Medical Xpress

Lowering LDL, the earlier the better

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Coronary atherosclerosis – a hardening of the arteries due to a build-up of fat and cholesterol – can lead to heart attacks and other forms of coronary heart disease (CHD). Lowering low-density lipoprotein (LDL), or "bad" cholesterol, 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 today at the American College of Cardiology's 61st Annual Scientific Session. The Scientific Session, the premier cardiovascular medical meeting, brings cardiovascular professionals together to further advances in the field.

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, MD, MPhil, MSc, 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.

Coronary heart disease is the most common cause of death and disability throughout the world. Treatment of CHD and its risk factors is costly and consumes a large proportion of health care expenditures. Dr. Ference believes that the results of this study suggest that focusing on prolonged and sustained reductions in LDL cholesterol beginning early in life has the potential to substantially reduce the global burden of CHD.