic Lateral Sclerosis (ALS). This form of ALS may be associated with difficulty swallowing and recurrent aspiration pneumonias, which, in turn, may warrant tracheostomy.[3] The 'drooling' of saliva can be managed by prescribing anti-cholinergic agents, and thereby provide symptom relief (response E).[4]

Recognition of sleep-disordered breathing is important in such patients, and in this particular case was suggested by the constellation of elevated serum bicarbonate levels (compensatory metabolic alkalosis), sleep complaints, and history of ALS. In patients with ALS, weakness of upper airway, diaphragm, and other respiratory muscles predispose them to develop sleep-disordered breathing.[5] Depression may occur and selective serotonin reuptake inhibitor (SSRI) antidepressants can be efficacious (response C). In experimental animals with sleep apnea, serotonergic agents can improve apnea but clinical studies have been disappointing.[6]

Although patients with alveolar hypoventilation may present with excessive daytime sleepiness, insomnia secondary to sleep-disordered breathing is not uncommon – especially in women.[7,8] Sleep-disordered breathing can worsen with sedative-hypnotic medications, although the effect is not large.[9] Nevertheless, in this particular patient with neuromuscular weakness and perhaps greater sensitivity to respiratory depressants, it would be unwise to prescribe a hypnotic as initial therapy for insomnia. Treatment directed at sleep-disordered breathing, the underlying cause for insomnia, would be more effective.

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