Induction Basics: Tips from the Trenches

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- ***Virtual CO MAT Learning Forum***

  1st Thursday 12:30pm-1:30pm

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  2nd Tuesday 7:30am-8:30am

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  **same topic each month*

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2019 Dates

- Tuesday, September 24
- Tuesday, October 22
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Buprenorphine Induction

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Agenda

- Goals:
  - To understand the stage of Induction within the phases of MAT with Buprenorphine when used for Opioid Use Disorder.
  - Do a little “myth busting” – academia vs reality
  - Demonstrate a thorough understanding of dosing guidelines to start patients on buprenorphine treatment
  - Recognize, anticipate, and treat complications of buprenorphine use in your patients during induction

Buprenorphine Care: Previous Approaches Compared With New Findings and Recommendations

- **Previous Approach / New Findings and Recommendations**
- A medical setting is needed for induction / Home induction is also safe and effective
- Do not exceed 12 mg on first day or 16mg on 2nd day / Retention in treatment and amelioration of WD symptoms often demands higher doses in first few days
- Benzodiazepine and buprenorphine coprescription is toxic / Buprenorphine should not be withheld from patients taking benzodiazepines - caution
- Relapse indicates that the patient is unfit for buprenorphine-based treatment / Relapse indicates the need for additional support and resources rather than cessation of buprenorphine treatment
- Counseling or participation in a 12-step program is mandatory / Behavioral treatments and support are recommended and provided as desired by the patient
- Drug testing is a tool to discharge patients from buprenorphine treatment or compel more intensive settings / Drug testing is a tool to better support recovery and address relapse
- Use of other substances is a sign of treatment failure and grounds for dismissal from buprenorphine treatment / Buprenorphine treatment does not directly affect other substance use, and such use should be addressed in this context
- Buprenorphine is a short-term treatment, prescribed with tapered dosages or for weeks to months / Buprenorphine is prescribed as long as it continues to benefit the patient

- Sabate´ E, ed. Adherence to Long-Term Therapies: Evidence for Action. World Health Organization. 2003. Accessed at www.who.int /chp/knowledge/publications/adherence_report/en on 21 September 2018. National Institute on Drug Abuse. Principles of effective treatment. Principles of drug addiction treatment: a research-basedguide. 3rd ed. 2012. Accessed at www.drugabuse.gov/publications/principles-drug-addiction-treatment-research-based-guide-third -edition/principles-effective-treatment on 16 May 2017. Massachusetts Department of Public Health Bureau of Substance Abuse Services. Practice guidance: responding to relapse 2013. Accessed at www.mass.gov/eohhs/docs/dph/substance-abuse/care-principles/care-principles-guidance- responding-to-relapses.pdf on 16 May 2017.American Society of Addiction Medicine. National practice guideline for the use of medications in the treatment of addiction involving opioid use. 2015. Accessed at www.asam.org /quality-practice/guidelines- and-consensus-documents/npg/complete-guideline on 25 February 2018 44. Knopf A. No proof that buprenorphine treatment requires counseling. Alcoholism & Drug Abuse Weekly. 2017;29:3-5. American Society of Addiction Medicine. The ASAM appropriate use of drug testing in clinical addiction medicine. 2017. drug-testing on 15 May 2017. Substance Abuse and Mental Health Services Administration. TIP 63: Medications for Opioid Use Disorder. Rockville: Substanceuse and Mental Health Services Administration; 2018. https://annals.org/aim/article-abstract/2708164/next-stage-buprenorphine-care-opioid-use-disorder

