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: Methadone IV to PO Conversion

### Background:

Methadone is used often in palliative care settings for chronic pain. Methadone is a lipophilic medication, which allows its administration by several routes, including parenteral or intravenous (IV). IV route of administration is used most in hospital settings when oral (PO) formulation is not feasible. Prior to discharge to the community, most patients are switched back to the oral route.

### Importance:

Accurate opioid conversion ratios are essential to minimize toxicity and maximize benefit. In current practice, the most common conversion ratio from PO to IV methadone is 2:1. Inversely, the conversion ratio is assumed to be IV to PO methadone of 1:2. Previously, in the literature, there has been discussion that this conversion from IV to PO methadone may be too aggressive and increase the risk of opioid toxicity; more conservative conversions of methadone routes of administration have been proposed. It is important for palliative care clinicians to review new literature and understand how it may or may not influence clinical practice.

### The Literature:

J Palliat Med. 2021 Mar;24(3):382-390.

**Switching Ratio from Parenteral to Oral Methadone 1:1.2 is Safer Compared with Ratio 1:2 In Patients with Controlled Cancer Pain: A Multicenter Randomized-Controlled Trial**

Objective: to compare success and side effects with two ratios from IV to PO methadone: 1:2 Versus 1:1.2 in hospitalized patients with cancer pain

Methods: Multicenter double-blind, RCT (n=44, n=39 evaluable patients)

Outcomes:

- Success defined by patients whose pain was well-controlled without any significant, methadone-related toxicity at 72 hours after switching from IV to PO methadone
- At 72 hours post-switching, "good" pain control was defined as a mean for the average score pain of ≤4 requiring ≤ 3 mean extra doses per 24 hours

Results:

- "Successes" (defined above): 100% of 1:1.2 ratio group, and 57.1% of 1:2 group (P=0.001)
- Efficacy:
  - Average pain was well-controlled throughout the study period for both groups; no differences between the two ratios were seen in terms of the need of extra rescue doses
- Toxicity:
  - Most common side effects were dry mouth, drowsiness, and myoclonus (at day +3)
  - More side effects in 1:2 ratio group
- Average methadone doses remained the same for 3 days after switch, and doses required reduction in the 1:2 group by day 7. Doses were not reported at day 7 for 1:1.2 (intervention) group.

Discussion:

- "Steady-state" data increases the strength of the conversion data
- Utilizing 1:1.2 IV to PO methadone conversion ratio has a superior safety profile
- Small sample size is a limitation

Conclusion:

- IV to PO Methadone ratio of 1:1.2 resulted in lower toxicity and no difference in analgesic effect *when monitoring for 72 hours…*

### Maria's thoughts:

- This is "steady state" conversion data, since they allowed the IV formulation to reach steady state prior to converting, which makes the data a bit stronger in terms of conversion ratios and safety profiles.
- I typically favor conservative dosing IF it allows patients to receive adequate pain control (obviously conservative dosing will be safer in terms of side effects)…
- Speaking of steady state… I wish they had continued to monitor past day 5 for the PO regimen to reach steady state to truly assess study outcomes
- Doses were not reported at day 7 for intervention group (1:1.2) this makes me wonder if they required dose escalations due to uncontrolled pain after PO regimen reached steady state?
- Surprised to see 8 out of 21 patients experiencing myoclonus... would wonder what other opioids & non-opioids these patients were taking
- Pain management study outcomes listing "good pain control" is difficult to interpret by using an average score on the pain scale. I wonder if they would have added a qualitative description from the patients regarding their report of pain to make this outcome stronger (such as patient reporting their pain "at goal" or patient reporting "well controlled" pain)… yes, ≤4 seems like an appropriate measure to determine "good pain control," but not everyone's pain scale is the same and not generalizable!

### Bottom Line:

- Using a more conservative conversion ratio improves tolerability
- I still worry that utilizing this conservative ratio would leave pain uncontrolled after new regimen reaches steady state

**CLINICAL PEARL:**
**Could consider utilizing IV to PO conversion ratio of 1:1.2 in patients at higher risk for opioid-related ADE (OSA, previous opioid intolerance, elderly); however, would monitor closely for analgesic effect around days 4-5.**