Compared effects of inhibition and exogenous administration of hydrogen sulphide in ischaemia-reperfusion injury

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Résumé en anglais	INTRODUCTION: Haemorrhagic shock is associated with an inflammatory response consecutive to ischaemia-reperfusion (I/R) that leads to cardiovascular failure and organ injury. The role of and the timing of administration of hydrogen sulphide (H2S) remain uncertain. Vascular effects of H2S are mainly mediated through K+ATP-channel activation. Herein, we compared the effects of D,L-propargylglycine (PAG), an inhibitor of H2S production, as well as sodium hydrosulphide (NaHS), an H2S donor, on haemodynamics, vascular reactivity and cellular pathways in a rat model of I/R. We also compared the haemodynamic effects of NaHS administered before and 10 minutes after reperfusion. METHODS: Mechanically ventilated and instrumented rats were bled during 60 minutes in order to maintain mean arterial pressure at 40 +/- 2 mmHg. Ten minutes prior to retransfusion, rats randomly received either an intravenous bolus of NaHS (0.2 mg/kg) or vehicle (0.9% NaCl) or PAG (50 mg/kg). PNU, a pore-forming receptor inhibitor of K+ATP channels, was used to assess the role of K+ATP channels. RESULTS: Shock and I/R induced a decrease in mean arterial pressure, lactic acidosis and ex vivo vascular hyporeactivity, which were attenuated by NaHS administered before reperfusion and PNU but not by PAG and NaHS administered 10 minutes after reperfusion. NaHS also prevented aortic inducible nitric oxide synthase expression and nitric oxide production while increasing Akt and endothelial nitric oxide synthase phosphorylation. NaHS reduced JNK activity and p-P38/P38 activation, suggesting a decrease in endothelial cell activation without variation in ERK phosphorylation. PNU + NaHS increased mean arterial pressure when compared with NaHS or PNU alone, suggesting a dual effect of NaHS on vascular reactivity. CONCLUSION: NaHS when given before reperfusion protects against the effects of haemorrhage-induced I/R by acting primarily through a decrease in both proinflammatory cytokines and inducible nitric oxide synthase expression and an upregulation of the Akt/endothelial nitric oxide synthase pathway.
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