



PCSS Guidance

Topic: Transfer from Methadone to Buprenorphine

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Guideline Coverage:

TIP #40, Treatment Protocols: Patients dependent on long-acting opioids (pgs. 52-54)

Clinical Questions:

1. Which patients receiving methadone should be considered good candidates for transfer to buprenorphine?
2. How should I transition a patient from methadone to buprenorphine?

Background:

Patients receiving methadone may seek transfer to buprenorphine treatment. There are a large number of clinical scenarios that would cause a patient receiving methadone to seek induction onto buprenorphine. It is incumbent upon the physician to weigh the clinical issues carefully prior to agreeing to assist in the transfer. If a patient is stable on methadone, it is generally not advisable to agree to transfer to buprenorphine without a careful evaluation of the factors motivating the desire to transfer. However, if in the physician's medical judgment, buprenorphine treatment is appropriate and the patient is well-informed of the risks and benefits, transfer may be a reasonable option.

Among the potential benefits of transfer to buprenorphine include lower risk of overdose or sedation, lower risk of QT prolongation and ventricular arrhythmias, less severe withdrawal if a dose is missed, the capacity to obtain medication at a local pharmacy and the option of treatment in a doctor's office.

A number of factors might motivate a patient's request to transfer from methadone. These include; a desire to no longer receive his or her treatment from an opioid treatment program, perceived stigma associated with receiving methadone, concern about having methadone in the house, a desire to travel frequently for work, concern about having a large numbers of methadone bottles in one's possession when traveling, concern about losing methadone bottles without the possibility of replacement, less need for the required counseling/medication dispensing/urine collection in regulated opioid treatment programs, and/or living a long distance from a treatment program. In some cases, the development of QT prolongation or a ventricular tachycardia has necessitated that methadone-maintained patients be transferred to buprenorphine to resolve these adverse cardiac effects (Hanon et al. 2010). In addition, some methadone-maintained patients seek induction onto buprenorphine as a transition to antagonist treatment.

Alternatively, the patient may not be doing well on methadone, continuing to use opiates, stimulants (cocaine or methamphetamines) or benzodiazepines and wish to leave the structure of an opioid treatment program. Finally, it is possible that a patient may be buying methadone on the street and is now seeking legitimate treatment.

Patient Education:

When a patient is seeking transfer from methadone to buprenorphine, it is advisable to determine if the request is based on realistic expectations. It is important for the prospective patient to know that, in an effort to lower the patient's level of opioid physical dependence, it is advised that most patients taper their

dose of methadone prior to transferring to buprenorphine. Unfortunately, for some patients, the transfer process may be associated with a period of discomfort, both from tapering methadone and from starting buprenorphine. Individuals on moderate to high-doses of methadone, over 60-100 mg, may not be able to taper without discomfort and a risk of relapse. As the methadone dose is tapered, if the patient begins to experience withdrawal that interferes with their functioning or leads to relapse, he/she can be advised that transfer at a later time may be advisable.

Coordination:

If the buprenorphine practitioner is not associated with the patient's methadone clinic, it will be important to work with the methadone physician and treatment team to coordinate the taper and the timing of the transfer. One should work with the methadone clinic staff to insure continuity of care and a smooth transition, and know that if the transfer fails, that the patient may return to methadone treatment. In some cases, the methadone clinic staff may oppose the patient's transfer. The buprenorphine prescriber should be cautious about being perceived as forcing the transfer, yet encourage the patient to advocate on their own behalf if needed and appropriate.

Recommendations:

Level of evidence: **Low - observational studies and a limited number of randomized studies**

Transfer Process:

Studies of transfer from methadone to buprenorphine are limited (Levin, Fishman, et al 1997; Breen, Harris et al 2003; Law, FD et al. 1997; Clark, Lintzeris et al, CPDD 2006; Salsitz et al. 2010) but offer helpful insights into the transfer process on both inpatient and outpatient settings. It is advisable for the patient to arrange a few days off from work, to go through the transfer.

