

## A serious complication of a common stress test

(MAY 2014)

**TO THE EDITOR:** We read with interest the article by Drs. Buitrago et al in the May 2014 issue of *Cleveland Clinic Journal of Medicine*, "Syncope during a pharmacologic nuclear stress test."<sup>1</sup> It highlights a known, serious interaction between adenosine and dipyridamole (the latter contained in the aspirin-dipyridamole combination Aggrenox) and associated asystole in patients undergoing pharmacologic cardiac stress testing. This interaction is known in the cardiology literature, as it was noted in the current guidelines for pharmacologic stress testing.<sup>2</sup> However, I would like to discuss a few points with the authors for a better understanding of the case.

First, the underlying rhythm before the development of complete atrioventricular (AV) dissociation and asystole was significant for second-degree AV block (Mobitz type I, Wenckebach). Second- or third-degree AV block is considered a contraindication to adenosine because of the risk of exacerbating these conditions. This underlying AV nodal disease made dipyridamole not the only culprit. In addition, the patient had been on two agents (labetalol and clonidine) that have AV nodal-blocking properties. Electrolyte imbalances such as hypokalemia, hypomagnesemia, and hypocalcemia are another reason for delayed conduction and PR prolongation, and electrolyte levels should be checked and corrected properly before the stress test or coronary angiography. It would have been helpful if the authors had discussed these points for a better understanding of the drug-drug interaction.

Because of the increasing trend to admit patients with chest pain to observation units to rule out myocardial infarction, the case has a valuable teaching point, especially for hospitalists and emergency physicians in charge of patients admitted with chest pain.<sup>3</sup> Since cardiologists rarely get involved in the care of these patients, careful review of medications before scheduling stress testing is of ultimate

importance and should be emphasized in the discussion.

Lastly, the number of combined medications that are available commercially is increasing, which puts patients at higher risk of drug interactions. Hospitalists and internists taking care of patients, especially elderly patients, admitted from nursing homes and taking multiple medications should pay extra attention when reviewing medications with brand names.<sup>4,5</sup> Furthermore, a 12-lead electrocardiogram should be reviewed, with special attention to the PR interval and QT segment. A pharmacy consultation could be valuable, especially in patients taking multiple drugs.<sup>6</sup>

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**IN REPLY:** We appreciate the interest and comments of Dr. Alraies. We would like to clarify that the patient's baseline electrocardiogram before the nuclear stress test was normal. Second-degree atrioventricular (AV) block (Mobitz type I) was evident only during adenosine infusion before ventricular asystole. The patient was on two AV nodal blockers (labetalol and clonidine) but had no underlying conduction disease. There is no contraindication to continuing these agents before pharmacologic stress testing. In addition,

the patient's electrolyte levels were within normal ranges before testing.

We agree that the valuable teaching point for clinicians is to appreciate the contraindication to and consequences of the use of dipyridamole-containing oral medications and either adenosine or regadenoson during pharmacologic stress testing. As Dr. Alraies points out, most cardiologists may be familiar with this interaction, but a large proportion of stress tests are ordered by emergency room physicians, internists, and hospitalists who are not. Still, the overall incidence of side effects with pharmacologic stress testing is very low and comparable to that with exercise testing, with safety enhanced by following the American Society of Nuclear Cardiology (ASNC) guidelines for performing stress myocardial perfusion imaging.<sup>1</sup> Avoidance of this interaction may be enhanced through education, but also by using checklists and building notifications into the electronic medical record when ordering pharmacologic stress testing. Of note, according to the ASNC guidelines, the use of intravenous dipyridamole as a stress agent is a safe alternative for pharmacologic stress testing in patients taking oral dipyridamole-containing medications.

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