Background

- Buprenorphine is a safe and effective treatment for opioid use disorder that offers patients a more widely available, accessible, convenient treatment option as compared to traditional opioid treatment programs
- The Drug Addiction Treatment Act (DATA) of 2000—an amendment to the Controlled Substances Act — allowed physicians who are not part of an OTP to prescribe buprenorphine with additional training and a waiver to the Controlled Substances Act.
- The Comprehensive Addiction and Recovery Act of 2016 (CARA) added nurse practitioners and physician assistants to the list of providers who can train to prescribe buprenorphine and become waivered.
- The law requires physicians to complete an 8-hour buprenorphine training conducted by an approved organization in order to prescribe it
- While buprenorphine is relatively safe, there are risks of overdose and death due to buprenorphine and there is a risk of diversion
  - Johnson R, Strain E, Amass L. Buprenorphine: how to use it right Drug Alcohol Depend. 2003;70(suppl 2):S59-S77. https://www.ncbi.nlm.nih.gov/pubmed/12738351.
  - SAMHSA/CSAT. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction 2004. https://www.ncbi.nlm.nih.gov/pubmed/22514846.
  - FSMB. Model Policy on DATA 2000 and Treatment of Opioid Addiction in the Medical Office FSMB Website. 2013. https://www.fsmb.org/Media/Default/PDF/FSMB/Advocacy/2013_model_policy_treatment_opioid_addiction.pdf.

The 3 Phases of Buprenorphine Treatment

- The 3 Phases of Buprenorphine Treatment Induction is the first of three phases of buprenorphine treatment. The three phases are the following:
- **1. Induction** 2. Stabilization 3. Maintenance
- During induction, buprenorphine is started.
- Goal of induction: To start buprenorphine treatment when the patient is in an appropriate state of withdrawal and to find your patient's ideal daily dose of buprenorphine
  - The patient should be in withdrawal as they take the first dose. This will avoid triggering severe withdrawal and also allow the titration of dose to an effective level for abstinence.
  - The ideal daily dose minimizes both side effects and drug craving.
    - file:///C:/Users/Front%20Range%20Clinic/Downloads/6-Induction%20(1).pdf

Phases of MAT

- For most of your patients with opioid use disorder:
  - The daily dose is 12 to 16 mg buprenorphine/day, but some patients are on 4 mg a day while others are on 24 mg – very individualized
  - The combination naloxone plus buprenorphine film or tablet may decrease abuse and diversion potential
  - Induction usually takes 2 to 4 days to complete
  - Stabilization - The stabilization period begins after induction and continues until your patient is no longer experiencing withdrawal symptoms or intense cravings.
    - This typically occurs at about 1-4 weeks following induction.
    - Side effects should be minimal or none.
    - Goal of Stabilization: Eliminate opioid use other than the partial agonist buprenorphine, as noted by patient reports and confirmed by urine drug testing During this phase
    - Recommend to monitor patients weekly, adjust dosing if needed, start psychosocial therapies along with medication assisted therapy
  - Maintenance - how long should a patient stay on Buprenorphine? Can be up to a year to lifetime
    - Goal of maintenance: Continue daily dose of buprenorphine to prevent relapse

MEDICAL EVALUATION BEFORE INDUCTION

- After determining that your patient is appropriate for OBOT, recommend completing the following before attempting induction
  - History & physical
  - Verification of patient list of medications
  - Screening for use of illicit drugs, misuse of prescription drugs, and alcohol use
  - Brief psychosocial assessment
  - Recommended Lab testing: Liver function tests, HIV and viral hepatitis serologies – patients with elevated liver function 3 to 5 times above normal should not be considered for buprenorphine – **but rx induction opportunity should rarely be withheld because don't have labs yet**
  - Urine toxicology – Screen for naturally occurring opioids (heroin is detected as morphine), synthetic and semisynthetic opioids (methadone, oxycodone), and other commonly abused drugs such as cocaine, amphetamines, and benzodiazepines
  - Pregnancy test

- Kraus M, Alford D, Kotz M, et al. Statement of the American Society of Addiction Medicine Consensus Panel on the Use of Buprenorphine in Office-Based Treatment of Opioid Addiction J Addict Med. 2011;5(4):254-263. https://www.asam.org/docs/advocacy/use-of-buprenorphinein-office-based-treatment-of-opioid-addiction.pdf. Accessed December 12, 2013

Prepare for Induction

- Patient Interaction Steps Before Induction
  - 1. Consent forms and treatment agreements
  - 2. Determine when and where to start induction (clinic / inpt. vs. home induction)
  - 3. Provide patient education about the induction, stabilization, and maintenance processes