As with any induction, the patient must be essentially free of opioid full agonists before taking the first dose of buprenorphine. It is not necessary to start with buprenorphine mono then transfer to buprenorphine/naloxone a few days later. The minimal absorption of naloxone is not likely to cause a precipitated withdrawal if the patient is in adequate withdrawal when he or she receives the first dose of buprenorphine.

With the long-acting agonist methadone, the timing of the first dose of buprenorphine may be more difficult to determine than when starting someone who is using a short acting-opioid. Methadone undergoes significant storage in body tissue, especially the liver, so the length of time until withdrawal is experienced is dependent upon factors such as hepatic function, dose of methadone, duration of methadone, etc. While a patient may know how long it takes to go into withdrawal while using heroin, he or she may not have ever missed a methadone dose and so be unaware of the timing of withdrawal symptoms.

Higher methadone doses and a shorter timeframe between last methadone dose are clinical concerns in the methadone to buprenorphine transfer process. Generally it is advisable to taper a patient to 20-30 mg methadone, and to maintain that dose for a week or more prior to initiating buprenorphine induction. Buprenorphine may be started 36-72 hours after the last methadone dose, but it is advisable to observe for objective signs of withdrawal (Clinical Opiate Withdrawal Scale of 13-15) and not rely only on time lapsed since the last methadone dose. The key to a smooth transition is not the length of time since the last methadone dose, but rather how much objective withdrawal the patient is in when he or she presents for the first buprenorphine dose. Both the doctor and the patient may be surprised to learn that it may take much longer than 36 hours to begin methadone withdrawal. Clonidine, anxiolytics, including benzodiazepines, non-steroidal anti-inflammatory agents may be used judiciously to assist the withdrawal process, and continued during the induction as well. Withdrawal anxiety will be one of the more common concerns.

Alternatively a patient may taper to the dose at which he or she reports discomfort, and if withdrawal signs are observed by the practitioner, the patient can then be started on buprenorphine with results similar to a taper to 30 mg methadone. (Breen, Harris, Lintzeris 2003)

One study from Australia, conducted on an inpatient unit with doses of buprenorphine that are not available in the U.S., presented at the College on the Problems of Drug Dependence (2006 Clark, Lintzeris) evaluated 3 induction schedules-low (0.8 mg qid on day 1 increasing to 32 mg by day 5; standard (4 mg day 1, increasing to 32 mg at day 5) or high (32 mg day 1 and maintain through day 5). The authors conclude that the high- and low-dose induction proved more tolerable than the standard induction. In addition, it was advised to wait as long as possible after the last dose of methadone to perform the

buprenorphine induction.

It may not be possible to admit a patient on high-dose methadone (over 40 mg) to an inpatient service, nor to taper methadone to 30 mg. After obtaining a COWS score of 15, it appears advisable to start at 2 mg, and continue to dose until the patient is comfortable, dosing up to 32 mg on day 1. If withdrawal is precipitated, management with ancillary medications is advisable. Discomfort may persist for up to 96 hours.

Post-transfer Management*

It may be helpful to maintain contact with the patient and provide reassurance and telephone consultation up to 3 times daily for the first few days. This can be an intensive process for the physician as well as the patient, so it may be inadvisable to start the transfer late in the week. After 3-5 days, the patient will be stable and comfortable, but it may be necessary to add medications to assist with some of the discomforts associated with the withdrawal/transfer process. The patient may lose patience with the discomfort and want to return to methadone. The clinician will need to work with the patient either to accomplish this, or to encourage him or her to wait a bit longer, by provide additional therapeutic support and/or increasing ancillary medications.

References:

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Salsitz EA, Holden CC, Tross SS, Nugent A. Transitioning stable methadone maintenance patients to buprenorphine maintenance. *J Addict Med* 2010; 4(2): 88-92.

Hanon S, Seewald RM, Yang F, Schweitzer P, Rosman J. Ventricular arrhythmias in patients treated with methadone for opioid dependence. *J Interv Card Electrophysiol* 2010; 28(1): 19-22.

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:

Randomized trial = **high**

Observational study = **low**

Any other evidence = **very low**

* Grading quality of evidence and strength of recommendations

British Medical Journal. 2004;328:1490-