

Letter to the Editor

ANGLE-CLOSURE GLAUCOMA AFTER DISCONTINUING DONEPEZIL HYDROCHLORIDE (ARICEPT)

To the Editor:

Donepezil hydrochloride (Aricept; Eisai America, Inc., Teaneck, NJ, and Pfizer, New York, NY) was only the second drug approved by the U.S. Food and Drug Administration for the treatment of mild-to-moderate Alzheimer's disease. We examined a patient who developed unilateral acute angle-closure glaucoma between 3 and 5 days of stopping donepezil hydrochloride 2.

A 55-year-old white female presented to the emergency room because of an intense right-sided headache of about 12 hours' duration. The patient also complained of nausea and vomiting, photophobia, and decreased vision. There was no past history or any family history of glaucoma. The patient's past medical history is remarkable for a total abdominal hysterectomy and the recent diagnosis of Alzheimer's disease. She had been treated for more than 8 years with estrogen replacement (Premarin; Wyeth-Ayerst, Philadelphia, PA). She had been regularly taking donepezil hydrochloride (10 mg, orally) at bedtime for about 4–6 months until she ran out of this medication. She was on no other prescription or over-the-counter medications.

On examination, the distant visual acuity was right eye (RE), count fingers at 2 feet, and left eye (LE), 20/400. The pupil RE was mid-dilated 5 mm and nonreactive. The pupil LE was 3 mm, reacting to light sluggishly to 2 mm. The right eye was markedly injected with corneal edema. Gonioscopy confirmed angle closure in the RE and occludable angles in the LE. The intraocular pressure was RE 48 mmHg and LE 12 mmHg. The patient was treated with topical antiglaucoma agents in addition to an emergent laser peripheral iridotomy when the cornea cleared. A prophylactic peripheral laser iridotomy was performed on the left eye the next day.

Many of the signs and symptoms of Alzheimer's disease are viewed to be a result of depression of cholinergic neurotransmission. Donepezil hydrochloride is postulated to exert its therapeutic effects by enhancing this cholinergic function, as it has been demonstrated to be highly selective for neural acetylcholinesterase. In clinical trials, the major side effects have been shown to be nausea, diarrhea, anorexia, and vomiting. Pharmacokinetic studies have shown that donepezil hydrochloride has an elimination half-life of about 70 hours, with the drug cleared mainly by renal excretion. A review of the literature shows no reports of acute angle-closure glaucoma having been described with donepezil hydrochloride.

Acute angle-closure glaucoma may be precipitated by topical mydriatics, systemic anticholinergics (e.g., antihistamines or antipsychotics), excitement, periocular botulinum toxin injection, or dim illumination. Pupillary block occurs when contact between the iris and lens creates an impediment in flow of the aqueous. We hypothesize that the patient's pupil may have likely been relatively predisposed to miosis given the biochemical characteristics of donepezil hydrochloride's action, an anticholinesterase. The abrupt discontinuation of the drug and its subsequent metabolism may have led to a rebound dilatation of the pupil. This dilatation led to iris–lens contact and subsequent pupillary block and angle closure. Anticholinesterase drugs themselves may precipitate attacks of angle closure in those predisposed with narrow angles. However, given the time frame during which the patient was previously on the medication and that the event occurred just days after its stoppage, we feel that this was the probable mechanism.

Although this is only a single case, there have been at least three additional cases tabulated from the "National Registry of Drug-Induced Ocular Side Effects" [personal communication, Dr. Frank Fraunfelder, letter October 25, 2001, Casey Eye Institute at Oregon Health & Science University, Portland]. This suggests that patients with Alzheimer's type dementia should probably have a screening eye exam prior to beginning treatment with donepezil hydrochloride. Rather serious consequences may result as a side effect of abruptly stopping the medication in a population already predisposed to forgetfulness.

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