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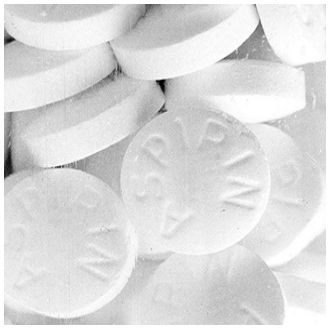
Genetic Modification and the Benefits of Aspirin



As far as antiplatelet therapies go, aspirin has been a gold standard for many years, and has been widely prescribed in low doses for the prevention of cardiovascular disease. However, a recent study conducted by Beth Israel Deaconess Medical Centre (BIDMC) and Brigham and Women's Hospital (BWH) reports something surprising. The study reveals that common genetic variation in the gene for catechol-O-methyltranferase (COMT) may actually modify the benefit of aspirin and may in fact confer slight harm in some people. The findings from the study have been published in the American Heart Association Journal Arteriosclerosis, Thrombosis and Vascular Biology.

COMT is an enzyme that plays a critical role in the metabolism of catecholamines. Catecholamines include epinephrine, norepinephrine and dopamine. These three hormones are involved in a broad spectrum of disorders including hypertension. The objective of this study was to gauge whether the COMT gene affected people's susceptibility to incident cardiovascular diseases such as myocardial infarction or ischaemic stroke. Since aspirin is so widely prescribed, the investigators also studied whether a genetic variation in COMT has an impact on its potential benefit.

Data for the study was collected from the Women's Genome Health Study involving more than 23,000 women who were followed for ten years in a randomised double-blind placebo controlled trial to analyse the impact of low-dose aspirin or Vitamin E for the primary prevention of incident cardiovascular disease.

This particular study itself focused on val158met, a common variant in the COMT gene. Women who were homozygous for the enzyme's high activity valine form, the val/vals were shown to have lower levels of catecholamines compared to those who were homozygous for the enzyme's low-activity methionine form, the met/mets. However, a surprising discovery was that the val/val women who were randomly assigned to aspirin had more cardiovascular events as compared to val/vals who were assigned to placebo. Thus, when the women with the val/val polymorphism were allocated to aspirin, their natural protection against incident cardiovascular disease was eliminated. At the same time, 28% of women who were met/met had fewer cardiovascular events when assigned to aspirin as compared to those assigned to placebo.

A possible explanation for this may be that val/val individuals have less epinephrine than met/met individuals. Since their COMT is more efficient at breaking it down, they may be naturally protected from cardiovascular disease. It might thus be a possibility that this effect is somehow modified by aspirin.

These findings highlight the need for further research to more clearly understand this discovery. Aspirin is prescribed to millions of individuals, but this study reveals that doctors need to be smarter about identifying the groups that are more likely to benefit from aspirin. According to study co-author Joseph Loscalzo, MD, PhD, Chairman of the Department of Medicine and Physician-in-Chief at BWH, "rather than give aspirin to all patients with risk factors for heart disease, we need to use modern genomics and genetics to identify those individuals for whom aspirin has the greatest benefit and the lowest risk of adverse effects."

Source: Medical News Today
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Published on : Fri, 25 Jul 2014