Letters to the Editor

Letters to the Editor will be published, if suitable, as space permits. They should not exceed 1000 words (typed double-spaced) in length and may be subject to editing or abridgment.

Response

We appreciate the great interest of Ribichini et al in our article on the effects of chronic ACE inhibition with perindopril on ACE, AT1 receptor, and nitric oxide synthase expression in human blood vessels. In their letter, Ribichini et al speculated that increased vascular AT1 receptor expression during chronic ACE inhibition, as we observed, may limit or reverse the beneficial effects of ACE inhibitors and promote restenosis after percutaneous injury or coronary stenting. Because our study was not designed to assess clinical outcomes of chronic ACE inhibition with perindopril, we cannot speculate whether increased vascular AT1-receptor expression during chronic ACE inhibition has detrimental effects on coronary artery restenosis as proposed by Ribichini et al.

In theory, it is possible that ACE inhibition–induced upregulation of vascular AT1 receptors may have some unwanted effects, because Ang II generated by ACE-independent chymase in humans may act on AT1 receptors to induce vasoconstriction, cell proliferation, or hypertrophy. However, the beneficial effects of ACE inhibitors are well supported by both animal and human studies. Indeed, ACE inhibitors have been shown to be effective in preventing and treating hypertension and chronic heart failure in large randomized, double-blinded, and placebo-controlled, multiple-center clinical trials. Moreover, the recently published HOPE studies further extend the benefits of chronic ACE inhibition to possible prevention or treatment of human coronary atherosclerotic disease. ACE inhibitors exert multiple beneficial cardiovascular effects by inhibiting plasma and tissue Ang II formation, augmenting tissue kinins levels, and increasing bioavailability of NO. All of these effects of chronic ACE inhibition oppose the Ang II–induced vasoconstrictor and proliferation–or growth-promoting effects.

Currently, there is no conclusive evidence to support the hypothesis that ACE inhibitors can promote, whereas AT1 receptor antagonists (ARBs) reduce, coronary restenosis after percutaneous coronary injury or stenting. Apart from the studies on the patients with the DD genotype as cited by Ribichini et al, there is no conclusive evidence to support the hypothesis that ACE inhibitors can promote, whereas ARBs reduce, coronary restenosis after percutaneous coronary injury or stenting. Likewise, ARBs have been shown to be either effective or inconclusive in preventing coronary restenosis in pigs or humans. We should wait for the outcomes of several large ongoing randomized, double-blinded, placebo-controlled, and multiple-center clinical trials before drawing a conclusion about whether ACE inhibitors can promote restenosis after percutaneous coronary injury or stenting.

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