

Hello lipid friends: This week brings the following dilemma. A clinician has a patient who is concerned about her lipids. She is a 47 y/o woman, family history of MI in parents >75 years of age; she's never smoked and has no CV medical surgical history; is normotensive; and vigorous but no regular aerobic activity; euglycemic.

Total cholesterol = 247 LDL-C = 175 HDL-C = 110 Triglycerides = 135

She wants to be on a statin. The clinician on the case has made a judgment about her lipids/risk profile that her high HDL protects her so much a statin is unwarranted. I am asked for an opinion.

DAYSRING ANALYSIS

One always has to take a close look at a lipid profile before acting on it. I think the lipid profile posted above is incorrect: in fact it is impossible

Total cholesterol is the sum of LDL-C + HDL-C + VLDL-C

VLDL-C is = TG/5 = 135/5 = 27

If the TG, HDL-C and LDL-C reported above are accurate, then her total cholesterol must be 175 + 110 + 27 = 312

Thus her Non HDL-C = 202 (normal is well under 160 using NCEP criteria or 130 using AHA Women's criteria)

In general increased amounts of HDL particles can offer CV protection through direct antiatherogenic action or by contributing to reverse cholesterol transport (RCT), but this lady still has a very significant amount of cholesterol in her LDL particles. Her Non HDL-C level is extremely high at 202. Both LDL-C and Non HDL-C are surrogates for beta-lipoproteins (apoB containing particles). Elevations of LDL-C and Non HDL-C would be extremely suggestive that she has a very high apoB level (VLDL, IDL and LDL particle concentration) and has familial hyperbetalipoproteinemia. The only way to truly answer this is to quantitate betalipoprotein concentrations.

You need to do an NMR lipoproteins and quantitate LDL and VLDL particles or do an Apolipoprotein B level: I suspect it will be very high and then you have a risk assessment and therapeutic decision to make. Please be aware that there are genetic disorders of hepatic lipase and cholesterol ester transfer protein (CETP) which cause significantly increased HDL-C and are associated with CV risk.

If you do a risk assessment using the Framingham equation (recommended by NCEP and the AHA) this woman would not be considered as very high risk. She is young, does not smoke or have elevated BP and has an HDL-C level that is very desirable. Lifestyle therapy would be advised to reduce her LDL-C to 160 mg/dL or below. If her LDL-C was above 190 mg/dL a drug would be appropriate therapy.

NCEP is nice and is put together as a guideline, but clinicians are always allowed to use their clinical judgment in treating individuals. This perimenopausal woman is entering a period of life where CV risk takes off. I much prefer preventing disease if safe and cost therapies exist. If her NMR particle concentration or apoB level is significantly abnormal which is certainly likely I would be very inclined to use pharmacotherapy after a trial of lifestyle. In general lifestyle is not going to work miracles in patients who have genetic apoB hyperproduction (Type IIa hyperlipidemia).

If one elected for a drug (and I would) to lower apoB in this perimenopausal woman one should consider a statin or a stain/Zetia. I prefer to recommend hydrophilic statins: Pravachol requires no follow-up LFT testing and has virtually no drug-drug interactions to worry about. Crestor would fall into that category but does not have the decade of safety data that Pravachol has. LFTs do have to be followed on Crestor. Of course Crestor would be used at a 5-10 mg dose and Prava at 40 mg.

As my readers know, I am very much convinced that statins should always be prescribed with Zetia: to keep sterols out and to up-regulate HMG CoA reductase in cholesterol hyperabsorbers (which makes the statin much more effective). So I would go with low dose statin and Zetia in this lady. If you want to go statin alone and follow apoB, go ahead. If the apoB did not drop on the statin, you then know you have a person who is hyperabsorbing cholesterol and has hepatic down-regulation of HMG CoA reductase. Zetia will turn that statin into a miracle drug: because by inhibiting cholesterol delivery to the liver, HMG levels are increased (upregulated) and the statin will then work.

References of the week:

Clinical Usefulness of Very High and Very Low Levels of C-Reactive Protein Across the Full Range of Framingham Risk Scores (Circulation. 2004;109:1955-1959.)

Conclusions—Both very low (< 0.5 mg/L) and very high (> 10 mg/L) levels of hsCRP provide important prognostic information on cardiovascular risk. hsCRP is clinically useful for risk prediction across a full range of values and across a full range of Framingham Risk Score.

Selenoprotein synthesis and side-effects of statins THE LANCET • Vol 363 • March 13, 2004

Statins are generally well tolerated, however, they do cause some unusual side-effects with potentially severe consequences, most prominently myopathy or rhabdomyolysis and polyneuropathy. We noted that the pattern of side-effects associated with statins resembles the pathology of selenium deficiency, and postulated that the mechanism lay in a well established, but often overlooked, biochemical pathway—the isopentenylolation of selenocysteine-tRNA. A negative effect of statins on selenoprotein synthesis does seem to explain many of the enigmatic effects and side-effects of statins, in particular, statin-induced myopathy.

Dayspring Travels:

Columbia and Greenville, SC
Anaheim, San Diego & LA Week of 5/17
Voorhees and Mountain Lakes, NJ
Dallas - Fort Worth and Tyler TX (last week May)

I just did (April 24) a CME presentation at the Annual MidAtlantic Nurse Practitioner Meeting at the University of Maryland. The lecture on Atherothrombosis in Women: Effects of Estrogen Receptor modulation was taped and is (will be) available from (I get no benefit)

All Star Media 9470 Campo Rd PMB #118 Spring Valley, CA 91977
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The selection number is 812-47 G2
The audio CD is \$12 and mp3 file \$10 plus shipping

As I type this I am sitting at St. Louis Airport watching some guardsmen take off in AF fighter planes and I am again saying thanks so much to those who give up so much to protect our way of life. Never forget them.

Best regards and happy lipiding

Tom