MICRODOSE BUPRENORPHINE INDUCTIONS

Jennifer Hartley

SUD ECHO

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A SNEAK ATTACK …

DISCLOSURES

Jennifer Hartley has nothing to disclose.

LEARNING OBJECTIVES

1. Define buprenorphine microdosing and become familiar with several protocols
2. Utilize the microdosing protocol favored by the inpatient addiction consult service at OHSU
3. Review case studies on microdosing from the inpatient consult service
4. Implement microdosing in the outpatient setting

WHAT IS MICRODOSING?

(No, it does not involve psychedelics.)

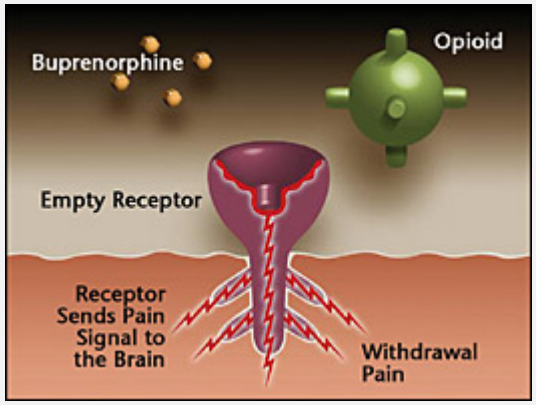
Microdose buprenorphine induction remains loosely defined as there are not yet widely validated standardized protocols.

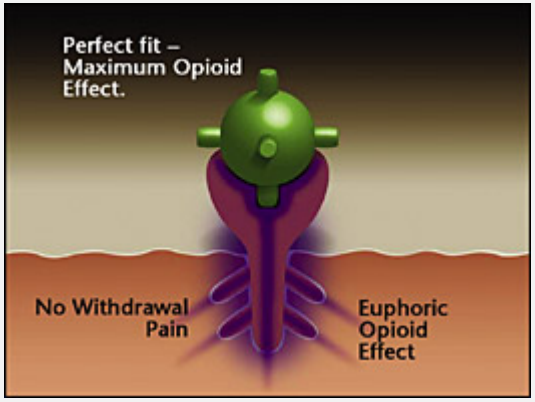
Essentially, it is an approach to starting buprenorphine that introduces the medication onto the receptors so slowly that no withdrawal of any kind is involved in the process.

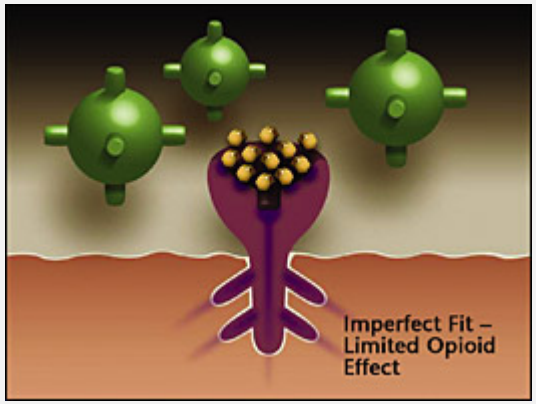
MICRODOSE BUPRENORPHINE INDUCTION: AN IMPORTANT DEVELOPMENT

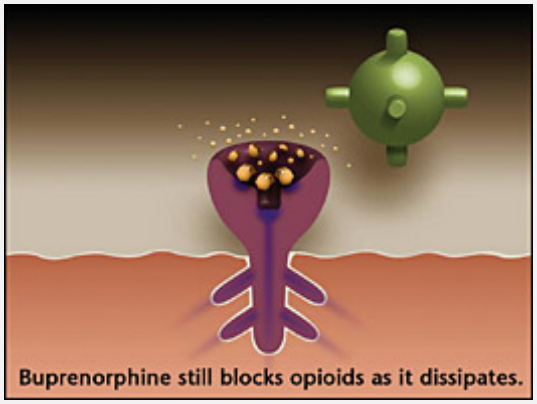
- Removes the need for patients to be in any degree of withdrawal when starting SL bup/nlx.
- Allows opioid pain medications to be administered simultaneously with induction.
- Lower risk for precipitating withdrawal.

REVIEW OF STANDARD INDUCTION









STANDARD VS. MICRODOSE

COWS OF 12	REMAIN ON FULL AGONISTS
4 mg + 4 mg	1 mg + 1 mg
8 mg + 4 mg + 4 mg	2 mg + 2 mg
	4 mg + 4 mg
	6 mg + 6 mg

