

### Pleiotropic Effects of Statins

#### **1. Are the pleiotropic effects of statins, including the anti-inflammatory effects, proportional to the degree of lipid lowering?**

##### **Question submitted by: anonymous**

Potent inhibitors of cholesterol biosynthesis, statins have been proven to be beneficial in both primary and secondary prevention of CVD. However, the overall benefits of statins, as observed in clinical trials, appear to be greater than what might be expected from changes in lipid levels alone, suggesting effects beyond cholesterol-lowering. Mounting evidence suggests that some of the cholesterol-independent or pleiotropic effects of statins include improvement in endothelial function, reduction of oxidative stress, inhibition of platelet aggregation, and stabilization of atherosclerotic plaques by attenuation of the inflammatory response.<sup>1</sup> In addition, statins have been shown to have beneficial extrahepatic effects, including enhancing immune function, protecting the CNS, improving renal

function, reducing serum uric acid levels, and improving bone mineralization.<sup>2</sup> Although proof in appropriately designed trials is currently lacking, there is data to suggest that, in high-risk patient groups, the pleiotropic effects of statins may be partially responsible for the observed reduction of morbidity and mortality, and proportional to the degree of lipid lowering.<sup>3</sup> While this is all very exciting, it's important to remember that although cholesterol-independent effects may be at play with statin therapy, LDL-C is a meddlesome metabolite, which raises havoc on our cardiovascular system in diverse and extensive ways. Therefore, LDL-C lowering needs to remain our priority in managing patients at risk for CVD, with goals less than 2.0 mmol/L in both moderate- and high-risk groups.<sup>4</sup>

##### References

1. Athyros VG, Kakafika AI, Tziomalos K, et al: Pleiotropic Effects of Statins—clinical Evidence. *Curr Pharm Des.* 2009;15(5):479–489.
2. Liao JK, Laufs U: Pleiotropic Effects of Statins. *Annual Review of Pharmacology and Toxicology* 2005; 45:89–118.
3. Palaniswamy C, Selvaraj DR, Selvaraj T, et al: Mechanisms Underlying Pleiotropic Effects of Statins. *Am J Ther* 2010; 17(1):75–78.
4. Genest J, McPherson R, Frohlich J, et al: 2009 Canadian Cardiovascular Society/Canadian Guidelines for the Diagnosis and Treatment of Dyslipidemia and Prevention of Cardiovascular Disease in the Adult – 2009 Recommendations. *Can J Cardiol* 2009; 25(10):567–579.

Answered by:

**Dr. Theodore K Fenske**

## Colchicine for the Prevention of Pericarditis

### **2. Does the use of colchicine prevent recurrence of pericarditis?**

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**Question submitted by: Hany Kamel, St-Laurent, Québec**

Imazio, *et al* just published a systematic review of colchicine for the prevention of pericarditis.<sup>1</sup> They found five randomized controlled trials comparing colchicine 1.0 to 2.0 mg on day one, then 0.5 to 1.0 mg per day, for preventing pericarditis after cardiac surgery (two trials) or following a single attack (three trials). They found that colchicine did indeed prevent pericarditis: the risk ratio was 0.40 (95% CI: 0.30 to 0.54). I calculate the absolute risk reduction as 18.9% (11.8% in the colchicine

treated patients versus 30.7% in untreated patients), so only five or six patients need be treated for one to six months to prevent one episode. None of the trials reported a serious adverse event (*e.g.*, death or requiring medical intervention), but gastrointestinal intolerance (*e.g.*, diarrhea) was numerically more common in the colchicine group and led to more withdrawals. The authors concluded that colchicine was safe and efficacious for the prevention of pericarditis.

#### Reference

1. Imazio M, Brucato A, Forno D, *et al*: Efficacy and Safety of Colchicine for Pericarditis Prevention. Systematic Review and Meta-analysis. *Heart* 2012. (epub ahead of print March 22, 2012).

Answered by:

**Dr. Thomas W. Wilson**

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