Predicting the Effectiveness of Beta-Blocker Therapy in Vasovagal Syncope

There has been a great deal of interest in the therapeutic role of beta-adrenergic blockade in patients suffering from vasovagal syncope. The efficacy of beta-blockers in these patients may be due to blunting of elevated catecholamine levels that precede vasovagal syncope (1). Notwithstanding the widespread use of beta-blockers in the past, some studies on chronic beta-blocker use have been less than encouraging and may suggest some benefit in older but not in younger patients, as mentioned in the recent article by Tan and Parry (2). That being said, might there be a better way to predict the favorable use of beta-blocker therapy in patients suffering from vasovagal syncope? In one study of patients with confirmed vasovagal syncope, all patients with a negative tilt test response during esmolol infusion had a negative tilt test response with oral metoprolol. Of the remaining patients with a positive tilt test response during esmolol infusion, 90% continued to have a positive response with oral metoprolol (3). In another study, a negative test with esmolol infusion among 112 patients with vasovagal syncope was again found to be an independent predictor for prevention of symptoms with oral metoprolol during follow-up of 2.7 ± 1.2 years (p < 0.0001) (4). Those authors concluded that “acute challenge with esmolol infusion appears to be an accurate predictor of response to chronic beta-blockers.” A negative head-up tilt test during propanolol infusion was similarly found to predict favorable responses to oral beta-blocker therapy in other studies, including a prospective trial of 296 patients (5–7). Thus, data on the effectiveness of a beta-blocker challenge during the head-up tilt test in patients with vasovagal syncope may be very helpful in formulating a therapeutic strategy.

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Reply

We thank Dr. Kapoor for his interest in our recent paper (1). As mentioned by Dr. Kapoor, beta-blockers had indeed found widespread usage in the treatment of vasovagal syncope in the past. Earlier uncontrolled studies (2,3) and 1 small randomized-controlled study (4) had demonstrated encouraging results, fueling this practice. However, recent randomized controlled trials (5,6), as well as the only multicenter, randomized, placebo-controlled trial published to date (7), have failed to demonstrate any beneficial effects with beta-blockers. There was a statistically nonsignificant trend to benefit in the subgroup of subjects ≥42 years of age, suggesting that further evaluation of the use of beta-blockers in older subjects may be warranted (8).

The studies cited by Dr. Kapoor were uncontrolled studies evaluating the role of intravenous beta-blockers in predicting treatment response to long-term oral beta-blocker therapy. Following the positive diagnosis of vasovagal syncope with a head-up tilt (HUT) test, a second HUT was performed to assess response to intravenous esmolol or propanolol (9–11). However, there has been a reasonable body of evidence demonstrating that the reproducibility of a positive HUT is low (12–15). The role of HUT as an instrument to evaluate treatment benefit is therefore limited, and can only be used in this context if a comparison is made with placebo (16).

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