

# Mirtazapine for suspected REM sleep behavior disorder and depression: A case report

Ouellet Jennifer A\*, Walke Lisa M and Kumar Chandrika

Department of Geriatrics, Internal Medicine, Yale University, USA

## Abstract

**Objective:** The objectives of this report are to a) review the clinical manifestations and therapy for REM Sleep Behavior Disorder in older adults with depression and b) explore the potential benefits of mirtazapine use for this condition.

**Methods:** A case report of an 85-year-old male with symptoms of REM Sleep Behavior Disorder and Depression.

**Results:** Symptoms of depression and disordered sleep improved after initiation of low dose mirtazapine.

**Conclusion:** Mirtazapine could be considered as a potential therapy for REM Sleep Behavior Disorder in patients with concurrent depression.

## Background

REM sleep behavior disorder (RBD) is a parasomnia characterized by dream enactment behaviors that emerge due to loss of atonia during REM sleep, affecting 0.3 to 1.15% of patients over the age of 60 [1]. RBD is associated with alpha synuclein-related diseases (e.g. Parkinson's Disease, Lewy Body Disease, multiple system atrophy) structural pontine lesions and orexin deficiency. It can also arise as a side effect to medications such as selective serotonin reuptake inhibitors (SSRI) and beta blockers [1,2]. Management includes avoidance or cessation of potentially offending medications and environmental modifications to avoid injury. For severe or refractory cases, first line pharmacotherapy includes melatonin and clonazepam [3].

## Case report

EC is an 85-year-old male with a history of multiple lacunar strokes and secondary parkinsonism who presented to the geriatrics clinic for follow up of cognitive impairment and gait instability. After two years of stable cognitive testing, his Saint Louis University Mental Status Examination (SLUMS) score decreased from 20/30 to 15/30 over eight months, indicating a decline in cognition. He also developed depressive symptoms with passive suicidal ideation and anorexia, and was found to have a positive screen for depression on the Geriatric Depression Scale (GDS) with a score of 6/15. Frequent dream enactment behaviors precluded his wife from sleeping in the same bed. He was not on any medications known to cause or exacerbate RBD, though he previously developed agitation with SSRI use. A polysomnogram two years prior had diagnosed obstructive sleep apnea and noted periodic limb movements during REM sleep. The patient's symptoms, however, had changed since this polysomnogram to include dream enactment behaviors. MRI brain was notable for bilateral basal ganglia infarcts, however he had no focal deficits on examination. Given depression, anorexia, and disordered sleep, EC was started on mirtazapine 7.5 mg qHS. Two weeks later, EC and his wife noted reduction in depressive symptoms and dream enactment behaviors. He was continued on low dose mirtazapine with sustained improvement.

## Discussion

The American Academy of Sleep Medicine diagnostic criteria for RBD include: 1) Repeated vocalizations or complex motor behaviors during sleep, 2) Evidence of above behaviors during REM sleep on polysomnogram or clinical history of dream enactment, 3) Evidence of loss of atonia during REM sleep on polysomnogram, and 4) Absence of more likely alternative diagnosis such as other sleep disorders or substance use. The differential diagnosis of RBD includes other sleep disorders (such as narcolepsy, nocturnal frontal lobe epilepsy, and periodic limb movements of sleep), dissociative states, and substance use [1]. Longitudinal studies have demonstrated conversion to an alpha synuclein-related neurodegenerative disease in up to 80% of patients with RBD, although RBD can predate a diagnosis of a neurodegenerative disease by decades [1,2].

Though patient EC had polysomnogram testing showing alternative sleep disorders (periodic limb movements of sleep and obstructive sleep apnea), the change in his disordered sleep symptoms combined with his parkinsonism warranted re-evaluation. Specifically, his complex motor behaviors and dream enactment behaviors raised the clinical suspicion for RBD.

It was apparent that the patient's lack of sleep and low mood were both substantially impacting both his day to day function and the ability of his wife to care safely for the patient at home. While we hypothesized that treatment of his disordered sleep would ultimately improve the patient's mood, we were concerned with the severity of depressive symptoms the patient was experiencing and made the clinical decision to first target his depression.

**Correspondence to:** Jennifer Ouellet, Geriatric Medicine Fellow, E.S. Harkness Memorial Hall, Building A 367 Cedar Street, Room 311, New Haven, CT 06510, USA, Tel: 401-451-5077; Fax: 203-688-4209; jennifer.ouellet@yale.edu

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Available treatment options generally base themselves on the premise that depression and sleep disturbances share a bidirectional relationship and so the adoption of measures that address specifically one of the conditions will reciprocally benefit the other [4]. The risks and benefits of several medications including mirtazapine, SSRIs, serotonin and norepinephrine reuptake inhibitors (SNRIs) and bupropion were considered for this patient with pre-existing disordered sleep and with prior adverse reactions to certain SSRIs. EC's clinical picture of depressed mood, poor sleep and anorexia made mirtazapine an attractive treatment option. There was concern, however, his prior reaction to SSRI medications and the known association of SSRIs and SNRIs with exacerbation of RBD [5] that he would experience worsening in his disordered sleep behaviors. A literature search revealed less risk of exacerbation of RBD with mirtazapine as compared to SSRI and SNRI medications, though case studies have been reported [6].

The decision was made to trial low dose mirtazapine to target the patient's depressive symptoms, with close clinical follow up and communication with the patient and his wife. The improvement in the patient's symptoms was so significant that use of an alternative agent for disordered sleep was not necessary. Mirtazapine's mechanism of action is primarily as a central presynaptic alpha2-adrenergic antagonist, resulting in increased release of both norepinephrine and serotonin. It also however, is a potent antagonist of H1 receptors. We hypothesized that successful treatment of his sleep-related symptoms with mirtazapine may be due to its anti-histaminergic properties, especially notable at lower doses. Of note, both SSRI and SNRI antidepressants lack anti-histaminergic properties [7]. Though there is no known role for histamine in the pathophysiology of RBD, the improvement

of symptoms in this patient could be due to histaminergic effects. Mirtazapine should be considered as an alternative treatment agent in high-risk elderly patients, especially those with comorbid anorexia or depression.

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