Combination Niacin-Statin Treatment Does Not Decrease Cardiovascular Events

According to a May 2011 announcement by the US National Heart, Lung and Blood Institute (NHLBI), the AIM-HIGH (Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides: Impact on Global Health) trial's data and safety monitoring board (DSMB) concluded that following 32 months of follow-up, high-dose extended-release niacin (Niaspan) offered no benefits beyond statins alone in reducing cardiovascular (CV) events, and there was no evidence this would change by continuing the trial.

The DSMB also noted a small unexplained increase in ischaemic stroke rates in the niacin group (1.6% versus 0.7%). Of the 28 strokes in the niacin group, 9 occurred in participants who had discontinued the drug at least 2 months and up to 4 years before their stroke. This contributed to a decision by the National Institutes of Health to stop the AIM-HIGH trial 18 months earlier than previously scheduled. However, the overall frequency of strokes was less than 1%, and previous studies have not linked niacin with strokes, while some studies have shown reductions in strokes.

There were 3,414 participants in the AIM-HIGH trial. They were all prescribed simvastatin; 515 received ezetimibe to maintain low-density lipoprotein (LDL) cholesterol levels at the target range of 40-80 mg/dL.

Participants in the trial (average age of 64 years) had LDL levels of about 71 mg/dL at baseline, but they were at risk of cardiovascular disease due to low high-density lipoprotein (HDL) cholesterol and high triglycerides (TG) levels. Pre-existing medical conditions included coronary artery disease (CAD) (92%), metabolic syndrome (81%), high blood pressure (71%), and diabetes (34%). More than half of participants had a myocardial infarction (MI) prior to entering the study. Participants who could tolerate high doses of niacin were randomised to niacin plus statin (n = 1,718), and to placebo (n = 1,696).

After 32 months of follow-up, participants in the niacin-statin arm showed a 22% increase in HDL, and a 25% decrease in TG (compared with those who took only a statin). The result was comparable to other studies and within the range of what was predicted, but the combination treatment did not reduce fatal or non-fatal MIs, strokes, hospitalisations for acute coronary syndrome (ACS), or revascularisation procedures.

The lack of effect on CV events is unexpected based on previous trials and observational studies. Researchers had expected a 6.5% event rate in the control arm, and recorded an overall event rate of 5.6% in the control arm and 5.8% in the intervention arm (total number of events was about 500). Most events were non-fatal MI and revascularisation procedures, but there were a substantial number of CAD deaths and hospitalisations for ACS.

This was not the first disappointing result of a trial attempting to decrease CV events by raising HDL. Fenofibrate (a HDL-raising drug) failed to reduce CV events in patients with diabetes (in the ACCORD [Action to Control Cardiovascular Risk in Diabetes] trial), even though there was a favourable effect on HDL and TG. In the ILLUMINATE (Investigation of Lipid Level Management to Understand its Impact in Atherosclerotic Events) trial, torcetrapib (another HDL-raising drug) actually increased the rate of CV events, even though it raised HDL and lowered LDL and TG.

However, there may still be interest in the HDL boosting strategy. An investigational drug, anacetrapib, which raises HDL and lowers LDL, when added to statin therapy, decreased LDL by almost 40%, dramatically increasing HDL by 138%, and there was no observed increase in MI, strokes, or mortality (over 24 weeks of treatment).

Although the AIM-HIGH trial has been terminated, patients in the trial will be followed for at least another 18 months. Ongoing analyses of data will drill down to HDL and LDL subtypes, and try to examine the cause of the ischaemic strokes. SMA

Source

National Institutes of Health, US Department of Health Services. NIH stops clinical trial on combination cholesterol treatment, 26 May 2011, News Release [online]. Available at: http://www.nih.gov/news/health/may2011/nhlbi-26.htm. Accessed 1 June 2011.