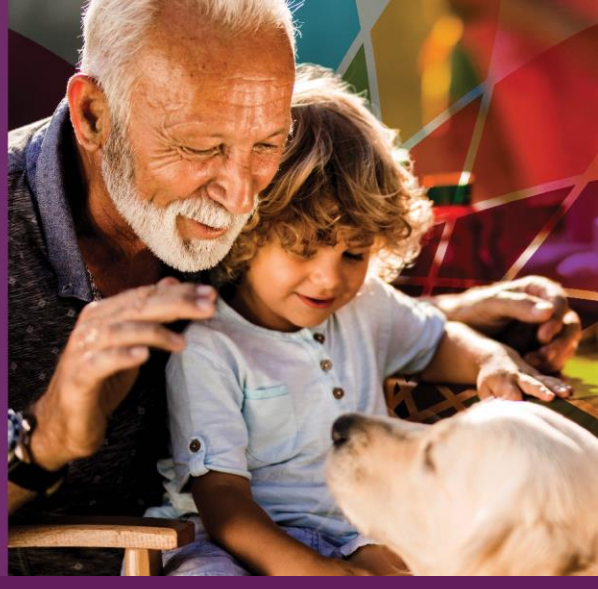
UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

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:

Reviewing New Literature: Buprenorphine for Chronic Pain

Background:

Pain is one of the most common symptoms experienced by patients with life-limiting illness, if not the most common. We know full opioid agonists are effective analgesic options for pain; however, opioids (full agonists) have risks such as respiratory depression, constipation, hyperalgesia, and misuse. Buprenorphine is a partial agonist of the mu opioid receptor and for this reason, it has a smaller side effect profile, with less likelihood of respiratory depression, and decreased potential for misuse due to lack of euphoric properties. Buprenorphine is commonly used in combination with naloxone (Suboxone®) or alone (Subutex®) for substance use disorder. Buprenorphine can also be prescribed to treat chronic pain but is not overly popular among providers due to fears (lack of mechanism understanding, analgesic ceiling, does not provide enough pain relief). Additionally, few studies have examined the use of specific formulations available in the US for the treatment of chronic pain. Multiple formulations, such as Buprenex, Belbuca, and Butrans, indicated for pain management are available in the United States. Various buprenorphine formulations may be appropriate for specific patient populations including the older adults, those at risk of opioid adverse drug events, and those with opioid use disorders.

Importance:

Buprenorphine can be used to treat pain in specific populations, although use is limited in palliative care given general limited experience in prescribing buprenorphine for pain. It is important for palliative care providers to be aware of the available evidence supporting the use of various buprenorphine formulations and the success of switching to buprenorphine from other opioid products.

The Literature:

J Pain Palliat Care Pharmacother. 2021 Aug 25;1-6.

Transdermal Buprenorphine Use for Pain Management in Palliative Care

Objective: Assess if the lower buprenorphine patch strengths that are available in the United States (5–20mcg/hr) can provide adequate analgesia for patients in a cancer palliative medicine clinic.

Methods:

- Single center, retrospective, observational chart review from 1/1/2016-9/30/2019 (n=68)
- Pain scores on numeric rating scale (0-10) at time of patch initiation and at various time points afterwards

Outcomes: Efficacy of TDB (transdermal buprenorphine) for cancer related pain, defined as no increase in pain score @ 28 days of use compared to reported pain score at initiation

Results: N = 68 patients (mean age 54 [SD 14.9], 12% with substance use disorder)

- At first follow-up appointment, 25 (46%) reported a decrease in pain and 15 (28%) reported no change in pain (total 74%). 16 patients (30%) reported at least a 2-point reduction in pain
- When TDB was initiated, 44 (65%) patients were prescribed a full mu-opioid agonist concomitantly for breakthrough pain
- The median duration of TDB was 94 days for all patients. For the subset of patients who did not discontinue prior to first follow-up, the median duration was 123 days.

Discussion:

- Patients initiated on TDB maintained stable pain scores throughout the study period
- Though many patients reported no change in pain score, over half of the patients included continued TDB for 3 months or longer.

Conclusion:

- Majority of patients initiated on TDB had stable or improved pain scores.

Alecia's Thoughts:

- Prior oral morphine equivalent (OME) requirements were low < 30mg before adding patch and patch strength not reported so could not assess actual conversion for efficacy
- Retrospective did not allow for pain score diary or average pain scores, pain scores taken at visits only, providing just one snapshot in time

JAMA Netw Open. 2021 Sep 1:4(9):e2124152.

Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain: A Systematic Review.

Objective: Examine the evidence on rotation to buprenorphine from full μ-opioid receptor agonists among individuals with chronic pain who were receiving long term opioid therapy.

