Correspondence

The Effects of Statins on Mortality Rates among Bacteremic Patients

Str—Liappis et al. [1] noted decreased mortality rates among bacteremic patients who were receiving statins, but they were not able to define the mechanisms by which this reduction in the mortality rate occurred.

It has recently been proposed that endothelial apoptosis could be the pivotal event in the pathogenesis of systemic inflammatory response syndrome, sepsis, acute respiratory distress syndrome, and multiple-organ dysfunction syndrome [2]. Endothelial apoptosis is caused by Staphylococcus aureus, lipopolysaccharides, and numerous other factors commonly associated with bacteremia and sepsis, and it can be prevented by the use of statins [2, 3].

Other forms of treatment have a demonstrated effect on endothelial apoptosis. Activated protein C [4], insulin [5], and increased shear stress [6] are antiapoptotic for endothelial cells in vitro and have been found to significantly improve the outcome for critically ill patients [7–9]. These studies and the study by Liappis et al. [1] support the hypothesis that endothelial apoptosis plays a central role in the pathogenesis of some diseases, and that the prevention of endothelial apoptosis can cause significant improvements in the patient’s outcome [2].

References


Reply

Str—We appreciate Dr. Štefanic’s letter [1] proposing that statin-mediated inhibition of endothelial apoptosis may be a central mechanism for the decreased mortality rate observed among the bacteremic patients in our study [2]. Statins may alter neointimal thickness and stabilize atherosclerotic plaques through the reduction of apoptosis in vascular smooth-muscle cells [3, 4], but there have been limited data on endothelial cell apoptosis [5]. It is premature to favor a single dominant mechanism when recent investigations reveal that the impact of statins seems to be multifaceted.

The diverse effects of statins on the host’s inflammatory responses implicate multiple mechanisms rather than a single mechanism related to endothelial apoptosis. Independent of their lipid-lowering effects, statins have the potential to decrease isoprenylated proteins that are necessary for leukocyte cellular signaling, an important component of the inflammatory response. Recent studies have shown that statins modulate endothelial cell–adhesion molecules and block leukocyte integrins [6–8], regulate chemotactic proteins [9], and modulate proinflammatory cytokines [10], in addition to being associated with other non–lipid-lowering biologic effects. Whether any or all of these effects contributed to our finding of decreased mortality rates remains to be elucidated.

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References

3. Guijarro C, Blanco-Colio LM, Ortego M, et al. 3-Hydroxy-3-methylglutaryl coenzyme A reductase and isoprenylation inhibitors induce...