VASODILATOR ACTIVITY OF HYDROGEN SULFIDE (H_2S) IN HUMAN ISOLATED MESENTERIC ARTERIES

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Hydrogen sulfide (H_2S) is a malodorous and hazardous gas that upon inhalation can produce toxic to lethal effects depending on the concentration (1), endogenously generated in mammalian cells from homocysteine and cysteine condensation, and *via* cysteine hydrolysis, by means of at least two different enzymatic pathways: cystathionine ß-synthase and cystathionine γ-lyase (1). High concentrations (50-160 µM) of H_2S have been detected in rat, human and bovine brain; and rat (45 – 300 µM) and human plasma (10-100 µM) (2). H_2S exerts a wide variety of biological effects at both central and peripheral levels (1). Vascular smooth muscle inhibitory effects of H_2S have been carefully characterized in isolated vessels of the rat, like the aorta and mesenteric arteries and the portal vein (3). Our study was aimed at investigating the vascular effects of H_2S on human isolated mesenteric arteries and to examine the underlying mechanisms involved. The effect of NaHS (as a donor of H_2S) was determined using noradrenaline (NA) pre-contracted human isolated mesenteric rings. NaHS evoked a concentration dependent relaxation (EC_{50} 57 µM). In contrast, homocysteine, an endogenous precursor of H_2S, failed to affect the human isolated mesenteric rings pre-contracted by noradrenaline. The vasorelaxant response to 1 mM NaHS (35 ± 10% of NA) was significantly reduced by removal of endothelium (5 ± 2 % of NA) or application of the nitric oxide synthase inhibitor L-NAME (5 ± 3 % of NA) or the inhibitor of cGMP production ODQ (5 ± 8 % of NA), ($P < 0.05$, $n = 6$ each). On the contrary, the adenylate _raduzi inhibitor, SQ 22536, failed to have any affect on the relaxation induced by NaHS. Inhibition of endogenous prostanoid production by indomethacin moderately reduced NaHS induced vasorelaxation. The role of potassium channels was also examined. Blockers of the Ca^{2+}-dependent potassium channel, charybdotoxin and apamin, failed to have any influence on the relaxant response to NaHS on this vascular tissue. In contrast, NaHS induced relaxation was demonstrated to be partially mediated by ATP-sensitive potassium channel activity, as glibenclamide suppressed the vasorelaxant effect of NaHS. In conclusion, endothelium dependent mechanism, prostanoid and cGMP generation and ATP-sensitive potassium channels represents important pathways for H_2S –mediated relaxation of human mesenteric arteries.

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