More about Cholesterol – Cholesterol Metabolism as a Target in the Combat against Hepatitis E Viruses

A hepatitis E virus infection involves interaction with the cholesterol metabolism. A research cooperation managed by the Paul-Ehrlich-Institut established that low intracellular cholesterol levels encourage the release of the virus. Inversely, high intracellular cholesterol levels result in a decomposition of the viruses within the infected cell. The results can have implications for the treatment of patients who have hepatitis E infections and may open new therapy options. Cellular and Molecular Gastroenterology and Hepatology reports on the results in its online edition of 15 February 2021.

The hepatitis E virus (HEV) is largely wide-spread in the developing countries and presents an increasing risk also for Europe and North America. Up to 20 million new infections per year have been recorded in the past few years. These can cause up to 44,000 deaths per year. There is no vaccine against the disease outside China. Treatment options are currently restricted to either the antiviral medicine Ribavirin, which may cause resistance, or pegylated interferon (PEG–74 IFN). Both treatment option may cause serious adverse effects.

It is known that HEV captures the so-called endosomal system of the host for its release from the infected cells. Endosomes and exosomes created from these are membrane enclosed functional areas (organelles) in the cells involved in the transport of proteins and lipids between and within cells. These endosomal structures are highly dependent on cholesterol.

What are the implications of the infection with HEV for the cholesterol metabolism? And – the other way round – how does the intracellular cholesterol content affect the release of HEV from the cells, and could cholesterol modulators be used in treatment? These were the questions addressed by Mirco Glitscher and colleagues at the Paul-Ehrlich-Institut under the supervision of Professor Eberhard Hildt, head of Division Virology in cooperation with scientists at the Federal Institut for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte, BfArM), the University Hospital at Aachen, and the Charité University Hospital at Berlin.

With the aid of various methods, the research consortium proved that a HEV infection lowers the lipid concentration in the serum. In infected cells, cholesterol values are reduced. Treatment with statins, a particular active ingredient group of lipid-reducing drugs, will increase virus levels (virus titres), and thus the viral load in chronically infected patents. In cell cultures, too, hepatitis E viruses were increasingly released after reducing the intra-cellular cholesterol levels by treatment with the statin Simvastatin. Inversely, the release of the virus is reduced by increasing intracellular cholesterol by low-density lipoproteins (LDLs) or 25-hydroxycholesterol. This happens by decomposition of the HEVs in cell organelles, the lysosomes. The decrease in virus release could also be brought about by increasing the intracellular cholesterol by means of active ingredients of medicines such as fenofibrate. Fenofibrate is also a lipid reducing drug of a category of active ingredients other than statins.
"Our studies show the significance of the interaction between cholesterol and the hepatitis E virus for the viral load and the course of the disease. It may be possible to use the findings from this research work to test new therapy options from the clinical point of view, in particular with regard to the use of lipid reducing drugs. Especially fibrates can present a favourable and efficient alternative to the current treatment options in this context", explained Professor Hildt with respect to the meaning of the results.

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