CHOLESTEROL & STATINS
AN UPDATE

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The previous SYNAPSE series of articles on "The Cholesterol Controversy" discussed how the theory linking dietary saturated fat, blood cholesterol and atherosclerosis was established by an American biologist in the 1950s and how the concurrent claims of a London physiology professor, that sugar not fat was mainly responsible for atherosclerosis, were ignored. We also highlighted the evidence that sugars, refined carbohydrates, starches and trans-fatty acids raise blood triglycerides (TRGs) and lower HDL-cholesterol, and that this TRGs/HDL ratio (the higher above 1 the higher the risk) is a more accurate indicator of risk for atherosclerosis than any other blood lipid profile risk ratios in common use.

At the same time we learned of the recent doubts about the validity of LDL as a reliable marker for risk of atherosclerotic, based principally on the finding that what routine laboratories measure as "LDL" is in fact a mixture of two distinct sub-fractions of LDL, one is a large light particle and the other a small dense particle. The small dense particle is the one involved in atherosclerosis. Hence, when "LDL is raised" in routine lipid profiles, one doesn't know whether the innocuous large particle, or the dangerous small particle, is largely responsible for the "raised LDL". Prescribing statins for a raised innocuous large particle LDL would therefore be inappropriate. How does one get round this problem of routine laboratories measuring only one total LDL?

We learned that a raised TRGs/HDL ratio is a surrogate marker for the raised small dense particle LDL. We also know that a high refined carbohydrate, starchy and trans-fat diet, the metabolic syndrome, and diabetes, are characterised by a raised TRGs/HDL ratio. Their association with atherosclerosis risk thus becomes clearer.

The above doubts about the reliability of routine LDL measurements to assess atherosclerotic disease risk, combined with the lack of randomised controlled data relating to the effect of different intensities of statins or different combinations of medications on specific LDL levels, led the American College of Cardiology/American Heart Association to eliminate specific LDL targets from their 2013 cholesterol guidelines.[1]

However, the National Lipid Association (US),[2] the European Society of Cardiology[3] and the Canadian Cardiovascular Society[4] continue to include LDL targets, which adds to the confusion since these targets are not evidence-based. Interestingly, Alberico Catapano, president of European Atherosclerosis Society and professor of pharmacology at Milan University, advises looking at the TRGs (especially when high) when managing LDL.[5] Remember the above observation that a high TRGs/HDL ratio is a surrogate marker for high small dense particle (bad) LDL.

The pathological basis of atherosclerosis is now well established to be a chronic inflammatory arterial disease.[6] Current research concentrates on which inflammatory cytokines are pro- or anti-atherogenic, and which drugs may promote anti-atherogenic cytokines or which dampen the effects of pro-atherogenic ones. Anti-tumour necrosis factor alpha (TNFa) is one of the pro-atherogenic cytokines and anti-TNFa therapy is associated with a reduced risk for all cardiovascular events.[7]

The cardiovascular beneficial effect of statins have traditionally been associated with their hypolipidaemic effects but has also been shown to be due to their anti-inflammatory action mediated via modulation of cytokine action. High blood glucose increases TNFa levels and atorvastatin is known to lower the post-glucose loading levels of TNF-a.[8] This also indicates at least one mechanism via which elevated blood glucose promotes atherogenesis and, therefore, how a high refined carbohydrate and starchy diet is pro-atherogenic.

It has also been shown that reduction of C-reactive protein (CRP) levels with statin treatment is independent from the reduction of LDL levels.[9] Lovastatin has been shown to prevent cardiovascular events in those coronary artery disease subjects with especially high CRP despite a favourable LDL profile.[10] Another study demonstrated that in subjects with CRP levels higher than 2mg/L, even with low LDL levels, rosuvastatin can decrease cardiovascular events.[11]

As you would expect, in all this pharmaceutical company-funded research activity, there will be no randomised controlled trials comparing the claimed anti-inflammatory and anti-atherogenic potential of omega-3 fatty acids[12] with those of statins. Omega-3 fatty acids are of both marine and plant origin. The latter are probably not only safer but definitely cheaper (such as flaxseed oil capsules) than pharmaceutical grade fish oil (distilled to remove any possible heavy metal contamination).

TAKE-HOME POINTS

1. The little known fact that LDL has two sub-fractions, one "good" and one "bad", and that only one total LDL is routinely measured, questions the reliability of conventional LDL levels for adverse cardiovascular events risk assessment. It is hard to justify statin therapy when the TRGs/HDL ratio and the CRP level are within normal limits, irrespective of LDL level, particularly in primary prevention. The TRGs/HDL ratio and the CRP should be the two most important risk indicators.[13]
2. The pro-atherogenic effects of sugars, other refined carbohydrates, starches and trans-fats have been re-emphasised. Drug therapy without correct dietary and lifestyle advice does not constitute adequate management of cardiovascular health.

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