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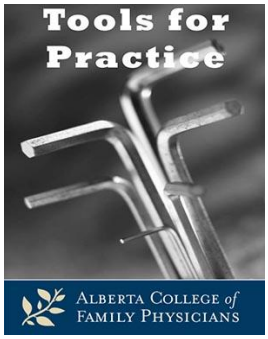
Reviewed: January 27, 2018
Evidence Updated: New RCTs
Bottom Line: Numbers changed, conclusion the same
First Published: December 16, 2013



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 seven people. One in 20 people (over placebo) will have to quit due to adverse events.

Evidence:

- Compared to placebo: Meta-analysis[1] of five randomized controlled trials (RCTs) with 2,589 diabetic peripheral neuropathy patients over ≤12 weeks.
  - ≥50% improvement in pain: Duloxetine 46% vs. placebo 30% (Number Needed to Treat (NNT)=7).
    - Mean pain scores improved by ~0.95 more with duloxetine than placebo (on 0–10 scale).
  - Adverse events leading to discontinuation: Duloxetine 60 mg/day 12.6% vs. placebo 5.8% (Number Needed to Harm (NNH)=20).
    - Adverse events included nausea (NNH=7), somnolence (NNH=14), dry mouth (NNH=14), and dizziness (NNH=22).
  - Increasing dose provides no advantage: No difference in response, but more adverse events.
  - Similar results in one other RCT[2] and several meta-analyses.[3-5]
- Compared to other neuropathic pain medications:
  - RCT[6] 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[7,8] or pregabalin[8,9] in neuropathic pain.

Context:

- Duloxetine is also efficacious in other chronic painful conditions, including fibromyalgia[1] (NNT=8), chemotherapy-induced neuropathic pain (NNT~9),[10] and osteoarthritis of the knee (NNT=6-8).[11,12]
- For depression, duloxetine has similar efficacy and overall safety to other second generation antidepressants, with no clear advantages compared to other agents.[13]
- 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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Tools for Practice is a biweekly article summarizing medical evidence with a focus on topical issues and practice modifying information. It is coordinated by G. Michael Allan, MD, CCFP and the content is written by practising family physicians who are joined occasionally by a health professional from another medical specialty or health discipline. Each article is peer-reviewed, ensuring it maintains a high standard of quality, accuracy, and academic integrity. If you are not a member of the ACFP and would like to receive the TFP emails, please sign up for the distribution list at http://bit.ly/signupfortfps. Archived articles are available on the ACFP website.