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DULOXETINE VERSUS PLACEBO FOR THE TREATMENT OF GERMAN WOMEN WITH STRESS URINARY INCONTINENCE (SUI)

Hypothesis / aims of study

Three published international Phase 3 randomised placebo-controlled trials in women with SUI have demonstrated improvements in incontinence and condition-specific quality of life (QoL) in women taking duloxetine [1-3]. The aim of this clinical trial was to study the effect of duloxetine on SUI in German women measuring the effect on incontinence episode frequency (IEF) by patient diaries and on QoL using the King's Health Questionnaire (KHQ), which has not been used in duloxetine studies before.

Study design, materials and methods

The analysis included 617 women aged between 28 and 86 years with predominant SUI who were enrolled in a randomized, blinded, placebo-controlled study performed by German urologists and urogynaecologists. SUI was diagnosed by either urodynamic studies within the previous 12 months or using a simple question from a short 2-question instrument (the S/UIQ) with one question asking about urge urinary incontinence (UUI) symptoms and one asking about SUI symptoms. Subjects had to have at least 7 episodes of urinary incontinence (UI) per week by patient diary and to have at least twice as many SUI episodes as UUI by S/UIQ. Subjects were randomly assigned to receive placebo (311) or duloxetine (306) for 6 weeks. Outcome was assessed using incontinence episode frequency (IEF) from patient-completed real-time paper diaries. The van Elteren test, stratified by baseline IEF severity, was used to analyze the primary variable, percent change in IEF. Secondary objectives included comparisons of response using the King's Health Questionnaire (KHQ) and the Patient Global Impression – Improvement (PGI-I) score.

Results

At baseline, the mean baseline IEF was 25 episodes per week; 436 (71%) subjects had a baseline IEF $\geq$ 14. Women taking duloxetine saw a significantly greater percentage reduction in IEF compared to those taking placebo; the reductions were significant for the whole group and also in the subgroup of women with at least 14 IEF episodes per week and amongst those with fewer than 14 episodes per week at baseline (see Table 1).

Table 1. Reductions in IEF:

IEF Reduction (median)	**Duloxetine**	**Placebo**	**P[a]**
All subjects	-46.4%	-22.2%	<.001
Baseline IEF < 14	-52.8%	-32.1%	<.05
Baseline IEF $\geq$ 14	-44.0%	-16.0%	<.001

[a] p-values obtained from the Van Elteren test

Significant improvements were seen in women taking duloxetine compared to placebo for the KHQ total score and for 6 out of 8 sub-domains (see Table 2).

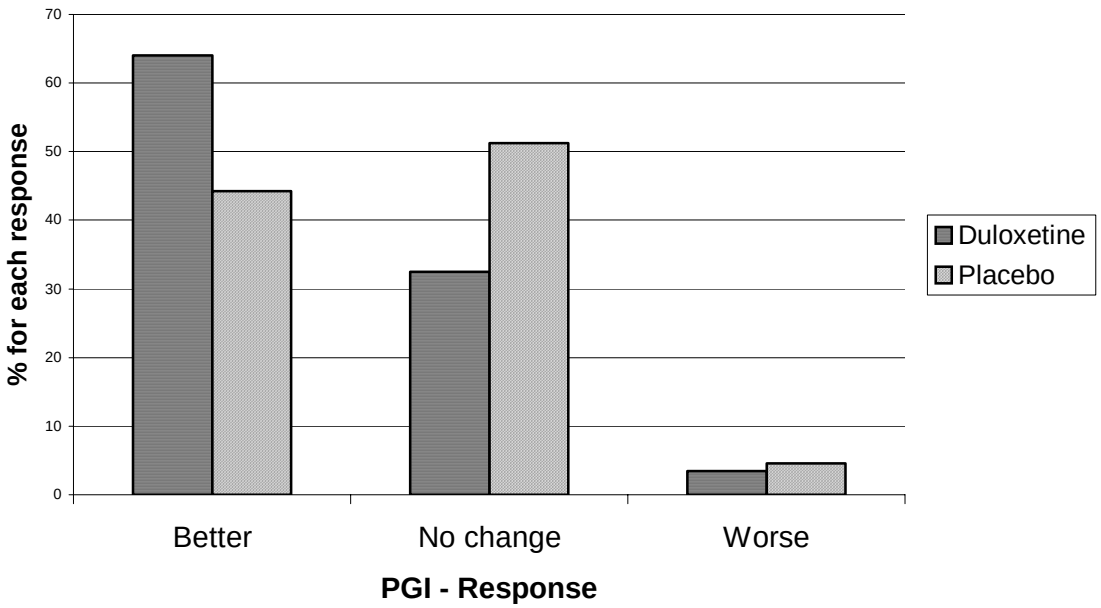
Table 2. Mean changes in KHQ scores:

	Duloxetine	**Placebo**	**P [b]**
Total score	-9.2	-2.6	<.0001
General Health Perception	-3.6	-0.8	=.092 ns
Incontinence Impact	-17.2	-9.5	=.0001
Role Limitations	-15.5	-7.1	<.001
Physical/Social Limitations	-10.1	-2.4	<.0001
Personal Relationships	-8.1	-1.5	<.001
Emotions	-10.1	-3.4	=.0001
Sleep/Energy	-1.6	-2.8	=.91 ns
Coping measures	-7.5	-1.3	<.0001

[b] ANCOVA test

Significant improvements in quality of life were also seen using the PGI-I instrument (see Figure).

Figure. PGI-I response *:



p<.001 (Cochran-Mantel-Haenszel test)

* All 'better' responses and all 'worse' responses grouped together

Discontinuation rates for adverse events were 2.9% for placebo and 17.3% for duloxetine (p <.001), with nausea being the most common symptom leading to discontinuation of duloxetine in 7.5% of all patients. Nausea was mild or moderate in 85% of subjects receiving duloxetine who reported nausea.

Interpretation of results

This study provides further evidence for the effectiveness of duloxetine in the treatment of SUI, including improvement in quality of life using the KHQ. The safety data are in line with previous published studies.

Concluding message

For women with predominant SUI, significant improvements in incontinence and quality of life were demonstrated.

References

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