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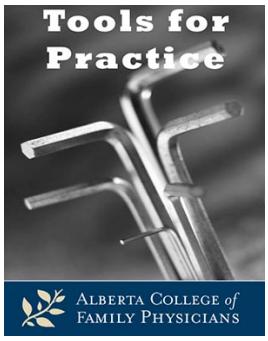

Duloxetine (Cymbalta®): Jack of All Trades, Master of None?

Clinical Question: How safe and effective is duloxetine for the treatment of chronic painful conditions?

Bottom-line: Compared to placebo, duloxetine appears efficacious in neuropathic pain, improving pain by 50% or more for one in six people. One in 18 people (over placebo) will have to quit due to adverse events.

Evidence:

- Compared to placebo: meta-analysis[1] of three Randomized Controlled Trials (RCTs) with 1,139 diabetic peripheral neuropathy patients over 12 weeks.
  - ≥50% improvement in pain: duloxetine 47% vs. placebo 29% (Number Needed to Treat (NNT) 6).
    - Mean pain scores improved 2.66 with duloxetine and 1.62 on placebo (on 0–10 scale).
  - Adverse events leading to discontinuation: duloxetine 60 mg/day 13.9% vs. placebo 8.3% (Number Needed to Harm (NNH) 18).
    - Adverse events included nausea (NNH 9), somnolence (NNH 14), dry mouth (NNH 17), and dizziness (NNH 21).
  - Increasing dose no advantage: no difference in response but more adverse events.
- Compared to other neuropathic pain medications:
  - RCT[2] of 804 diabetic peripheral neuropathy patients treated with either duloxetine 60 mg/day or pregabalin 300 mg/day for eight weeks.
    - ≥50% improvement in pain: duloxetine 40% vs. pregabalin 28% (NNT 9).
    - ~12% discontinued treatment due to adverse effects in both groups.
    - Trial sponsored by manufacturer of Cymbalta®.
  - Previous small trials showed no conclusive difference between duloxetine and amitriptyline[3,4] or pregabalin[4,5] in neuropathic pain.

Context:

- Duloxetine is also efficacious in other chronic painful conditions, including fibromyalgia[6] (NNT 8), chemotherapy-induced neuropathic pain (NNT ~9),[7] and osteoarthritis of the knee (NNT 6–8).[8,9]
- For depression, duloxetine has similar efficacy and overall safety to other second generation antidepressants, with no clear advantages compared to other agents.[10]
- Duloxetine trials are at moderate-to-high risk of bias: industry funding, short duration, high risk of selective outcome reporting, high drop-out rates, multiple outcomes without adjustment and possible selective publication.

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