Are statins 'smart bombs'?

(AUGUST 2006)

TO THE EDITOR: In their recent article (*Cleve Clin J Med* 2006; 73:760–766), Dr. Shishehbor and colleagues assert that statins lower the risk of cardiovascular events beyond the expected reduction attributable to cholesterol-lowering alone, and that this extra benefit might be explained by their potent anti-inflammatory action. Therefore, in addition to weight loss, exercise, and smoking cessation, statin therapy would represent the best therapeutic option to modulate inflammation. For these pleiotropic effects, statins are called "smart bombs" in an accompanying editorial.[1]

However, angiotensin II plays a significant role in the initiation and perpetuation of inflammatory processes.[2] Consequently, angiotensin-receptor blockade has also been shown to be related to a decrease in markers of systemic inflammation,[3] which may result in a reduction, or potentially a reversal, of atherosclerosis, as well as other inflammation-associated cardiovascular diseases.[4] In fact, angiotensin-converting enzyme inhibitors have been shown to have the broadest effect of any drug in cardiovascular medicine, reducing the risk of myocardial infarction, stroke, diabetes, renal impairment, and, above all, total mortality.[5]

On the other hand, total mortality is still a hard nut for statin trials to crack. Furthermore, the negative pleiotropic effects of statins should also be taken into account, as they may lead to the documented poor compliance with this therapy.[6] In fact, the relevance of subjective adverse effects for discontinuation of drug use is likely more pronounced in clinical practice than in clinical trials.[7]

Therefore, we don't know whether statins are really smart. We know, however, they are bombs to handle with care.

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IN REPLY: Drs. Mascitelli and Pezzetta raise valid points regarding angiotensin-receptor blockers and their impact on clinical outcomes. A number of drugs currently used to treat various aspects of cardiovascular disease and diabetes exert part of their benefit through modulation of inflammation and oxidative stress.[1–3]

Statins have also been shown in numerous animal and human studies to exert potent systemic anti-inflammatory and antioxidant properties.[4,5] Therefore, it is believed that some of the benefit associated with the reduction in cardiovascular outcomes with statin therapy is related to these pleiotropic effects.[6]

We agree that statins, like many other drugs, are associated with side effects; however, this class of drugs remains among the most widely studied.[7] Therefore, with proper attention to symptoms and signs, side effects associated with this class of drugs are manageable.

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LETTERS TO THE EDITOR

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