Age-related differences in responses to hydrogen sulfide in the bladder of spontaneously hypertensive rats

Suo Zou¹, Takahiro Shimizu¹, Shogo Shimizu¹, Hideaki Ono^{1,2}, Yohei Shimizu^{1,2}, Yurika Hata^{1,2}, Masaki Yamamoto¹, Takaaki Aratake^{1,3}, Yoshiki Nagao¹, Tomoya Hamada¹, Youichirou Higashi¹, Motoaki Saito¹

¹Dept. of Pharmacol., Kochi Med. Sci., Kochi Univ., ²Cent. for Innovative and Translational Med., Kochi Univ.,

³Research Fellow of Japan Society for the Promotion of Science

We have confirmed that hydrogen sulfide (H₂S) is a possible relaxation factor in the rat bladder, and H₂S-induced bladder relaxation is impaired in 18-week-old (18W) spontaneously hypertensive rats (SHRs), which show bladder dysfunctions. We compared effects of NaHS and GYY4137 (H₂S donors) on bladder contractility and micturition reflex, and H₂S contents and expression of enzymes related to H₂S biosynthesis (CBS, MPST and CAT) in the bladder between 12W and 18W male SHRs. Effects of NaHS (1×10^{-8} to 3×10^{-4} M) were evaluated on carbachol (10^{-5} M)-induced pre-contracted bladder strips. Under urethane-anesthesia, effects of intravesically instilled GYY4137 (10^{-8} to 10^{-6} M) on the rat micturition reflex were examined. The H₂S contents and expression of CBS, MPST and CAT were measured by methylene blue method and western blotting. Compared to 12W SHRs, NaHS-induced maximal relaxation of bladder strips was significantly decreased, GYY4137-induced intercontraction intervals prolongation was attenuated, the bladder H₂S content and expression level of CBS, MPST and CAT in the bladder dome was higher in 18W SHRs. These results indicate that H₂S-induced bladder relaxation in SHRs is impaired time-dependently, suggesting that early intervention in SHRs with H₂S donors may prevent the development of hypertension-mediated bladder dysfunctions.