PATIENT INSTRUCTION ON HOW TO TAKE BUPRENORPHINE - SUBLINGUAL

- Remind patients of key points relevant to successful induction covered the day of induction. These include:
  - The possibility of taking recommended comfort medications for residual withdrawal symptoms or requesting additional comfort medications as needed
  - Taking doses as directed; not taking a dose on their own unless this has been carefully explained and authorized by you
  - Reminders of the importance to abstain from the opioid they were using and other substances
  - Advise patients that each buprenorphine tablet or film will take some time to dissolve under their tongues (6-15 min is safe bet – different formulations)
  - While the medication is dissolving, they should not talk, drink, or swallow.
  - While the tablet is dissolving, they will salivate a lot, so they will need to tilt their heads forward to avoid swallowing the saliva.
  - Suggest rinsing their mouths or eating a mint prior to taking buprenorphine to help with the taste.
  - Your patients should not try to take more than two tablets or films at one time.

Induction

- Review patient education in detail before induction day and if done in office, repeat the key points on induction day. Follow a checklist to assure that all patient education points are reviewed with all of your patients.
- The following patient education points are important to emphasize before induction and again on induction day:
  - Be in withdrawal at induction: Advise your patients not to use opioids for the appropriate amount of time to be in withdrawal at induction in order to prevent precipitated withdrawal. This may be 12 to 24 hours for many opioids and potentially longer for long-acting opioids. Utilize COWS SCALE
  - Patients often know the timing from experiences with running out of the drug they take.

- Gunderson E. Models of Buprenorphine Induction PCSSMAT Train. 2014. http://www.pcssmat.org/wp-content/uploads/2015/02/Buprenorphine-Induction-OnlineModule.pdf. Accessed March 3, 2016.

INDUCTION CHECKLIST ASSESSMENT TO ENSURE APPROPRIATE USE

- Appropriate Diagnostic Criteria Verified - patient meets appropriate diagnostic criteria for opioid dependence
- Prescription Drug Monitoring - Opioids/CNS Depressants
  - Checked patient's prescription profile in the Prescription Drug Monitoring Program (PDMP), as appropriate
- Reviewed all medications (e.g., benzodiazepines, other opioids, CNS depressants) and illicit substances to assess for appropriateness of co-prescribing
- Risks and Side Effects Discussed the risks and side effects described in professional labeling and Medication Guide with patient including
  - potential for abuse and misuse / potential for fatal additive effects with benzodiazepines and other CNS depressants, including alcohol
    - https://www.btodrems.com/Portal/Content%20Library/Appropriate%20Use%20Checklist.pdf

INDUCTION CHECKLIST ASSESSMENT TO ENSURE APPROPRIATE USE

- Conditions of Safe Storage Explained or reviewed conditions of safe storage of medication
  - Reinforced importance of secure storage and keeping the medication out of the sight and reach of all others, especially children
- Limited Amount of Medication Prescribed limited amount of medication at first visit
  - enough to last until next visit
- Professional Counseling Provided or referred to professional counseling and support services
- Scheduled Next Visit Scheduled next visit at interval commensurate with patient stability
  - Weekly, or more frequent, visits are recommended for the first 4-8 weeks
    - https://www.btodrems.com/Portal/Content%20Library/Appropriate%20Use%20Checklist.pdf

SAFE MEDICATION STORAGE AND DISPOSAL

- A guideline by the AMA (2017) recommends that providers
  - Talk to their patients about opioid misuse, letting them know that 70% of misused opioids come from family and friends
  - Proper storage of their Buprenorphine is important - Individuals not tolerant of opioids can overdose on a relatively low dose
  - Risks to children should be emphasized; "Even very brief exposure to buprenorphine formulations can result in sedation, respiratory depression, cerebral anoxia, and death"
    - Following exposure of even a few seconds, children should receive immediate medical attention and observation for 24 hours
      - SAMHSA. Sublingual and Transmucosal Buprenorphine for Opioid Use Disorder: Review and Update Winter 2016. https://store.samhsa.gov/shin/content//SMA16-4938/SMA16-4938.pdf. .

