Activation of Muscarinic Receptors Inhibits Neurogenic Nitric Oxide in the Corpus Cavernosum

AM Senbel, AM Hashad, FM Sharabi, TT Daabees

Faculty of Pharmacy- Alexandria University, Department of Pharmacology & toxicology- 21521, Egypt

Objective: The functional role of cholinergic transmission in erection is still far from being fully elucidated. This work aims to further elucidate the modulatory role of neostigmine on NO in the corpus cavernosum and to highlight whether cholinergic transmission in the penis modulates sildenafil action.

Methods: The isolated rabbit corpus cavernosum and measurement of intracavernosal pressure in the anesthetized rat model were used. Results: Neostigmine (0.02 mg/kg) reduced increase of intracavernosal pressure/mean arterial pressure (ICP/MAP) next to cavernous nerve stimulation. Higher doses (0.06 and 0.4 mg/kg) potentiated ICP/MAP rise and atropine (1.5 and 10 mg/kg) did the opposite. In vitro, neostigmine (10-5 and 10-4 M) potentiated neurogenic relaxations and this effect was significantly inhibited by hexamethonium (10-4 M) or Nω-propyl-L-arginine (3x10-5 M) and partially but significantly reduced in the presence of atropine. Lower dose neostigmine (10-7 M), inhibited electrically-induced relaxation over the range of 1-4 Hz, atropine (10-6 M) almost abolished this inhibitory effect as well as NG-nitro-L-arginine (10-5 M). It was also significantly reduced by selective nNOS inhibitor Nω-propyl-L-arginine (3x10-5 M). Nicotine (10-4 M) significantly potentiated electrically-induced relaxations amounting to 84.625±8.06% at 1 Hz and potentiated the effect of sildenafil synergistically. Hexamethonium did the opposite. The potentiatory effect of sildenafil on neurogenic erection was significantly reduced by low dose neostigmine both in-vitro and in-vivo.

Conclusions: This study provides evidence that muscarinic receptors may modulate NO synthesis in nitrergic nerves by inhibiting nNOS and high level of cholinergic stimulation may activate nicotinic receptors to promote erection probably by potentiating NO synthesis in nitrergic nerves.