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Beta-Blockers and Depression

To the Editor: We read with great interest the thought-provoking Clinical Case Conference by Laura K. Kent, M.D., et al., published in the August 2009 issue of the *Journal*, which described the finding of takotsubo cardiomyopathy after ECT (1). We hope to expand on the discussion regarding the role of beta-blockers in the course of depression treatment, an issue frequently raised by colleagues and trainees. We have searched the medical literature over time and have not found conclusive evidence to support a clear causal role of beta-blockers in depression.

Since Dr. Stoudemire et al. (2) posed, in 1984, that there is very little evidence to link propranolol with mood disturbance, subsequent studies have consistently challenged the dogma that beta-blockers cause depression. A meta-analysis (3) examined 15 randomized, controlled studies involving 35,000 subjects taking beta-blockers for the treatment of myocardial infarction, heart failure, or hypertension and demonstrated no statistical difference between beta-blockers and placebo with respect to depression, although beta-blockers were associated with increased incidence of fatigue and sexual dysfunction. The absolute incidence of depressive symptoms was six per 1,000 subjects (95% confidence interval=–7 to 19). A prospective multicenter trial (4) of 254 subjects taking beta-blockers and 127 comparison subjects measured serial Beck Depression Inventory scores. This study showed no significant difference between groups in the rate of depression at 3, 6, and 12 months, even with an alpha set at <0.10. Dr. Kent et al. suggested that beta-blockers may cause depression more often in women than men. However, Crane et al. (5) examined a cross-sectional sample of 84 women (>65 years old) 6 to 12 months after myocardial infarction and did not find any elevated risk of depression (using the Geriatric Depression Scale) among women who were taking beta-blockers (5).

The aforementioned studies teach us that it is important to distinguish fatigue from depression, that a temporal association between beta-blocker use and depression does not seem to exist (up to 12 months), and that there is no evidence to support a gender difference. When the preponderance of evidence does not support a long-held belief, it is the responsibility of the medical community to adopt a new clinical paradigm. It may be time to change the prevailing wisdom in our field so as not to prevent our patients from receiving beta-blockers for cardiovascular benefits. We support the decision to continue the beta-blocker for the patient discussed in the Clinical Case Conference.

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Dr. Kent Replies

To the Editor: We thank Dr. Xiong et al. for their thoughtful response to our article. They make the point that studies on beta blockade have distinguished fatigue from depression, have highlighted that there does not seem to be a temporal association between beta-blocker use and depression (up to 12 months), and that there is no evidence to support a gender difference.

Dr. Xiong et al. state that while we suggested that depression in the setting of beta-blockade use is seen more frequently in women, Crane et al. (1) examined 84 women and found no difference in depression symptoms between women who did and did not use beta-blockers. Although that study suggested that the use of beta-blockade does not cause depression in women, the study had several limitations, including its cross-sectional design, making it difficult to identify causation (even though this is more of an issue when an association is found). We also wish to make the point that very large doses of beta-blockade were used in our case study relative to the doses administered to women in the Crane et al. study, who were post-myocardial infarction and received only conventional doses, thus limiting comparability.

We agree that Van Melle et al. (2) showed no significant difference between groups in the rate of depression at 3, 6, and 12 months. However, the vast majority of these subjects were men (78% in both non-beta-blocker and beta-block-