WITHDRAWAL AT INDUCTION

- Patient education prior to induction includes describing the target state of withdrawal that is needed before taking the first dose of buprenorphine.
- The target level of withdrawal is mild to moderate, but if a person induces too soon and Precipitates Withdrawal - lower retention, less faith in rx as a good tool moving forward, unpleasant
- Immediately before induction, good practice to use an objective measure - like the Clinical Opioid Withdrawal Scale (COWS) – to evaluate withdrawal symptoms. An objective measure is important, for example, because patients may exaggerate their symptoms to avoid discomfort. When patients have a mild to moderate COWS score of 12 to 16, they are often ready for the first dose. Some providers go as low as 5 or as high as 24 on the COWS scale, but ideally > 10.
- Other withdrawal scales, such as the Subjective Opiate Withdrawal Scale (SOWS) and the Objective Opiate Withdrawal Scale (OOWS), may also be used.
- The COWS measures withdrawal symptoms with observations of the following:
  - Resting Pulse Rate / Sweating / Restlessness / Pupil Size / Bone or Joint Aches / Running Nose or Tearing
  - GI Upset / Tremors / Yawning / Anxiety or Irritability / Goose-flesh Skin
  - If doing in house induction - Be sure to look for objective signs of withdrawal to help confirm reports of subjective symptoms.

EFFECT OF OPIOID TYPE ON INDUCTION

- Determine the formulation your patient has been taking, short acting vs. long acting/extended release, because it can affect induction in several ways.
  - Note that some opioids, including fentanyl, oxycodone, and morphine are available in different formulations.
- Short acting opioids
  - Most patients who present for buprenorphine treatment are dependent on short-acting opioids. Heroin and many abused prescription narcotics are short acting opioids.
  - Abstinence timing for short-acting is 12-16 hours; for intermediate-acting is 17-24 hours
- Long acting opioids
  - Due to their longer action, patients on long-acting opioids must start abstaining from their medication for longer before their induction to evoke withdrawal.
  - Patients may need more "comfort" medicine (e.g., non-opioid analgesics, anxiolytic used sparingly and very carefully, antidiarrheal agents, antiemetics, antispasmodics) to help with remaining withdrawal after the first day until a stable daily dose is established.
  - Differences in the activity of these two types of opioids at the mu opioid receptors make precipitated withdrawal much more likely for long-acting opioids than for short-acting opioids, so treat induction for long-acting opioids with care.
  - Methadone is a long-acting opioid. Transferring from methadone requires some additional details and will be covered separately another time / Abstinence timing for methadone is 30-120 hours

Buprenorphine Induction Protocol Examples

- https://www.ncbi.nlm.nih.gov/books/NBK64246/
- Eduacte on COWS greater than 12-15 (caution with arbitrary times, i.e. waiting 12, 24, 36 hrs) / Must educate on precipitated WD potential / Must educate on proper administration
- 8mg films – ½ film every 2 hrs until out of WD, fall asleep, or 12 mg on first day (max 16 on 2nd day)
- 8mg films – ½ tid for day 1, then 1 film bid day 2 and after
- 8mg films - ¼ film every 90 minutes until out of WD, fall asleep, or 12 mg on first day (max 16 on 2nd day)
- 8mg films – 1 film in am, ½ film in afternoon, ½ - 1 film at night (caution with 16mg/1st day)

“In-House” / Office Induction

- Observed inductions Recommendations
  - Evaluate the level of withdrawal with the COWS.
  - Wait until a COWS score of 12-15 is observed
  - Instruct the patient how to take the medication, under the tongue, no talking and swallow when fully dissolved
  - Administer the first dose of 2-4 mg under observation in the office or inpatient setting.
  - Keep the patient in the office for at least an hour to determine the effect of the first dose, and then document the effect of the first doses in the medical record.
  - Depending on the amount and type of opioid use, the first day's dose may range from 2 to 16 mgs. Lower doses are required in patients with a lower level of physical dependence.
  - If withdrawal occurs after the patient leaves the office, request that the patient return for withdrawal assessment. This will be time-consuming, discouraging and not likely to happen. Avoid this complication by taking the time to assure moderate withdrawal discomfort prior to the first dose.
  - If the individual in the office is pressing for relief and the doctor is still not certain that he is in sufficient withdrawal then a low dose of 2 mg can be given and doses provided for later in the day.
  - May Remain in contact with the patient by telephone during the first day or two. even in the case of a successful induction, as doses may need to be adjusted prior to the next office visit.
  - Give sufficient medication only until the next visit, within 3-7 days

