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- Research

TESTOSTERONE MODULATES PLATELET AGGREGATION AND ENDOTHELIAL CELL GROWTH THROUGH NITRIC OXIDE PATHWAY

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Abstract

The aim of the present study was to investigate the effect of testostorone on the modulation of cellular events associated with vascular homeostasis. In rat aortic strips, 5-20 minutes treatment with physiological concentrations of testosterone significantly increased nitric oxide production. The rapid action of the steroid was suppressed by the presence of an androgen receptor antagonist (flutamide). We obtained evidence that the enhancement in nitric oxide synthesis was dependent on the influx of calcium from extracellular medium, because in the presence of a calcium channel blocker (verapamil) the effect of testosterone was reduced. Using endothelial cell cultures we demonstrated that the androgen directly acts at endothelial level. Chelerythrine or PD98059 compound completely suppressed the increase in nitric oxide production, suggesting that the mechanism of action of the steroid involves PKC and MAPK pathways. It is known that endothelial-NO released to the vascular lumen serves as an inhibitor of platelet activation and aggregation. We showed that testosterone inhibited platelet aggregation and this effect was dependent on endothelial nitric oxide synthesis. Indeed, the enhancement of nitric oxide production elicited by the androgen was associated with endothelial cell growth. The steroid significantly increased DNA synthesis after 24 h of treatment, and this mitogenic action was blunted in the presence of the NOS inhibitor L-NAME. In summary, testosterone modulates vascular endothelial cell growth and platelet aggregation through its direct action on endothelial nitric oxide production.