TRANSITIONS IN METHADONE AND BUPRENORPHINE

ME SUD LEARNING ECHO
8/8/24

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LEARNING OBJECTIVES

1. Offer a framework for a patient to choose methadone versus buprenorphine depending on their goals and drug use patterns.

2. Gain comfort in a 5-day process for patients switching from buprenorphine to methadone, allowing them to CONTINUE methadone to avoid opioid withdrawal.

METHADONE V. BUPRENORPHINE

- Easier to get on than buprenorphine, don't have to be in opioid withdrawal to start
- Less complicated induction
- Wrap around OTP services
- Higher fentanyl doses?

- Safer in higher doses
- Therapeutic doses can be achieved relatively quickly
- Lower risk of diversion
- Less stigma?
- No dedicated clinic, can get from primary care (no more X-waiver)
- Partial opioid agonist "ceiling effect" on respiratory depression

MY PATIENT IS ON SUBOXONE BUT STILL USING FENTANYL S THEY WANT TO START METHADONE

- Can do immediately, no waiting period
- Partial mu opioid agonist (buprenorphine) → Full agonist (methadone takes over all the receptors)

- The other way around (methadone to buprenorphine) is a bit trickier but CAN be done (in the outpatient clinic!)

MANY OF THESE SLIDES WERE TAKEN FROM ADDICTION MEDICINE PHYSICIAN, VINCE MARIANO MD

TRANSITION STRATEGIES

- Standard/Traditional Buprenorphine Induction
- Low-dose Buprenorphine Induction
- Buprenorphine Inductions with intermediary opioids
- Antagonist-assisted Buprenorphine Induction

STANDARD INDUCTIONS

- General principles:
  - Gradual reduction of methadone until patient experiences mild withdrawal between doses
  - Stop methadone and monitor for signs of withdrawal
  - Start buprenorphine with a low dose and increase slowly over multiple days until withdrawal symptoms dissipate
- Wide variability between published protocols from different institutions
  - Starting methadone dose, when to start buprenorphine, initial buprenorphine dose, buprenorphine formulation, speed of buprenorphine dose increases, duration of induction

