Combination of alfuzosin and tadalafil exerts an additive relaxing effect on precontracted human corpus cavernosum

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INTRODUCTION

- Lower urinary tract symptoms (LUTS) and erectile dysfunction (ED) are highly prevalent in 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 (tadalafil, sildenafil, vardenafil) are the first line treatment of erectile dysfunction (ED)³. However, there is still an unmet need for the management of men who do not respond to PDE5 inhibitors such as diabetic or neurologically impaired patients.
- It has been reported that 71% of non responders to tadalafil monotherapy (20 mg on demand) have an improvement of ED when alfuzosin 10mg once daily (OD) is combined⁴. Moreover, a recent pilot study suggested that untreated ED is more effective than sildenafil alone to enhance erectile function⁵.

AIM OF THE STUDY

- We evaluated in vitro the effect of alfuzosin, tadalafil or the combination of both drugs on precontracted human cavernosal strips.

**RESULTS**

**Effect of alfuzosin on the relaxation induced by tadalafil on NE-induced cavernosal contraction**

<table>
<thead>
<tr>
<th>Pretreatment</th>
<th>None</th>
<th>Alfuzosin 10⁻⁷M</th>
<th>Alfuzosin 10⁻⁷M (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emax (%)</td>
<td>75.0 ± 4.2</td>
<td>81.6 ± 3.9</td>
<td>83.4 ± 3.7</td>
</tr>
<tr>
<td>pED2</td>
<td>7.2 ± 0.1</td>
<td>7.5 ± 0.1</td>
<td>7.6 ± 0.1</td>
</tr>
</tbody>
</table>

Significant difference between groups for Emax and pED2

**Effect of tadalafil, alfuzosin or a combination of both on EFS-induced cavernosal contraction**

- The combination of tadalafil and alfuzosin is more efficient to inhibit human cavernosal contraction induced by increasing EFS frequency than each compound alone.

**Effect of alfuzosin or tadalafil on the nitrergic non-adrenergic non-cholinergic (NANC) relaxation induced by EFS on NE-precontracted cavernosal strips**

The pre-treatment of strips with tadalafil 10⁻⁷M has no effect on the amplitude of nitrergic NANC relaxation induced by EFS while tadalafil 10⁻⁶M tends to enhance the amplitude of relaxation although this effect is not significant. In contrast, tadalafil increases in a dose dependent manner the duration of the relaxation induced by EFS.

The pre-treatment of strips with alfuzosin at 10⁻⁷M significantly increases the amplitude and, to a lesser extent, the duration of EFS-induced relaxation. Alfuzosin at 10⁻⁶M does not modify the relaxation response induced by EFS.

**Effect of the combination of alfuzosin & tadalafil on the nitrergic non-adrenergic non-cholinergic relaxation induced by EFS on NE-precontracted cavernosal strips**

- The combination of tadalafil 10⁻⁷M and alfuzosin 10⁻⁸M, significantly increases the amplitude of the relaxation and its effect is significantly greater than tadalafil 10⁻⁷M alone suggesting an additive effect of the combination.

In addition, the combination of tadalafil 10⁻⁷M and alfuzosin 10⁻⁸M also prolongs the relaxation to EFS to a greater extent than tadalafil 10⁻⁷M or alfuzosin 10⁻⁸M alone.

**CONCLUSIONS**

- In vitro, the combination of alfuzosin and tadalafil is more efficient than each compound alone to relax the adrenergic tone or to enhance nitrergic relaxation.
- As a considerable population of patients with erectile dysfunction do not respond to PDE5 inhibitors, such a combination therapy deserves further investigation in well-designed placebo-controlled studies in patients complaining of erectile dysfunction and not responding to tadalafil alone.