Delirium Associated with Donepezil in a Patient with Alzheimer's Disease: a Case Report

Kamyar Mollazadeh-Moghaddam, Pharm.D[1, 2, 3]
Arsia Jamali, MD[1,3]
Fatemeh Adili-Aghdam, MD[1]
Shahin Akhondzadeh, Ph.D.[4]

1 Students' Scientific Research Center, Tehran University of Medical Sciences, Tehran, Iran.
2 National Drug and Poison Information Center, Deputy of Food and Drug, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3 Milad Clinical Research Center, Milad Hospital, Tehran, Iran.
4 Psychiatric Research Center, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, Tehran, Iran.

Corresponding author:
Shahin Akhondzahdeh Ph.D., FBPharmacolS. Psychiatric Research Center, Roozbeh Psychiatric Hospital, Tehran University of Medical Sciences, South Kargar Street, Tehran 1333795914, Iran.
Tel: +98-21-66418466
Email: s.akhond@neda.net

Donepezil, a member of the acetylcholinesterase inhibitor family, is approved for management of cognitive impairments as well as behavioral complications in patients with neurodegenerative Alzheimer's disease. Generally, donepezil is regarded as a safe medication in patients with Alzheimer's disease although there have been reports of several minor adverse events including gastrointestinal disturbances. Herein we describe a patient with Alzheimer's disease who demonstrated delirious behavior upon treatment with donepezil.

Keywords: *Alzheimer's disease, donepezil, delirium*

Iran J Psychiatry 2013; 8:1: 59-60

Donepezil, a member of the acetylcholinesterase inhibitor family, is approved for management of cognitive impairments as well as behavioral complications in patients with neurodegenerative Alzheimer's disease. Generally, donepezil is regarded as a safe medication in patients with Alzheimer's disease although there have been reports of several minor adverse events including gastrointestinal disturbances. It is not a surprise to observe and document additional adverse effects of a medication as it is more widely administered.
Herein, we describe a patient with Alzheimer's disease who showed delirious behavior upon treatment with donepezil.

Case presentation

A 63 year old Caucasian high school graduated man, who has been a known case of Alzheimer's disease according to DSM-IV-TR and criteria of National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) (1) since 3 years ago, was visited in February 2012. At the time of diagnosis, his Mini-Mental State Examination (MMSE) score was 26/30. His past medical history was otherwise unremarkable. With worsening of his cognitive functional state, the patient was treated with 10 mg/day donepezil. On the next day, the patient appeared delirious and was referred to our center due to agitation and confusion. Based on reports by family members, following the dosage increase of the medication, the patient was unable to recognize family members consistently, showed difficulty in awareness of time, acted aimlessly, and became emotionally irritable and violent with the family member attempts to assist him. At the time of referral, his MMSE score was 8/30. Upon general and neurologic examination, no relevant sign was evident. Routine laboratory examinations, serum creatinine and ammonia as well as liver and thyroid function tests were in normal limits. After withdrawing donepezil, patient's symptoms

improved gradually in course of one day. Patient became alert and returned to his baseline cognitive functional state although he was unaware of his previous delirious behaviors. At 6 months follow-up, the patient demonstrated no delirious behavior and his mild cognitive impairments have not progressed substantially.

Discussion

To the best of our knowledge, this is the second reported case of delirium in a patient upon treatment with donepezil. In 2003, Kawashima and Yamada reported a patient with Alzheimer's disease who was presented with delirium three days after increasing the dosage of donepezil from 3 mg/day to 5 mg/day (2). This patient also recovered in two days following withdrawal of the medication and his recovery was maintained at 5 months follow-up. Two months subsequent to donepezil discontinuation based on a decision by family members, patient's aggressive behaviors disappeared and no similar event was repeated. Along the same line, emergence of violent actions during treatment with donepezil and disappearance of symptoms with medication withdrawal is reported by Bouman and Pinner in a patient with dementia in 1998 (3). Similarly, in 2003, Bianchetti and Trabucchi presented a patient suffering from Alzheimer's with mild cognitive impairments that demonstrated aggressive and agitated behaviors toward relatives and attempted self-harm following increase in starting dose of 10 mg/day donepezil from 5 mg/day (4). In line with these cases, Lo Coco and Cannizzaro described a patient who showed inappropriate sexual behaviors during treatment with donepezil (5) .

Notably, in 1996, Traepacz et al. reported a patient with Alzheimer's disease who showed signs of neurotoxicity and cholinergic delirium following dosage increase of Tacrine, another member of acetylcholinesterase inhibitors which is not currently widely used due to its associated adverse events, to 160 mg/day (6). This patient also recovered to a great extent although he did not return to his baseline function after 5 months of tacrine withdrawal.

Although this case does not prove donepezil as a cause of delirium, incidence of delirium following treatment with this medication and spontaneous recovery of the patient subsequent to its withdrawal, suggest physicians should be cautious in prescribing acetylcholinesterase inhibitors.

References

1. McKhann G, Drachman D, Folstein M, Katzman R, Price D and Stadlan EM. Clinical Diagnosis of Alzheimer's Disease: Report of the Nincds-Adrda Work Group under the Auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. Neurology 1984; 34: 939-944.
2. Kawashima T and Yamada S. Delirium Caused by Donepezil: A Case Study. The Journal of clinical psychiatry 2002; 63: 250-251.
3. Bouman WP and Pinner G. Violent Behavior-Associated with Donepezil. The American journal of psychiatry 1998; 155: 1626-1627.
4. Bianchetti A, Trabucchi M, Cipriani G. Aggressive Behaviour Associated with Donepezil Treatment: A Case Report. International journal of geriatric psychiatry 2003; 18: 657-658.
5. Lo Coco D and Cannizzaro E. Inappropriate Sexual Behaviors Associated with Donepezil Treatment: A Case Report. Journal of clinical psychopharmacology 2010; 30: 221-222.
6. Trzepacz PT, Ho V, Mallavarapu H. Cholinergic Delirium and Neurotoxicity Associated with Tacrine for Alzheimer's Dementia. Psychosomatics 1996; 37: 299-301.