Methods:

- Literature review through November 2020
- Included peer-reviewed original research reporting specific outcomes of rotation from long-term opioids to buprenorphine Quality of evidence assessed with Grading of Recommendations Assessment, Development and Evaluation (GRADE) system

Outcomes: precipitated opioid withdrawal, pain intensity or severity, pain interference, Treatment success (completion of protocol, willingness to continue buprenorphine long term, and reduced interest in additional opioids), mental health condition (depression and insomnia), adverse effects, and health care use (hospitalizations and outpatient visits)

Results: N =22 studies included; 5 RCTs (22.7%), 7 case-control or cohort studies (31.8%), and 10 uncontrolled pre-post studies (45.5%)

- Buprenorphine rotation protocols were diverse in formulation of buprenorphine used (Suboxone – buprenorphine/naloxone versus Buprenorphine alone) and dosing strategies

CLINICAL PEARL: Buprenorphine may be a favorable option for pain control in patients at higher risk for full opioid agonist-related adverse effects

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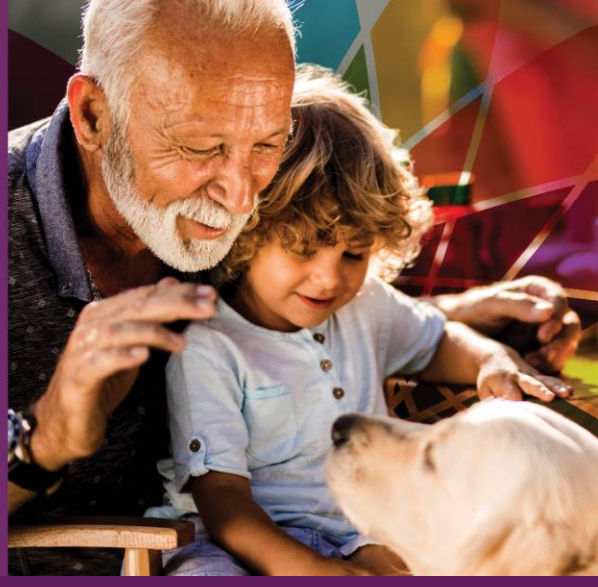

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- Precipitated opioid withdrawal (defined as worsening withdrawal symptoms after receipt of the first dose of buprenorphine) was rare, according to very low– to low-quality evidence. The incidence of precipitated withdrawal ranged from 3% to 6%
- Rotation to buprenorphine was associated with decreased pain severity in 12 of 17 studies (very low to low quality evidence); heterogeneity exists in timing and frequency of pain assessments
- Evidence suggested that rotation to buprenorphine can be accomplished successfully in participants with chronic pain who were receiving long term opioid therapy
- Rotation to buprenorphine was associated with little harm to patients, as suggested by 4 RCT and 6 uncontrolled observational studies
- Most common ADE were mild and included headache, GI upset (N/V/C), dizziness, or sedation
- No accidental or intentional overdoses or deaths attributed to buprenorphine in any of the studies
- There was insufficient evidence to definitively support an association between outcomes of mental health conditions (eg, depression, anxiety, and insomnia) and buprenorphine rotation

Discussion:

- Buprenorphine appeared to be noninferior to full MOR agonists in controlling pain
- Findings highlighted benefits of buprenorphine rotation but also that the state of the science is in its early stages
    - Did not identify an optimal approach for rotation from full MOR agonists
    - Wide range of baseline full MOR agonist doses, starting buprenorphine doses, and buprenorphine formulations
- Future research should address the optimal starting dose, formulation, and administration frequency of buprenorphine that are based on baseline total daily dose, ideally in the form of a standard equipotency ratio

Conclusion: Buprenorphine was associated with reduced chronic pain without precipitating opioid withdrawal or serious adverse effects in patients with chronic pain who used long term opioid therapy

Alecia's thoughts:

- Most studies reviewed were deemed to be low or very low quality given small sample sizes and lack of prospective, randomized study designs
- Not all studies measured pain scores the same way, making comparison between studies difficult, in addition to the variety of buprenorphine doses, formulations, etc..
- Diverse populations of patients – some with no diagnosis of OUD/SUD, some with opioid dependence given underlying chronic pain condition, some with SUD

Bottom Line:

- Studies have shown that buprenorphine is an option for pain management in certain chronic pain populations
- Buprenorphine seems to be a safe alternative to other opioids, and the risk of withdrawal when switching from other long term opioid therapies seems to be relatively low which can be minimized further with microinduction protocols
- Optimal starting dosages, formulation, and administration frequency are less clear from available data
- Given that the available formulations in the US are lower doses in comparison to other available formulations across the world, generalizability of data becomes more complicated
- It is possible that patients with lower OME requirements will have a better response to buprenorphine given the limited doses available in the US, especially of Butrans® patch formulation
- Remember that buprenorphine can be utilized for pain control in patients without any underlying SUD or opioid dependence… it may be a favorable option in patients that are more susceptible to opioid-related ADE such as respiration depression, sedation

CLINICAL PEARL: Buprenorphine may be a favorable option for pain control in patients at higher risk for full opioid agonist-related adverse effects