ACUTE CORONARY SYNDROMES

Autologous delipidated HDL infusion is safe and feasible in patients with ACS

Researchers from the USA have reported the safety and feasibility of a novel HDL-cholesterol therapy—serial infusion of autologous HDL delipidated plasma—in patients with acute coronary syndrome (ACS).

An increasing body of evidence suggests that low HDL cholesterol concentration is an independent risk factor for cardiovascular disease. Furthermore, raising HDL cholesterol levels has been associated with regression of atherosclerosis and could provide additional benefit over lowering LDL cholesterol levels alone.

The cardioprotective effects of HDL cholesterol are thought to be related to the reverse cholesterol transport mechanism. Through its interaction with the ATP-binding cassette transporter (ABCA1), HDL removes cholesterol from macrophages and transports it to the liver for excretion. The naturally occurring percentage of lipid-poor preβ-like HDL—the active form of HDL for cholesterol removal—is very low, at just 5%. Most HDL is present as mature αHDL, which does not interact with ABCA1. Therefore, therapies to increase levels of preβ-like HDL have been hypothesized to increase reverse cholesterol transport.

In the first-in-man Lipid Sciences Selective Delipidation Trial (LS-001), Dr Ron Waksman and colleagues used a strategy of HDL apheresis, delipidation, and reinfusion to raise levels of preβ-like HDL in patients with ACS. The investigational device employed in this trial—the Lipid Sciences Plasma Delipidation System-2—uses solvents to selectively remove cholesterol from αHDL particles, forming preβ-like HDL particles for reinfusion.

A total of 28 patients aged 18–85 years presenting with non-ST-segment elevation myocardial infarction or unstable angina were enrolled in the study. The median age was 55 years; 89% of patients had a history of hyperlipidemia and 89% were receiving statins at baseline. Patients were randomly assigned to undergo HDL delipidation therapy ($n = 14$) or receive placebo ($n = 12$), which involved removal of plasma and reinfusion without treatment, in seven sessions at weekly intervals.

Patients in the delipidation group had a 28-fold increase in preβ-like HDL levels from baseline. Laboratory analysis revealed only minor changes in blood chemistry and blood cell counts, from before apheresis to after reinfusion. 15 patients experienced a total of 28 adverse events, with no significant differences between delipidation and control groups. The most common adverse event was transient, procedure-related hypotension, which resolved with fluid supplementation. No instances of toxicity were reported. Intravascular ultrasonography in 26 patients showed a numerical decrease from baseline in mean total atheroma volume in the delipidation group, but this change was not significant.

"It is clear that this technique is very promising for the management of ACS," comments Professor John Kastelein from the Academic Medical Center in Amsterdam, the Netherlands, who was not involved in the study. "It would be reassuring, however, if a statistically significant regression of coronary atheroma could be demonstrated by this technique, before embarking on a large ... trial," he concludes.

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Original article Waksman, R. *et al.* A first-in-man, randomized, placebo-controlled study to evaluate the safety and feasibility of autologous delipidated high-density lipoprotein plasma infusions in patients with acute coronary syndrome. *J. Am. Coll. Cardiol.* **55**, 2727–2735 (2010)