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VASCULAR DISEASE

ALDH2 GENOTYPE INFLUENCES THE PROTECTION OF ENDOTHELIUM AGAINST ISCHEMIC INJURY BY SYSTEMIC NITRITE

ACC Poster Contributions
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Session Title: Platelets and Thrombosis
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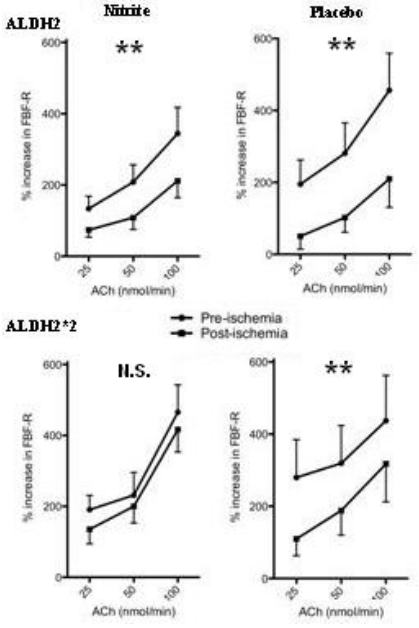
Background: The nitrite anion has been shown to prevent ischemia-reperfusion (IR) injury in animal models, with ALDH2 suggested to underlie this protection. We hypothesised that systemic sodium nitrite would protect endothelial function in healthy volunteers with the wild-type ALDH2, but not in those with the low-function ALDH2*2 genotype.

Methods: 18 subjects of East Asian origin who gave informed consent were recruited to this randomised, double-blind placebo-controlled crossover study. Venous occlusion plethysmography was used to measure increases in forearm blood flow to intra-arterial acetylcholine, pre- and post-ischemia. Sodium nitrite or saline placebo was given intravenously at a dose of 1 mcg/kg/min during the last 10 of 20 minutes of ischemia. Data were normalised to the control arm. Genotyping was done after completion of all studies. Two way repeated measures ANOVA was used throughout.



Results: Ischemia + placebo significantly reduced endothelial function ($p<0.001$, $n=9$ for both). Nitrite protected endothelium in the *2 group ($p=0.16$, $n=9$), but not in the wild-type group ($p<0.001$, $n=9$).

Conclusions: ALDH2 status affects protection from IR injury by nitrite, though protection was only seen in those with the *2 genotype. The reaction of nitrite with the wild-type enzyme may produce more oxidative stress than with the variant enzyme, abrogating the protective effect. Further work is needed to ascertain if nitrite protects in wild-type individuals at other doses.