**Fatal Lung Toxic Effects Related to Dronedarone Use**

Dronedarone is a derivative of amiodarone that aimed to reduce the extracardiac adverse effects while preserving its antiarrhythmic effects for treatment of atrial fibrillation (AF). In the ATHENA trial (A Placebo-Controlled, Double-Blind, Parallel Arm Trial to Assess the Efficacy of Dronedarone 400 mg bid for the Prevention of Cardiovascular Hospitalization or Death from Any Cause in Patients with Atrial Fibrillation/Atrial Flutter), dronedarone reduced cardiovascular hospitalization and death in patients with non-permanent atrial fibrillation (AF) with other cardiovascular risk factors. However, an experimental study suggested that dronedarone might have toxic effects on the lung greater than or equal to amiodarone. We describe 2 cases of fatal and near-fatal lung toxic effects associated with dronedarone use.

**Report of Cases. Case 1.** A 72-year-old woman was hospitalized with progressive dyspnea for 3 weeks. She had symptomatic paroxysmal AF, and amiodarone was initiated 2 years ago. Ten months before admission, she was enrolled into the ATHENA trial, in which amiodarone therapy was stopped for 1 month prior to switching to dronedarone. At the time of admission, she had already been using dronedarone for 9 months. Chest radiography on admission showed bilateral diffuse pulmonary infiltrates, and thoracic computed tomography revealed diffuse ground glass opacities involving both lungs (Figure, A and B). Treatment with empirical board-spectrum antibiotics failed, and she developed progressive respiratory failure necessitating mechanical ventilation 20 days later. All microbiological examination findings were negative. Trans-bronchial biopsy revealed features compatible to bronchiolitis obliterans with organizing pneumonia (BOOP) described in amiodarone-induced lung toxic...
effects (Figure, C).³ Pulse methylprednisolone therapy was tried, but she subsequently died 4 days later.

Case 2. An 83-year-old man with history of hypertension and diabetes mellitus presented with new-onset AF. He was treated initially with 6 days of intravenous and then 4 days of oral amiodarone (a total of 4.6 g), which was subsequently switched to oral dronedarone for 4 days. He was transferred to our hospital for management of AF. On admission, dronedarone therapy was stopped, but he developed progressive dyspnea 2 days later. Chest radiography and thoracic computed tomography revealed diffuse ground glass opacities over both lungs, compatible with BOOP (Figure, D and E). Treatment with broad-spectrum antibiotics failed, and he developed respiratory failure necessitating mechanical ventilation. All the microbiological investigation findings were negative. His condition improved with pulse methylprednisolone therapy, and he was successfully weaned off from the ventilator.

Comment. Although it is arguable that both patients were treated with amiodarone before switching to dronedarone, the temporal sequence of their onset of respiratory symptoms as well as similar radiological features would suggest that dronedarone may in fact play an important role in the pathogenesis. Furthermore, the lung toxic effects appear to occur both after the short- and long-term exposure to dronedarone. Our observations suggest that serial monitoring of chest radiography is needed in patients receiving dronedarone, especially in those with prior exposure to amiodarone.

Chung-Wah Siu, MD
Marie P. Wong, MD
Chung-Man Ho, MBBS
Chi-Leung Lam, MBBS, PhD
Hung-Fat Tse, MD, PhD

Author Affiliations: Divisions of Cardiology (Drs Siu and Tse) and Respiratory Medicine (Drs Ho and Lam), Department of Medicine (Drs Siu, Ho, Lam, and Tse), and Department of Pathology (Dr Wong), Li Ka Shing Faculty of Medicine, The University of Hong Kong, Pokfulam, Hong Kong.

Correspondence: Dr Tse, Division of Cardiology, Department of Medicine, The University of Hong Kong, K1929B Queen Mary Hospital, Pokfulam, Hong Kong (hftse@hkuc.hku.hk).

Author Contributions: Study concept and design: Siu and Ho. Acquisition of data: Siu, Ho, Lam, and Tse. Analysis and interpretation of data: Wong, Lam, and Tse. Drafting of the manuscript: Siu and Tse. Critical revision of the manuscript for important intellectual content: Siu, Wong, Ho, and Lam. Administrative, technical, and material support: Siu, Wong, and Lam. Study supervision: Siu and Tse.

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References

EDITOR’S NOTE

Dronedarone Use and Fatal Lung Toxic Effects?

Siu et al have observed a rare potential adverse effect of dronedarone in patients who have had previous exposure to amiodarone. Dronedarone is an antiarrhythmic agent that can be useful in some patients with nonpermanent atrial fibrillation who have not had recent heart failure. Many clinicians, including cardiologists, are currently using this drug in specific patient populations, including young individuals, at least initially, in preference to long-term oral therapy with amiodarone, a more highly toxic agent. Nonetheless, it is clinical observations like these, and not randomized controlled studies, which can (and often do) serve the purpose of alerting us to new and important consequences of our therapies. The implied warning provided by this report in these 2 patients who have had prior exposure to amiodarone should be taken seriously, and newly described adverse effects should be actively sought and reported by physicians using newly developed approved drugs of all types.

Nora Goldschlager, MD

RESEARCH LETTERS

Bridging the Chasm: Effect of Health Information Exchange on Volume of Laboratory Testing

Sharing patient information between health care providers, including through health information exchanges (HIEs), has been proposed as one of the essential changes to improve the quality and efficiency of the health care system in the United States.¹ It has been estimated that HIEs could decrease health care costs across the country by approximately $78 billion annually.² Despite numerous potential advantages of HIEs, there are few studies documenting their benefits.³ This lack of objective information might have slowed down their acceptance.⁴ Studies that demonstrate tangible evidence of benefits provided by HIEs are urgently needed. Provider surveys show that reduction in duplicate testing is one of the most commonly expected benefits.⁵ We therefore investigated whether the introduction of an HIE between 2 academic medical centers was associated with a reduction in volume of laboratory testing.

Methods. We conducted a retrospective study to investigate whether the availability of laboratory test results