LDL-C Limbo: How Low Will You Go?

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About Megan

- Megan, 81, is hypertensive.
- Her history shows that at age 72 she had coronary bypass surgery.
- At this time, she stopped smoking.
- Recently, she was re-hospitalized for an acute coronary syndrome but she declined repeat angiography.
- Her lipid profile is HDL-C 1.1 mmol/L and LDL-C 2.9 mmol/L.
- Megan takes acetylsalicylic acid, 81 mg, orally, daily; ramipril, 10 mg, orally, daily; hydrochlorothiazide, 12.5 mg, daily, orally and atorvastin, 10 mg, orally, daily.

For another case, go to page 64.

For millennia, the genes of our ancestors adapted to subsistence, not surplus. In the present era of all-you-can-eat consumerism, this inheritance condemns one in three of our population to vascular death. Lowering the serum LDL cholesterol (LDL-C) reduces the toll of this metabolic paradox. There are benefits for seniors of having even lower LDL-C levels and lipid lowering therapy in seniors will be discussed.

How low to go?

The last Canadian recommendations for prevention and management of coronary disease were issued in 2003, based on a decade of placebo-controlled clinical trials that confirmed efficacy and safety through cholesterol reduction. Since 2002, four secondary prevention trials[2-5] have reported additional benefits with even lower LDL-C levels in stable and acute coronary patients. These studies showed that 11% to 22% of acute coronary patients displayed further improvements in mortality, coronary events and rates of revascularization with LDL-C < 2.0 mmol/L compared to the conventional target of 2.5 mmol/L.

Remarkably, a lower limit of LDL-C was always associated with a better outcome and benefit was observed independent of baseline levels. Moreover, no excess adverse effects occurred in patients with plunging LDL-C (*e.g.,* 0.9 mmol/L)[2] compared to cohorts whose lipids lingered at conventional targets while receiving similar statin doses.

How to go low?

A recent meta-regression analysis[2] compared clinical trials aimed at lowering cholesterol. These trials employed either dieting, gastric surgery and bile adsorbing resins or statins. These trials found that the LDL-C level, not the method of lipid lowering, correlated best with the cardiovascular outcome. This strongly endorses the use of all methods to reduce LDL-C, especially when higher statin doses are problematic. Blocking intestinal cholesterol absorption with oral ezetimibe, 10 mg, daily, may be effective alone but can be combined with statin doses to achieve up to 50% LDL-C reduction. Slow release oral niacin, 500 mg to 2,000 mg, daily, for every hour of sleep can be useful in combination with statins.

A recent, large trial of fenofibrate[3] in Type 2 diabetics showed only a reduction in MI and the need for coronary revascularization. The best results come from combining pharmacologic tactics with cigarette cessation, dieting (including fish and fish oils), weight loss, exercise, as well as optimal BP and blood glucose control.

Too old to go low?

Several studies have reported the benefits of lipid therapy in the elderly. The Provastatin in Elderly individuals at Risk of Vascular disease (PROSPER) trial[4] randomized 5,804 high-risk subjects from 70 years of age to 82 years of age to pravastatin or placebo.

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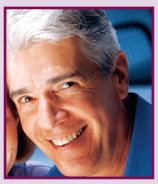
About Geoff



- Geoff, 55, is a married executive and exercise enthusiast.
- His CT scan reveals calcium in two coronary arteries, but a later exercise sestimibi test reveals everything to be normal at 15 mets.
- Geoff's only atherosclerotic risk is his father who died unexpectedly at the age of 57 from a MI.
- His lipid profile is HDL-C 1.4 mmol/L and LDL-C 3.2 mmol/L.

Over a period of three years, the trial found:

- a significant reduction (15%) in cardiac death and MI (10.1% vs. 12.2%), but not in stroke,
- no decrease in cognitive or other functions,
- no reduction in all-cause mortality and
- an elevated cancer incidence in the treatment arm.

In other assessments of seniors in lipid trials and meta-analysis,[6] positive cardiovascular outcomes have also seen a consistent reduction in stroke (27%) and no significant excess in non-cardiovascular demise. Even with the mortality issues of seniors put aside, reducing their high incidence of non-fatal (and recurrent) vascular events can be valuable.[6]

No caveats?

In statin therapy, each dosage increment raises the risk of hepatic and myopathic side-effects to one to three per cent, while lowering LDL-C by about nine per cent. Fortunately, the vast majority of complications are mild and reversible, while the excess of serious or fatal reactions is extremely low at about 0.01%. Follow creatine phosphokinase and liver function carefully if niacin or fibrates are combined with a statin.

Toxicity is promoted by factors such as:

- low body weight,
- low muscle mass,
- hypothyroidism,
- liver disease and
- concurrent medications that compete for the statin clearance pathway (*e.g.,* diltiazem).

Finally, the physcians must consider the cost and inconvenience for the patient of yet, more pills in older patients with multiple comorbidities whose healthcare philosophies may differ from the doctor's.

In July 2004, the US National Cholesterol Education Program published an update for more aggressive options in high-risk patients. High-risk patients were those who had any two atherosclerotic risk factors, including cigarette smoking, diabetes, metabolic syndrome or a history of past coronary events. Given the volume and strength of studies reported in 2005 alone, it is expected that 2006 will see very low LDL-C guidelines made standard.

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Take-home message

- Lower LDL-C is better, even when the baseline is not high.
- Statins are big players in a many-pronged approach.
- The high-risk have the most to gain.
- Raising the statin dose lowers LDL-C about 9% more.
- Ezetimibe and slow-release niacin tablets help to reach targets.
- Drugs for other purposes can induce statin toxicity.

References

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