Los niveles bajos de proteína transportadora de ésteres colesterilo se asocian con el riesgo de enfermedad cardiovascular

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Elevated blood low-density lipoproteins (LDL) cholesterol concentrations are major cardiovascular disease risk factors and lowering their levels has been the focus of behavioral and pharmacological preventive and therapeutic measures to decrease heart disease in the population. Conversely, raising high-density lipoprotein (HDL) cholesterol levels may have similar or greater cardiovascular benefit. Molecular mechanisms and genetics of cardiovascular disease and aging: Basic and clinical approaches.

CETP is a protein that shuttles cholesterol throughout the body, thus controlling the levels of HDL, LDL, and very-low-density lipoprotein (VLDL) in the blood. Some studies suggested that inhibition of CETP was associated with increased HDL cholesterol concentrations. Therefore, inhibiting this protein became the target for pharmacological therapy to reduce cardiovascular risk by increasing HDL-cholesterol concentrations. However, in a clinical trial testing that hypothesis, heart disease unexpectedly advanced in a surprising number of participants, despite achieving significant increases in HDL-cholesterol.

To better understand the basis for those paradoxical effects, Ordovas and colleagues examined CETP activity in 1,978 Caucasian men and women with a mean age of 51 years-old and no history of heart disease. They analyzed 15 to 18 years of study visits looking for first cardiac events including heart failure, heart attack, angina, stroke and peripheral vascular disease.

By the end of the follow-up period, 320 men and women had experienced their first cardiac event. Interestingly, participants with low CETP activity were 18 percent more likely to develop cardiovascular disease than people with CETP activity above the median.

A more in-depth investigation of the statistical models eliminated the possibility that age, sex and common risk factors such as smoking, weight, diabetes, and cholesterol levels interfered with the findings that clearly differ from previous studies suggesting that inhibiting CETP activity would bring a cardiovascular benefit by raising HDL.

However, we need to emphasize that this information is based on a single observational study. The relationship between CETP activity and HDL levels carries many unknowns. In the meanwhile, other CETP inhibitors are in the pipeline and they may overcome some of the initial adverse side effects. At this time there is not enough research to discount the possibility that raising HDL levels through CETP inhibitors may reduce the risk of heart disease.

Vasan RS, Pencina MJ, Robins SJ, Zachariah JP, Kaur G, D''Agostino RB, Ordovas JM. Association of circulating cholesteryl ester transfer protein activity with incidence of cardiovascular disease in the community. Circulation (2009) 120(24):2414-20

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