ENHANCEMENT OF THE RENAL VASOCONSTRICTOR BUT NOT THE ANTI-NATRIURETIC RESPONSE TO INHIBITION OF HYDROGEN SULFIDE PRODUCTION DURING NITRIC OXIDE BLOCKADE IN THE ANESTHETIZED RAT.

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Hydrogen sulfide (H$_2$S), a newly discovered vasorelaxant, is produced endogenously in the vasculature from L-cysteine mainly by the action of the enzyme cystathionine $\gamma$-lyase (CSE). Using immunohistochemical study we have recently found that CSE expressed mainly in the renal vasculature (renal arterioles and glomeruli) as well as in the collecting duct. To understand the role of CSE mediated H$_2$S production in the kidney, we examined the renal responses to incremental dosages of the CSE inhibitor, DL-propargylglycine (PAG; 20, 50 and 100µg/min/kg), infused directly into the left renal artery in anesthetized rats. A possible interaction of H$_2$S with other vasodilator, nitric oxide (NO) was also examined in these experiments by evaluating renal responses to PAG in rats pretreated with (n=10) or without (n=12) NO synthase inhibitor, nitro-L-arginine methyl ester (L-NAME; 50µg/min/kg). Total (RBF) as well as regional (cortical; CBF and medullary; MBF) blood flows were measured by Transonic and laser-Doppler flowmetry and glomerular filtration rate (GFR) was determined by inulin clearance. PAG administration directly in the kidney decreased the urinary excretion rate of sulfate (marker for H$_2$S production) similarly both in control and in L-NAME pretreated rats without significant changes in plasma sulfate concentration or arterial pressure.
Nevertheless, compared to the responses in control rats, PAG infusion resulted in
greater decreases in renal hemodynamic parameters in L-NAME pre-treated rats. At
highest dose of PAG, these responses in control vs L-NAME pre-treated rats were as
follows: RBF, -26±3\% vs -49±3\%; CBF, -16±2\% vs -45±8\%; MBF, +6±8\% vs -32±8\% and
GFR, -28±10\% vs -57±6\%). However, PAG at the highest dose caused similar
decreases in urine low (-40±5\% vs -42±7\%) and sodium excretion (-50±7\% vs -56±4\%)
in both groups of rats while the fractional excretion of sodium was decreased in control
rats (-22±7\%) but not in L-NAME pretreated rats (+16±11\%). These data demonstrate
that endogenous H$_2$S is a potent renal vasodilator as well as natriuretic agent which act
synergistically with NO to regulate kidney function. These findings also suggest that the
renal tubular action of H$_2$S is dependent on intact NO system.

**Keywords:** hydrogen sulfide, nitric oxide, DL-propargylglycine, renal hemodynamics,
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