

VARDENAFIL FOR OVERACTIVE BLADDER IN WOMEN: A PILOT RANDOMIZED CONTROLLED TRIAL

Hypothesis / aims of study

Antimuscarinic drugs are frequently used as the first-line therapy for overactive bladder (OAB) in women. However, it is widely acknowledged that these drugs are not fully effective in a substantial proportion of patients and produce side effects limiting their chronic use. Preclinical studies indicate that phosphodiesterase type 5 (PDE5) inhibitors used for treating erectile dysfunction in men could offer some benefits in the treatment of OAB. For example, it has been reported that PDE5 inhibitors directly inhibit afferent detrusor excitability and that the PDE5 inhibitor-induced relaxation of detrusor smooth muscle may be associated with cGMP- and cAMP-dependent signaling pathways.

The aim of the present single-center, randomized, double-blind, placebo-controlled, parallel-group study was to evaluate the efficacy and safety of a PDE5 inhibitor, vardenafil (10 mg orally twice daily) in the treatment of OAB in women.

Study design, materials and methods

The study was conducted in the ambulatory of the Department of Gynecology and Oncological Gynecology, Military Institute of Medicine, between February 2011 and December 2012. Women with symptoms of OAB lasting for ≥ 3 months, with an average ≥ 8 micturitions/24 h and ≥ 3 urgency episodes/24 h (with or without incontinence), and with no satisfactory response to prior antimuscarinic therapy were recruited to the study.

Thirty three subjects (mean age \pm S.D.: 64.3 \pm 7.1 yr) were randomized to receive vardenafil (n=17) or placebo (n=16) over a period of 4 weeks. The primary endpoints were changes from baseline to a 4-week follow-up visit in the mean number of micturitions, urgency and urgency incontinence assessed with the 3-day micturition diaries. Secondary endpoints included changes in health-related quality of life (HRQoL) assessed by a 10-point Visual Analog Scale (VAS).

Results

There were no differences in basic sociodemographic and clinical parameters between the vardenafil and placebo group. Vardenafil was significantly more effective than placebo in reducing the mean number of urgency episodes/24h from the baseline to follow-up assessment (-6.4 vs. -2.93; $p < 0.05$, the Student's t-test). This represented a 62% reduction from baseline in the vardenafil group as compared to a 31% reduction in the placebo group. Vardenafil was also significantly more effective than placebo in reducing the mean number of urgency incontinence episodes/24h (-4.4 vs. -1.8; $p < 0.05$). The reduction in the mean number of micturitions/24h was also larger in the vardenafil group but this trend did not reach significance (-3.8 vs. -0.8; $0.05 < p < 0.1$). There was a statistically significant difference in favor of vardenafil over placebo for the secondary endpoint, i.e. HRQoL ($p < 0.01$). No serious side effects or exacerbations of pre-existing medical conditions were noted in the study group. The most common side effect reported by the patients receiving vardenafil (6 of 17) was headache.

Interpretation of results

The significant improvement in two (urgency episodes and urgency incontinence episodes) from three primary endpoints with vardenafil was accompanied by the significant improvement in HRQoL.

Concluding message

Vardenafil (10 mg orally twice daily) may offer some benefits for women suffering from OAB who showed no satisfactory response to prior antimuscarinic therapy. Further studies are needed to fully assess the efficacy and safety of vardenafil in the treatment of OAB symptoms.

References

1. Andersson KE, Chapple CR, Cardozo L, Cruz F, Hashim H, Michel MC, Tannenbaum C, Wein AJ. Pharmacological treatment of overactive bladder: report from the International Consultation on Incontinence. *Curr Opin Urol.* 2009;19(4):380-394.
2. Oger S, Behr-Roussel D, Gorny D, Lebret T, Validire P, Cathelineau X, Alexandre L, Giuliano F. Signalling pathways involved in sildenafil-induced relaxation of human bladder dome smooth muscle. *Br J Pharmacol.* 2010;160(5):1135-1143
3. Behr-Roussel D, Oger S, Caisey S, Sandner P, Bernabé J, Alexandre L, Giuliano F. Vardenafil decreases bladder afferent nerve activity in unanesthetized, decerebrate, spinal cord-injured rats. *Eur Urol.* 2011;59(2):272-279

Disclosures

Funding: The study was supported by the National Science Centre (grant no. NN407098836) **Clinical Trial:** Yes **Public Registry:** No **RCT:** Yes **Subjects:** HUMAN **Ethics Committee:** Ethics Committee for Human Studies at the Military Institute of Medicine **Helsinki:** Yes **Informed Consent:** Yes