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THE EFFECT OF BASELINE SEVERITY ON THE EFFICACY OF DULOXETINE IN THE TREATMENT OF WOMEN WITH STRESS URINARY INCONTINENCE (SUI)

Hypothesis / aims of study

Four published randomised placebo-controlled trials involving nearly 2000 women with SUI have demonstrated consistent significant improvements in incontinence and condition-specific quality of life [1-4]. The aim of this *post* hoc analysis of the integrated database from these trials was to assess the relationship between incontinence severity and duloxetine response using four grades of incontinence severity based on baseline weekly incontinence episode frequency (IEF).

Study design, materials and methods

The analysis included 1913 women aged 22-83 years with predominant SUI who were enrolled in randomized, blinded, placebo-controlled studies performed in 16 countries on 5 continents. SUI was diagnosed using a clinical algorithm 90.2% predictive for urodynamic stress incontinence [5]. Subjects were randomly assigned to receive placebo (955) or duloxetine (958) for 12 weeks. Outcome was assessed using incontinence episode frequency (IEF) from patient-completed real-time paper diaries and the validated Incontinence Quality of Life (I-QOL) questionnaire score. The severity of baseline incontinence was divided into four strata from <7 IEF/week to ≥21 IEF/week (tables). The van Elteren test was used to analyze the percent change in IEF and an ANCOVA model was used to analyze the change in I-QOL scores.

Results

Table 1 displays the results for the IEF analysis. The placebo response in the least severe group was high and enhanced compared with more severe groups, consistent with effects previously reported [6]. Duloxetine demonstrated a median percent decrease in incontinence of at least 50% in all groups, although this was not superior to the placebo response in the least severe subgroup. The separation of duloxetine response from placebo response in the other subgroups varied between 21.62% and 32.85%.

Table 1. Median Percent Change in IEF/week by Treatment and Severity Subgroups

Baseline IEF/week severity subgroup	Mean (median) baseline IEF per week for the subgroup	Treatment	n	Median % IEF Change[a]	P-value[b]
< 7	4.95 (5.00)	Duloxetine	85	-50.32	
		Placebo	94	-52.98	.271
≥7 to <14	10.11 (10.00)	Duloxetine	294	-59.42	
		Placebo	320	-37.80	<.001
≥14 to <21	16.98 (16.90)	Duloxetine	178	-61.12	
		Placebo	204	-28.27	<.001
≥21	34.55 (29.75)	Duloxetine	267	-54.61	<.001
		Placebo	308	-31.11	

[a]Using pooled diary approach (comparing all baseline diaries to all post baseline diaries)
[b]P-values obtained from the Van Elteren test with the stratification variable being the study

Table 2 displays the results for the I-QOL analysis. In all but the least severe group, the I-QOL treatment differences were statistically significant and exceeded the within-treatment minimum clinically important difference (MCID) established for I-QOL in women with SUI (6.3 points) [7]. The treatment differences also exceeded the between-treatment MICD for I-QOL (2.5) in these groups. [7]

Table 2. Mean Improvement in I-QOL Score by Treatment and Severity Subgroups

Baseline IEF/week severity subgroup	Mean (median) baseline I-QOL score for the subgroup	Treatment	n	Mean I-QOL Score Change	P-value[a]
< 7	75.38 (79.55)	Duloxetine	99	4.76	.820
		Placebo	94	5.83	
≥7 to <14	68.25 (71.59)	Duloxetine	333	7.61	.023
		Placebo	325	5.09	
≥14 to <21	62.84 (65.91)	Duloxetine	193	9.61	.004
		Placebo	207	5.91	
≥21	56.38 (57.95)	Duloxetine	298	12.15	<.001
		Placebo	312	6.64	

[a]P-values were obtained using Type III sum of squares from an ANCOVA that included change in I-QOL as dependent and baseline I-QOL, treatment, and study as independent variables.

Interpretation of results

The data support the significant and clinically important efficacy of duloxetine in women with SUI who are experiencing one or more incontinent episodes per day. Significant differences were not demonstrated in women with very mild incontinence who also had high baseline I-QOL scores. The challenge of demonstrating a significant treatment response in women with mild disease is a phenomenon observed in many disease states. Given the natural fluctuation of SUI and the limited room for improvement with mild disease, it is difficult to demonstrate a significant impact of any treatment in patient groups who have very mild indicators of disease at baseline. However, physiologically, patients with mild SUI should have the least damaged continence mechanism that should therefore be best able to respond to duloxetine's mechanism of action.

Concluding message

For women who average at least one incontinence episode per day, significant and important improvements in incontinence and incontinence-specific quality of life were demonstrated.

References

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FUNDING: Lilly Research Laboratories