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Beta-Blockers in Syncope: The Jury Is Still Out

Madrid et al. (1) are to be commended for assessing the efficacy of beta-blockers in neurocardiogenic syncope. Syncope is a common problem, and beta-blockers are commonly used to attempt to treat this disorder despite a paucity of randomized data.

Unfortunately, design limitations preclude this study from providing definitive answers as to the role of beta-blocking drugs in neurocardiogenic syncope. Previous papers have identified predictors of beta-blocker success, including the presence of tachycardia during the tilt table test, the need for isoproterenol to induce syncope, and an acute response to beta-blockers (2,3). By including a high percentage of tilt-negative patients (60%), the investigators may have inadvertently diluted a potential treatment effect. The researchers’ own data in their Figure 2 suggest a differential response to study medication based upon the result of the tilt table test. We agree with Madrid et al. (1) that tilt tests are not an ideal diagnostic modality, but a better tool is not presently available. We are now validating objective criteria quantitatively for the causes of syncope that make use of a structured history to diagnose neurocardiogenic syncope (1). Without such a tool, a positive tilt test remains the diagnostic standard.

In the accompanying editorial to the Madrid et al. (1) article, Dr. Sra (5) correctly points out that tilt tests are not an ideal diagnostic modality, but a better tool is not presently available. We are now validating objective criteria quantitatively for the causes of syncope that make use of a structured history to diagnose neurocardiogenic syncope (1). Without such a tool, a positive tilt test remains the diagnostic standard.

In the accompanying editorial to the Madrid et al. (1) article, Dr. Sra (5) correctly points out that the assessment of therapy in neurocardiogenic syncope is difficult. A single recurrence of syncope is not an ideal end point due to symptom clusters and long symptom-free periods. This problem is not unique to syncope research; it is also seen in other disorders such as paroxysmal atrial fibrillation. We have previously reported that the time to first syncope recurrence after a positive tilt table test correlates very well with the frequency of syncope after a positive tilt table test (6). Time to first syncope recurrence is an appropriate end point for such studies, but it can be supplemented with other end points such as syncope burden and presyncope burden.

We agree with Dr. Sra (5) about the need for a large-scale multicenter trial to answer the question of beta-blockers for neurocardiogenic syncope. We are presently conducting a multinational, double-blind, placebo-controlled study of oral metoprolol in patients with at least three lifetime episodes of neurocardiogenic syncope and a positive head-up tilt table test. In the study, which is funded by the Canadian Institutes of Health Research, we are enrolling 220 patients, each of whom will be on blinded therapy for one year. The primary end point is time to first syncope recurrence, and secondary end points include the burden of syncope and presyncope, and the quality of life over the full year.

Madrid et al. (1) may eventually be found to be correct in concluding that atenolol specifically and beta-blockers in general are not effective in decreasing or delaying symptoms in patients with neurocardiogenic syncope. However, the final answer is not yet known.

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REPLY

We appreciate the interest of Sheldon et al. in our article and the opportunity to respond to his letter. We are aware of his concerns regarding the methodology of our study, considering the diagnosis of vasovagal syncope based on the typical clinical history. We do not question the great clinical value of the tilt test, but in this technified medicine we also need to consider the value of simple things such as the anamnestic and physical examination. We recognize the progress in the knowledge of physiology, which the tilt test has rendered, but nevertheless it is not the gold standard for the diagnosis of vasovagal syncope, with its limited sensitivity and specificity and its dependence on the protocol.

In our study, only those patients with a clear anamnesis of vasovagal syncope were included. In fact, more than 700 patients with unexplained syncope were evaluated, and in the end only 50 patients were eligible for the study, including those patients with clear clinical history of vasovagal syncope who were highly symptomatic. A complete study to discard other possible causes of syncope was carried out in all patients. Moreover, there was no new etiological diagnosis of syncope during the follow-up (1). We want to emphasize that despite the lack of efficacy of atenolol, the