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JOURNAL ARTICLE

The potent relaxant effect of adenosine in rabbit corpora cavernosa is nitric oxide independent and mediated by A2 receptors

L. Mantelli, S. Amerini, F. Ledda, G. Forti and M. Maggi

In the present study the effect of adenosine and adenosine analogues on rabbit isolated cavernosal smooth muscle has been evaluated in comparison with the effect of acetylcholine and electrical field stimulation. In the presence of guanethidine and indomethacin, acetylcholine and electrical field stimulation relaxed the rabbit corpus cavernosum, which was precontracted with phenylephrine. The nitric oxide synthesis inhibitor, N omega-nitro-L-arginine-methyl ester (L-NAME), greatly reduced the relaxation induced by electrical stimulation and completely abolished the relaxant effect of acetylcholine. A concentration-dependent relaxation of the rabbit corpus cavernosum was produced by adenosine; this effect was not modified by L-NAME, but was reduced by adenosine deaminase. On the other hand, the adenosine-induced relaxation was potentiated by the inhibitor of adenosine deaminase, erythro-9-(2-hydroxy-3-nonyl) adenine and by the adenosine uptake inhibitor dipyridamole. Moreover, the effect of adenosine was antagonized by the unspecific adenosine receptor antagonist 8-phenyltheophylline. The receptor subtypes involved in cavernosal relaxation were characterized by using selective receptor antagonists: 1,3-di propyl -8-cyclopentyl xanthine, a blocker of A₁ receptors, did not modify adenosine-induced relaxation. This effect was, however, antagonized by the A₂-receptor antagonist CGS15943. A relaxant effect was also obtained with nanomolar concentrations of two synthetic adenosine analogues, the preferential A₂ receptor agonist 5'-N-ethylcarboxamidoadenosine and the A_{2a} selective agonist CGS21680. These results demonstrated that adenosine has potent relaxant activity on the corpus cavernosum, acting through a mechanism different from the nitric oxide pathway, and that receptors involved in the effect of adenosine belong to the A_{2a} subtype.

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