

Vitamin E Reduces Cardiovascular Disease in Individuals with Diabetes Mellitus and the Haptoglobin 2-2 Genotype

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Introduction. Individuals with both Diabetes Mellitus (DM) and the Haptoglobin (Hp) 2-2 genotype are at increased risk of cardiovascular disease. As the antioxidant function of the Hp 2-2 protein is impaired we sought to test the pharmacogenomic hypothesis that antioxidant vitamin E supplementation would provide cardiovascular protection to Hp 2-2 DM individuals. Methods and Results. We determined the Hp genotype on DM participants from two trials (HOPE and ICARE) and assessed the effect of vitamin E by Hp genotype on their common prespecified outcome, the composite of stroke, myocardial infarction and cardiovascular death. Data was analyzed with a fixed-effect model. These results were input into a simulation model, the Evidence Based Medicine Integrator, in order to estimate their long term implications in a real-world population from Kaiser Permanente. Meta-analysis of the two trials demonstrated a significant overall reduction in the composite endpoint in Hp 2-2 DM individuals with vitamin E (odds ratio 0.58 (95% CI 0.40-0.86) p=0.006). There was a statistically significant interaction between the Hp genotype and vitamin E on the composite endpoint. In these trials, Hp typing of 31 DM individuals and treating with vitamin E those with the Hp 2-2 prevented one myocardial infarct, stroke or cardiovascular death. Lifelong administration of vitamin E to Hp 2-2 DM individuals in the Kaiser population would increase their life expectancy by three years. Conclusions. A pharmacogenomic strategy of screening DM individuals for the Hp genotype and treating those with Hp 2-2 with vitamin E appears to be highly clinically effective.