Letter to the Editor

Donepezil Helps Alleviate Nightmares Associated With Posttraumatic Stress Disorder and Other Psychiatric Conditions: A Report of 4 Cases

To the Editor: Many patients with the diagnosis of posttraumatic stress disorder (PTSD) or a history of emotional trauma report recurrent nightmares. Though there is a widespread prevalence of nightmares in patients with various psychiatric conditions, there are few treatments available to treat or manage this symptom.^{1,2} Prazosin has been shown in some studies to help with nightmares related to PTSD.¹⁻⁷ Donepezil is approved by the US Food and Drug Administration for mild-to-severe Alzheimer's dementia.^{8,9} Donepezil is a reversible inhibitor of the acetylcholinesterase enzyme. The enzyme acetylcholinesterase breaks down the neurotransmitter acetylcholine. In this way, donepezil may allow a greater concentration of acetylcholine in the brain, thereby improving cholinergic function.¹⁰ The following is a series of cases in which nightmares in patients with various diagnoses responded well to 10 mg of donepezil at bedtime.

Case 1. Mr A, a 63-year-old white retired captain of the US Army, had participated in the Vietnam War and Operation Desert Storm. He has a history of PTSD (*DSM-IV* criteria) and opioid abuse, which started after he was put on treatment with opioids due to war injuries. He had participated in combat several times during his active duty service. Mr A had a history of recurrent nightmares. Most of his nightmares were related to wartime situations and almost always included a situation in which he was not able to escape, could not move during the dream, and felt awake during the dream. At his 1-month outpatient follow-up after he was started on donepezil 10 mg/d, his nightmares were very few, and in fact he reported some pleasant dreams after being placed on donepezil treatment.

Case 2. Ms B, a 64-year-old divorced white woman diagnosed with hepatitis C, was admitted as an inpatient for major depressive disorder, recurrent, severe without psychotic features (*DSM-IV* criteria), and an overdose. She stated she had been depressed for years and had inability to sleep because of recurrent nightmares that she was dying, which woke her up. She was also having nightmares about something terrible happening to her. The day after donepezil 10 mg daily at bedtime was started, she reported that she was having pleasant dreams, including one in which she was walking her dog in her neighborhood.

Case 3. Mr C, a 41-year-old Iraqi immigrant, was tortured during Saddam Hussein's regime and had a diagnosis of PTSD (*DSM-IV* criteria). He reported waking up screaming and having horrible nightmares. At his 1-month outpatient follow-up after he was started on donepezil 10 mg/d, he reported that his nightmares significantly subsided and his sleep improved.

Case 4. Ms D, a 56-year-old white woman, had a history of bipolar I disorder (*DSM-IV* criteria). She reported repeated nightmares. At her 1-month outpatient follow-up after she was started on donepezil 10 mg/d, she reported significant improvement in her nightmares.

Acetylcholine plays an important role in the sleep-wake cycle. Cholinergic projections from the forebrain act as a relay center for the brainstem-cortical arousal system and modulate cortical activity and thus promote wakefulness or rapid eye movement (REM) sleep.^{11–13} We do not know the exact mechanism of action of donepezil and the improvement in the nightmares. However, considering that most of the nightmares are associated with REM sleep, there could be an intimate association of level of acetylcholine available and nightmares. On the basis of successful management of nightmares in these few cases with donepezil, we hypothesize that the low levels of acetylcholine could lead to sleep disturbance and nightmares. These results are only preliminary, and more

controlled studies are needed to validate or reject this hypothesis and address the problem of nightmares in the population of psychiatric patients.

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Author affiliation: Department of Psychiatry, Craft Behavioral Health, LLC, Jacksonville, Florida. Potential conflicts of interest: None reported. Funding/support: None reported. Acknowledgment: The author thanks Cara McKee-Farooque for manuscript review and editing. Ms McKee-Farooque reports no potential conflict of interest relative to

the subject of this letter. Published online: August 30, 2012.

Prim Care Companion CNS Disord 2012:14(4):doi:10.4088/PCC.12l01355 © Copyright 2012 Physicians Postgraduate Press, Inc.