Clinical Resource Guide: Buprenorphine

INTRODUCTION TO BUPRENORPHINE IN THE HOSPICE SETTING

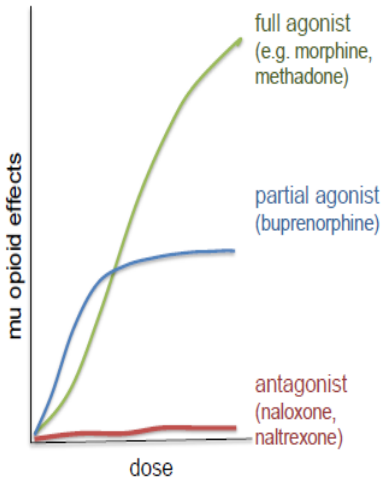
Chronic pain affects ~ 30% of Americans, and as the populations ages, this percentage continues to increase. Over the last three decades, opioids prescribed for the management of chronic pain have also been on the rise. Unfortunately, these prescribing trends combined with improper opioid use and diversion have contributed to the national opioid epidemic, resulting in increased rates of opioid addiction and opioid overdose-related deaths.

Buprenorphine is a medication indicated for the management of chronic pain and in the treatment of opioid use disorder. Although the formulations and doses of buprenorphine for these indications differs, the mechanism of action is the same. Buprenorphine is a partial opioid agonist, meaning it has activity at the opioid receptor, but resulting in a lower risk of overdose or developing physical dependence. These advantages have led to an increased utilization of the drug. Despite these benefits, there are challenges to using buprenorphine at the end of life.

Pharmacist Corner Objectives

1. Identify characteristics of buprenorphine that decrease risk of opioid-related adverse events
2. Identify formulations of buprenorphine and indication of use for each
3. Summarize process for converting buprenorphine to a full opioid agonist

MEDICATION EFFECTS ON OPIOID RECEPTOR BY TYPE



- ***Full opioid agonists:*** opioid effect increases with dose
- ***Partial opioid agonists***: ceiling effect occurs as doses increase, reducing pain relieving benefits, but also reducing risks of opioid-related side effects or adverse events
- ***Opioid antagonists***: block the opioid receptor to prevent opioid activity

BUPRENORPHINE MECHANISM OF ACTION

PHARMACOLOGY	IMPLICATION
Partial mu receptor agonist	• Potent analgesia with dose-related ceiling on respiratory depression • Doses can be customized to be safe AND effective
Kappa receptor antagonist	• Drowsiness can be a common side effect of opioid use • Patients often develop a tolerance to this after a few doses • Symptom relief can increase that patient's ability to get rest, often improving alertness, comfort and quality of life
Delta receptor antagonist	• The goal of opioid therapy is reduced symptom burden and increased quality of life, not quickening death • Near the end of life, patients may require doses of opioids that keep them sedated in order to be comfortable • Establish goals of care early with your hospice team

BUPRENORPHINE CONSIDERATIONS IN THE HOSPICE SETTING

Buprenorphine has a high affinity for the opioid receptor, which is beneficial when being used for opioid use disorder, as it can prevent full opioid agonists (fentanyl, oxycodone, etc.) from achieving the euphoric effects contributing to continued use/misuse/abuse. This strong bond and receptor activity result in decreased risk of opioid related adverse events, such as respiratory depression. While these are desirable outcomes when managing chronic pain or opioid use disorders, in the hospice setting, where the goal of care is usually centered on comfort, the use of buprenorphine can interfere with the efficacy of full opioid agonists (ex.: morphine) from being an effective medication for pain and/or dyspnea. Understanding the reason for using buprenorphine and the patient's goals of care are critical to setting a treatment plan involving this medication.

CONVERTING FROM BUPRENORPHINE TO FULL OPIOID AGONISTS

BUPRENORPHINE FORMULATION	INDICATION	AVAILABLE DOSES
Buprenorphine sublingual (*Subutex®*)	Opioid use disorder	2mg, 8mg
Buprenorphine/naloxone sublingual (*Suboxone®*)	Opioid use disorder	2mg/0.5mg, 4mg/1 mg 8mg/2mg, 12mg/3mg
Buprenorphine patch (*Butrans®*)	Chronic pain	5mcg/hr, 10mcg/hr, 15mcg/hr, 20mcg/hr
Buprenorphine buccal film (Belbucca®)	Chronic pain	75mcg, 150mcg, 300mcg, 450mcg, 600mcg, 900mcg

Buprenorphine Formulation	Equianalgesic Conversion Ratio	Equivalent Dose
Butrans® patch to oral morphine	1:70 to 1:115 (buprenorphine to morphine)	50mg of oral morphine/day = 0.43-0.71mg buprenorphine/day (18-36mcg/hr)
Butrans® patch to fentanyl transdermal	0.8mcg : 0.6mcg (buprenorphine to fentanyl)	20mcg/hr transdermal buprenorphine = 12mcg/hr transdermal fentanyl; 12mcg/hr of transdermal fentanyl ~30mg morphine/day

The conversion ratio of buprenorphine formulations to morphine (or any other full opioid agonist) can be variable, as patient specific are taken into consideration. It is important to note that the total daily amount of buprenorphine administered by the patch or the buccal film (both used for chronic pain) is significantly less than the amount received in the form of the sublingual film or the sublingual tablets (for treatment of opioid use disorder). Therefore, if a patient is being treated with Suboxone® for a history of substance use disorder but is experiencing significant pain as a result of metastatic cancer, this patient may require a significantly higher dose of a full opioid agonist than a patient on a Butrans® patch.

Prior to transitioning, it is important to have conversations with patients who with a history of substance use disorder to discuss risk mitigation strategies to prevent the patient from returning to use.

Buprenorphine Conversion to Full Opioid Agonist

1.) Discuss goals of care, understand patient thoughts regarding buprenorphine therapy if history of addiction.
2.) Stop buprenorphine
3.) Initiate immediate-release opioid regimen with prn dosing schedule
    a. Ex: oxycodone IR 5mg po every 4 hours prn pain
    b. Ex: hydrocodone 10mg/APAP 325mg po every 4 hours prn pain
4.) Follow-up
    a. Evaluate pain following transition to immediate release regimen
    b. Calculate daily opioid equivalents
    c. Pending prn opioid usage, may consider initiation of long-acting opioid
    d. Continue prn immediate-release opioid regimen for breakthrough pain
5.) Repeat
    a. Repeat Step 4 as often as necessary to ensure patient achieves pain goal
    b. Modify pain management regimen as often as necessary
6.) Consult BetterRX with any questions, issues or concerns.

References

1. Johnson RE, Fudula PJ, Payne R. Buprenorphine: considerations for pain management. *J Pain Symptom Manage.* 2005; 29:297-326.
2. Mercadante S, Villari P, Ferrera P, et al.
   Safety and effectiveness of intravenous morphine for episodic breakthrough pain in patients receiving transdermal buprenorphine. *J Pain Symptom Manage.* 2006;32:175-9.
3. Jalili M, Fathi M, Moradi-Lakeh M, Zehtabchi S. Sublingual Buprenorphine in Acute Pain Management: A Double-Blind Randomized Clinical Trial. *Ann Emerg Med.* 2012; 59:276-80. PMID 22115823.
4. Mercadante S, Casuccio A, Tirelli W, Giarratano A. Equipotent doses to switch from high doses of opioids to transdermal buprenorphine. *Support Care Cancer.* 2009; 17: 715-8.

