A better treatment for saphenous vein graft disease after coronary artery bypass surgery: Might statins be the answer at the right dose to the right patient at the right time?

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Central Message

Cardiac surgeons are often frustrated with venous graft failures. Finding a pharmacologic agent that helps mitigate graft failures would be of immense value. Is the right dose of statin the answer?

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Surgical methods to harvest and graft veins into coronary arteries are well optimized so pharmacologic interventions are often explored as the next step to maintain saphenous vein graft (SVG) patency. Aspirin and statin drugs are actual pharmacologic treatments for SVG disease.¹

Statin became a multipurpose drug because of their pleiotropic effects beyond cholesterol lowering.² Statins at the optimal dose to the right patient and at the appropriate time may be the answer for surgeons frustrated with SVG disease progression despite tireless efforts to optimize surgical revascularization procedures.

SVG disease pathophysiology has 3 main phases: early thrombosis (up to 30 days) followed by smooth muscle hyperplasia (up to 1 year) and atherosclerosis (after 1 year).

Ideally, one would want to delay the disease development at the earliest point and consequently avoid SVG stenosis and failure. Because statins are already used successfully to treat hypercholesterolemia and long-term SVG disease, it is reasonable to test these agents short term with higher doses. Kulik and colleagues did just that.³

A well-designed pilot trial comparing the effects of atorvastatin (intense [80 mg/day] and moderate [10 mg/day] doses) on early graft occlusion of 173 patients who underwent SVG for coronary artery bypass surgery. The moderate dose was not better than the intense dose according to computed *P* values with an α set at 0.05. If more broadly aimed at SVG disease, including either occlusion or stenosis, better response was recorded, albeit not yet significant.

RIGHT DOSE

When we analyze experiments with negative results, it is essential to make sure that the drug was effective. Low-density lipoprotein levels clearly showed a highly

significant decrease between moderate and intense doses, reassuring that, for what statins are better known for, the different doses are acting accordingly. It also may mean that plasma low-density lipoprotein levels below a certain level has marginal, if any, influence on the development of SVG disease at 1 year.

RIGHT PATIENT

The closest statistically significant result was, unfortunately, elevated liver enzymes in 3 patients in the intense treatment group compared with none in the moderate group. Treatment discontinuation, however, was due to patient preferences (side effects) or physician insistence on open label treatment. The pharmacogenomic properties of statins may guide to a personalized medicines with fewer risks and more efficiency.⁴⁻⁶

RIGHT TIME

If the pathophysiology of SVG disease is correct, statins are effective at the late atherosclerotic phase. In the earlier phases (ie, thrombosis and/or smooth muscle hyperplasia), other pharmacologic agents are likely better candidates. A good response to long-term prevention of SVG disease

using statins⁷ and other lipid-lowering drugs⁸ has been documented.

RIGHT TRIAL

The authors should be congratulated for their efforts at bringing trustworthy negative data to such an important medical problem.

The publication of well-controlled negative results is important because it helps to prepare more realistic evidence-based systematic review^{9,10} to guide medical treatments.

As we keep learning from well-controlled negative clinical studies, the next trials will have improved chances to yield more efficacious treatments for important medical problems.

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