

Pretreatment of Patients With Atrial Fibrillation Who Undergo Electrical Cardioversion

To the Editor:

We read with interest the study by Madrid et al¹ in a recent issue of *Circulation*. They investigated the role of pretreatment with amiodarone alone or combined with irbesartan in patients with long-lasting persistent atrial fibrillation, and concluded that adding irbesartan to amiodarone reduces recurrences. Nonetheless, some points should be stressed. They reported no significant difference in the baseline concomitant medication between the two groups. However, the percentage of both β -blockers, and calcium-channel blockers, is higher in the irbesartan group (15% versus 7%, $P=0.09$, and 9% versus 5%, $P=0.3$, respectively). Because both decrease intracellular calcium, we believe that both medications should be considered together.

When Tieleman et al² first demonstrated the role of calcium-lowering drugs in reducing recurrences of atrial fibrillation after electrical cardioversion, the proportion of patients taking calcium antagonists or β -blockers before cardioversion was of borderline significance ($P=0.06$ and $P=0.08$, respectively). When considering the overall intracellular calcium-lowering drugs, the proportion became significant ($P=0.04$). Arranging the Madrid et al data in a similar way, the percentage of calcium-lowering drugs might become statistically significantly lower in the amiodarone group. This could explain part of the lower recurrence rate of atrial fibrillation in the irbesartan group. Moreover, the findings that most of the benefit of irbesartan occurred during the first 2 months after cardioversion supports our hypothesis that the higher prevalence of calcium lowering drugs in the irbesartan group plays a role in the benefit of irbesartan.

As we and other groups have demonstrated, calcium-lowering drugs significantly decrease the early recurrence of atrial fibrillation,^{2,3} whereas an angiotensin I type 1 receptor blocker is expected to improve the structural remodeling during a period of months.⁴

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Response

We appreciate Dr Stabile's interest in our article and the opportunity to respond to his letter. Calcium channel blockade has been shown in several studies to prevent the shortening of

atrial refractoriness that occurs during atrial fibrillation. In the study published by De Simone et al,¹ patients treated with verapamil plus propafenone had a lower rate of recurrence within 3 months (33 versus 8%). Other important studies, like that published by Van Noord et al,² had disappointing results. In that particular study, all other antiarrhythmic drugs were omitted, except for β -adrenergic blockers. In our study, different combinations of drugs and the higher use of β -adrenergic blockers together with calcium-channel blockers in the group of patients treated with irbesartan (24%) compared with the amiodarone group (12%) may have had a role in the potential benefit of irbesartan. However, there are other possible mechanisms; these include decrease of wall stress, modulation of refractoriness, interference with ion currents, modification of sympathetic tone, stabilization of electrolyte concentrations, and possible effects on transmembrane action potentials and currents.³

Although electrical changes may be present after conversion of atrial fibrillation (which could be ameliorated with verapamil), the effect of structural changes may predominate (these could be modified with irbesartan). Efforts to reduce the structural changes that occur during atrial fibrillation may be more useful in preventing recurrences than efforts designed to minimize the electrical changes. Administration of irbesartan may have an antifibrotic effect due not only to its ability to diminish the synthesis of collagen type I, but also to its capacity to stimulate the degradation of collagen type I fibers. It may be important to intervene early, if possible, to prevent atrial structural remodeling before it occurs.

We agree with Dr Stabile that the pretreatment of patients with atrial fibrillation who undergo electrical cardioversion is important and will be the subject for continuous improvement.

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