Abstract: P6003
Coronary artery spasm: a consequence of impaired nitric oxide/hydrogen sulphide signalling?

Authors:
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Background: Coronary artery spasm (CAS) represents a major cause of patient morbidity, with variable clinical response to prophylaxis with calcium antagonists and generally poor symptomatic relief with organic nitrates. The precipitation of CAS with acetylcholine may reflect impaired nitric oxide (NO) release and/or signalling. We have recently demonstrated that platelets from patients with CAS exhibit markedly impaired anti-aggregatory responses to the NO donor sodium nitroprusside (SNP) (“NO resistance”).

Purpose: In the current experiments we sought to determine whether N-acetylcysteine (NAC), which is known to potentiate haemodynamic responses to organic nitrates, reverses NO resistance in platelets from CAS patients.

Methods: Patients with CAS were studied during acute (n=11) and chronic (n=24) phases of symptoms. NAC (10 g/24 hours) was infused together with low dose NTG (2.5 μg/min) in patients presenting with acute exacerbations, and platelets were studied ex vivo. In blood samples taken from chronic CAS patients, in vitro studies were performed to evaluate the possible role of H2S release (via cysteine formation) from NAC in putative potentiation of NO effect.

Results: (1) In acute patients, NTG/NAC infusion resulted in increases in platelet response to SNP (p=0.003); (2) In vitro studies showed that incubation with NAC or the H2S donor NaHS potentiated SNP responses (Figure 1A); (3) Effects of NAC were reversed by co-incubation with aminooxyacetic acid (AOAA) and D, L-propargylglycine (PAG), inhibitors of enzymatic cysteine bioconversion to release H2S (Figure 1B).

Conclusion: CAS-associated impairment of platelet NO signaling reflects a deficiency of the H2S/NO interaction, and can be reversed using exogenous H2S donors, including NAC.

Figure 1A: Impact of increasing concentrations of NAC and NaHS (10-100μM) on anti-aggregatory responses to fixed concentration of SNP (10 μM). 2-way ANOVA: drug concentrations: F=11.1 p<0.0001; NAC versus NaHS: F=9.0 p=0.004.

Figure 1B: Alteration of anti-aggregatory effect of SNP (10 μM) combined with NAC (100 μM) by: PAG (3.3 mM) and AOAA (0.5 mM).

Figure 1
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Figure 1