TWO PRIMARY METHODS

1. Start a 20 mcg buprenorphine transdermal patch and gradually introduce SL bup/nlx. Then taper full agonist.

2. Start sublingual bup/nlx at very low doses and uptitrate. Then taper full agonist.

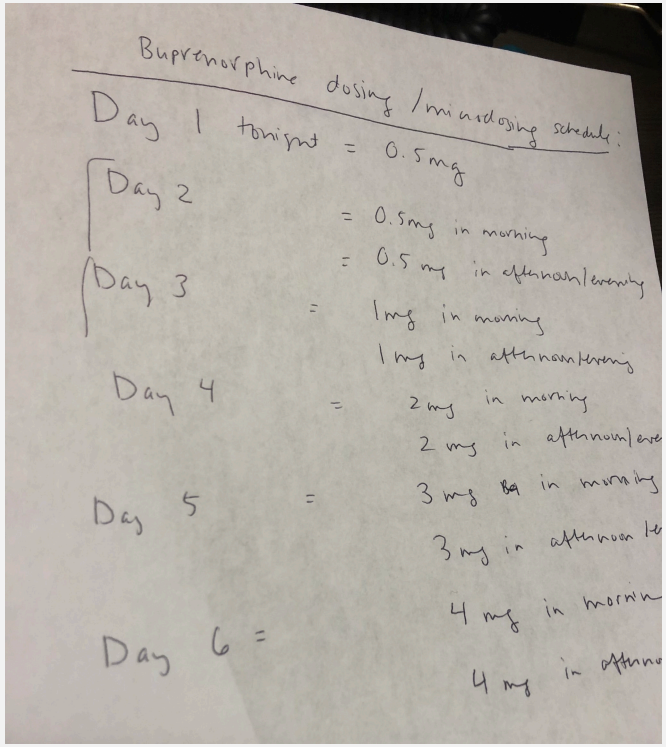
THE LITERATURE

- First research done in Switzerland using 0.2 mg compounded doses yielded the "Bernese Method" starting with 0.5 mg doses and titrating up.
- Small number of published case reports in US and Canada have used a variety of protocols with both patches and SL dosing.
- Have transitioned from methadone doses as high as 100 mg methadone.

FASTEST PROTOCOL TO DATE: LEMBKE & RAHEEMULLAH IN JAMA, MARCH 2019

- 20 mcg bup patch for 24 hours
- Day 1, give 2 mg SL bup/nlx + 2-4 mg prn doses q 2-4 hours for maximum dose of 8 mg.
- Day 2, give total from Day 1 + 2-4 mg prn doses q 2-4 hours for max dose of 16 mg.
- Remove patch after 48 hours. Discontinue full agonists not yet tapered.

HOW WE STARTED THE PROCESS (THANKS TO TWITTER)



IMPACT TRANSDERMAL PATCH PROTOCOL:

- Place two 10 mcg bup transdermal patches (= 20 mcg patch)
- Continue both long and short-acting opioids.
- For short-acting, can start SL bup/nlx at 24 hours; for long-acting, wait 48 hours.
- Begin SL dosing with 1 mg BID (1/2 tab).
- Day 2: 1 mg BID
- Day 3: 2 mg BID
- Day 4: 4 mg BID
- Day 5: 6 mg BID
- Day 6: 8 mg BID

IMPACT CASE 1

- 36 yo man severe OUD and meth use disorder, admitted w/ RLE osteomyelitis.
- Methadone 5 mg AM, 2.5 mg PM started to manage withdrawal with plan to titrate up and maintain as outpatient.
- But – pt had been at 90 mg methadone previously and felt over-sedated. Frustrated by "revolving door" of pain and use. Needed mental health treatment, which he could obtain at a clinic that also prescribed bupe. BUT – afraid of withdrawal and increased pain.
- Agreed to microdose approach.

- Patch kept on for 3 days before sublingual started.
- Day 1 of SL: 1 mg + 1 mg half hour later.
- Day 2: Pt noted better pain control and mood, asked to reduce oxycodone dose.
- Day 6 (at 8 mg bid) pt had increased pain and question of withdrawal symptoms – increased irritability. Additional 4 mg dose given mid-day. Irritability resolved.
- Day 7: Methadone discontinued on with no adverse symptoms. Oxycodone continued and tapered prior to discharge.

IMPACT CASE 2

- 44 yo woman w/ severe meth use disorder, OUD in sustained remission.
- Admitted for disarticulation of R hip 2/2 chronic RLE osteomyelitis, cellulitis.
- Initially on hydromorphone PCA and oxycodone with ketamine after surgery.
- Discussion of SL bup/nlx for long-term pain control initiated early in hospitalization with pt in agreement.

- Induction deferred due to pt feeling overwhelmed
- Turnover of team, high census led to pt being ready for discharge to SNF without suboxone having been started. Still on oxycodone.
- SNF will not manage standard induction and microdose induction had already been offered to pt.
- Patch to the Rescue! ☺

- Primary team holds pt for an extra day to get induction underway.
- SNF will administer remaining SL up-titration doses and then oxycodone taper.
- Patch placed for 24 hours
- SL bup/nlx started 1 mg bid
- Pt discharged to SNF the following day. Suboxone titration and oxycodone taper went smoothly.

POTENTIAL LIMITATIONS

1. Withdrawal symptoms

- To date, the only symptoms have been mild, vague and non-specific.
- include insomnia, restless legs and irritability.
- none can be definitively attributed to withdrawal.

1. Cost, insurance coverage of buprenorphine patch as outpatient
2. Complexity and patient compliance
3. Duration of microdose inductions

FUTURE DIRECTIONS & DISCUSSION

1. Changes to protocol for methadone > 100 mg, other long-acting opioids (e.g. fentanyl patch)
2. Choosing "classic" over microdose
3. Timing for SL dosing after placing bup patch
4. Use in opioid treatment programs
5. Outpatient microdose induction protocols using 0.5 mg SL bup/nlx

SAMPLE OUTPATIENT SL PROTOCOL

- Day 1: 0.5 mg (1/4 tab)
- Day 2: 0.5 mg BID
- Day 3: 1 mg BID (1/2 tabs)
- Day 4: 2 mg BID
- Day 5: 4 mg BID
- Stop or taper full agonists

CONCLUSIONS

1. Microdose inductions are safe and feasible for inpatient and outpatient settings

2. The main benefits are avoiding planned withdrawal and minimizing risk of precipitated withdrawal associated with conventional buprenorphine induction

3. Downsides of microdose buprenorphine induction include the cost of buprenorphine patches, duration of induction, issues of complexity and compliance in outpatient settings