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Hydrogen Sulfide and Homocysteine Transsulfuration Pathway in the Progression of Kidney Fibrosis

Hee-Seong Jang, Jee In Kim, Sang Jun Han, Kwon Moo Park

Department of Anatomy, Kyungpook National University School of Medicine

Background: Hydrogen sulfide (H2S) produced by cystathionine β-synthase (CBS) and cystathionine ɣ-lyase (CSE) in the transsulfuration pathway of homocysteine has diverse role in pathophysiological condition. The role of H2S in kidney fibrosis remains to be defined despite involvement of hyperhomocysteinemia in kidney fibrosis. Here, we investigated the role of H2S and its acting mechanism in unilateral ureteral obstruction (UO)-induced kidney fibrosis in mice.

Methods: Left ureter of mice was tied completely using 6/0 nylon under anesthetization with pentobarbital sodium. Some mice received daily intraperitoneal administration of sodium hydrosulfide hydrate (NaHS; 1.12, 5.6, or 28 μg/kg BW, Sigma-Alrich), a H2S donor, or 0.9% NaCl (vehicle), beginning on day one after UO for a period of 6 days.

Results: UO decreased expressions of CBS and CSE in the kidney with decrease of H2S concentration. Treatment of sodium hydrogen sulfide (NaHS, a H2S producer) reduced kidney fibrosis and prevented the loss of kidney function following UO, but did not induce significant changes of blood pressure in both sham-operated and UO-induced mice. Treatment with NaHS during UO reduced UO-induced oxidative stress including superoxide formation, hydrogen peroxide, and MDA production with preservations of catalase, copper-zinc superoxide dismutase (CuZnSOD), and manganese superoxide dismutase (MnSOD) expression, and glutathione level. In addition, NaHS mitigated decreases of CBS and CSE expressions, and H2S concentration in the kidney. NaHS treatment attenuated UO-induced increases in levels of TGF-β1, activated Smad3, and activated NF-κB and infiltration of inflammatory cell in the kidney.

Conclusion: This study provided the first evidence of involvement of the transsulfuration pathway and H2S in UO-induced kidney fibrosis, suggesting that H2S and its transsulfuration pathway may be a potential target for development of therapeutics for fibrosis-related diseases, including kidney fibrosis.

Key Words: 황화수소, 섬유화, 활성산소
Hydrogen sulfide, Fibrosis, Oxidative stress