Pericardioversion Dofetilide Does Not Suppress Immediate and Subacute Recurrences of Persistent Atrial Fibrillation

To the Editor:

Dofetilide is an important new antiarrhythmic drug for the treatment of persistent atrial fibrillation (AF). Recently, Singh and colleagues reported that dofetilide dose-dependently converts persistent AF to sinus rhythm and that it helps to maintain sinus rhythm. The authors do not describe 2 important issues that are obvious from the data. First, Table 2 shows that electrical cardioversion is unsuccessful in almost 30% of procedures in patients receiving pretreatment with 250, 500, or 1000 μg of dofetilide per day during 3 days; there is a far lower 20% failure rate in placebo patients. This is in sharp contrast with other drugs. Second, dofetilide does not ameliorate the rate of AF recurrence during the first few weeks after conversion (Figure 3). Subacute recurrences tend to cluster in the 2 weeks after the shock. This period contains strong triggers for recurrence, possibly related to the reversal of electrical remodeling. Dofetilide starts to suppress AF recurrence only after this initial, vulnerable phase has passed. These observations suggest that dofetilide does not change the immediate and subacute (ie, until a few weeks after shock) arrhythmia outcome of electrical cardioversion. This is disappointing and strongly argues in favor of supportive measures such as concomitant pericardioversion verapamil or other, more effective antiarrhythmic drugs. If not, many patients will not reach the more or less stable postcardioversion phase in which late recurrences occur relatively infrequently. Especially for those who need sinus rhythm to suppress symptoms, enhancing the immediate and subacute outcome of cardioversion may make the difference between a good and a bad quality of life.

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Response

We would like to thank Van Noord and colleagues for their valuable comments regarding our article on the conversion and maintenance of sinus rhythm with dofetilide. Regarding the success of cardioversion, as will be published in a correction, the percent of successful cardioversion for the dofetilide 500 μg BID group was 81%, not 71%. As is seen in Table 2 from the article, 62 of 77 patients in the dofetilide 500 μg group converted compared with 68 of 84 patients in the placebo group. Therefore, there was no difference in cardioversion for the dofetilide versus placebo groups. In fact, 23 of these 62 patients in the dofetilide 500 μg group also converted pharmacologically.

In response to Van Noord and colleagues’ comment about the initial relapse rates over the first 2 weeks, we would like to offer the probabilities of remaining in sinus rhythm at 7, 14, and 30 days. At 7 days, these were 0.90, 0.93, 0.88, and 0.91 for the dofetilide 125 μg, 250 μg, and 500 μg and placebo groups, respectively. At 14 days, the rates were 0.60, 0.69, 0.77, and 0.58, respectively. At 30 days, the rates were 0.51, 0.60, 0.69, and 0.47, respectively. These data demonstrate, as do the results of the study by Tieleman et al., a separation of the probabilities after 7 days, indicating that dofetilide suppresses recurrence earlier than can be appreciated from the published figure.

Furthermore, the studies of verapamil and other antiarrhythmic drugs they mentioned used different definitions for successful cardioversion. Unfortunately, this is true of much of the cardioversion literature. Specifically, in the study by DeSimone et al that they quoted, successful cardioversion was defined as 3 beats of sinus rhythm, compared with our definition of sinus rhythm for 24 hours.

It is likewise difficult to compare studies with widely differing patient populations. Specifically, our population consisted of 59% to 69% of patients with NYHA class II to III heart failure and structural heart disease compared with a predominantly hypertensive population in DeSimone et al’s study and few patients with significant heart disease in Tieleman et al’s study. In summary, the data support the use of dofetilide for both cardioversion and maintenance of sinus rhythm, especially because the drug has been shown to be safe, even in heart failure patients.

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