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Buprenorphine for Pain:

a safer alternative for opioid-
dependent patients?

Howard Kornfeld, MD
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- This session will be recorded
- Slides will be distributed and recording will be posted to the CHCF website
- Use “raise my hand” or Q&A/chat to ask a question

Today's Speaker



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Disclosure:

The speaker has not received any
pharmaceutical funding in the last 8 years.

Agenda

- Understanding waiver requirements
- Rationale: why use buprenorphine for pain?
- Induction options
- Understanding formulations
- Inpatient management
- Functional restoration
- Insurance coverage
- Common challenges

Understanding Waiver Requirements

What is a waiver?

- DATA 2000 (Drug Abuse and Treatment Act) for FDA approved medications for addiction, waives provisions of the Narcotic Addict Treatment Act
- Not required to treat pain, even when addiction is a factor
- When addiction is prominent (involving street opioids, for example), generally a good idea
- Managing patient caps:
 - 30 first year
 - 100 ongoing (may be 200, pending federal legislation)

Buprenorphine basics

- Onset of action: 30-60 minutes
- Tight receptor binding
- Analgesic action: up to 8 hours
- No apparent analgesic ceiling effect below 300 mg MME
- Excellent safety profile
- Lack of immunosuppressive effect
- Relatively few drug/drug interactions
- No accumulation in renal impairment

Rational for Opioid Rotation to Buprenorphine

The "High" Dose Patient

- >50 -120 or more morphine milligram equivalent (MME) per day
- 2016 CDC guidelines:

Carefully reassess evidence of individual benefits and risks when considering increasing dosage to ≥ 50 morphine milligram equivalents (MME)/day,

Avoid increasing dosage to ≥ 90 MME/day or carefully justify a decision to titrate dosage to ≥ 90 MME/day"

Rationale for Opioid Rotation to Buprenorphine

The “Low” Dose Patient

- Although not exceeding CDC guidelines, common clinical situation would be that of poor efficacy, disrupted sleep, depression and anxiety, challenging or unwilling to taper or discontinue, prolonged course of treatment.

Rationale for Opioid Rotation to Buprenorphine

Medical complications from long-term opioid therapy

- Hypogonadism: erectile dysfunction, osteopenia
- Sleep apnea
- Weight gain or loss
- Deconditioning and sedentary lifestyle
- Disturbed circadian rhythm
- Constipation and opioid bowel disease, SIBO (small intestine bacterial overgrowth)
- Opioid induced hyperalgesia
- Theoretical immune suppression
- Dysregulation of the hypothalamic pituitary adrenal axis

How to Convince Patients to Switch

- Better symptom management
- Less sedation
- Resolution of recurrent withdrawal symptoms
- Potential resolution of sleep apnea, hormonal abnormalities
- Able to taper off of anti-depressants and neuroleptic drugs
- Regulatory environment not conducive to staying on full agonist opioids
- Schedule 3 rather than 2
- Functional restoration can be effective

Conversion from High Dose Full Opiate Agonists to Sublingual Buprenorphine Reduces Pain Scores and Improves Quality of Life for Chronic Pain Patients

After 2 months on sublingual buprenorphine, patients' mean pain score decreased from 7.2 to 3.5, with 34 of 35 patients reporting a pain decrease.

Poster presented by Daniel Novinson, MPH, Jonathan Daitch, MD, Danielle Daitch, BA, Michael Frey, MD, Carol Mitnick, ARNP, Joseph Pergolizzi Jr, MD

References for Buprenorphine Induction Protocols

- Provider Clinical Support System for Medication Assisted Treatment (PCSS-MAT)
- The NIDA Treatment Improvement Protocol (TIP 40)
- buppractice.com, updated December 2013

NOTE:

*All three protocols were developed with funding from SAMSHA or NIDA

*PCSS-MAT and TIP 40 are inaccurate regarding peri-operative management

Buprenorphine transdermal (patch) bridge

Methadone:

Convert first to long-acting opioid (30-50% less than the calculated equivalent)

<50 mg methadone: 3-4 days long-acting opioids

50-100 mg methadone:

Replace 50% with long-acting opioid for 3-4 days,
then the other 50% for 3-4 days
(overlapping or cross taper)

>100 mg methadone:
cross-taper method in 3 or more steps

Buprenorphine transdermal (patch) bridge

Before the induction day, prescribe:

- Buprenorphine patches
four 5 mcg/hr or two 10 mcg/hr patches (box of four),
- Buprenorphine sublingual 2 mg #60
mono product – without naloxone – if no addiction
- 4 days of short-acting opioids
slightly less than current long-acting opioid dose

Avoid long-acting opioids on the day of the induction.

Short-acting opioids can be used as needed for pain.

