

Future of statins in sepsis: a review on its safety and efficacy

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Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to infection. Statins [Hydroxymethylglutaryl-CoA reductase inhibitors] not only lower cholesterol levels but also have been proposed as adjunctive therapy in sepsis due to their pleiotropic effects. They act on several stages in sepsis: the generation of proinflammatory cytokines, modulation of leukocyte and monocyte functions, and reduction of oxidative stress as well as improvement in endothelial function and platelet activity. However, it has been argued if the observed beneficial effect of statins in sepsis is related to preadmission or post-admission use of statins. Also, the positive impact of statins on the clinical outcome of patients with sepsis has shown conflicting results. Accordingly, this review will discuss recent evidence regarding the use of statins in sepsis. Also, adequate use of statins based on the right drug, at the right time, at the right dose and in the right population will be discussed. The information in this review shows that the effect of statins is a drug, not a class effect, with the most effective drug in sepsis being simvastatin. Besides, it highlights the importance of proper timing and dosing of statins to manifest their antibacterial and pleiotropic effects. Finally, the effect of statins in sepsis is restricted to early phases of sepsis or sepsis prevention, not sepsis complicated with organ dysfunction or septic shock. However, more *in vivo* and clinical trials are required to determine the final decision about statin use in sepsis. may improve brain metabolism, restore mitochondrial ATP production, decrease reactive oxygen species production, reduce inflammation, and increase neurotrophic factors' function. It has been shown that KD mimics the effects of fasting and the lack of glucose/insulin signaling, promoting a metabolic shift towards fatty acid utilization. In this work, the author reports a number of successful case reports treated through metabolic ketosis. The available evidence suggests that, in the future, treatment of sepsis may benefit from including statin therapy. Given their pleiotropic effects related to many pathophysiological determinants of sepsis, statin therapy may be the next logical step in the search for adjuvant therapy.

However, there have been no RCT of statins in sepsis, and large randomized controlled clinical trials with clinically relevant primary endpoints are desperately needed. It is imperative to test the efficacy and safety and the benefit/adverse effects of statins administered at the onset of sepsis, as well as in patients with severe sepsis or septic shock admitted into ICUs.

REFERENCES

1. Albert MA, Danielson E, Rifai N, Ridker PM. Effect of statin therapy on C-reactive protein levels: the pravastatin inflammation/CRP evaluation (PRINCE): a randomized trial and cohort study, *JAMA*, 2001, vol. 286 (pg. 64-70)
2. Alfon J, Pueyo PC, Royo T, Badimon L. Effects of statins in thrombosis and aortic lesion development in a dyslipemic rabbit model, *Thromb Haemost*, 1999, vol. 81 (pg. 822-7)
3. Almog Y, Novack V, Eisinger M, Porath A, Novack L, Gilutz H. The effect of statin therapy on infection-related mortality in patients with atherosclerotic diseases, *Crit Care Med*, 2007, vol. 35 (pg. 372-8)
4. Almog YM, Shefer AM, Novack VM, et al. Prior statin therapy is associated with a decreased rate of severe sepsis [Article], *Circulation*, 2004, vol. 110 (pg. 880-5)
5. Andrews P, Azoulay E, Antonelli M, et al. Year in review in intensive care medicine, 2006. II Infections and sepsis, haemodynamics, elderly, invasive and noninvasive mechanical ventilation, weaning, ARDS, *Intensive Care Med*, 2007, vol. 33 (pg. 214-29)

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