LDL低下療法は早く開始するほどよい

LDL療法は若年で開始した方が高齢で開始するよりも有意に優れている

Lowering LDL early in life is significantly better than treating with statins when older

LDL低下療法を若年で開始した方が遅く開始するよりも冠動脈疾患（CHD）のリスクが3倍低下したとのスタディ結果が、第61回American College of Cardiology学会で発表された。動脈硬化が発現する前の早い時期にLDLコレステロールを低下させた方が当然心筋梗塞（MI）軽減にはより有効であろうと思われるが、この仮説を立証するのは困難であった。この仮説を調査するには、従来の無作為化トライアルであれば非常に大人数の無症状の若年者を何十年も追跡する必要がある。これの替わりとして研究者らは、Mendelian無作為化コントロールトライアル（mRCT）と呼ばれる新たなスタディデザインを用いて、その各々がLDLコレステロールレベル低下と関連する9つの一塩基多型（SNPs）の影響を調査した。その結果、9つのSNPs全てが、生涯におけるLDLコレステロールが1mmol/L（38.67mg/dl）低下するごとに一貫してCHDリスクが50～60%低下するのに関連のあることが示された。LDLを2mmol/L（77.34mg/dl）低下させることにより、CHDリスクはほぼ80%低下させることができた。

Full Text

Coronary atherosclerosis can lead to myocardial infarction and other forms of coronary heart disease (CHD). Lowering low-density lipoprotein (LDL) reduces the risk of CHD, and researchers found that lowering LDL beginning early in life resulted in a three-fold greater reduction in the risk of CHD than treatment with a statin started later in life, according to research presented at the American College of Cardiology's 61st Annual Scientific Session.

By the time most people begin treatment to lower LDL, CHD has often been quietly developing for decades. Because coronary atherosclerosis begins early in life, lowering LDL at a younger age may produce even greater reductions in the risk of CHD. Researchers sought to test this hypothesis by using genetic data to conduct a series of "natural" randomized controlled trials involving over one million study participants.

"Our study shows that the benefit of lowering LDL cholesterol depends on both the timing and the magnitude of LDL reduction," said Brian A. Ference, M.D., MPhil, MS.c., FACC, director of the cardiovascular genomic research center at Wayne State University School of Medicine and the study's principal investigator. "The increased benefit of lowering LDL beginning early in life appeared to be independent of how LDL was lowered. This means that diet and exercise are probably as effective as statins or other medications at reducing the risk of CHD when started early in life."

Lowering LDL cholesterol at an early age, before the development of atherosclerosis, would understandably be more effective at reducing heart attacks, but testing this hypothesis has proven difficult. A conventional randomized trial would have to follow a very large number of young, asymptomatic people for several decades to test this hypothesis. As an alternative, researchers used a novel study design called a Mendelian randomized controlled trial (mRCT) to study the effect of nine single-nucleotide polymorphisms (SNPs), or single-letter changes in DNA sequence, each of which is associated with lower levels of LDL cholesterol. Because each of these SNPs is allocated randomly at the time of conception, inheriting one of these SNPs is like being randomly allocated to a treatment that lowers LDL cholesterol beginning at birth. The researchers found that all nine SNPs were associated with a consistent 50-60 percent reduction in the risk of CHD for each 1 mmol/L (38.67 mg/dl) lower lifetime exposure to LDL cholesterol. Lowering LDL by 2 mmol/L (77.34 mg/dl) could reduce the risk of CHD by almost 80 percent.

"The results of our study demonstrate that the clinical benefit of lowering LDL can be substantially improved by initiating therapies to lower LDL cholesterol beginning early in life," Dr. Ference said.

Dr. Ference reports no conflicts of interest.

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