

## HDL cholesterol — How do I raise my patients good cholesterol?

Quratulain Shaikh, Ayeesha Kamran Kamal

Stroke Service and Vascular Fellowship Program, International Cerebrovascular Translational Clinical Research Training Program (Fogarty International Center and National Institute of Neurologic Disorders and Stroke), Aga Khan University Hospital, Karachi, Pakistan.

Correspondence Author: Ayeesha Kamran Kamal. Email: ayeesha.kamal@aku.edu

### What are the new concepts about HDL?

HDL is the smallest and densest of the lipoproteins because of its high protein content. Proteins make up about 50% of its mass and apolipoprotein A-I (apoA-I) accounts for 70% of that protein component. There are several mechanisms by which HDL protects against atherosclerosis, including reverse cholesterol transport, anti oxidant effects, anti-inflammatory effects, anti-thrombotic effects, and modification of endothelial function. HDL has been proven to be inversely related to stroke risk. HDL function rather than its absolute level may predict atherosclerotic disease better in some subsets of patients where the HDL functions as perhaps pro inflammatory. This explains those patients who develop coronary artery disease and stroke despite very high HDL levels.

### What do the Current Guidelines Recommend?

The Adult Treatment Panel (ATP) and American Diabetes Association (ADA) guidelines recommend that dyslipidemic therapy be geared at achieving target LDL-C goals in persons with low HDL-C levels and that serum HDL-C levels are a secondary target. The Expert Group on HDL, a working group reporting on low HDL-C levels, advised additional treatment with a fibrate or niacin in persons with diabetes, the metabolic syndrome, or HDL levels <40 mg/dL.

### What are the available drugs?

#### Fibrates:

Raising HDL and lowering triglycerides with gemfibrozil has been shown to reduce major cardiovascular events, even in the absence of LDL-lowering. The reduction in stroke risk with gemfibrozil treatment was evident after 6 months, and those with the lowest HDL-C at baseline seemed most likely to benefit from treatment.

#### Niacin:

Niacin doses of 1 to 2 g per day can increase in HDL-C of 20% to 30%. The extended-release (ER) niacin preparation is better tolerated. Trials of niacin in cardiovascular disease have not evaluated stroke as an independent end point.

#### Statins:

Statins have been shown to reduce the risk of ischaemic stroke by about 20% in multiple large studies. Each 10% reduction in LDL-C is estimated to reduce the risk of stroke by 15.6%. The effect of statins may vary among patients, with those with low HDL-C and elevated triglycerides more likely to benefit from statin therapy.

#### Combination Therapy:

Combination therapy may hold the key to the most dramatic increase in HDL-C, and combinations of statin and niacin have demonstrated 18% to 21% increase in HDL-C. The HDL Atherosclerosis Treatment Study (HATS) highlighted the benefits of combining statin therapy with niacin where major clinical events were reduced and atherosclerosis halted at angiographic level. ARBITER-2 study demonstrated that ER-niacin added to statin therapy may halt the progression of atherosclerosis, as measured by carotid intima-media thickness among CHD patients with low HDL-C levels.

#### VA-HIT Trial:

This trial was done from September 1991 to August 1998 and it demonstrated that CHD events were significantly reduced by treating patients with the fibric acid derivative gemfibrozil 1200 mg/d when the predominant lipid abnormality was low HDL. CHD events were reduced by 11% with gemfibrozil for every 5-mg/dL (0.13-mmol/L) increase in HDL-C. During gemfibrozil treatment, only the increase in HDL C significantly predicted a lower risk of CHD events; by multivariable analysis, neither triglyceride nor LDL-C levels at baseline or during the trial predicted CHD events.

### What does this mean for clinicians practicing in Pakistan?

All these studies reinforce the fact that dyslipidaemia is a vascular risk factor and controlling our patients' bad cholesterol and improving their good cholesterol is crucial for prevention of further vascular events. Pakistani population's food habits and the recent trends towards refined diet and fast food are all leading to an increase in the number of population at risk of vascular events. This calls for more attention by health care providers to this subject and defining targets for

control and reference.

HDL cholesterol should be improved through diet rich in omega 3 fatty acids like fish and exercise. Drugs like Statins and Niacin can improve HDL levels by approximately 20% and are the mainstay of treatment.

### **Acknowledgement and Disclosure Statement**

The International Cerebrovascular Translational Clinical Research and Training Program (ICT\_CRT) at the Aga Khan University are supported by funds from the Award Number D43TW008660 from the Fogarty International Center and the National Institute of Neurologic Disorders and Stroke. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Fogarty International Center or the National Institutes of Health.

---

### **Recommended Reading**

1. Sanossian N, Saver J, Navab M, Ovbiagele B. High-Density Lipoprotein Cholesterol: An Emerging Target for Stroke Treatment. *Stroke* 2007; 38: 1104-9.
2. Brewer HB Jr. Increasing HDL cholesterol levels. *N Engl J Med* 2004; 350: 1491-4.
3. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, Jacobs DRJ, Bangdiwala S, Tyroler HA. High-density lipoprotein cholesterol and cardiovascular disease: four prospective American studies. *Circulation* 1989; 79: 8-15.
4. Gemfibrozil for the secondary prevention of coronary heart disease in men with low levels of high-density lipoprotein cholesterol. Veterans Affairs High-Density Lipoprotein Cholesterol Intervention Trial Study Group. *N Engl J Med* 1999; 341: 410-8.
5. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults (adult treatment panel III). *JAMA* 2001; 285: 2486-97.
6. Dyslipidemia management in adults with diabetes. *Diabetes Care* 2004; 27: 68S-71.