Buprenorphine transdermal (patch) bridge

Simultaneously (on the first day of the induction):

- Discontinue long-acting opioids
- Place up to 20 mcg/hour of buprenorphine patch. Keep patch on for 3-4 days.
- Continue short-acting opioids as needed for pain

Buprenorphine transdermal (patch) bridge

- Discontinue short-acting opioids the night before starting sublingual buprenorphine. Keep the patch in place.
- Give 1 mg (half-tablet) buprenorphine; observe 30 minutes. Can add 1 mg dose later that day.
- Increase dose by 2 mg every 3 days as needed to control pain and cravings, to a maximum of 24 mg.
- Some physicians titrate up at a faster pace.
- Once higher doses of sublingual buprenorphine are tolerated, discontinue the patch.

Fentanyl transdermal (patch) induction

- Transition patients to fentanyl 25 or 50 mcg x 3-7 days.
- Stop short-acting opioids for at least 24 hours prior to sublingual buprenorphine.
- Remove fentanyl patch, and give 1-2 mg sublingual buprenorphine; observe for 20 minutes.
- Increase to 8 mg if needed to manage withdrawal symptoms on the first day, and up to 24 mg over 3-7 days, as needed.

Home Induction

- Promising reports in literature
- See PCSS-MAT protocol (pcssmat.org) (Provider Clinical Support System for Medication Assisted Treatment)
- Facilitated by transdermal buprenorphine bridge
- Support in home is needed
- Return office visit in short interval

Sublingual Buprenorphine Tablets

- If 2 mg tablets of buprenorphine is too high (nausea, sweating, dysphoria), consider:
 - Cutting them in half (they often break)
 - Having the patient swallow the pills (this reduces the bioavailability substantially)
 - Using compounded buprenorphine at lower doses (usually in the form of gelatin troche's)
 - Buccal mucoadhesive (75 mcg to 900 mcg) per buccal film to be dosed q12 hours

Buccal Film

- Less than 30mg oral mg morphine equivalents (MME): start at 75 mcg per day or q12 hours
- 30-89mg oral MME: 150 mcg q12 hours
- 90-160mg oral MME: 300 mcg q 12 hours
- Greater than 160mg oral MME: “consider alternative analgesic”

Formulation	Doses Available	Indication
Transdermal patch (Butrans)	buprenorphine: 5, 7.5, 10, 15, and 20 mcg/hour, every 7 days	Pain
Low dose buccal film (Belbucca)	buprenorphine: 75, 150, 300, 450, 600, 750, 900 mcg, twice daily	Pain
High dose buccal film (Bunavil)	buprenorphine/naloxone: 2.1mg/0.3mg, 4.2mg/0.7mg, and 6.3mg/1mg	Addiction
Sublingual tablets (Subutex, Suboxone, Zubsolv)	buprenorphine: 2mg, 8mg buprenorphine/naloxone: 2mg/0.5mg, 8mg/2mg; 1.4mg/0.36mg, 2.9mg/0.71mg, 5.7mg/1.4mg, 8.6mg/2.1mg, 11.4mg/2.9mg	Addiction Off-label for pain
Sublingual film (Suboxone)	buprenorphine/naloxone: 2mg/0.5 mg, 4mg/1mg, 8mg/2mg, 12mg/3mg	Addiction Off-label for pain
Implant	Buprenorphine: 80 mg (equivalent to <8 mg SL)	Addiction Off-label for pain
Compounded	Many options	Pain

A Case Series (Kornfeld & Manfredi, 2010)ness of Full Agonist Opioids in Patients Stabilized on Buprenorphine Undergoing Major Surgery:

- Patients were maintained on buprenorphine up to the time of surgery.
- Postoperative pain was adequately controlled using full agonist opioids.

	Surgical Procedure	Length of stay (days)	Pain assessment at discharge	Preoperative buprenorphine (mg)
1	Right-side colectomy	9	"Pain free"	24
2	Knee replacement (R)	4	"Excellent pain management"	12
3	Knee replacement (L)	3	"Excellent analgesia"	12
4	Small bowel resection	5	"Good analgesia"	2
5	Bilateral mastectomy w/ reconstruction	4	"Pain fluctuates . . . responds to hydromorphone"	8
6	Breast reconstruction	2	"Good pain control"	6
7	X-STOP removal	3	"Excellent pain control"	16

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Functional Restoration Clinic

- Psycho-educational group
- Psychological therapy
- Physical therapy

Insurance coverage

- Medi-Cal
 - Addiction? No authorization needed (sublingual only)
 - Pain? Requires authorization
 - Pharmacies sometimes deny in error (sent to managed care plan instead of State Fee for Service Medi-Cal)
- Commercial insurance
 - Authorization requirements vary

Common Challenges and Opportunities

- Escalation/persistence of pain
- Euphoric recall of full agonists
- Adding full agonists to buprenorphine
- Tapering full agonists back to buprenorphine alone
- Benzodiazepines, zolpidem-like drugs
- ADHD: stimulant-dependent patients
- Ineffective SSRI's, SNRI's
- Unnecessary neuroleptic drugs
- QTc considerations

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Local anesthetic effect:

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Questions & Answers