In this issue of Critical Care, Christensen and colleagues [1] present data suggesting that patients who chronically take statins have improved survival during acute hospitalizations and for at least 1 year thereafter. Over the last decade, the pleiotropic effects of statins have been increasingly elucidated. Perhaps most intriguing are the effects statins appear to have on the immune system, especially the modulation of diffuse or systemic inflammation. There is a growing body of observational literature suggesting that statins can actually reduce hospital mortality through mechanisms far beyond those that can be explained by reductions in cardiovascular events.

Statins for acutely hospitalized patients: randomized controlled trials are long overdue

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See related research by Christensen et al., http://ccforum.com/content/14/2/R29

Abstract

From the earliest studies of statins for control of plasma cholesterol, observations have been made that the reductions in mortality observed occurred in a manner seemingly independent from what could be anticipated from cholesterol lowering alone. Over the last decade, the pleiotropic effects of statins have been increasingly elucidated. Perhaps most intriguing are the effects statins appear to have on the immune system, especially the modulation of diffuse or systemic inflammation. There is a growing body of observational literature suggesting that statins can actually reduce hospital mortality through mechanisms far beyond those that can be explained by reductions in cardiovascular events.
lipophilic statins seem to be more potent, but it is not clear that this will translate into better in vivo results [5].

Adding strength to the association observed by Christensen and colleagues [1], current users, new users, and long-term users derived similar benefit whereas users of other cholesterol-lowering drugs had no associated benefit and indeed effects seemed to go the wrong direction. Other subgroups that fared the best with statin use include patients with gastrointestinal disease, trauma, poisoning, cancer, or mechanical ventilation. Effects did not seem to differ as to whether the patient was surgical or medical. The survival benefit persisted out to 1 year of follow-up. At least one randomized trial in critically ill patients with infection has been completed. It was not large enough to address clinical outcomes but did demonstrate a reduction in inflammatory cytokines in the statin arm [6].

Given the results derived from observational data from a very large and still rapidly growing literature on the benefits of statins, prospective randomized trials are now clearly indicated. At least one such trial, conducted by the National Institutes of Health ARDS [Acute Respiratory Distress Syndrome] Clinical Trials Network [7], is targeting an enrollment of 1,000 patients and is under way in patients with acute lung injury (ALI) due to infection. Several aspects of statins, including the simplicity with which statins can be used in the hospital setting, their low cost, and their relative safety, make the opportunity to evaluate this class of agents in prospective trials even more exciting. These drugs have the potential to actually prevent the development of sepsis, make sepsis less severe, reduce the incidence of ALI/ARDS, and reduce mortality.

Abbreviations
ALI, acute lung injury; ARDS, acute respiratory distress syndrome; CI, confidence interval.

Competing interests
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