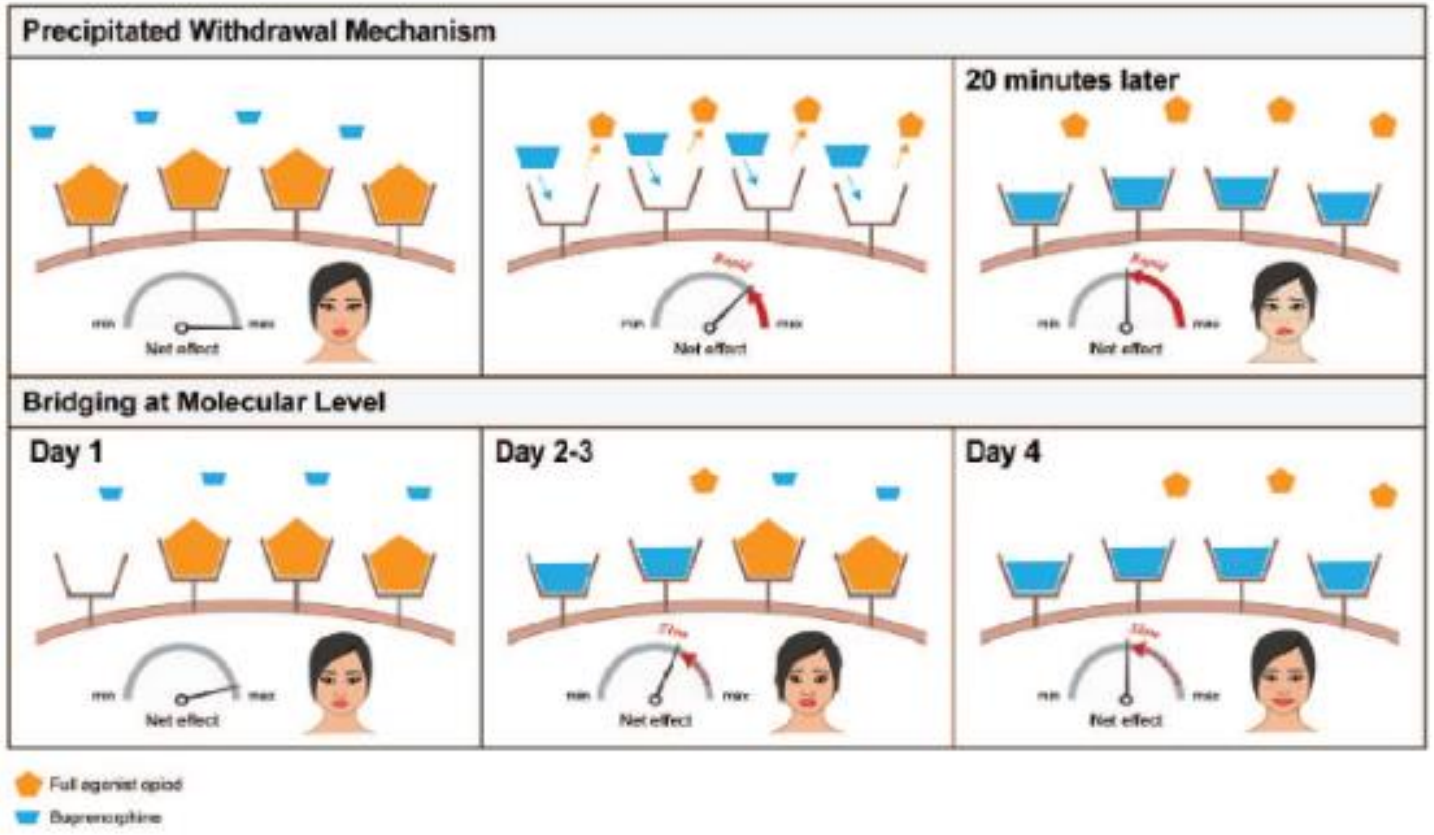
TABLE 1. Published Guidelines for Transfer of Patients From Methadone to Buprenorphine*

