

Combination of alfuzosin and tadalafil exerts an additive relaxant effect on human detrusor and prostatic tissues in vitro

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Background: Lower urinary tract symptoms (LUTS) suggestive of benign prostatic hyperplasia (BPH) and erectile dysfunction (ED) are highly prevalent in aging men and are strongly linked. Alpha(1)-blockers such as alfuzosin are effective monotherapies for LUTS. Phosphodiesterase type 5 (PDE5) inhibitors such as tadalafil are the first-line treatment for ED. Both drugs act by two different mechanisms of action on common urogenital target organs and, thus, may have additive effects.

Objectives: We evaluated in vitro the effects of alfuzosin, tadalafil, and the combination of both on human detrusor and prostatic smooth muscle.

Design, Setting, and Participants: Prostatic and bladder tissue were obtained from patients (n=20 and n=17, respectively) undergoing cystoprostatectomy for bladder cancer.

Measurements: In organ baths, isolated prostatic strips and isolated bladder strips were incubated with vehicle, tadalafil (10(-6) M and 10(-5) M), alfuzosin (3x10(-8) M or 10(-6) M and 10(-5) M) or a combination. Concentration-response curves (CRCs) to norepinephrine were generated on prostatic strips and detrusor strips precontracted with carbachol. Strips were also submitted to electrical field stimulation (EFS).

Results and Limitations: When alfuzosin and tadalafil were combined, the maximal relaxation to norepinephrine on carbachol-precontracted detrusor strips was significantly increased compared with tadalafil alone, and EFS-induced detrusor contractions were better inhibited compared with each compound alone. Tadalafil significantly inhibited norepinephrine-induced prostatic strip contractions by reducing the maximal effect, whereas alfuzosin shifted the CRC of norepinephrine to the right. Combining both tadalafil and alfuzosin resulted in a greater relaxant effect. Likewise, the combination was more effective at reducing EFS-induced contractions compared with each compound alone.

Conclusions: The combination of alfuzosin and tadalafil exerts an additive effect of inhibiting adrenergic smooth muscle tone of prostatic tissue and EFS-induced detrusor contractions and conversely, of enhancing adrenergic relaxation of detrusor precontracted with carbachol. These experiments provide experimental support for the clinical investigation of the combination of alpha1-blockers and PDE5 inhibitors in the treatment of LUTS.

Editorial Comment

Prescription of an association of alpha-blockers and PDE-5 inhibitors has been increasingly in clinical practice, since lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) are commonly associated. Also, it has been demonstrated a positive effect of PDE-5 in LUTS. On the other hand, it has been demonstrated that LUTS would predispose to sexual dysfunction. Therefore, an emerging concept is that the combination of an alpha-blocker and a PDE-5 inhibitor is the most effective therapy to treat LUTS secondary to BPH. The present study demonstrated in vitro that the combination of alfuzosin and tadalafil shows an additive relaxant effect on human prostate and detrusor tissue, and therefore, the association could be more effective than monotherapy in relieving LUTS associated with BPH.

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