HOME INDUCTION

- Many clinicians now complete induction for a substantial portion of their buprenorphine patients at home.
- At-home buprenorphine induction is a safe and convenient option for some patients.
- Several studies found at home induction to be as effective as office-based induction. Patients who have been on buprenorphine previously may be comfortable with home re-induction.
    - Alford D, Labelle C, Richardson J, et al. Treating Homeless Opioid Dependent Patients with Buprenorphine in an Office-Based Setting Soc Gen Intern Med. 2007;22:171-176. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1824722/. Accessed October 9, 2013. Lee J, Grossman E, DiRocco D, et al. Home buprenorphine/naloxone induction in primary care J Gen Intern Med. 2009;24(2):226-232.
- Note, however, that in an expert consensus opinion, ASAM recommends home induction be offered only by a provider who is experienced with buprenorphine treatment
    - American Society of Addiction Medicine (ASAM). The ASAM National Practice Guideline For the Use of Medications in the Treatment of Addiction Involving Opioid Use June 2015. https:// www.asam.org/docs/default-source/practice-support/guidelines-and-consensus-docs/asamnational-practice-guideline-supplement.pdf. Accessed October 6, 2015.
- Follow-up visit is recommended; between 3 and 7 days

Home Inductions

- Inductions not directly observed by physician
  - file:///C:/Users/Front%20Range%20Clinic/Downloads/Buprenorphine_Home_Induction_James_Walsh_MD_10-05-2017.pdf
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2628995/
- It is expected that the physician will provide explicit instructions on how and when to start buprenorphine/naloxone with clear requirements for maintaining telephone contact if needed and follow up appt
- One recent observational cohort study found that participants with patient-centered home-based inductions had similar reductions in opioid use and greater reductions in any drug use than those with standard-of-care office-based inductions

- Alford DP, LaBelle CT, Richardson JM, O'Connell JJ, Hohl CA, Cheng DM, Samet JH. Treating homeless opioid dependent patients with buprenorphine in an office-based setting. J Gen Intern Med. 2007 Feb;22(2):171-6. Johnson RE, Strain E, Amass L: Buprenorphine: how to use it right: Drug and Alcohol Dependence, Volume 70, Issue 2, May 21,2003, pages S59-77 Lee JD. Grossman E. Di Rocco D. Gourevitch M. Home Buprenorphine/Naloxone Induction in Primary Care. J Gen Intern Med 24(2): 226-32 December 1,2008 Nielsen S, Hillhouse M, Weiss RD, Mooney L, Sharpe Potter J, Lee J, Gourevitch MN, Ling W. (2013) The relationship between primary opioid and buprenorphine-naloxone induction outcomes in a prescription opioid dependent sample. Am J Addict, in press. TIP 40. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction: Laura McNicholas. Consensus Panel ChairM.D. Ph.D.

Home Inductions

- Unobserved induction remains outside the TIP Guidelines, remains under investigation, and there is no evidence to support its use by inexperienced clinicians or with unstable patients
- Most Inductions done at Front Range Clinic are at home / how we got here……
- If a physician decides to pursue this strategy, it is advisable to use after patient education, in previously treated patients who are known to be reliable, or for patients who demonstrate clear documented knowledge of the risks of unobserved induction and are willing to come to the office in the event of problems.
- If a patient has expressed significant fear of withdrawal, he/she may not be a good candidate for home induction due to the potential for starting buprenorphine too early and causing a precipitated withdrawal.
- Patients should be provided with explicit written instructions regarding the subjective and objective assessment of opioid withdrawal, the timing and dose of buprenorphine, and phone numbers for assistance.
- The physician should maintain close telephone / office contact with the patient during the course of the unobserved induction and document these interactions
- The patient should be seen within 2- 7 days of starting buprenorphine.
- Many unobserved home inductions are likely performed without adverse consequences. However it is important to note that the majority of the research and clinical care guidelines on the use of buprenorphine are based upon observed induction.