	ASAM (United States) 2015[5]	Common-wealth of Australia 2014[6]	British Columbia (Canada) Ministry of Health 2017[9]	CCBHO (Pittsburgh, PA) 2013[40]	New Zealand Ministry of Health 2014[19]	NHS (United Kingdom) Fife 2011[41]	WHO 2009[18]	SAMHSA (United States) 2018[42]
Before BUP administration								
METH dose and taper guidance	NA; patients on 30–40 mg will be less comfortable	Gradual dose reductions to ≤60 mg/d	Taper to <60 mg, ideally ≤30 mg/d, for 6–7 d	Gradual taper to ≤30 mg/d for 5–7 d	NA	Reduce to ≤30 mg	Taper to 30 mg	Taper to 30–40 mg/d for ≥7 d
Time between last METH dose and first BUP dose	24–72 h	NA	≥24 h, preferably 48–72 h	48–72 h	≥24 h	≥24 h, preferably 36 h	≥24 h	≥24 h, preferably ≥36 h.
Withdrawal symptoms before BUP administration	Mild-moderate withdrawal (COWS 11 to ≥12)	Moderate withdrawal (COWS ≥13, SOWS ≥16)	COWS > 12	"Clear objective signs of withdrawal"	Moderate withdrawal COWS > 12	COWS 13–24	"Ideally when withdrawal signs are evident"	COWS ≥ 12
BUP administration: day 1								
Initial dose	2–4 mg	2 mg	BUP/NLX 4 mg/1 mg†	2 mg	2 mg	2 mg if equivocal objective signs of withdrawal, 4 mg if clear signs of moderate withdrawal	NA	BUP/NLX 2/0.5 mg–4/1 mg
Additional dosing guidance	Prescribe increments of 2–4 mg if no withdrawal symptoms evident after 60–90 minutes	If initial dose does not cause precipitated withdrawal after 1 h, may give additional 6 mg Supplementary doses: COWS <6: no additional BUP; COWS 6–12: additional 4 mg; COWS ≥13: additional 8 mg	Increments of 2 mg/0.5 mg BUP/NLX up to a maximum of 12 mg/3 mg If need for additional dose uncertain, consider prescribing one or two 2 mg/0.5 mg BUP/NLX tablets as take-home doses	2 mg every 2 h as needed; maximum 8 mg	Additional 6 mg after 1 h if the initial dose does not precipitate withdrawal Supplementary doses (every 1–3 h): COWS < 6 = no BUP; COWS 6–12 = additional 4 mg; COWS ≥ 13 = additional 8 mg	Additional 2–4 mg depending on COWS (cut-offs not specified) score and pupil size; maximum 8 mg	NA	Additional dosing in increments of BUP/NLX either 2 mg/0.5 mg or 4 mg/1 mg every 2 h as needed; maximum 8 mg
BUP day 2 and beyond								
Starting dose	Not addressed	Total dose of day 1 +: COWS 0–5, SOWS <8: −4 mg COWS 6–12, SOWS 8–15: −4 mg COWS ≥13, SOWS ≥16: −8 mg Maximum 32 mg	If no withdrawal symptoms since last BUP, continue once-daily dose of the total amount of BUP/NLX administered on day 1, titrating as needed in subsequent days, aiming for target dose ≥16 mg/4 mg	Start with day one total dose +4 mg BUP; if still symptomatic after 2 h, give 4 mg to a total of 16 mg on day 2	Dosing on days 2–4: total amount from day 1 +: COWS 0–5: +4 mg COWS 6–11: +4 mg COWS > 12: +8 mg Maximum 32 mg	Total day one dose + 2–4 mg if obvious withdrawal features present, otherwise repeat day 1 dose	NA	Maximum 16 mg, otherwise document rationale for higher dose
Dose range	Generally 8–16 mg; maximum 24 mg/d	Most patients require 12–24 mg; some as little as 4–8 mg, others as much as 32 mg/d (maximum)	Target dose of BUP/NLX ≥16 mg/4 mg; maximum 24 mg/6 mg/d	8–24 mg	Generally 12–24 mg; maximum 32 mg/d	NA	Generally 8–24 mg/d; maximum 32 mg/d	BUP/NLX mg/0.5 mg–4 mg/1 mg; maximum 8 mg/2 mg

Reproduced from Lintzeris et al, *J Addict Med*, 2022

LOW-DOSE BUPRENORPHINE

- General principles:
  - Continue with current opioid (heroin, fentanyl, methadone, etc) while gradually introducing buprenorphine at low doses to prevent displacement of opioids at mu-receptor to avoid precipitated withdrawal.



Reproduced from Ghosh et al, *Canadian J Addict*, 2019

BERNESE METHOD

- Modified versions now available

Box 1: Outpatient microdosing induction schedule for buprenorphine–naloxone

- Day 1: 0.5 mg once a day
- Day 2: 0.5 mg twice a day
- Day 3: 1 mg twice a day
- Day 4: 2 mg twice a day
- Day 5: 3 mg twice a day
- Day 6: 4 mg twice a day
- Day 7: 12 mg (stop other opioids)

Randhawa et al, *CMAJ*, 2020

OPTION 1: OUTPATIENT 2MG TO 8MG FILMS

- Methadone to 60mg or as low as tolerated
- Coordinate with patient's OTP
- Send in 2mg films of buprenorphine-naloxone, pause if withdrawal symptoms are present
- Close follow up
- Day 1: Take 0.5mg (1/4 of a 2mg film) three times throughout the day. Continue regular dose of methadone.
  Day 2: Take 1mg (1/2 of a 2mg film) three times throughout the day. Continue regular dose of methadone.
  Day 3: Take full 2mg film three times throughout the day. Continue regular dose of methadone.
  Day 4: Take 4mg (2x 2mg film) three times throughout the day. Continue regular dose of methadone (last day).
  Day 5: Take full 8mg film twice or three times throughout the day. Do not take methadone today.

