INTRODUCTION:

Alpha1-adrenergic blockers are considered the most effective monotherapy for lower urinary tract symptoms (LUTS) suggestive of BPH and phosphodiesterase 5 inhibitors are the first line treatment of erectile dysfunction (ED). LUTS and ED are highly prevalent in aging men and are strongly linked, independently of age. Recently, it has been shown that tadalafil could improve LUTS. Furthermore, a recent placebo-controlled study showed no clinically relevant hemodynamic interaction between alfuzosin and tadalafil. We aimed to evaluate the effect of alfuzosin, tadalafil or a combination of both on human prostatic tissue.

METHODS:

Prostatic tissue were obtained from 7 patients undergoing cystoprostatectomy for infiltrating bladder cancer. Prostatic strips were mounted isometrically in a 5 ml organ bath filled with Krebs-HEPES buffer maintained at 37°C and bubbled with 95% O2 and 5% CO2, pH 7.4. Following an equilibration period, concentration-response curves (CRC) to norepinephrine (NE) were performed from 10^-8 to 10^-4 M. Then following a 20 min incubation period with either vehicle, or tadalafil (10^-5 M), or alfuzosin (3.10^-8 M) or a combination of both compounds, CRC to NE was repeated.

RESULTS:

Preincubation of the strips with tadalafil 10^-5 M significantly inhibited contractions induced by NE (p<0.05, two-way ANOVA). In presence of tadalafil the maximal effect (Emax) of contraction induced by NE on prostatic strips was reduced to 57.4 ± 2.0% of maximal contraction of first CRC versus 71.4 ± 1.7% in presence of vehicle (p<0.05, one-way ANOVA). In presence of both 10^-5 M alfuzosin and 10^-5 M tadalafil, Emax of NE was reduced to 51.3 ± 1.7% compared to control group (p<0.05). In presence of both compounds, CRC to NE was performed. Alfuzosin (3.10^-8 M) shifted the CRC to NE to the right by 4.8 fold (p<0.05, Student t test) while tadalafil (10^-5 M) had no effect on CRC. The combination of both compounds shifted the CRC to NE to the right by 5.6 fold when compared to CRC with tadalafil alone (p<0.01, one-way ANOVA). Combination of alfuzosin and tadalafil exerted an additive relaxant effect on human prostate.

CONCLUSION:

Alfuzosin and tadalafil exert an additive relaxant effect on human prostate. The value of such a combination therapy in BPH patients with LUTS deserves further investigation in placebo-controlled studies.

SIU 2007 ABSTRACT

Combination of alfuzosin and tadalafil exerts an additive relaxant effect on human prostate

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INTRODUCTION

Lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) are highly prevalent among aging men and are strongly linked, independently of age and cardiovascular comorbidities1.

Alpha1-adrenergic blockers such as alfuzosin are considered the most effective monotherapy for LUTS suggestive of benign prostatic hyperplasia (BPH)2.

Phosphodiesterase 5 (PDE5) inhibitors such as tadalafil are the first line treatment for ED3.

There is evidence from three recent phase II double-blind placebo-controlled studies that PDE5 inhibitors including tadalafil significantly improve LUTS/BPH4-6.

The combination of tadalafil (10-5M) and alfuzosin (3.10-8M) exerted a greater inhibitory effect on NE-induced contractions of human prostatic strips compared to

There is no clinically relevant hemodynamic interaction between alfuzosin 10mg once daily and tadalafil 20mg once daily6.

AIM OF THE STUDY

We aimed to evaluate in vitro the effect of alfuzosin, tadalafil or a combination of both drugs on human prostatic tissue.

RESULTS

***P<0.001 versus vehicle

CONCLUSIONS

Alfuzosin and tadalafil exert in vitro an additive inhibitory effect on norepinephrine-contracted human prostatic tissue.

These results support that a combination of tadalafil and alfuzosin could be an effective therapy to treat LUTS associated with BPH.

The value of combining both drugs in BPH patients with LUTS deserves further investigation in placebo-controlled studies.