PCSS Guidance

Topic: Buprenorphine Induction

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Guideline Coverage:
This topic is fully addressed in: **TIP 40. Clinical Guidelines for the Use of Buprenorphine in the Treatment of Opioid Addiction:** Laura McNicholas, Consensus Panel Chair M.D. Ph.D. U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES. Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment
http://www.kap.samhsa.gov/products/manuals/index.htm

Clinical Questions:
1. What can I do to insure a successful buprenorphine induction?
2. How can I determine if the patient is ready?
3. Do I have to do the induction in my office?
4. What do I do if the patient experiences a precipitated withdrawal?

Background:
Buprenorphine induction, performed at the right time, remains one of the most satisfying procedures a patient and his/her physician can experience. While there may be initial fears or concerns about precipitating withdrawal, if the patient presents with objective signs of withdrawal and doses are slowly titrated upwards, the patient will leave the office much happier than he/she has been in a long time. The physician will see immediate positive results -- a rare occurrence in clinical practice.

The goal of the induction phase is to transfer the patient from an abused opioid to a dose of buprenorphine which will provide relief from withdrawal and make induction the first step to assist the patient in discontinuing or markedly diminishing use of other opioids. Even during induction phase, the physician must emphasize the need for counseling to manage the behavioral issues related to opioid use and to address the social, medical and psychiatric problems associated with opioid dependence.

The Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment, Treatment Improvement Protocol Number 40 provides clear guidelines and protocols for buprenorphine induction. Trainings in the use of buprenorphine emphasize the need to observe and document mild-to-moderate withdrawal from the opioid of choice prior to giving the first dose of buprenorphine.

General Principles:
To help the patient prepare for buprenorphine induction, it is important to work closely with him/her during the screening process to determine how long it will take to attain mild to moderate opiate withdrawal symptoms. It is also important to learn how fearful the individual is of withdrawal, as this fear may complicate the induction process. It is helpful to ask the patient to recall what his or her first withdrawal symptoms are and advise that it is while experiencing these that he/she should be walking into the office. If the patient is not sure, it may be useful to ask the patient to experiment and hold off as long as possible from opiate use to determine and record the length of time it takes from last use until he/she absolutely needs relief from withdrawal. Many patients are surprised that they can go without their opioid for much longer than anticipated. This period will vary by patient based on a number of factors. These include the patient's level of tolerance and the dose of substance that they ingest. In general, this should take 12-16 hours for short-acting opioids (heroin, hydrocodone. oxycodone-immediate release), 17-24 for intermediate-acting opioids (oxycodone-sustained release), and 30-48 hours, or longer, for long-acting opioids such as methadone. The longer one can hold off on giving the first dose of buprenorphine, the easier the induction

will be, so waiting beyond these above time ranges is advisable. The Clinical Opiate Withdrawal Scale (COWS) is easy to use and can be inserted into the medical record to document withdrawal. The COWS is available at:
http://pcssmat.org/wp-site/wp-content/uploads/2013/10/2.15.12-CLINICAL-OPIATE-WITHDRAWAL-SCALE.pdf.

Some physicians may choose to use buprenorphine mono product for the first few days, especially in patients being transferred from methadone. This is generally not necessary, and can cause patient objections and complaints when buprenorphine/naloxone is started. In some cases buprenorphine induction and stabilization may last a week or more. The COWS can be used at each office visit during the first week to assess for continued withdrawal. To help assure that the patient comes in for their next visit, medication should be prescribed only until the next visit. During the first weeks the patient should be seen regularly (once to twice per week) and not given a month's supply after the first visit.

1. Observed inductions

Recommendations:
Level of Evidence: **High** - **Clinical trials**

1. Evaluate the level of withdrawal with the COWS.
2. Wait until a COWS score of 6-10 is observed (see Nielsen et al. 2013).
3. Instruct the patient how to take the medication, under the tongue, no talking and swallow when fully dissolved.
4. Administer the first dose of 2-4 mg under observation in the office or inpatient setting.
5. 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.
6. 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.
7. 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.
8. 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.
9. 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.
10. Give sufficient medication only until the next visit, within 3-4 days

2. Inductions not directly observed by physician: Home Inductions

Background:
Since the approval of buprenorphine for office practice, increasing numbers of patients have been treated with buprenorphine and physicians have become more comfortable using the medication. Although data are not currently available, we can safely speculate that a large number of individuals have started and stopped buprenorphine with and without physician input. One observational study reported on the successful unobserved induction in a cohort of 41 individuals. A larger observational study in 101 individuals has reported outcomes for home induction (Lee. et al. 2009). In this study, researchers provided significant patient education, including a detailed handout, that covered how and when to start buprenorphine/ naloxone. In this trial, home-based buprenorphine induction was feasible and appeared safe. If the physician has previously treated a returning patient, has conducted an observed induction with this patient, and trusts that he/she has a history of responsible use of his medication, the patient and physician may decide to re-start buprenorphine without direct physician observation. It is. however, possible that a physician may see a new patient in an office consultation, and decides, due to problematic office logistics, to prescribe buprenorphine for home induction. It is expected that the physician will provide explicit instructions on how and when to start buprenorphine/naloxone, alone with clear requirements for maintaining telephone contact. While home induction may be growing, we must emphasize that there is limited safety data on not maintaining the patient under direct observation during induction. 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 (Cunningham et al. 2011).

Recommendations:
Level of Evidence: **Low/Moderate - Further controlled studies needed uncontrolled case series, expert opinion**

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.

1. 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 burepnorphine too early and causing a precipitated withdrawal.
2. 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.
3. The physician should maintain close telephone contact with the patient during the course of the unobserved induction and document these interactions.
4. The patient should be seen within 2 days of starting buprenorphine.
5. All telephone calls and contacts should be documented in the physician's medical record. 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.

3. Management of precipitated withdrawal

Recommendations:
Level of Evidence: **Low-clinical experience**
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:**

1. Repeated 2 mg doses of buprenorphine every 1-2 hours
2. Clonidine 0.1 mg every 8 hours (caution regarding hypotension)
3. Antiemetics for nausea
4. Non-steroidals for arthralgias and myalgias

Some patients may resist supportive treatment and return to full agonist opioid use as a method to self-medicate their precipitated withdrawal.

References:

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. U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES. Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment http://www.kap.samhsa.gov/products/manuals/index.htm

Wesson D, Ling W The Clinical Opiate Withdrawal Scale (COWS) Journal of Psychoactive Drugs V 35 (2) April-June 2003 p 253-61

PCSS Guidances use the following levels of evidence*:
High = Further research is very unlikely to change our confidence in the estimate of effect
Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the
estimate.
Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to
change the estimate.
Very low = Any estimate of effect is very uncertain.

Type of evidence:
Randomised trial = **high**
Observational study = **low**
Any other evidence = **very low**

* Grading quality of evidence and strength of recommendations
British MedicalJoumal. **2004:328:1490-**