Early evidence shows 'good' cholesterol could combat abdominal aortic aneurysm

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New research provides early evidence that 'good' cholesterol may possess anti-aneurysm forming properties. In laboratory-based investigations, scientists found that increased levels of high-density lipoproteins (HDL), the so-called good cholesterol, blocked the development of aneurysms – dangerous 'ballooning' in the wall of a blood vessel – in the body's largest artery, the aorta.

The researchers say their findings – which are published in the American Heart Association scientific journal *Atherosclerosis* Thrombosis *and* Vascular Biology – lay the foundations for further investigations into ways of raising HDL cholesterol as a possible therapeutic intervention for the condition.

Abdominal aortic aneurysms can rupture and kill without warning. They are responsible for 6,000 deaths in England and Wales each year. There are no therapeutic treatments for aneurysms. Patients are monitored until the aneurysm reaches what is considered to be a critical size where it is at significant risk of rupturing – 5cm in diameter – and then it is repaired by surgery.

The study, led by researchers from St George's, University of London, found that elevating the amount of HDL cholesterol in the abdominal area of the aortic artery in mice both reduced the size of aneurysms that had already grown and prevented abdominal aortic aneurysms from forming at all.

The researchers say that while more work is needed to understand the exact mechanism by which HDL cholesterol effects aneurysms, their investigations indicate that raising HDL cholesterol influences the activity of the aortic artery's cells, which are the building blocks of its structure and function.

They found that elevated levels of HDL had two key influences on the cells. Firstly, it altered the signals sent between cells, which, in turn, reduced the activity of a protein called ERK1/2 that is known for its cell growth properties. Secondly, it increased levels of HDL cholesterol induced programmed cell death, which is an essential part of the cell lifecycle that sees old cells replaced with new ones.

The study focused on mice models of the area of the aorta just above the kidney (the suprarenal region) and the region that is just below the kidney and most commonly associated with aneurysm formation in humans (the infrarenal region). The researchers hope that the effects seen in these specific areas of the aortic artery will help explain basic mechanisms of aneurysm formation.

Dr Cockerill says: "HDL cholesterol is made up of a complex family of heterogeneous particles that may vary in composition, size and function. Whilst we have shown that elevating the concentration of the so-called 'good-lipid' can modulate site-specific cellular responses and inhibit aneurysm formation, it is important to learn more about changes that occur on HDL complexity in addition to the effects in the artery's responses that influence aneurysm development."

The researchers say that, in principle, if raising HDLs can be induced using a drug, it could offer a preventative measure to reduce the chance of an aneurysm developing for individuals considered at high risk of aneurysms. It could also offer a treatment option for patients from early diagnosis that could negate the need for surgery. But they point out that

much more research is need before this becomes a reality.

The next phase of the investigations, which the researchers hope to begin this year, will see the researchers conduct laboratory tests with families of drugs that can elevate HDLs and reproduce the observed effects on aneurysms.

More information: Evelyn Torsney, Grisha Pirianov, Nicoletta Charolidi, Azza Shoreim, David Gaze, Slaveia Petrova, Ken Laing, Trevor Meisinger, Wanfen Xiong, B. Timothy Baxter, Gillian W. Cockerill, Elevation of Plasma High-Density Lipoproteins Inhibits Development of Experimental Abdominal Aortic Aneurysms, Arteriosclerosis, Thrombosis, and Vascular Biology. 2012; 32: 2678-2686

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