UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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TODAY'S TOPIC:

Neuropathic Pain Management: Gabapentinoid to Duloxetine Rotation in Palliative Cancer Patients

Background:

Around 30% of cancer patients experience neuropathic pain (NP) related to their condition, and treatment typically involves combining non-opioid medications like gabapentin or pregabalin (gabapentinoids) with opioids. However, using these medications together can increase the risk of opioid-related side effects, such as sedation and respiratory depression. Despite the limited evidence supporting gabapentinoids for cancer-related neuropathy (as discussed in a previous issue: Gabapentinoids for Cancer-Related Neuropathy; Vol 1 No 10), they remain commonly used in the oncology setting. On the other hand, duloxetine, a serotonin-noradrenaline reuptake inhibitor, is considered a safer alternative. It is currently the only medication recommended by the American Society of Clinical Oncology (ASCO) for managing chemotherapy-induced neuropathic pain, although its use has been subject to some debate. Nonetheless, duloxetine is the established guideline-recommended treatment for painful neuropathy in cancer patients.

Importance:

Gabapentinoid rotation to duloxetine in palliative care patients with cancer who are receiving concurrent opioids is important because it offers a potentially safer approach to managing neuropathic pain. Gabapentinoids, though commonly used, have limited evidence for effectiveness in cancer-related neuropathy and can exacerbate opioid toxicity. Duloxetine, being guideline-recommended by ASCO for chemotherapy-induced neuropathy, provides an alternative that may reduce the overall medication burden and improve symptom control. It is important for palliative care clinicians to be aware of the updated evidence surrounding this topic.

The Literature:

J Pain Symptom Manage. 2024 Sep 26:S0885-3924(24)01038-8.

Gabapentinoids Rotation to Duloxetine in Palliative Care Patients With Cancer Receiving Concurrent Opioids

Objective:

- To investigate how often individuals concurrently receiving opioids and gabapentinoids were rotated to duloxetine in an outpatient palliative care setting

Methods:

- Retrospective chart reviews during 2022
- Reviewed 2,240 patient charts. Narrowed down to 96/392 patients who were receiving gabapentinoids and opioids
- **Primary Outcome:**
  - Patients rotated to duloxetine
- **Secondary Outcomes:**
  - Demographics (age, gender, race, ethnicity, marital status), primary cancer diagnosis, dose of gabapentinoid (expressed as the gabapentin equivalent dose, calculated by multiplying the dose of the pregabalin X 6.6), gabapentinoid dose reduction, dose of duloxetine, Morphine Equivalent Daily Dose (MEDD), Edmonton Symptom Assessment System (ESAS), whether a rotation discussion took place

Results:

Comparison of Symptoms, MEDD, Dose of Gabapentinoids, and Side Effects During Each Visit

	First Visit	Second Visit	Third Visit
Median time -months- from the first visit (IQR)		1.4 (0.9–2.0)	3.2 (2.1–4.0)
Median pain score (IQR)	6 (3–8)	6 (3–7)	5 (4–7)
Median ESAS (IQR)	39 (24–56)	36 (23–50)	34 (21–48)
Median MEDD -mg- (IQR)	20 (6–60)	40 (10–84)	35 (8–79)
Gabapentinoids, N (%)			
Gabapentin	84 (88)	69 (72)	63 (66)
Pregabalin	11 (12)	12 (13)	8 (8)
Both	1 (1)	-	-
None	-	15 (16)	25 (26)
Median Gabapentin equivalent dose -mg- (IQR)[a]	900 (600–1800)	800 (300–16,500)	600 (0–1125)
Gabapentin side effects, N			
Fatigue	2	5	3
Sedation	1		
Dizziness	1		
Duloxetine, N		20	20
Duloxetine and gabapentin		14	12
Duloxetine alone		4	6
Duloxetine and pregabalin		2	2
Median duloxetine dose (IQR)		40 (30–60)	60 (30–60)
Duloxetine side effects, N			
Constipation		1[b]	1[c]
Fatigue		1[b]	-
Drowsiness		-	1[c]

[a]The dose was considered 0 for the patients in whom the gabapentinoids were discontinued; comparing the first and the third visit $P=0.000$ (related samples Wilcoxon Signed Rank Test).
[b]Both patients were also on gabapentin.
[c]One patient was on gabapentin and the other on pregabalin.ESAS = Edmonton symptom assessment system; IQR = interquartile range; MEDDc = morphine equivalent daily dose; N = number.

- Malignancies were diverse and included 17 (18%) breast, 16 (17%) head and neck, 13 (14%) gastroenterological, 10 (10%) gynecological, and 40 (42%) other
- A rotation took place in 24 patients during the first consultation, in 8 during the second visit, and in 2 more at the third visit, for a total of 34 (35% with a 95% CI: 26–46)
- Median gabapentinoid equivalent daily dose decreased from 900 to 600 mg ($P<0.001$) between the first consult and the third visit
- Only 3 patients reported side effects to duloxetine and they were also on gabapentinoids

Conclusion:

- Only a minority of palliative care patients with cancer on gabapentinoids and opioids were transitioned to duloxetine

Anneliese's Reflections:

- There were limitations of this retrospective review that made drawing a clinically relevant conclusion difficult
  - MEDD scores, pain scores, and ESAS as an average of ALL medication groups combined were reported
    - Authors did not report MEDD scores, pain scores, and ESAS between medication groups or over time between groups… this would have been an interesting comparison between groups that stayed on gabapentinoids or switched to duloxetine
    - Without these patient-reported outcomes, it is hard to draw clinically relevant conclusions about this data
  - It is unknown why the medication rotations happened, knowing this could have strengthened the data
  - Neuropathic pain syndrome was not differentiated between chemotherapy-induced neuropathy versus cancer (disease)-related neuropathy
    - Duloxetine preferred in chemotherapy-related neuropathy
    - If neuropathy in the setting of cancer, a change may not be necessary
- There is limited evidence to support gabapentinoids versus duloxetine in the treatment of chemotherapy-related pain as limited clinical trials have been released comparing these medications head-to-head, having more information about pain syndrome and reason for rotation would be helpful

Bottom Line:

- Counsel patients on risks vs. benefits on concurrently receiving gabapentinoids with opioids
- There is opportunity for outpatient centers to complete medication use evaluations with more defined methods and less limitations to asses their current populations' needs
- No current articles compare duloxetine versus gabapentinoids for cancer-related neuropathy (either chemotherapy-induced or disease-related)
  - Opportunity for further research specifically looking at pain scores, ESAS, and MEDD between gabapentinoids and duloxetine

CLINICAL PEARL: It is difficult to draw conclusions on efficacy and safety of the rotation from gabapentinoids to duloxetine in cancer-related neuropathy