Canadian Mental Health Association
Mental health for all

Thames Valley
Family Health Team

Buprenorphine/Naloxone Microdosing: The Bernese Method

A Brief Summary for Primary Care Clinicians

Disclaimer:

Microdosing principles are currently not included in any clinical practice guidelines for the management of Opioid Use Disorder, rather it is an off-label practice that has been included in clinical practice amongst addiction specialists. It is therefore important to obtain informed consent prior to initiating it with a patient. Microdosing is frequently used at the London Rapid Access and Addictions Medicine (RAAM) Clinic with good results.

What is Microdosing?

The Bernese Method uses the principle of Microdosing to initiate a patient onto buprenorphine/naloxone (bup/nlx) maintenance therapy. The theoretical background of this method is based on the following principles:

1) Repetitive administration of very small buprenorphine doses with sufficient dosing intervals (e.g. 12 hours) should not precipitate opioid withdrawal
2) Because of the long receptor binding time, buprenorphine will accumulate at the opioid receptor
3) Over time, an increasing amount of a full μ-agonist will be replaced by buprenorphine at the opioid receptor

Therefore, overlapping induction of buprenorphine with ongoing use of opioids, from the unregulated drug market or prescription, including maintenance doses of a full μ-agonist (e.g. methadone or sustained release oral morphine), is possible without precipitating severe opioid withdrawal. Mild withdrawal symptoms may be experienced during the induction.

Although dosing schedules vary, principles of the Microdsoing method include:

1) Prescriber starts with a low dose of buprenorphine, overlapping with other opioid use
2) Small buprenorphine dose increases over time
3) Tapering or of opioid use at sufficient dose of buprenorphine (or sometimes an abrupt cessation

Why use it, and who is a good candidate?

Microdosing may have considerable advantages despite taking longer for the overall induction than the traditional protocol. It may be useful for <u>most</u> patients. In more detail:

- It may be helpful for patients fearing withdrawal or experiencing severe symptoms during conventional induction, or who have failed conventional induction due to inability to tolerate withdrawal symptoms

- It may also be beneficial when a switch to buprenorphine is desired for patients maintained on a full μ-agonist such as methadone or slow-release oral morphine (SROM)
- It is no longer necessary to wait for withdrawal before induction, so patients who may not be able to attend daily appointments due to work commitments, etc. are good candidates
- As withdrawal is avoided, there is better treatment retention with buprenorphine/naloxone
- It may have more providers willing to prescribe buprenorphine/naloxone, as the induction is not as complex

Who Should Be Referred to the RAAM Clinic for Induction and Stabilization of Opioid Agonist Therapy (OAT)*?*

- Patients who are on high dose fentanyl patches of 100mcg/hr or greater
- Patients who are using street fentanyl (due to the uncertain risk of precipitated withdrawal)
- Injection drug users
- Methadone conversions

Monitoring Considerations:

If choosing to use Urine Drug Screens (UDS) to assist with monitoring, emphasize that they are being utilized as a patient safety tool. These may be used with each client visit, or as the practitioner deems appropriate.

Reasons to use a UDS are to ensure client safety, augment honesty and accountability, and to inform treatment. It is often the case that clients are unaware of the mixed components of their drug from the unregulated market, or how combining medications, like benzodiazepines, can put them at further risk. UDS can help us assist them in their recovery. Contaminants such as Levamisole are detected by lab chromatography.

Using the Microdosing method, follow-up appointments may be at a weekly interval, based on individual client's stability. You may choose to have a few days of brief daily follow-up appointments with opioid cessation, to allow for timely titration of buprenorphine/naloxone to a comfortable dose.

How do you prescribe buprenorphine/naloxone via the *Microdosing Method?*

OPTION 1

ONCE DAILY DOSING

<u>Short-acting Opioid</u>:

Day	Buprenorphine	Opioid
1	0.5 mg daily	Maintain dose
2	1.0 mg daily	Maintain dose
3	1.5 mg daily	Maintain dose
4	2.0 mg daily	Maintain dose
5	2.5 mg daily	Maintain dose
6	3.0 mg daily	Maintain dose
7	4.0 mg daily	Stop short-acting opioid
See the patient on Day 7, after 4mg of Bup/Nlx, and give another 2mg every 1h until comfortable, to a max of 12mg that day. You may instead choose to give an additional 2mg as needed on Day 7, with daily follow-ups thereafter, and increases of 2mg to 4mg/day as needed, until comfortable. Final maximum dose is typically 16mg/day (but often can be less)		

<u>Long-acting Opioid:</u> (Including Fentanyl, Fentanyl Patches, and Methadone)

