
Aims: 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.

Materials & methods: 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 (CA, USA).

Results: Meta-analysis of the two trials demonstrated a significant overall reduction in the composite end point 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 end point. In these trials, Hp typing of 69 DM individuals and treating those with the Hp 2-2 with vitamin E 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 3 years.

Conclusion: 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.