LOGISTICS

- Prescribe 12 2mg films – written no more than TID (I've had trouble with some insurances sending 1 week worth BID bc technically you only need 4 days of the 2mg film as part of the 5 day protocol).
  - Technically for this protocol you need 11.25 of the 2mg strips (3/4 film on day 1, 1.5 film on day 2, 3 film on day 3, 6 film on day 4, switch to 8mg films on Day 5).
    - Some insurances only cover BID dosing but ideally you can get 12 of the 2mg films somehow (voucher/PA), easiest being 2mg TID x 4 days (to get the 12 aka 11.25 strips you need).
- Would send in 12 strips of the 2mg and then on day 5 send in 8mg films BID-TID. Try not to have the switch from 2 to 8mg films happen over a weekend.
- CLOSE FOLLOW UP (daily) with careteam

PRINT/EMAIL FOR PATIENT TO FOLLOW

Microinductions

Standard microinduction

**Please note: the below doses refer to buprenorphine. If you are taking Subxone it contains two medications, buprenorphine and naloxone. The buprenorphine dose is listed first on your Suboxone films.

Day 1: take 0.5 mg (1/4 of a 2 mg film) three times, in the morning, at mid-day and in the late afternoon. Take your regular dose of methadone.

Day 2: take 1 mg (1/2 of a 2 mg film) three times, in the morning, at mid-day and in the late afternoon. Take your regular dose of methadone.

Day 3: take 2 mg (one whole 2 mg film) three times, in the morning, at mid-day and in the late afternoon. Take your regular dose of methadone.

Day 4: take 4 mg (two whole 2 mg films) three times, in the morning, at mid-day and in the late afternoon. Take your regular dose of methadone.

Day 5: today you will switch from 2 mg films to 8 mg films. You will need to pick these up at your pharmacy. Take 8 mg (one whole 8 mg film) two times today. If you feel like you need more Suboxone, for example if you are having cravings for opioids or symptoms of withdrawal, you can take a third 8 mg film. DO NOT TAKE METHADONE TODAY.

Rapid microinduction

**Please note: the below doses refer to buprenorphine. If you are taking Subxone it contains two medications, buprenorphine and naloxone. The buprenorphine dose is listed first on your Suboxone films.

Day 1: Take 0.5 mg (¼ of a 2 mg film) every 3 hours. Take 8 doses (a total of two 2 mg films). Take your usual dose of methadone.

Day 2: Take 1 mg (½ of a 2 mg film) every 3 hours. Take 8 doses (a total of four 2 mg films). Take your usual dose of methadone.

Day 3: Today you will switch from 2 mg films to 8 mg films. Start the day by taking 12 mg (one and a half 8 mg films). DO NOT TAKE METHADONE TODAY. Take an extra 4 mg (½ of an 8 mg film) later in the day if you need it.

Touch base with your doctor at this point to determine the next steps in dosing.

RHODE ISLAND ADDICTION MEDICINE EXPERTISE/LOCAL STANDARDS (VINCE MARIANO, MD)

OPTION 2: INPATIENT BUTRANS PATCH

- If no time limitations, general recommendations would be:

  Day 1 – 80mg methadone + 20mcg/hr Butrans patch

  Day 2 – 80mg methadone + 20mcg/hr Butrans patch + 1mg SL buprenorphine QID

  Day 3 – 80mg methadone + 20mcg/hr Butrans patch + 2mg SL buprenorphine QID

  Day 4 – Discontinue methadone and Butrans + 4mg buprenorphine QID

  Day 5 – 8mg SL buprenorphine TID if withdrawal/cravings inadequately managed

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OPTION 3: SLOWER UPTITRATION

- Methadone 80mg
- Day 1: 0.5mg once
  Day 2: 0.5mg BID
  Day 3: 1mg BID
  for 7-14 days
- Stop/hold if withdrawl

TAKE HOME POINTS

- There are a number of different protocols for transitioning from buprenorphine to methadone but little evidence to suggest certain methods are superior than others
- Protocols can be tailored to individual patient's needs

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