Letters to the Editor

Statins do lower cardiovascular mortality

To the Editor

The point/counterpart in the recent issue of the Journal of Clinical Lipidology confronts the anti-statin view of Ed-die Vos, MEng, and the pro-statin view of Alan Sniderman, MD. I would like to add my experience to this debate.

As a family physician who sees potential victims of atherothrombotic disease (ATD) decades before they actually become victims of ATD, I have the benefit of being able to have determined ATD risk and to offer dyslipidemic therapy to my patients with the usual dyslipidemias that lead to ATD, rather than just to patients with Type II hyperlipoproteinemia. Some of my patients decline my offer of treatment and others accept it. My treatment involves, in most cases, the use of super statins to drive low-density lipoprotein cholesterol down to plaque regression levels and to raise, if possible, high-density lipoprotein cholesterol. I may combine the superstats with resins to achieve the desired goals of therapy because resins can achieve high rates of plaque nonprogrresssion.

Cigarette smoking is the leading cause of death in ATD. Of the past 4 ATD deaths in my patients, occurring over the past 10 years, all have been patients who refused my offer of treatment of their dyslipidemia. A little more than 10 years ago a treated patient of mine died of ventricular tachycardia, but he was in his mid-80s and had given advanced directives to do nothing in the event of a cardiac catastrophe. The former group had 2 current cigarette smokers, 1 nonsmoker, and 1 who had smoked cigarettes in the distant past.

I understand that my report is anecdotal. However, in my experience, Eddie Voss is just plain wrong.

William E. Feeman Jr, MD
Bowling Green, OH, USA

http://dx.doi.org/10.1016/j.jacl.2013.06.008

References

2. Feeman WE Jr. Poster presentation at The Lipid Regulatory Hypothesis 2013 Annual Symposium of the National Lipid Association. May 2013; Las Vegas, NV.

Large high-density lipoprotein cholesterol at birth and its early postnatal changes

We appreciated the report by Kwiterovich et al about high-density lipoprotein cholesterol (HDL-C) subfractions in infants at birth and follow-up (FU) at 2 to 3 months. They demonstrated a strong maternal-to-infant correlation for the largest HDL-C (H5C) level at birth, suggesting that maternal cholesterol is transferred predominantly to fetal HDLs and promotes the formation of H5C. In addition, the H5C level in infants at FU was 3.2-fold greater than that at birth. The investigators speculated that neonatal programming could be responsible for the persistence of a higher H5C at FU. These results were very interesting to us because we also investigated HDL-C subclasses in term and preterm infants at birth and at 1-month FU.

Our study included 81 appropriate-for-gestational-age infants; 25 late preterm infants (LPIs) and 56 term infants (TIs). At birth and at 1 month, serum lipoprotein analyses were performed with the high-performance liquid chromatography method, which measured cholesterol levels in 12 lipoprotein subclasses. At birth, the large HDL-C level was significantly higher in LPIs (mean ± SD: 11.9 ± 6.3 mg/dL) than in TIs (8.6 ± 1.7 mg/dL). However, very large HDL-C levels showed no difference (6.3 ± 3.7 mg/dL and 6.2 ± 3.4 mg/dL, respectively). At FU, very large and large HDL-C levels in TIs (8.9 ± 4.7 mg/dL and 15.9 ± 6.2 mg/dL, respectively) were 1.4- and 1.8-fold greater than levels at birth. However, a 21% decrease in the very large HDL-C level (5.0 ± 2.8 mg/dL) and no change in the large HDL-C level (11.9 ± 7.7 mg/dL) were seen in LPIs. Our results confirmed that higher large and very large HDL-C levels persisted during the early postnatal period in TIs. These findings are compatible with those by Kwiterovich et al. However, in LPIs, postnatal changes in large and very large HDL-C levels were impaired. A previous study in preterm infants also found that large HDL particles persisted for 1 month but did not increase. Kwiterovich et al hypothesized that infants with a low H5C level may have a predisposition to very low-density lipoprotein (VLDL) production and are more likely to be dyslipidemic later in childhood under some programming.

Kwiterovich et al hypothesized that infants with a low H5C level may have a predisposition to very low-density lipoprotein (VLDL) production and are more likely to be dyslipidemic later in childhood under some programming.
mechanisms. In our study, LPIs at FU had significantly higher large and medium VLDL-cholesterol levels, as well as lower levels in large and very large HDL-C. This distinct lipoprotein phenotype may contribute to the development of cardiovascular diseases if it persists. Studies of adolescent twin pairs suggest that genetic factors account for the association between low birth weight and high LDL cholesterol levels, whereas intrauterine factors rather than genetic factors possibly play a role in the association between low birth weight and low HDL-C levels.5

Preterm infants, even those who were born otherwise healthy, have a unique postnatal change in the HDL-C subclass. Understanding the metabolism of lipoproteins during the early postnatal period could provide useful information for establishing better personalized lipid nutrition and cardiovascular risk assessments for the improvement of long-term outcomes.

Tomoo Okada, MD
Nobuhiko Nagano, MD
Shigebaru Hosono, MD
Tokyo, Japan

http://dx.doi.org/10.1016/j.jacl.2013.05.006

References


Response to the letter from Okada et al

The letter from Okada et al is of interest because their prior research has indicated that high-density lipoprotein (HDL) cholesterol levels are higher in preterm than in full-term infants at birth, a difference that may persist at adolescence. Their work supports the tenet that further research is needed on the importance of HDL during intrauterine life and in the immediate postnatal period and perhaps beyond.

Okada et al found that large HDL particles were not elevated at birth by using high-performance liquid chromatography that measured 12 lipoprotein subclasses. We measured the size and concentration of 15 lipoprotein subclasses by nuclear magnetic resonance spectroscopy. We found significant heterogeneity among the size and concentrations of the largest HDL subclass, namely that designated H5C. Some infants had markedly increased H5C, whereas some had smaller amounts, and others had barely detectable levels. Immunochemical measurement of apolipoprotein C-I (apoC-I) in Dr Alaupovic’s laboratory indicated a strong and linear relationship between apoC-I levels and H5C concentrations. Our hypothesis is that this is related to the effect of apoC-I which can stimulate lecithin-cholesterol acyl transferase but can inhibit the uptake of cholesterol from cholesteryl ester transfer protein and scavenger receptor class B type 1. Both effects should promote a large HDL particle.1 ApoC-I did not promote higher triglycerides in the infants, either at birth or at follow-up. These effects of apoC-I on H5C and triglycerides in infants are diametrically opposite of those found in the parents of these children. Thus, it appears that HDL metabolism is different than that in adults and perhaps has some important but incompletely understood role in infant intrauterine and postnatal development.

I wish to point out that we previously studied a large, biracial group of infants in whom the prominent large HDL was present in approximately 1 in 5 infants, absent in another 20% and intermediate in the other 60%.2

A genetic or prominent environmental factor is presumably affecting the phenotypes and appears to be operating through apoC-I. In this first study we also documented the presence or absence of the large HDL by density gradient ultracentrifugation, supporting the nuclear magnetic resonance spectroscopic findings of large H5C in both studies.2 Thus, it is unlikely that our observations are due to methodological issues.

Peter O. Kwiterovich, MD
Baltimore, MD, USA

http://dx.doi.org/10.1016/j.jacl.2013.06.009

References
