272

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CLINICAL EFFICACY OF SOLIFENACIN TREATMENT IN MEN WITH DETRUSOR OVERACTIVITY AND LOW DETRUSOR CONTRACTILITY

Hypothesis / aims of study

Although treatment approaches to OAB can include behavioural, pharmacological and surgical intervention, pharmacological management remains the mainstay of therapy. Solifenacin is a once-daily oral antimuscarinic agent and it has demonstrated to improve urgency and other symptoms of OAB and was associated with an acceptable level of anticholinergic side effects. In a recent paper Athanasopulos and co-workers have suggested that a combination treatment with alpha-blocker plus tolterodine improves quality of life and did not adversely affect urinary function in men with OAB and BOO. However, no study has investigated the efficacy of antimuscarinic agents in men with OAB and low detrusor contractility. The primary objective of the present study was to evaluate the clinical efficacy of solifenacin treatment in men with OAB and low detrusor contractility.

Study design, materials and methods

This is a pre- and post-test design study. Following informed consent, subjects underwent initial screening and men aged $\geq$ 40 years were eligible if by 7-day bladder diary they had urinary frequency (8 or more micturitions per 24 hours) and urgency, with or without urgency incontinence (1 or more episodes per 24 hours) together with coexistence of detrusor overactivity (DO) and detrusor underactivity (UDA). DO was defined as the urodynamic presence of involuntary detrusor contractions of $\geq$ 10 cmH2O with volume at 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 not taken. A complete urodynamic study was performed the day of enrolment (baseline) and at day 120. As primary endpoint we estimated the efficacy of solifenacin treatment. For this purpose, the primary efficacy measure were change in the number of urge incontinence episodes per week and the evaluation of patient perception of treatment benefit assessed by “Patient Perception of Bladder Condition (PPBC). Secondary efficacy measures were total micturation per 24hr, urgency episodes per 24hr and IPSSQoL that were evaluated at baseline and day 120 of treatment. All adverse events (AEs) were recorded. AEs were noted by direct observation and spontaneous patient report, and classified as mild (not interfering with usual function), moderate (interfering to some extent with usual function), or severe (interfering significantly with usual function). The prevalence of acute urinary retention (AUR) after treatment was also recorded. 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 clinical 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

A total of 49 patients were enrolled. Mean patients age was 65 (CI99% 57 to 68). A total of 45 men (92%) completed the study and the cumulative dropout rate was 8% (n=4). No patient discontinued because of lack of effectiveness. Few men discontinued because of AEs (6%) or lost during follow-up (2%). The mean changes (%) in clinical parameters from baseline to day 120 were evaluated. The number of urge incontinence episodes per week decreased significantly after treatment (mean changes –-6.8; CI 99% -8.8 to –4.5) ($p<0.001$) as well as the patient perception of treatment benefit assessed by PPBC (mean changes -2.2; CI 99% -2.7 to –1.65) ($p<0.001$). The number of total micturation (mean changes –2.82; CI 99% -3.52 to –2.12; $p<0.001$) and urgency episodes per 24hr (mean changes –2.0; CI 99% -3.02 to –0.77; $p<0.001$) was reduced after solifenacin treatment. The quality of life increased respect to baseline. In particular significant change in IPSSQoL scoring was found (mean changes –1.1; CI 99% –2.8 to –0.9) ($p=0.006$). After solifenacin treatment slight changes in Qmax during UDS (mean changes –0.6 ml/s; CI 99% -1.1 to 1.4 ml/s; $p=0.007$) and PVR (mean changes 6 ml; CI 99% 4 to 8.7 ml; $p=0.152$) were found and these were not clinical significance. The most common AEs reported were dry mouth (11.1%), constipation (4.4%). The prevalence of AUR after solifenacin treatment was equal to 2% (1/45). We have further considered how of observed changes in clinical parameters could be imputable to solifenacin. Using a general linear model for repeated measures we found that none of the changes found in clinical parameters were imputable to solifenacin treatment. Here we listed the eta square coefficients with respective p values.

UUI per week	Eta square=0.054; $p<0.001$
PPBC	Eta square=0.628; $p<0.001$
Voids per 24hr	Eta square=0.730; $p<0.001$

Urgency episodes per 24hr Eta square=0.651; p<0.001
IPSSQol Eta square=0.23; p=0.009

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 efficacy in men with urodynamically proven DO and DUA. This antimuscarinic significantly improved all symptoms of OAB. Our regression analysis indicated that changes found in clinical parameters were principally imputable to solifenacin treatment. Low prevalence of AUR was observed and there were clinical significance changes in Qmax during UDS and in PVR.

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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