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:

Gabapentinoids for Neuropathic Pain: Review

Background:

Gabapentinoids, specifically pregabalin (Lyrica®) and gabapentin (Neurontin®), are widely used to manage neuropathic pain. Gabapentinoids are within the anticonvulsant class of medications. Gabapentinoids bind to voltage gated calcium channels, which decreases the release of glutamate, noradrenaline (norepinephrine), and substance P. This mechanism contributes to their anticonvulsant, analgesic, and anxiolytic actions. Of note, pregabalin is a controlled substance, specifically a Schedule V medication (low potential for abuse relative to substances listed in Schedules IV and above). Pregabalin and gabapentin are used for a variety of neuropathic pain syndromes, and their evidence differs based on the particular neuropathic syndrome.

Importance:

Gabapentinoids are commonly used in palliative care. Palliative care clinicians should be aware of the evidence behind their use for neuropathic pain and reasons to select one gabapentinoid over the other.

The Literature:

Cochrane Database Syst Rev. 2019 Jan 23;1(1).
Pregabalin for neuropathic pain in adults
Review

Methods: 45 studies in Review
- 28 studies (n= 8251) Postherpetic Neuralgia (PHN) + Peripheral Diabetic Neuropathy (PDN)
- 8 studies (n=1991) Mixed neuropathic pain
- 2 studies (n=160) Neuropathic cancer pain

Outcomes:
- Participant-reported: pain intensity reduction of 30% or greater, reduction of 50% or greater, global impression of clinical change (PGIC) and global impression of clinical change (PGIC) of very much improved

Results:
- Efficacy:
  - Higher quality evidence exists for benefit of pregabalin for diabetic neuropathy and post-herpetic neuralgia
  - Pregabalin at 150mg/day is generally ineffective with the exception of for PHN
  - Mixed neuropathic pain:

Pregabalin 600mg/day	Relative Benefit	NNTB*
30% pain reduction	1.2	8.2
50% pain reduction	1.5	7.2

*NNTB: Number needed to benefit

  - Neuropathic cancer pain:
    - Did not include efficacy outcomes highlighted in Cochrane Review; unable to include in analysis
    - Very low quality evidence per Cochrane Review
    - Pregabalin vs. Placebo: not much difference
    - Pregabalin vs. Amitriptyline vs. gabapentin vs. placebo all revealed a decrease in pain scores
- Safety

Pregabalin Dose	Somnolence RR*	Somnolence NNTH**	Dizziness RR	Dizziness NNTH
150mg	2.2	12	1.3	Not calculated
300mg	3.0	9.5	3.6	4.8
600mg	4.4	5.2	4.0	3.8

*Risk Ratio
**NNTH: number needed to treat for an additional harmful outcome

Conclusion:
- Pregabalin at oral doses of 300mg-600mg/day has proven to be beneficial for PHN and PDN; evidence for other types of neuropathic pain is very limited like neuropathic cancer pain.
- Common side effects include: somnolence and dizziness

Cochrane Database Syst Rev. 2017 Jun 9;6(6).
Gabapentin for chronic neuropathic pain in adults
Review

Methods: 37 studies in review
- 20 studies: Postherpetic Neuralgia (PHN) + Peripheral Diabetic Neuropathy (PDN)
- 4 studies: Mixed neuropathic pain
- 3 studies: Neuropathic cancer pain

Outcomes:
- Participant-reported: pain intensity reduction of 30% or greater, reduction of 50% or greater, global impression of clinical change (PGIC) and global impression of clinical change (PGIC) of very much improved

CLINICAL PEARL: Gabapentinoids can be trialed for neuropathy unrelated to diabetes or shingles, although data is limited. Discontinue gabapentinoid if no relief after adequate trial (~4 weeks and targeted dose achieved).

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Results:

- Efficacy:
  - Higher quality evidence exists for benefit of gabapentin for diabetic neuropathy and post-herpetic neuralgia
  - Mixed neuropathic pain:

Outcome	Risk Ratio
50% pain reduction	1.5
PGIC very much improved	2.0
PGIC much or very much improved	2.2

  - Neuropathic cancer pain:
    - One study only examined 10 days of treatment (max dose 1800mg/day) compared to placebo, with similar pain control between groups
    - Gabapentin 2700mg/day vs placebo for chemo-induced neuropathic pain over three weeks had no difference between groups
    - Gabapentin 1800mg/day vs. pregabalin 600mg/day vs. amitriptyline 100mg/day x 4 weeks revealed a decrease in pain scores for all groups

- Safety

Side effect	Participants	Risk Ratio	NNH*
Somnolence	4288	2.8	11
Dizziness	4739	2.9	8.0
Peripheral Edema	3325	4.1	20
Ataxia	510	5.5	8.5

*NNH: number needed to harm

Conclusion:

- Doses needed to achieve pain control were > 1800mg/day in divided doses
- Most evidence is for its efficacy in PHN and PDN and evidence for other types of neuropathic pain is limited
- Over half of those treated with gabapentin will not have worthwhile pain relief

Bottom Line:

- Gabapentinoids have little evidence for their efficacy for neuropathy not related to diabetes or shingles
- Unfortunately, it is fairly common (>50%) that patients might not get adequate pain relief from gabapentinoids. Discontinue if patients perceive little or no benefit after adequate trial
- Adequate trial of gabapentin could be defined as: dose titration to >1800mg/day or highest tolerated dose if below 1800mg/day and continuation for at least 4 weeks after reaching max tolerated dose
- Adequate trial of pregabalin could be defined as: dose titration to ~300mg/day, or maximum tolerated dose for at least 4 weeks
- Counsel patients on side effects of gabapentinoids such as somnolence or dizziness and beware of prescribing other sedating medications concomitantly

Are you interested in knowing what data IS out there for uses commonly seen in palliative care settings? Stay tuned for next week…

CLINICAL PEARL: Gabapentinoids can be trialed for neuropathy unrelated to diabetes or shingles, although data is limited. Discontinue gabapentinoid if no relief after adequate trial (~4 weeks and targeted dose achieved).