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SPONTANEOUS CONTRACTIONS IN THE TRANSITION ZONE OF PROSTATES FROM MEN WITH BENIGN PROSTATIC HYPERPLASIA OR ENLARGEMENT ARE SIGNIFICANTLY REDUCED BY COMBINATION THERAPY

Hypothesis / aims of study

There is ample evidence to suggest that patients treated with low dose PDE-5 inhibitors have an improvement in their lower urinary tract symptoms (LUTS) secondary to prostate enlargement or benign prostatic hyperplasia (BPH); however, the precise mechanism by which PDE-5 inhibitors exert their effects is not known. The aim of this study was to examine the direct effect of a clinically used PDE5 inhibitor, sildenafil, compared to an existing well established treatment for BPH, the α1 antagonist tamsulosin, in a novel model of human prostatic contractility.

Study design, materials and methods

Transition zone (TZ) tissue (10mm X 15mm) from the prostate gland was obtained from consenting patients undergoing transurethral resection of prostate or radical prostatectomy. Transition zone tissue was placed into ice-cold RPMI medium supplemented with 5% fetal calf serum and antibiotics (penicillin at 300 units/ml, streptomycin at 300 µg/ml and amphotericin at 1 µg/ml). Contractile recordings were made from prostatic preparations (5mm X 10mm) using standard tension recording techniques as we have previously described. A paired Student's t-test was used to test for statistical significance ($P < 0.05$).

Results

All specimens contracted spontaneously at a frequency of 1.9 +/- 0.2 contractions per minute; the average duration of each contraction was 13.1 +/- 1.6 seconds. In the TZ of the human prostate, the amplitude of the spontaneous contractions was 0.23 +/- 0.02 N/g (n=22). Sildenafil (10µM) reduced the frequency (by ~40%) and amplitude (by ~27%), of spontaneous contractions recorded in the TZ of the human prostate gland (n=8) ($P < 0.05$). Tamsulosin (0.1nM) reduced the amplitude (by ~27%), but not the frequency of spontaneous contractions recorded in the TZ of the human prostate gland (n=9) ($P < 0.05$). The combination of tamsulosin following sildenafil resulted in a reduction in amplitude by 87% and frequency by 87% (n=4) ($P < 0.01$). The combination of sildenafil following tamsulosin resulted in a reduction in amplitude and frequency by 70% and 65%, respectively (n=6) ($P < 0.05$). The non-specific α1 antagonist, 1µM prazosin, had no significant effects on the spontaneous contractions (n=5) ($P > 0.05$).

Interpretation of results

Using this model of human prostatic smooth muscle tone, we have demonstrated that the *α1 adrenoceptor antagonist* tamsulosin and the *PDE-5 inhibitor* sildenafil directly reduce the spontaneous contractility of the transition zone of the human prostate gland. Our results provide: 1) further validation for the use of PDE-5 inhibitors in the treatment of lower urinary tract symptoms associated with BPH, and 2) proof of mechanism data to support the use of combination therapy utilising α1 antagonists with PDE-5 inhibitors.

Concluding message

The potential to use PDE-5 inhibitors, in combination with lower doses of 'uroselective' α1 antagonists such tamsulosin may prove to be a better strategy than current treatment regimens, especially in patients with comorbidities.

Disclosures

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