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:

Opioid-Induced Hyperalgesia (OIH) in Chronic Pain

Background:

Opioid-induced hyperalgesia (OIH) is a paradoxical increase in pain perception after opioid administration and it is typically difficult to treat. Many palliative care patients are at risk for OIH because both opioid dose and duration of treatment directly correlate with risk of OIH. Although the mechanism of OIH is mediated by more than one system, the most studied mechanism is opioid-induced increase in NMDA currents in the dorsal horn. Naturally, ketamine, an NMDA antagonist, is being investigated to whether it can prevent or attenuate this effect. The most robust data for use of ketamine and dexmedetomidine is from the anesthesia literature (See Parts 1 and 2).

Importance:

Palliative care patients often have high OME requirements and are at risk for OIH, which has proven difficult to treat. It may be difficult to extrapolate data from other specialties/studies, so it is important for palliative care clinicians to be aware of the evidence, albeit minimal, within the palliative care or chronic pain population.

The Literature:

Clin J Pain. 2021 Oct 26;38(1):49-57.

Opioid-induced hyperalgesia in patients with chronic pain: A systematic review of published cases

Methods:

- Literature review through December 2020 according to PRIMSA criteria relating to adults or children experiencing chronic pain (pain > 3 months duration)
- Included cases, case reports, cohort, and case-control studies

Outcomes:

- OIH management successful defined as baseline pain intensity was decreased by at least 30% or by at least 1 category for pain evaluations based on categorical verbal scales
- Reduction in opioid dose considered "strong" if reduced by > 60%

Results: n=41 articles describing 72 cases between January 1986 and December 2020

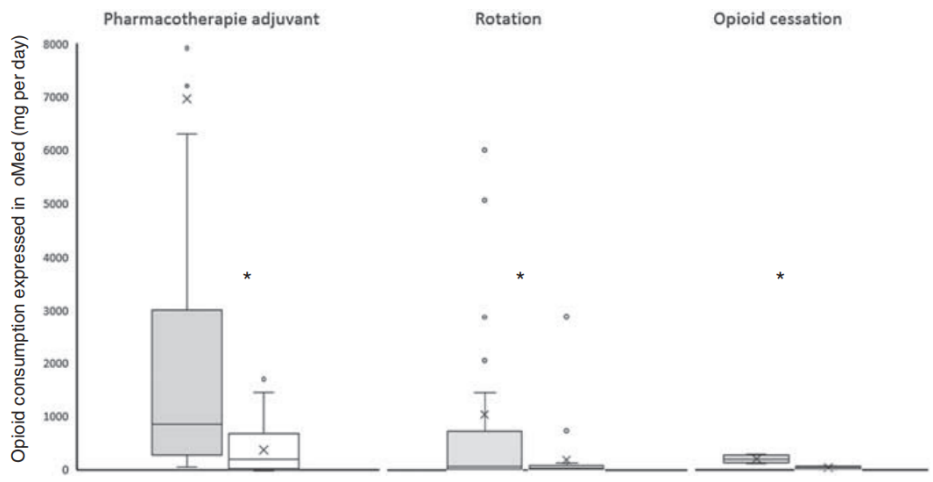
- 51% male, average age 46 years old; 7.5/10 average pain score, median OME = 850mg, 96% patients with refractory pain despite opioid dose increases, 33% experienced diffuse pain/clearly extended to other anatomic areas in absence of disease progression, 27.7% experienced allodynia
- *Main strategies to combat OIH: adjuvant pharmacotherapy (47.7%), opioid rotation (36.9%), and opioid cessation (10.7%)*
    - Principal opioid prescribed for rotation was methadone
    - Ketamine IV most frequently prescribed adjuvant (44.1%) followed by dexmedetomidine 35.3%)
        - *Ketamine dose: 0.12-1.5mg/kg/h; duration range 1-28 days*
        - *Dexmedetomidine dose: 0.5-0.8mcg/kg/h; duration range 1-7 days*

TABLE 2. Success of OIH Management in Patients With Chronic Pain Treated With Opioids According to Strategy Used and Origin of Pain (Cancer or Non-cancer)

Strategy	Total Number of Cases	Successful, n (%)	Not Successful	No Data
Opioid cessation	7	4 (57)	0	3
Malignant	4	2 (50)		
Nonmalignant	3	—		
Rotation of opioids	24	19 (79)	0	2
Malignant	22	19 (86)		
Non-cancer	2			
Methadone	22	17 (77)	0	3
Other opioids	2	2 (100)	0	0
Adjuvant therapies	33	24 (72)	2	7
Cancer	12	10 (83)	2	—
Non-cancer	21	14 (66)	0	7
Ketamine	12	10	0	1
Dextrometorphan	1	1	0	0
Dexmedetomidine	13	5	2	6
Clonidine	1	1	0	0
Propofol	2	2	0	0
Lidocaine	1	1	0	0
Mexiletine	1	1	0	0
Naloxone*	2	2	0	0

Success was defined as a decrease in pain of at least 30% relative to baseline on a pain scale, or a change of at least one category on a verbal scale (from severe to moderate or moderate to weak).
*Naloxone was used in combination with propofol or ketamine.

Figure 2. Opioid consumption before and after the 3 strategies of OIH management



Conclusion: Adjuvant pharmacotherapy was most successful approach for treating OIH, resulting in largest decrease in opioid requirements. OIH can be resolved when it is diagnosed and managed.

Bottom Line:

- Three options were reviewed to combat OIH: opioid cessation, opioid rotation, or adjuvant pharmacotherapy
- It is unlikely that opioid cessation is feasible option for our patients, especially those with pain related to disease burden
- If adjuvant pharmacologic therapy is not ideal or clinically appropriate, could consider rotation to another opioid. Methadone was most often used and had fairly high success rate…
- This review does highlight the potential utility of ketamine in the treatment of established OIH in patients with chronic pain
- A range of doses and duration of ketamine (and other adjuvant pharmacotherapy) have been utilized to combat OIH making it difficult to extrapolate effective dosing strategies; Of note, ketamine dose range was higher in this review than in literature examining prevention of OIH

CLINICAL PEARL: Adjuvant pharmacotherapy (ie. ketamine) or rotating to another opioid (ie. methadone) may be helpful for reducing OIH