Influence of the glutathione peroxidase 1 Pro200Leu polymorphism on the response of glutathione peroxidase activity to selenium supplementation: a randomized controlled trial.

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BACKGROUND: A genetic variant at codon 200 (Pro200Leu) of the gene encoding for glutathione peroxidase 1 (GPx1), a selenium-dependent enzyme, is associated with lower enzyme activity; however, the evidence is limited to in vitro and observational studies. Objective: The objective was to determine whether the GPx1 Pro200Leu genetic variants modify the response of whole-blood glutathione peroxidase (GPx) activity to selenium supplementation in patients with coronary artery disease in New Zealand.

DESIGN: The results from 2 parallel-design, double-blind trials were combined. Participants were randomly assigned to receive a daily supplement of 100 μg Se as l-selenomethionine (n = 129) or placebo (n = 126) for 12 wk. Plasma selenium and whole-blood GPx activity were measured at baseline and at week 12. Participants were genotyped for the GPx1 Pro200Leu polymorphism.

RESULTS: Selenium supplementation increased whole-blood GPx activity by 5 (95% CI: 4, 7) U/g hemoglobin (P < 0.001); however, the magnitude of the increase did not differ by genotype (P = 0.165 for treatment-by-genotype interaction). In an exploratory analysis, a significant nutrient-gene interaction was apparent when baseline plasma selenium concentrations were included in the regression model (P = 0.006 for treatment-by-genotype × baseline selenium concentration interaction). Increases in GPx activity were 2-fold higher in Pro homozygotes than in participants carrying a Leu allele when baseline selenium concentrations were ≤1.15 μmol/L (P < 0.05).

CONCLUSIONS: These results indicate that GPx1 Pro200Leu variants do not substantially modify the response of whole-blood GPx to selenium supplementation in individuals with relatively high plasma selenium concentrations. A nutrient-gene interaction was observed when the baseline selenium concentration was low, but this requires independent confirmation. This trial was registered at www.actr.org.au as ACTRN12605000412639 and ACTRN12606000197538.

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