Day	Buprenorphine	Opioid
1	0.5 mg daily	Maintain dose
2	1.0 mg daily	Maintain dose
3	1.5 mg daily	Maintain dose
4	2.0 mg daily	Maintain dose
5	2.5 mg daily	Maintain dose
6	3.0 mg daily	Maintain dose
7	4.0 mg daily	Maintain dose
If long- AND short-acting opioids, stop short-acting opioids here and maintain long-acting opioid dose. You may also choose to begin a taper of long-acting opioids at this point, though we have not found it necessary		
8	5.0 mg daily	Maintain dose
9	6.0 mg daily	Maintain dose
10	7.0 mg daily	Maintain dose
11	8.0 mg daily	Maintain dose
12	10.0 mg daily	Maintain dose
13	12.0 mg daily	Maintain dose
14	12.0 mg daily	Stop all remaining opioid therapy
Follow-up appointment at Day 7 to monitor progress and outline taper of long-acting opioid if you choose. See the patient on Day 14, after 12mg of Bup/Nlx, and give another 2mg every 1h until comfortable, to a max of 16mg that day.		

OPTION 2

TWICE DAILY DOSING

<u>Short-acting Opioid</u>:

Day	Buprenorphine	Opioid
1	0.5 mg once daily	Maintain dose
2	0.5 mg twice daily	Maintain dose
3	1.0 mg twice daily	Maintain dose
4	2.0 mg twice daily	Stop short-acting opioid therapy
At 4mg Suboxone, the client may fully stop all short-acting opioids without a taper. The Suboxone dose can then be adjusted as needed, adding 2mg every 1h until comfortable, to a max of 12mg that day.		

<u>Long-acting Opioid</u>: (including Fentanyl, Fentanyl Patches, and Methadone)

Day	Buprenorphine	Opioid
1	0.5 mg once daily	Maintain dose
2	0.5 mg twice daily	Maintain dose
3	1.0 mg twice daily	Maintain dose
4	2.0 mg twice daily	Maintain dose
If long- AND short-acting opioids, short-acting opioids can be stopped here.		
5	3.0 mg twice daily	Maintain dose
6	4.0 mg twice daily	Maintain dose
7	12 mg once daily	Stop all remaining opioid therapy
Follow-up appointment at Day 7 after 12mg of Bup/Nlx, and give another 2mg every 1h until comfortable, to a max of 16mg that day.		

note that microdoses apply to the active component buprenorphine, not naloxone

Community Pharmacy Considerations:

It is advisable to check with the patient's community pharmacy to ensure they have buprenorphine / naloxone to dispense. If you are unsure if the pharmacy has dispensed it using the Microdosing method previously, it is a general courtesy to forward them a copy of the Microdosing Method along with your prescription. They may need a "heads up" that tablets may need to be split to accommodate the smaller doses required in Microdosing.

Carries and Observed Doses for Microdosing:

In general, inductions involve all observed doses at the pharmacy. Daily dispensing will also ensure accuracy and ease of any associated opioid taper. Twice daily dosing may have one observed dose and one carry, or be dispensed in blister packs for the week.

Missed Dosses During Microdosing Induction:

If one dose is missed during induction, consider repeating the previous day's dose and continue the schedule.

If two doses are missed, consider restarting the schedule.

Withdrawal Management:

Diphenhydramine, loperamide and acetaminophen/ibuprofen may be of benefit for any potential withdrawal.

Local Support for Clinicians:

If you require any assistance or just want to double check your plan, consider contacting the local Rapid Access Addiction Medicine Clinic.

Or consider using e-Consult (https://otnhub.ca/patient-care/) with Addiction Specialist Dr. Ken Lee

Or contact Dr. Ken Lee via email (ken.lee@sjhc.london.on.ca);

Or Medical Mentoring for Addictions and Pain (https://ocfp.on.ca/cpd/collaborative-networks/mmap)

Or consultation with Katie Dunham, NP (katie_dunham04@hotmail.com).

References:

Hämmig, R., Kemter, A., Strasser, J., von Bardeleben, U., Gugger, B., Walter, M., Dürsteler, K.M. and Vogel, M., 2016. Use of microdoses for induction of buprenorphine treatment with overlapping full opioid agonist use: the Bernese method. *Substance abuse and rehabilitation*, *7*, p.99.

Buprenorphine / Naloxone - The Bernese Method: A Primer for the Clinician. Prepared by the *PHS Health Care Columbia Street Community Clinic and St. Paul's/VGH/RAAC clinicians* (Vancouver, BC).

Dosing schedules adapted from the *Rapid Access Addictions Medicine Clinic / Clinicians London ON.*

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