

COMBINATION THERAPY OF TAMSULOSIN WITH SOLIFENACIN REDUCES PROSTATE VASCULAR DENSITY WHILE TAMSULOSIN MONOTHERAPY INCREASES PROSTATE PERfusion IN PATIENTS WITH PREDOMINATELY STORAGE LUTS: RESULTS OF A PILOT STUDY

Hypothesis / aims of study

The combination of an antimuscarinic with an α -blocker is the recommended treatment option for male storage lower urinary tract symptoms (LUTS). Previous studies indicate that the therapeutic effect of α -blockers occurs independent of prostatic relaxation and perhaps involving a direct effect on blood vessels. There is strong evidence that improves prostate perfusion and decrease oxidative stress markers. In contrast, it is unclear if anticholinergics affect prostatic perfusion. Here in, we tried to assess prostate vascularity before and after Tamsulosin monotherapy and combination with anticholinergic treatment.

Study design, materials and methods

In a prospective, randomized study we recruited treatment naïve patients with prostate volume ≥ 30 mls and predominantly storage LUTS, who had maximum urine flow rate (Qmax) ≥ 10 ml/s, post-void residual (PVR) < 100 ml, scored ≥ 3 in the International Prostate Symptoms Score urgency question. The recruited patients had at least 3 urgency episodes per 24h, daytime frequency ≥ 8 and at least 2 nocturia episodes as documented in a 3-day bladder diary. Patients with neurogenic bladder, PSA > 4 ng/ml, recurrent urinary tract infections or a history of urinary tract malignancy were excluded.

The study was designed and powered to identify changes in the detected vascular surface from baseline to week 26, as well as in prostate and adenoma volumes. The primary end point was the mean percentage changes in the detected vascular surface as measured by the colour pixel Doppler (CPD). All patients were submitted to transrectal ultrasonography at baseline and at the end of the study. The CPD was assessed by a sequence of Doppler images from prostatic apex to base using a 5mm step using a stepper. The image processing software (Image J) used to manually delineate the visible vessels and calculate the pixels contained within the selected area. The total number of prostate pixels was extracted from a 3D prostate model, which was created for volumetric measurements. We calculated the CPD as a percentage of vascular surface to the total prostate volume ((Total Vessels Pixels / Total Prostate Pixels)*100). Paired t-test was used for intragroup variability and Mann-Whitney test for intergroup variability. The local ethics committee approved this study and all recruited patients gave their written informed consent.

Results

A total of 80 men were enrolled in the study. At baseline, both groups were comparable for bladder diary, questionnaire scores, prostate parameters and demographics. Sixty-three men completed the study (Group I: n=31, Group II n=32). At baseline both groups were comparable for CPD ($1.3 \pm 1.1\%$ in Group I and $1.7 \pm 0.9\%$ in Group II), prostate size (48.93 ± 13.6 ml vs. 52.63 ± 31 ml) and adenoma volume (24.45 ± 10.2 ml vs. 28.37 ± 21.4 ml).

At the end of the treatment there was a marked increase (149.3%) in the CPD in the monotherapy group that corresponds to $1.9 \pm 1.0\%$ of total prostate vascular surface, as opposed to a reduction (-19.8%) in the combination group, corresponding to $1.0 \pm 0.6\%$ of total prostate vascular surface. After treatment an increase was noted in total prostate volume (9.2%) in the monotherapy group as opposed to a decrease (-9.5%) in the combination group (comparative p<0.001). Similar changes were found in adenoma volume (+17.4% vs. -12.5%, p<0.001).

Interpretation of results

To our knowledge, this is the first analysis of a randomized population focusing on the effect of the combination of Solifenacin and Tamsulosin on the detected vascular surface of prostates in patients with benign prostatic enlargement who present with predominantly storage LUTS.

The results of this study confirm that Tamsulosin monotherapy positively affects the perfusion of prostate gland. In contrast, the combination therapy and Solifenacin seems to reduce the detected vascular surface. These changes are proportional to volumetric changes of prostate and adenoma in both groups. Whether antimuscarinics and, in this case Solifenacin, may cause prostatic ischemia leading to reduction of the prostate and adenoma volume remains to be further investigated, as well as possible associations of these morphometric changes of the prostate with symptomatic improvement. As both muscarinic and adrenergic receptors exist in the prostate, the role of prostate muscarinic receptors needs to be examined, also in association with the acknowledged function of adrenergic receptors.

Concluding message

The results of this pilot study suggest that both Tamsulosin and Solifenacin affect prostatic perfusion. It is unclear if muscarinic receptor blockage predominates over the adrenergic receptors at the level of prostatic arterioles or whether our findings reflect actions via an indirect alternative pathway.

Disclosures

Funding: None **Clinical Trial:** Yes **Public Registry:** No **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** Approved by the Ethics Committee of Hippokrateion Hospital of Thessaloniki and by the Committee of Bioethics of Aristotle University of Thessaloniki, Greece **Helsinki:** Yes **Informed Consent:** Yes