TESTOSTERONE-INDUCED VASORELAXATION INVOLVES L-CYSTEINE/H_2S PATHWAY IN RAT AORTA

Bucci Mariarosaria, Roviezzo Fiorentina, Brancaleone Vincenzo, Di Lorenzo Annarita, *Rizzo Giovanni, Vellecco Valentina, *Fiorucci Stefano, Cirino Giuseppe

Department of Experimental Pharmacology, Faculty of Pharmacy, University of Naples -Federico II- Naples, Italy *Department of Clinic and Experimental Medicine, Molecular Biology Laboratory, University of Perugia, Italy

Acute administration of testosterone (T) induces a rapid relaxation in vascular tissues of different species, including human, suggesting a non genomic effect of this hormone on vascular reactivity. Different mechanisms have been proposed to explain testosterone-induced vasodilatation. Here we investigate on the involvement of H_2S together with nitric oxide (NO) in the vasorelaxant effect of T on isolated rat aortic rings. Androgen antagonist nilutamide and specific inhibitors of endothelial nitric oxide synthase activation have been used to assess androgen receptor and endothelial derived-NO involvement respectively. H_2S production in isolated aortic rings and in aorta homogenates incubated with testosterone was evaluated. In testosterone-stimulated rat aorta, cystathionine β-synthetase (CBS) and cystathionine γ-lyase (CSE) mRNA levels at different time points were measured by QRT-PCR. Testosterone (10 nM - 30 μM) induced a concentration and endothelium-dependent vasodilatation. Inhibition of eNOS-hsp90 dependent activation by geldanamycin but not LY 294002, that interferes with eNOS phosphorylation, significantly reduced testosterone-induced vasorelaxation. Androgen receptor blockage by nilutamide partially inhibited testosterone-induced vasorelaxation. Propargylglycine, a specific inhibitor of CSE significantly inhibited testosterone-induced vasodilatation. H_2S measurement in tissues stimulated with testosterone revealed a significant increase of this gaseous mediator. Tissue incubation with testosterone (1h and 3h) induced in rat aorta an increase of mRNA levels of either CSE or CBS with a different time frame.
In conclusion, testosterone-induced vasodilatation involves the L-cysteine/H_2S pathway as well as NO production.