Abou-Raia S, Abou-Raia A, Helmi M. Duloxetine for the management of pain in older adults with knee osteoarthritis: randomised placebo-controlled trial. Age and Ageing 2012; 41: 646–652

Design: randomized clinical trial

Study question: Is duloxetine more effective than placebo for the treatment of knee osteoarthritis (OA)?

Population/sample size/setting:

- 288 patients (241 women, 47 men, mean age 68) treated for knee OA at the University of Alexandria, Egypt
- Eligible if they met American College of Rheumatology for OA of Grade I-III, with knee pain at least 40 points on a 100 point scale for at least 14 days per month for three consecutive months
- Exclusion criteria included BMI greater than 32 kg/m^2, joint inflammatory diseases, neuropsychiatric problems including cognitive impairment, liver or renal disease, or taking other antidepressants

Interventions:

- Randomization was to either 60 mg duloxetine qd for 16 weeks or identical appearing placebo for 16 weeks
    - Concomitant rescue medication including NSAID and acetaminophen up to 4 g/day was permitted, but could not be increased over the pre-trial doses

Outcomes:

- Primary outcome was pain response; patients were classified as responders if they had an improvement in the pain or function score of 20% or more
- Secondary measures were the Western Ontario and McMaster University OA Index (WOMAC) function and knee stiffness scales, and the use of rescue medication such as NSAID or acetaminophen
- Patients were also asked about activities of daily living (ADL) such as bathing, grooming, dressing, eating, transferring brom bed to chair, and toileting
- 254 of the 288 patients (88%) completed the study
    - In the duloxetine group, 6 were lost to followup, 9 discontinued because of adverse events, and 5 discontinued for lack of efficacy
    - In the placebo group, 5 were lost to followup, 6 discontinued because of adverse events, and 2 discontinued for lack of efficacy
- The responder rates at 16 weeks were 48% in the duloxetine group and 9% in the placebo group

- WOMAC function scores were significantly better with duloxetine than with placebo; WOMAC stiffness scores were not significantly improved in either group
- The duloxetine group had more constipation, nausea, cough myalgia, arthralgia, hyperhidrosis, and palpitations than the placebo group, but there were no deaths or severe life-threatening events in either group

Authors' conclusions:

- Older adults with knee OA treated for 16 weeks have greater pain reduction with duloxetine than with placebo
- The duloxetine group also appeared to decrease its use of NSAID and acetaminophen compared to the placebo group
- WOMAC functional scores also improved more with duloxetine than with placebo
- The side effect profile of non-life-threatening events was not insignificant with duloxetine and should be borne in mind with older OA adults

Comments:

- The definition of a responder as having a 20% improvement in pain or function is easier to meet than more usual definitions of 30% or 50% response, but the differences between duloxetine and placebo were clinically important in any event
- The sponsor appears to have been the University of Alexandria, and the drug manufacturer appears not to have funded the study

Assessment: Adequate for evidence that duloxetine more effectively decreases knee OA pain in older adults than placebo, but there is a side effect profile of constipation and other symptoms that should be considered if the drug is given to older adults