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URODYNAMIC SAFETY OF SOLIFENACIN TREATMENT IN MEN WITH DETRUSOR OVERACTIVITY AND LOW DETRUSOR CONTRACTILITY

Hypothesis / aims of study

Storage symptoms are mainly attributable to detrusor overactivity that is associated in up to 40 to 60% with voiding disorders. Antimuscarinics remain the most widely used medical treatment for detrusor overactivity. In a recent paper Abrams and co-workers have suggested that tolterodine did not adversely affect urinary function in men with OAB and BOO and there was no evidence of clinically meaningful changes. Among men who desire treatment antimuscarinics are not given to men with low detrusor contractility. There are speculative concerns that the inhibitory effect of antimuscarinics on detrusor contraction could further reduce the detrusor contractility and determine a significant increase of acute urinary retention. In this study we prospectively evaluated the urodynamic safety of solifenacin treatment in men with detrusor overactivity plus low detrusor contractility.

Study design, materials and methods

In this open-label study with pre- and post-test design. All men (older than 40 years) with an urodynamic proven detrusor overactivity (DO) and detrusor underactivity (UDA) were enrolled. DO was defined as the urodynamic presence of involuntary detrusor contractions of $\geq$ 10 cmH2O with volume to first contraction less than 350 ml. DUA was defined as a bladder contractility index (BCI) of less than 100. BCI quantification was obtained according to the following formula: PdetQmax - 5Qmax. All enrolled men received 5mg of Solifenacin once a day for 120 days. The solifenacin administration was started the day of enrolment (Baseline). Medications (30 days supply) were dispensed during the study visit. Patients were instructed to tape any medications untaken back into the blister pack, to account for any selective adherence. During follow-up visits, blister-packed medications were counted, including medications untaken. A complete urodynamic study was performed the day of enrolment (baseline) and at day 120. As primary endpoint we estimated the safety of solifenacin treatment by measuring the changes from baseline to day 120 of following urodynamic parameters: BVE, BCI, BOOI, Qmax obtained during UDS, PdetQmax PVR and measured after UDS. The prevalence of acute urinary retention (AUR) after treatment and total IPSS were evaluated at baseline and day 120 of treatment was also recorded. Sample size was determined assuming that all continuous variables were analysed by a t student-test for paired data. Using a 2-tailed alpha-level of 0.01 with 90% power and assuming a difference in means of Qmax obtained during UDS pre- and post-treatment equal to 2.5 ml/s with a standard deviation of difference in the response of matched pairs equal to 4 ml/s, 43 patients were required. Allowing for an approximate 15% dropout rate, we aimed to enrol 49 men. Statistical analysis was performed using SPSS 11.0 (SPSS, Inch., Chicago, Illinois) software. An alpha value threshold of 0.01 was used. All statistical tests were two-tailed. Continuous variables were normally distributed (Shapiro-Wilk test $p<0.01$) and were presented as mean and IC99% and analyzed using a Student t-test for paired data. A multivariate general linear model was used to assess the clinical significance of the changes in urodynamic parameters (dependent variables) after treatment with solifenacin (independent variable). In this regard eta squared coefficient was utilized and all coefficients were weighted for voided volume.
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Results

The mean changes (%) in urodynamic parameters from baseline to day 120 were evaluated. Qmax during UDS decreased weakly after treatment (mean changes –0.6 ml/s; CI 99% -1.1 to 1.4 ml/s) (p=0.007). PdetQmax decreased after treatment (mean changes -6.4 cmH_2O; CI 99% -8.7 to -4.0 cmH_2O) ($p<0.001$). An indicator of urethral resistance index such as BOOI decreased after treatment (mean changes –7.5; CI 99% -10.5 to –4.6) ($p<0.001$). BCI, and indicator of contractility decreased weakly after treatment (mean changes –3.8; CI 99% -6.7 to –0.9) (p=0.001). BVE as indicator of voiding efficacy decreased after treatment (mean changes -4.4; CI 99% –8.4 to -0.4) (p=0.006). PVR increased after treatment (mean changes 6 ml; CI 99% 4 to 8.7 ml) (p=0.152). The prevalence of AUR after solifenacin treatment was equal to 2% (1/45). We have further considered how much of observed changes in urodynamic parameters could be imputable to solifenacin. Using a general linear model for repeated measures we found that none of the changes found in urodynamic parameters were imputable to solifenacin treatment. Here we listed the eta square coefficients with respective p values.

Qmax during UDS	Eta square=0.007; p=0.425
PdetQmax	Eta square=0.072; p=0.011
BOOI	Eta square=0.057; p=0.024
BCI	Eta square=0.064; p=0.016
BVE	Eta square=0.023; p=0.156
PVR	Eta square=0.001; p=0.963

Interpretation of results

Our study presents attractive methodological characteristics. We have carried out our analysis on the same subject using a pre- and post-test design. Controls are an essential component of any research design because they test evaluation criteria and detect extraneous contributions to the evaluation. Ideally, the experimenter attempts to control all outside variables except for the one(s) to be measured. This is a critical point of all studies. The attractive feature of this design is that the treatment comparisons are “within subjects” rather than “between subjects”. In this scenario we found that solifenacin is safe in men with urodynamically proven DO and DUA. Although mean changes in several urodynamic parameters were statistically significant from baseline to day 120, they were not clinically significant since a very prevalence of AUR was found. Additionally we found that most of changes in urodynamic parameters were due to case. Our regression analysis indicated that changes found in urodynamic parameters were not imputable to solifenacin treatment.

Concluding message

The results of present study seem to suggest that solifenacin is utilizable as medical therapy in men with detrusor overactivity with low detrusor contractility. Further study should be performed in order to confirm our results.

References

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