UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

January 26, 2024 Vol. 4, No. 2

Palliative Care Pharmacy Team:

Clinical Pharmacy Specialist:

Maria Felton Lowry, PharmD, BCPS, BCGP
Assistant Professor
University of Pittsburgh School of Pharmacy, Department of Pharmacy and Therapeutics
Palliative Care Clinical Pharmacy Specialist
UPMC Palliative and Supportive Institute

Cell: 412-627-8473
Office: 412-864-2899
Email: lowrymf@upmc.edu

If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

Duloxetine (Cymbalta®) for Osteoarthritis Pain

Background:
Osteoarthritis (OA) is common in the older adult population. Standard treatments include (but are not limited to) acetaminophen, systemic and topical non-steroidal anti-inflammatory (NSAID) medications, or injections. Some of these treatments (NSAIDs in particular) may pose a higher risk to patients when considering patient's comorbidities (heart failure, renal disease). In a search for alternative options to manage OA pain, antidepressants such as SNRIs have been studied in this population, especially if central sensitization component may be present. Duloxetine is a serotonin and norepinephrine reuptake inhibitor and a weak inhibitor of dopamine reuptake and is the most studied centrally-acting agent for OA; it is even listed in the 2019 American College of Rheumatology/Arthritis Guideline for OA (although admittedly, with limited references). Of course, duloxetine has risks associated with use; it requires dose adjustment or avoidance depending on degree of kidney disease and has other classic SSRI/SNRI class-related adverse effects such as increased bleeding risk, serotonin syndrome, hyponatremia, and sexual dysfunction.

Importance:
Osteoarthritis is the most common form of arthritis and prevalence likely increase as the population continues to age. It is important for palliative care clinicians to be aware of the literature surrounding alternate therapies that may assist with managing pain related to OA.

The Literature:

BMC Musculoskelet Disord. 2022 Feb 5;23(1):115.

Duloxetine in Osteoarthritis (DOA) study: effects of duloxetine on pain and function in end stage hip and knee OA – a pragmatic enriched randomized controlled trial

- Methods: multicenter, open-label RCT
  - 8-week duloxetine trial vs. usual care in adult patients with end-stage knee and hip OA with level of centralized pain (neuropathic-like symptoms) when placed on waiting list for total joint arthroplasty by orthopedic surgeon
    - Exclusions: patients who underwent hip or knee joint procedures in past year, received intra-articular injections in past 3 months, significant peripheral nerve injury, cognitive disorder making questionnaire unreliable, planned for total hip or knee arthroplasty during study duration
  - Patients screening positive on Modified painDETECT (mPDQ) questionnaire which evaluates neuropathic pain symptoms (mPDQ $\geq$ 12)
  - Duloxetine 30mg x 1 week, increased to 60mg, continued until weeks 9 and 10 when it was tapered back to 30mg x2 weeks prior to discontinuation
- Outcomes: Primary: pain in index knee or hip, measured with pain domain of Knee injury and Osteoarthritis Outcome Score (KOOS) or hip disability and osteoarthritis outcome score (HOOS)
- Results: N=111 (n=57 duloxetine, n=54 usual care); 55% knee OA, mean age: 62.7 years
  - Duloxetine group scored 11.3 points better on pain domain on KOOS/HOOS
  - Joint-specific sub-analyses revealed that knee OA improved more significantly than hip OA with hip OA group not having clinically relevant/significant change in score on HOOS
  - mPDQ score were significant lower in duloxetine group versus usual care; joint specific analysis revealed knee OA patients with lower scores and hip OA patients had no difference
  - 94.7% of patients in duloxetine group experienced and adverse effect (AE): Headache, somnolence, dry mouth, and nausea were the most common AEs
- Conclusion: "Adding duloxetine treatment to usual care seems to be especially beneficial for end-stage knee OA patients with neuropathic-like symptoms/central sensitization. End-stage hip OA patients seem to be non-responsive to duloxetine"

Cochrane Database Syst Rev. 2022 Oct 21;10(10):CD012157

Antidepressants for hip and knee osteoarthritis

- Methods: Cochrane Review 2022
- Results: RCTs included with patients with OA compared use of antidepressants to placebo or alternative comparator with focus on efficacy trials
  - 9 trials included, 7 of which included only knee OA with sizes ranging from 36-388 participants (other 2 had combination hip + knee OA)
  - Durations between 8-16 weeks
  - Duloxetine 60-120mg most studied (n=6 RCTs), with milnacipran, fluvoxamine, and nortriptyline each studied once, all versus placebo
  - SNRI studies (duloxetine) had mean reduction in pain of 0.68 points (95% CI -0.98-0.38; 7 studies, 1773 participants) which is not clinically relevant
  - No difference in quality of life
  - Adverse events higher in antidepressant groups (NNH: 1000)
- Conclusion: "There is high-certainty evidence that use of antidepressants for knee osteoarthritis leads to a non-clinically important improvement in mean pain and function…High-certainty evidence indicates antidepressants result in more adverse events and moderate-certainty evidence indicates more withdrawal due to adverse events."

Bottom Line:

- Overall, data lacks clinically meaningful results for the use of duloxetine for OA-related pain
- Most evidence suggests some improvement for knee OA pain in the setting of centralized pain with neuropathic pain characteristics
- Evidence does not support use for hip OA
- As always, there is a risk for adverse effects which seems prevalent in all studies

CLINICAL PEARL: Duloxetine has limited evidence for use in osteoarthritis pain