UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

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

TODAY'S TOPIC:

New Literature: Rotation of Gabapentinoids

Background:
Gabapentinoids, specifically pregabalin (Lyrica®) and gabapentin (Neurontin®) are widely used to manage neuropathic pain syndromes. If a patient is not responding to one gabapentinoid, it may make sense to transitions to another gabapentinoid.

Importance:
Gabapentinoids are commonly used in palliative care. All previous rotation studies have been unidirectional (ie. gabapentin to pregabalin) and further studies needed to determine this in clinical practice. Palliative care clinicians should be aware of the evidence for rotation strategies and dosing equivalencies to aid in switching from one gabapentinoid to another, if clinically appropriate.

Previously, studies have shown 6:1 conversion factor, from gabapentin to pregabalin. (Pain Med. 2011 Jul;12(7):1112-6.)

The Literature:

Am J Ther. 2013 Jan;20(1):32-6.*
Compared unidirectional switch from gabapentin to pregabalin with two rotation strategies:
1. Direct switch
    - Stop gabapentin, initiate pregabalin at next scheduled dose period
2. Cross-taper
    - Co-administer 50% of gabapentin dose + 50% of desired pregabalin dose for 4 days
    - Discontinue gabapentin after day 4 and increase pregabalin to target dose after day 4

Transitioning patients from gabapentin to pregabalin could be achieved by either approach
*Note: this study was a pharmacokinetic modeling study and not replicated in clinical setting.

J Pain Palliat Care Pharmacother. 2021 Mar;35(1):13-22.
Strategies for Rotation between Gabapentinoids in the Inpatient Setting
Methods: Single-center retrospective cohort study (n=67) 46% mixed neuropathic pain, 15% nociceptive pain, 9% inflammatory pain
Outcome:
- Primary: Proportion of patients rotated using direct switch versus cross-taper strategy
- Secondary: Successful rotation (ie. stable or improved numeric rating scores from baseline to day 3 to stable dosing), dose-ratio used, incidence of adverse effects associated with rotation

Results:
- 87% of patients were rotated using the direct switch strategy with the majority rotating from gabapentin to pregabalin
- Average starting dose (n=67): gabapentin 900mg/day and pregabalin 150mg/day
- Median cross taper duration was 2 days
- 95% of patients who underwent a direct switch had a successful rotation whereas 78% of those who underwent cross-taper had a successful rotation
- Adverse reactions experienced pre- or post-rotation (n=14) were tremors, somnolence, dizziness, neutropenia
- Dose ratios for those in the equal analgesia group with normal renal function were plotted and a new curve was generated and compared to prior dose ratios from an algorithm utilizing bioavailability data previously published (N Z Med J. 2019 Mar 8;132(1491):101-103.) and a new dose conversion algorithm was proposed:

Table 6. Proposed dose conversion algorithm.

Dose ratio	GBP TDD (mg)	GBP per dose (mg)	PGB TDD (mg)[a]
3	≤300	≤100	≤100
4	600–900	200–300	150–200
5	1200	400	200–300
6	1800	600	300
7	2400–2700	800–1000	400
8	≥3000	≥1100	450–600

Abbreviations: GBP: gabapentin; PGB: pregabalin; TDD: total daily dose.
[a]Given in two divided doses.

Discussion:
- This is the first study to describe rotation both to and from gabapentin
- "It may be reasonable to use a more conservative ratio when rotating from gabapentin given pregabalin's consistently high bioavailability compared to the variable bioavailability of gabapentin"
- This was in the inpatient setting, so less conservative dosing rotation can be employed, given close monitoring parameters

Bottom Line:
- Utilized 10% difference on NRS to be clinically important difference, this may be questionable…
- This study needed 126 patients to reach power and they only included 67, which could make smaller differences in the data undetectable
- It is possible that dosing conversion is not linear between gabapentin and pregabalin.
- If using the 6:1 ratio of gabapentin to pregabalin dosing, it is important to note that at some dose ranges, this conversion may be too conservative whereas at other doses/situations it may be too aggressive.
- Direct conversion is the most widely used strategy for conversion between gabapentinoids and has been proven safe
- The above table can be utilized as a guide when converting from gabapentin and pregabalin, would encourage use of clinical judgement and need to adjust dose based on patient-specific factors (renal function, elderly)

CLINICAL PEARL: Direct switch between gabapentinoids is the most often used conversion strategy and can be done safely. Utilize dose conversion tables as a guide and consider patient-specific factors when determining an appropriate dose of new gabapentinoid.