Education Handout Example

Buprenorphine - Beginning Treatment

Day One: Before taking a buprenorphine tablet you want to feel lousy from your withdrawal symptoms. Very lousy. It should be at least 12 hours since you used heroin or pain pills (oxycontin, vicodin, etc.) and at least 24 hours since you used methadone.

Wait it out as long as you can. The worse you feel when you begin the medication, the better it will make you feel and the more satisfied you will be with the whole experience.

You should have a least 3 of the following feelings:

- twitching, tremors or shaking
- joint and bone aches
- bad chills or sweating
- anxious or irritable
- goose pimples

- very restless, can't sit still

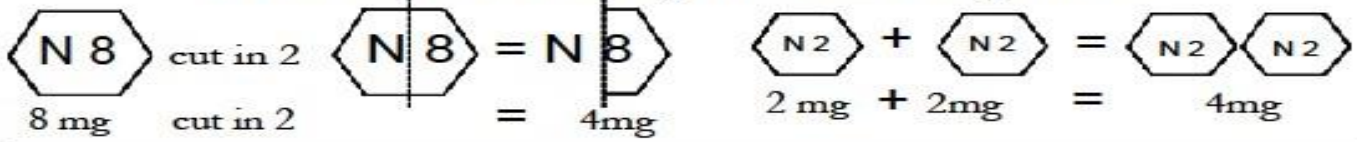
- heavy yawning

- enlarged pupils

- runny nose, tears in eyes

- stomach cramps, nausea, vomiting, or diarrhea

First Dose: 4 mg of Buprenorphine (Bup) under the tongue.
This is one half of an 8 mg tablet or two 2 mg tablets:



Put the tablet (one half tablet of 8mg tabs, or two tablets if 2mg tabs) under your tongue. Keep it there. If you swallow Bup tablets they will not work, the medicine is best absorbed through the thin skin on the bottom of your tongue.

It takes 20-45 minutes for the medication to be absorbed and have an effect. Feel better? Good, the medicine is working. Still feel lousy after 45 minutes? Don't worry, you just need more medication.

At 1-3 hours (60-180 minutes) after your first dose, see how you feel. If you feel fine after the first 4 mg, don't take any more, this may be all you need. If you have withdrawal feelings, take another 4 mg dose under your tongue.

Later in the day (6-12 hours after the first dose), see how you feel again. If you feel fine, don't take any more. If you have withdrawal feelings, take another 2 or 4 mg dose under your tongue.

Do not take more than 12 mg of Bup on the first day.

Most people feel better after the 4-12 mg on the first day. Still feel really bad, like a bad withdrawal? Call your doctor right away. You can call or page any time during the day if you are having difficulty.

Management of precipitated withdrawal

- If an unexpected precipitated withdrawal occurs during the early phases of the induction period, supportive treatment with or without medication will be necessary.
- Types of supportive treatment: support continuation of the Buprenorphine
  - Repeated 2 mg doses of buprenorphine every 1-2 hours
  - Clonidine 0.1 mg – 0.2 mg every 6- 8 hours (caution regarding hypotension)
  - Antiemetics for nausea
  - Non-steroidals for arthralgias and myalgias
  - More intensive Psychosocial support - Some patients may resist supportive treatment and return to full agonist opioid use as a method to self-medicate their precipitated withdrawal

Conclusions

- Find a Mentor
- Easier than it sounds
- We give much more dangerous medicines for less severe issues
- MAT has been a game changer in treating Opioid Use Disorder
- Close Follow up is key to retention and leads to a gentler induction and stabilization
- Lesley Brooks email; lbrooks.alliance@nocoha.org

Case Examples / Questions