“Post-marketing surveillance reveals new information on amiodarone optic neuropathy”

Cheryl Guttman
in Fort Lauderdale

INITIAL frequent ophthalmic examinations may be beneficial for patients who have started on the anti-arrythmic agent amiodarone to enable timely detection of amiodarone-associated optic neuropathy and the prompt discontinuation of the medication may afford the best chance for vision recovery, said Lenworth N Johnson MD, at the annual meeting of ARVO.

Dr Johnson is professor of ophthalmology and neurology, University of Missouri-Columbia. His comments were based on a review of cases of amiodarone-associated optic neuropathy (AON) undertaken by the investigators from the Research on Adverse Drug Events and Reports group, a project supported by grants from the National Heart, Lung and Blood Institute, the National Cancer Institute, the American Cancer Society, and the Department of Veterans Affairs.

The study encompassed 294 cases that were reported to the Food and Drug Administration Adverse Event Reporting System (FDA-AERS), developed among patients enrolled in clinical trials, or described in the published literature.

The reported histories demonstrated that AON typically presented within the first year after amiodarone initiation and usually within the first four to six months. However, while its clinical presentation was sometimes acute, the onset was more often insidious and almost one-third of patients were asymptomatic.

Vision at presentation ranged from 20/15 to light perception and was 20/200 or worse in at least one eye in about 20% of patients. Follow-up information on visual outcome was available for 62 cases.

Cause-and-effect relationship unproven

Among the 48 cases where amiodarone was withdrawn, visual acuity worsened in about 20% of those eyes, but the majority (58%) benefited with visual acuity improvement after the medication was withdrawn. In contrast, among 14 cases where amiodarone treatment was continued, only seven per cent of eyes had vision improvement whereas acuity was unchanged in 86%.

“In the absence of a prospective, randomised, double-masked, controlled clinical trial, it is not possible to say there is a direct cause-and-effect relationship between amiodarone and the development of optic neuropathy. However, this is the largest review of cases of AON, and based on their features, it seems reasonable to advocate close ophthalmic surveillance during the first year of starting amiodarone. Our suggestion would be to examine patients at baseline and then every three months throughout the first year. If no problems are detected, then the examination schedule can be extended to annually thereafter,” said Dr Johnson, speaking on behalf of the RADAR group.

Of the 294 cases of AON reviewed, 214 were from the FDA-AERS, 57 appeared in published case reports, and the other 23 were mentioned as adverse event reports in clinical trials.

“It is unfortunate that the majority of these cases were reports to the FDA because those often contain limited information regardless of the submitting source. We encourage US physicians to report adverse events to the FDA MedWatch program and to provide as much detail as possible in those reports,” Dr Johnson said.

The 294 patients had a mean age of 66 years (range 30 to 94) and were predominantly men (74%). The dose of amiodarone being taken ranged between 57 and 1,200mg per day with a median of 200mg. The indication for therapy was equally divided between atrial fibrillation and other atrial or ventricular arrhythmias.

“Patients treated with amiodarone are generally older, and older age is also a feature of patients who most often develop nonarteritic anterior ischemic optic neuropathy (NAION). While cardiac arrhythmia has never been identified to be a risk factor for NAION, a prospective study of amiodarone-treated patients would be needed to reveal an association between these ocular events and certain types of cardiac arrhythmias,” Dr Johnson said.

Vision loss developed anywhere between one and 84 months after amiodarone initiation, but the median onset was six months. Optic disc oedema was seen in 85% of eyes.

Optic neuropathy manifestations vary

Based on temporal characteristics and optic nerve appearance, the cases could be divided into several clinical categories. Almost half (44%) of patients experienced insidious onset AON, while 29% of eyes presented with retrobulbar optic neuropathy, and 21% manifested with acute onset optic neuropathy. Pseudotumor cerebellar intraocular pressure was the presenting feature in eight per cent of cases while six per cent had a delayed-progressive onset optic neuropathy characterised by presentation with visual symptoms but development of optic disc oedema only after amiodarone was discontinued.

“Amiodarone has a long half-life that ranges from 35 to 110 days, which explains the latter presentation pattern,” Dr Johnson said.

“Ocular adverse events that are due to drug toxicity usually present with simultaneous bilateral involvement, which contrasts with the common finding of initial monocular presentation in these patients”


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