

REDEFINING RESPONSE IN OVERACTIVE BLADDER SYNDROME – IMPACT ON QUALITY OF LIFE

Hypothesis / aims of study

Overactive bladder (OAB) was redefined by the International Continence Society (ICS) as urgency, with or without urge incontinence, usually with frequency and nocturia. This definition places urgency as the central and driving symptom of OAB; as such, we propose that reduction of urgency should be a primary target for the assessment of the effectiveness of any treatment for OAB. There remain, however, numerous different ways in which treatment results are reported, confounding comparison of efficacy between studies, and highlighting the need for a standardized outcome measure in OAB. In addition, the symptoms of overactive bladder (OAB) can have a profound negative impact on patient quality of life (QoL), therefore, it is important that any measure of drug efficacy in OAB must be accompanied by improvements in QoL. Based on these principles, the pooled analysis presented here evaluates three potential new definitions of treatment response, which accommodate the ICS definition of OAB, and relates the impact of pharmacological treatment according to these composite endpoints on improvements in QoL.

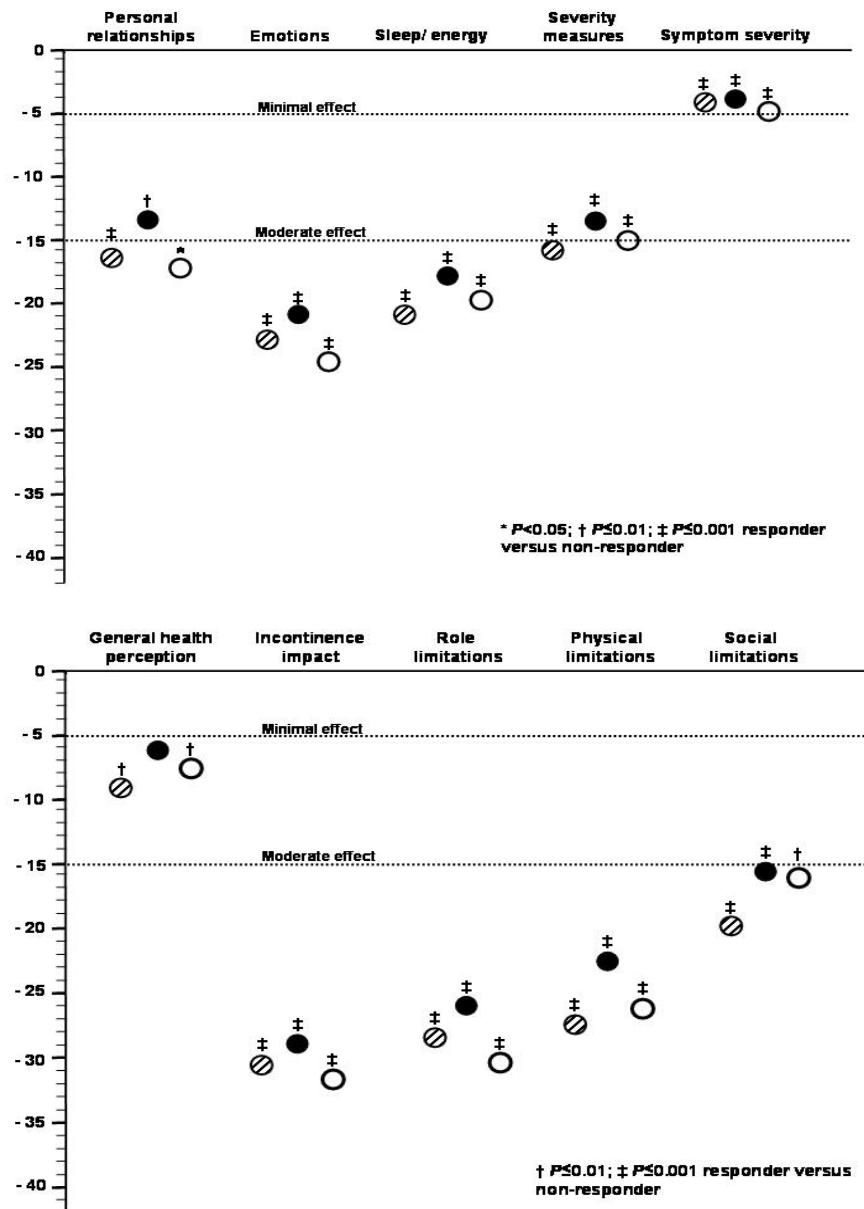
Study design, materials and methods

Data from two multinational, double-blind, randomized Phase III studies with similar protocols were pooled. Patients (n=1726) were randomized to receive solifenacin 5 mg od, solifenacin 10 mg od or placebo (or tolterodine as an active comparator in one study; data from this treatment arm was not included in this pooled analysis). Data on urgency, incontinence, micturition frequency and nocturia (the symptoms included in the analysis) were collected from 3-day micturition diaries, which were evaluated at baseline and at weeks 4, 8 and 12. Based on these data, treatment response was evaluated in three ways, as follows: 1) a $\geq 50\%$ reduction in every baseline symptom; 2) a $\geq 50\%$ reduction in urgency episodes and ≥ 1 other baseline symptom; and 3) resolution of urgency and ≥ 1 other baseline symptom, where resolution was defined as the presence of the symptom at baseline but not at endpoint (for micturitions, subjects with normalization of micturition frequency [< 8 episodes/day at endpoint] were included). QoL was compared in responders versus non-responders using the King's Health Questionnaire (KHQ), completed at baseline and weeks 4 and 12, for all treatment groups and for all three responder definitions. The studies included in this analysis were conducted according to the principles of the Declaration of Helsinki, and received approval from the appropriate Ethical Committee or Institutional Review Board.

Results

Treatment with solifenacin at either dose resulted in significantly higher response rates versus placebo for all three response definitions: for solifenacin 5 mg, solifenacin 10 mg and placebo, response rates were, respectively: 27%, 30% and 17% for definition 1; 53%, 58% and 39% for definition 2; and 20%, 25% and 12% for definition 3 ($P \leq 0.001$ for all solifenacin groups vs placebo). Irrespective of the responder definition used, and the treatment administered, responders experienced significantly greater improvements at least 9 of the 10 domains of the KHQ versus non-responders (the solifenacin 5 mg group is shown as representative in Figures 1a and b). The two definitions associated with the greatest QoL changes in patients classified as responders were: a $\geq 50\%$ reduction in urgency episodes and at least one other symptom; and resolution of urgency and at least one other symptom.

Figure 1. Baseline to endpoint changes in scores for the first five (a) and second five (b) domains of the KHQ in responders for each of the three response definitions.



Hash markings = a $\geq 50\%$ reduction in every baseline symptom; full circle = a $\geq 50\%$ reduction in urgency and ≥ 1 other symptom; empty circle = resolution of urgency and ≥ 1 other symptom

Interpretation of results

Symptom improvements (response rates as defined in this analysis) derived from solifenacin treatment in patients with OAB are paralleled by patient-reported improvements in QoL. Based on the associated improvements in QoL, irrespective of the treatment administered, the two responder definitions that appear to be the most appropriate measures are: a $\geq 50\%$ reduction in urgency episodes and ≥ 1 other baseline symptom; and resolution of urgency and ≥ 1 other baseline symptom. Establishing which is the most appropriate definition of response to pharmacological treatment in OAB will require further investigation.

Concluding message

The composite endpoints of treatment response defined here may be considered a good starting point on which to base a standardized measure of treatment response in OAB, accurately reflecting the current ICS definition of OAB and associated with improvements in QoL.

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