EDITORIAL COMMENT

Reduction in Dipyridamole-Induced Single-Photon Emission Computed Tomography Myocardial Defect Size by Beta-Blockers

Time to Re-Examine the Patient Preparation Protocol for Pharmacologic Stress Testing*

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Over the past decade, pharmacologic coronary artery vasodilation in combination with single-photon emission computed tomography (SPECT) myocardial perfusion imaging has become an increasingly popular approach to the noninvasive detection of coronary artery disease. Numerous studies document comparable diagnostic accuracy of myocardial perfusion imaging with dynamic exercise and with pharmacologic coronary artery vasodilation (1). Single-photon emission computed tomography imaging after either dipyridamole or adenosine infusion has provided a valuable diagnostic tool in patients who are unable to exercise to target heart rate. In addition, pharmacologic coronary artery vasodilation should be substituted for dynamic exercise in the detection of coronary artery disease by SPECT imaging in patients with left bundle branch block or an implanted electronic pacemaker. In these patients, exercise-induced tachycardia can result in SPECT defects in the absence of coronary artery stenosis. At times pharmacologic stress has been substituted for dynamic exercise in patients receiving beta-adrenergic blockers because a beta-blocker might prevent the patient from reaching the target heart rate with exercise and interfere with the induction of myocardial ischemia (2). However, Sharir et al. (3) have cautioned that beta1-blocker would not directly dilate coronary arteries, it is likely that the observed reduction in coronary vascular resistance and increase in coronary blood flow is an indirect result of negative inotropic, negative chronotropic and, possibly, anti-ischemic effects.

Beller et al. (8) showed that in a setting of severe single-vessel coronary artery stenosis, dipyridamole infusion induces the coronary steal phenomenon by reducing post-stenotic subendocardial blood flow while maintaining or increasing post-stenotic subepicardial flow. In contrast, metoprolol can increase subendocardial blood flow to the post-stenotic myocardium in the presence of dipyridamole, resulting in improved regional wall thickening (5). This may result from reduced myocardial compression of intramyo-
cardiac subendocardial vessels through the negative inotrope effect of the beta-blocker. Beta-blockers may also help maintain intramyocardial coronary collateral flow by a similar mechanism, and this may avert the coronary steal phenomenon otherwise induced by dipyridamole. Additionally, beta-blockers may reduce ischemia by slowing the heart rate, thereby facilitating diastolic coronary flow.

Indirect support for the postulate that beta-blockade ameliorates maldistribution of blood flow induced by dipyridamole infusion comes from a dipyridamole echocardiographic study reported by Lattanzi et al. (9). Patients were tested with and without antianginal drugs, including propranolol in 27 patients. The sensitivity of dipyridamole echocardiography fell from 91% off antianginal therapy to 65% on therapy (p < 0.01). Dipyridamole echocardiography depends upon maldistribution of myocardial blood flow away from the subendocardium to induce regional wall motion abnormality, an effect that was prevented by antianginal treatment. It appears that beta-blockers, by averting this maldistribution of myocardial blood flow, can prevent detection of coronary artery stenosis during pharmacologic myocardial perfusion imaging with dipyridamole.

**What are the limitations of the Taillefer et al. (4) study?** The study is small—21 patients completed the study protocol. This may well have prevented the identification of a statistically significant effect of beta-blockade on per-patient sensitivity for the detection of coronary disease with dipyridamole infusion. Study size did not prevent statistically significant reductions in quantitative perfusion defect size with metoprolol. Study design did not include patients in whom coronary disease was absent; therefore, the effects of beta-blockers on test specificity, normalcy rate, and overall accuracy are unclear. The study was performed with acute intravenous rather than chronic oral beta-blocker administration and thereby differs from the usual clinical scenario encountered in patients presenting for dipyridamole myocardial perfusion imaging. Furthermore, the results obtained with the beta1-selective blocker, metoprolol, may not be the same for treatment with nonselective beta-blockers, such as propranolol or carvedilol.

**What then are the clinical implications of the findings reported by Taillefer et al. (4)?** Several studies have suggested that antianginal drugs interfere with detection of coronary artery disease with pharmacologic coronary artery vasodilation (3,10). Taillefer et al. (4) now present data focusing specifically on the interference of metoprolol with detection of coronary disease with dipyridamole myocardial perfusion testing. In patients referred for dipyridamole myocardial perfusion imaging for the purpose of determining the presence or extent of coronary disease, strong consideration should be given to withholding beta-blockers for four to five half-lives (e.g., 36 to 48 h) before testing. When the purpose of testing is to assess the clinical effectiveness of antianginal treatment, the beta-blocker should be continued. The decision to withhold beta-blockers for diagnostic testing must be considered carefully for each individual patient. Although small, there is a finite risk of life-threatening complications, including severe hypertension or an unstable coronary syndrome with beta-blocker withdrawal (11–14). Therefore, withholding beta-blockers for diagnostic testing may not be appropriate in high-risk patients. When beta-blockers are withheld for 36 to 48 h before diagnostic testing, the patient should be advised of the importance of promptly seeking medical care if symptoms of ischemia appear or escalate. New clinical studies are needed to determine more precisely the duration that beta-blockers, and other antianginal drugs should be withheld to avoid compromising the sensitivity of myocardial perfusion imaging with pharmacologic stress. Finally, because dipyridamole acts by preventing the inactivation of adenosine by adenosine deaminase and by preventing adenosine reuptake (15), it is likely that beta-blockers will interfere with detection of coronary disease with adenosine as well as with dipyridamole perfusion imaging. Further studies will be needed to confirm the effects of beta-blockers on dipyridamole perfusion imaging and to determine whether the sensitivity of adenosine perfusion imaging is compromised similarly.

In conclusion, the new data presented by Taillefer et al. (4) suggest that beta-blockers should be withheld temporarily before dipyridamole infusion for detection of coronary artery disease by myocardial perfusion imaging. The decision to withhold beta-blockers for diagnostic testing should be carefully considered on a case-by-case basis.

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**REFERENCES**


