

CLINICAL VIGNETTE

Mirtazapine Abating Neuropsychiatric Symptoms in Dementia

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Introduction

Mirtazapine is an atypical antidepressant distinct from other classes of antidepressants that include selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), serotonin modulators, tricyclics, and monoamine oxidase inhibitors (MAO). It is referred to as a noradrenergic and specific serotonergic antidepressant (NaSSA). Mirtazapine inhibits alpha-2adrenergic receptors, and antagonizes H1 histamine receptor, and 5-HT_{2A}, 5-HT_{2C}, and 5-HT₃ serotonin receptors, but does not affect 5-HT₁ receptors. It also has a moderate to weak effect on peripheral cholinergic, alpha-1adrenergic, dopaminergic and muscarinic receptors.^{1,2}

Case

A 101-year-old female with severe late-onset Alzheimer's dementia with behavioral disturbances, sleep disturbance and progressive weight loss, resides in a skilled nursing facility for long-term care. At baseline she is oriented only to self; and does not know location or year.

Her most prominent neuropsychiatric symptoms were audio-visual hallucinations and delusions without insight. These usually consist of seeing people who are not there. One of her more disconcerting hallucinations is seeing a small boy crying in the corner of her room. This recurrent hallucination caused fear, tearfulness and emotional distress.

The patient also has persistent weight loss despite medical evaluation and treatment recommendations from a dietician and a speech pathologist. Her low oral intake was concerning as a symptom of depression. In the past, she had taken mirtazapine with adequate weight gain, but the medication was discontinued at request of her power of attorney (POA) after her weight improved.

The patient appeared frail and cachectic, with recorded weight loss of 20 pounds over the past 18 months. Her body mass index (BMI) decreased from 19 to 15. She appeared visibly distressed, staring out her window into the facility's courtyard where residents and their families congregated. She stated that they were going to "break into her room and steal her valuables". She was at her baseline, only oriented to self, and did not know where she was or the year. She became tearful when she looked at the corner of her room and reported seeing a small boy crying.

Given her low appetite, poor sleep quality, and concern for severe mood disorder with psychotic features, we re-initiated mirtazapine 15mg orally at bedtime. We expected improvement in overall mood and sleep quality and that her weight would increase, or stop decreasing.

At one-month follow-up visit, her weight remained stable. Her mood improved and she was pleasantly engaged during the examination. She was sleeping better and was more awake in the morning, and participated more in personal care and eating. She had decreased active delusions and paranoia. She continued to acknowledge seeing people in the room, but did not report the boy crying in the corner and denied other distressing hallucinations.

There is a paucity of literature regarding the effect of mirtazapine on neuropsychiatric symptoms in patients with dementia. The Study of Mirtazapine for Agitated Behaviours in Dementia (SYMBAD) trial by Banerjee et al evaluated the use of mirtazapine for the treatment of agitation in Alzheimer's disease.³ But we found no published trials examining the effect of mirtazapine on hallucinations in demented patients.

Several case reports describe improvement in visual and auditory hallucinations in patients with Parkinson's disease.^{4,5} However, there are several theories regarding the pathogenetic mechanisms of visual hallucinations in Parkinson's disease making them distinct from hallucinations in dementia.⁶⁻⁸

Hallucinations are not uncommon in patients with dementia, and unless they are distressing to the patient, may not necessarily require treatment. Our patient was experiencing considerable distress over her hallucination. Our team needed to determine what was the cause of her underlying hallucinations and delusions. Hallucinations can occur with severe depression and in these cases, the depression should be addressed. There are reports that describe mirtazapine as an effective agent in psychotic depression.^{8,9} We decided that her hallucinations were related to exacerbation of depression, and perhaps contributing to her severe cognitive dysfunction.

Because the patient's hallucinations improved with the initiation of mirtazapine, it is possible that she had an underlying untreated depression with psychosis. It is difficult to determine if her hallucinations were due to her dementia, depression, or a combination of both. However, we suspect

that the beneficial impact of mirtazapine on mood and sleep may have contributed to her improvement in severe delusions and hallucinations.¹⁰

We did not initially consider that worsening cognitive impairment was a prominent effect of sleep deprivation.¹¹⁻¹³ In laboratory settings, sleeping less than seven hours per night resulted in cumulative deficits in behavioral alertness and vigilant attention^{14,15} causing psychosis in patients with underlying dementia and/or severe depression.

It can be difficult to evaluate depression in demented patients. Tools to diagnose depression in patients with dementia, such as the Cornell Scale rely on caregiver or examiner observation. Increased awareness and use of these scales may assist in diagnosing and treating depression in patients with dementia and may alleviate secondary symptoms of depression.

Pires et al., report sleep deprivation may result in a mental status that resembles depression or anxiety.¹⁶ Often these patients have decreased cognition, low mood, increased irritability, low energy, poor insight and judgment, and other signs of psychologic dysfunction such as psychosis, hallucinations and delusions. Patients with underlying neurocognitive dysfunction may have more apparent symptoms even after one night of sleep disturbance. Most if not all of these symptoms may disappear when normal sleep is restored.¹⁶

In conclusion, this patient's low mood, poor appetite and sleep dysfunction may have resulted in severe depression with psychosis or vice versa, causing her distressing hallucinations. Mirtazapine was effective in managing hallucinations along with the underlying depression and psychosis. The diagnosis and management of depression in patients with dementia can be underestimated or undetected due to patient's inability to express emotions and symptoms.

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