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:

Another Tool in your Palliative Care Toolbox: Lidocaine Series Part 3

Question: What happens when lidocaine works? Then what?

Background:

Lidocaine's use in palliative care continues to be variable, including dosing regimen and duration as seen with Part 1 and Part 2 of the Lidocaine series. If lidocaine therapy was successful, an emerging strategy for ongoing pain relief is to use other anti-arrhythmics in place of lidocaine as data is limited for duration of benefit after discontinuation of lidocaine IV (continuous infusion or bolus) for chronic pain. Other anti-arrhythmics are administered orally. Mexiletine is classified as a 1B anti-arrhythmic agent like lidocaine. Both medications inhibit fast sodium channels to reduce neuropathic pain and could reduce neuropathic pain. Half-life of IV lidocaine is 1.5-2 hours, and half-life of mexiletine is 9-12 hours. If lidocaine is beneficial for patients with ongoing, refractory, chronic neuropathic pain it is possible to switch to a similarly acting oral anti-arrhythmic, mexiletine.

Importance:

It is important for palliative care clinicians to be aware of longer term options for lidocaine-responsive, chronic, neuropathic pain.

The Literature:

J Pain Palliat Care Pharmacother. 2020 Jun;34(2):90-98.

A Multi-Centered Case Series Highlighting the Clinical Use and Dosing of Lidocaine and Mexiletine for Refractory Cancer Pain

Methods:

- Retrospective, multi-centered case series (n=10)

Results:

- Lidocaine Regimen: Lidocaine bolus average 1.6±0.69mg/kg, resulting in loading dose of 94.5±48.9mg (median = 100.1) infused over average of 24±20.7 minutes, followed by continuous infusion (n=8) at average rate of 1.1±0.2mg/kg/hr for average starting infusion of 69.4mg/hr.
- Mexiletine Regimen Range: 150mg PO daily – 400mg PO BID ; starting dose average was 400±123mg/24 hours divided twice or three times daily; final dose average was 500±168mg/24 hours (median 450mg) divided three times daily.
- Conversion Strategy: (proposed by authors, cases had variable cross-titration plans)
  - Day 0: Start mexiletine, continue IV lidocaine but at 50% of dose
  - Day 1 (24 hours after initiation of mexiletine): discontinue IV lidocaine and continue mexiletine
  - Day 2 (48 hours after initiation of mexiletine): Consider increase of mexiletine, depending on tolerability and efficacy
- Secondary outcomes:
  - Overall 21.1% decrease in average Morphine Equivalent Daily Dose (MEDD) from 24 hours prior to lidocaine through 24 hours after final mexiletine dose achieved
  - Side effects appear to be dose-related, consistent with previous literature. Confusion, agitation, hallucination occurred in one patient 2 days post-discharge on highest dose of mexiletine (800mg/day)
  - Interesting note: Lidocaine levels were not obtained during lidocaine infusion for any of the ten patients

Conclusion:

- "This study proposes a conversion recommendation from intravenous lidocaine to oral mexiletine for treatment of neuropathic pain in the setting of malignancy. Intravenous lidocaine is an effective option, and conversion to oral mexiletine appears to be safe and efficacious in patients who had a positive response to lidocaine. Consider an initial mexiletine dose of 150 mg every 8 hours, increased to a target dose of 200 mg every 8 hours, if tolerated."

Bottom Line:

- Overall, it is possible to convert patients from IV lidocaine to PO mexiletine
- This conversion appears to be well-tolerated with minimal neurotoxicity when started at lower dose range
- Cross-titration is likely necessary given short half-life of lidocaine and longer half-life of mexiletine
- Prior to making this conversion, it is important to be mindful of drug interactions with mexiletine (amiodarone, antiretrovirals, clozapine, immunotherapy, desvenlafaxine, CYP1A1, CYP2D6 inhibitors) and other comorbidities (cardiac, renal, hepatic function).

CLINICAL PEARL:

Conversion of IV lidocaine to PO mexiletine has been reported in the literature, and could be considered for refractory, chronic, neuropathic pain for those patients responsive to lidocaine.