Skljarevski V, Desaiah D, et al. Efficacy and Safety of Duloxetine in Patients With Chronic Low Back Pain. Spine 2010;35:E578-585.

Reviewed, no change to conclusions, February 2017

Design: Randomized clinical trial

Population/sample size/setting:

- 236 patients (144 women, 92 men, mean age 51) treated for chronic low back pain at 18 clinical sites in Brazil, France, Germany, Mexico, and the Netherlands
- Eligibility criteria were age over 18, at least 6 months of low back pain without radicular symptoms or signs (proximal thigh symptoms were eligible for inclusion)
- Exclusion criteria were clinical or radiographic evidence of spinal stenosis, grade 3 or 4 spondylolisthesis, spinal fracture, history of more than one low back operation, back surgery within past 12 months, invasive procedures to reduce low back pain in past month, MAO inhibitors in past 14 days, disability compensation, psychiatric disorders BMI over 40

Main outcome measures:

- Numerous outcomes and analyses were done; the principal designated outcome was Brief Pain Inventory Severity (BPI-S) average pain in the past week from patient diaries, with scores recorded at visits during week 4, wee7, and week 13
- Randomized to either duloxetine (n=115) or placebo (n=121) for a total of 13 weeks of treatment
- Randomization was stratified on the basis of whether the patient was or was not using NSAID regularly; the method of randomization (and method of allocation concealment) is not otherwise described
- Duloxetine administered at starting dose of 60 mg qd for 6 weeks; if there had not been a 30% reduction in the average BPI-S at the end of 6 weeks, the patient was considered a non-responder, and the dose was increased to 120 mg for the duration of the study; the placebo group similarly had its “dose” increased if it had not responded at the 6 week point
- For BPI-S, duloxetine group improved more than placebo (reduction of 2.32 points vs. 1.50 points, p=0.004 at week 13)
- Some secondary outcome measures also were better in duloxetine group; Patient’s Global Impression of Improvement (PGI-I) was 2.59 in duloxetine vs. 3.16 in placebo ($p<0.001$; low score good, high score bad)
- Rowland-Morris Disability changes also favored duloxetine: 3.60 vs. 1.93
- Response rates, defined as a 30% improvement in BPI-S average pain, were more frequent in the duloxetine group: 53.2% vs. 40%
- Serious adverse events occurred in 4 duloxetine patients (hypertensive encephalopathy, osteoarthritis, transient ischemic attack, wrist fracture) and 1 placebo patient (MI)

- Rate of discontinuation because of adverse effects was greater in duloxetine than placebo group: 31(27%) vs. 23 (19%), but the groups did not differ significantly in discontinuation rates because of any specific adverse event

Authors' conclusions:

- Duloxetine demonstrates a significant reduction in chronic low back pain compared to placebo
- The analysis was based on the acute response, and may not reflect the long term effect
- Duloxetine was safe and well tolerated; the adverse effect profile was ot different from that reported in previous duloxetine studies

Comments:

- While it is reported that the randomization was stratified on NSAID use, the randomization method is not otherwise described, and concealment of allocation is not mentioned; this cannot be assumed
- The difference in improvement between groups, while statistically significant, is modest and possibly due to a fairly large sample size
- The last recorded response was at 13 weeks, which is fairly short
- The investigators did not have access to the complete database, which remained in the custody of the corporate sponsor; the analysis of the data was complex, and the statistical analysts were not blinded to the group assignments
- Placebo was the comparison group; duloxetine was not compared with any established treatment (SSRI, TCI)
- Withdrawal due to adverse effects were reported as not differing between groups for any specific effect; however, this can easily be arranged if the categories of adverse effects are multiplied until the numbers in any category are too small to produce statistically significant differences; this may suggest that the analysis was chosen by the statisticians working for the pharmaceutical company in order to minimize the adverse effect differences

Assessment: Inadequate (randomization not well described, small group differences, only short term results reported, incomplete control of data by investigators)