

THE EFFECT OF PRIOR TREATMENT EXPERIENCE AND INCONTINENCE SEVERITY ON THE PLACEBO RESPONSE OF STRESS URINARY INCONTINENCE (SUI)

Aims of Study

The placebo response of stress urinary incontinence is sizeable but variable. In four large randomized clinical trials examining the role of duloxetine hydrochloride in the treatment of women with stress urinary incontinence, the placebo reduction in incontinence episode frequency (IEF) varied between 27 and 40%. Other authors have reported placebo effects as high as 75% [1]. The aim of the current analysis was to examine the relationship between previous treatment experience and baseline incontinence severity with placebo response.

Methods

921 assessable women aged 24 to 83 years received placebo in four 12-week randomized clinical trials evaluating pharmacological therapy for SUI in 16 countries in Africa, Australia, Europe, North America, and South America. Predominant SUI was diagnosed using a clinical algorithm demonstrated to be 90.2% predictive for urodynamic stress incontinence. Subjects were randomly assigned to receive placebo (n = 955) or duloxetine (n = 958) for 12 weeks. Weekly incontinence episode frequency (IEF) was calculated before and after randomization using subject-completed real-time paper diaries. At baseline, subjects reported their experience with prior continence surgery and with current pelvic floor muscle training (PFMT) using standardized questions. Analysis included Pearson correlations and the Wilcoxon two-sample test. All analyses are based on intent-to-treat principles.

Results

The placebo group had an average IEF of 17 per week. 55% of assessable placebo-treated subjects averaged ≥ 14 IEF/week, 11.8% had prior continence surgery, and 16.5% currently performed PFMT. The overall median decrease in IEF with placebo was 33% but ranged from a low of 11% to a high of 57% for individual countries. The placebo response was lower in women with more severe SUI ($p=.07$), in those who had prior continence surgery ($p=.26$), and for those using PFMT ($p=.02$). In comparison, decreases in IEF with active treatment were nearly identical in these subgroups (Table).

	Current PFMT		Prior Surgery		Baseline IEF Severity	
	No	Yes	No	Yes	<14/wk	≥ 14 /wk
Placebo	33.3%	23.6%	33.3%	25.0%	36.4%	29.6%
Duloxetine	51.5%	51.9%	50.0%	52.0%	50.0%	53.3%

Table. IEF reduction by subgroup for placebo and duloxetine

There was a significant positive correlation ($\rho = .44$; $p < .0001$) between the placebo response within a country and that country's utilization rate for PFMT (Figure). The IEF reduction/PFMT utilization rate relationships ranged from a 57% IEF reduction with placebo in a country with a 0% PFMT utilization rate to 21% reduction in a country with a 46% PFMT utilization rate. There were geographic differences in placebo response that paralleled the utilization rates for PFMT (Figure).

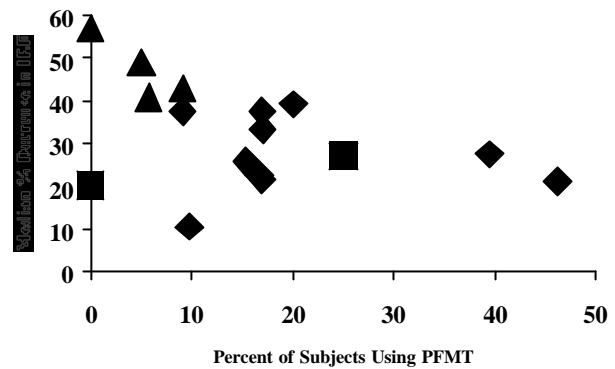


Figure. Placebo response versus PFMT use rates by country. Diamonds = countries in Western Europe, North America, and Australia with at least 18 subjects; squares = countries in Western Europe with 8 or fewer subjects; triangles = countries outside Western Europe, North America, and Australia. $\rho = .44$; $p < .0001$.

Conclusions

Treatment naivety, as reflected by low utilization rates of PFMT, seems to be a significant predictor of an increased placebo response in clinical trials for SUI. There is also a trend for an enhanced placebo response in women with less severe SUI and for a lower placebo response in those with a history of prior continence surgery.

References

1. CE Dubeau, V Khullar. Drug impact on the SUI component of mixed incontinence: is it all placebo effect. 2002 American Urogynecologic Society meeting, San Francisco.