Endogenous Hydrogen Sulfide Mediated Cutaneous Vasodilation is Attenuated in Essential Hypertensive Humans

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Hydrogen sulfide (H_2S) is an endothelium-dependent hyperpolarizing factor (EDHF) implicated in the pathogenesis of hypertension-induced vascular dysfunction. H_2S is synthesized enzymatically through cystathione-γ-lyase (CSE) and 3-mercaptopyruvate transferase (MPST) in the cutaneous vasculature and induces vasodilation directly and through nitric oxide synthase (NOS)-dependent mechanisms.

Objective: Our aim was to determine the role of endogenously produced H_2S in the cutaneous microcirculation of essential hypertensive humans. We hypothesized that *in vivo* H_2S-mediated vasodilation would be attenuated and *in vitro* H_2S enzymatic activity would be reduced in Stage I hypertensive adults.

Methods: Seven Stage I unmedicated hypertensive (HTN: 24-hour ambulatory systolic 144±5mmHg, diastolic 86±3mmHg) and 7 normotensive (NTN: 110±5mmHg, 72±2mmHg) men and women were instrumented with intradermal microdialysis fibers serving as (1) control (Ringers), and (2) NOS-inhibited (L-NAME), (3) enzymatic H_2S-inhibited (aminooxyacetic acid; AOAA), and (4) dual enzymatic H_2S+NOS inhibition during dose-response perfusion of acetylcholine (Ach: 0.001, 0.01, 0.1, and 1.0mM). Red blood cell flux (laser-Doppler flowmetry) was measured and cutaneous vascular conductance was calculated (%CVC_{max}). Skin biopsy samples were obtained and H_2S producing enzymatic activity was measured (amperometric assay).

Results: Ach-induced vasodilation was attenuated in HTN compared to NTN adults ($p<0.001$). Enzymatic H_2S-inhibition blunted the cutaneous vasodilatory response to Ach in NTN (80±6 vs. control: 90±5 %CVC_{max}; $p=0.002$) adults but had no effect in HTN adults (70±6 vs. control: 70±8). Similarly, NOS-inhibition reduced the response to Ach in NTN adults (50±8 %CVCmax, $p<0.001$ vs. control), but had no effect in HTN adults (59±4%CVC_{max}). Dual inhibition did not further reduce Ach-induced vasodilation compared to NOS-inhibition alone in either group. CSE and MPST were expressed in all skin samples and enzymatic activity was reduced in HTN samples (45±1 vs 35±4 H_2S[nM]/h; $p<0.05$).

Conclusions: Endogenous H_2S-mediated vasodilation is functionally absent and H_2S producing enzymatic activity is reduced in the cutaneous microcirculation of essential hypertensive humans.