The Importance of Missed Doses in Methadone Maintenance Treatment (MMT)

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Methadone safety is a critical issue. The June 2013 issue of CPSO's Methadone News (1), discusses newly-released information from the Office of the Chief Coroner which highlights an increase in methadone-related deaths from 60 in 2009 to over 100 in 2011. A study published this year, also noted an increase in methadone related deaths in Ontario from 2006 to 2008, most of them accidental (2). The last issue of Pharmacy Connection published an analysis of medication incidents involving methadone processes. (3)

A major clinical issue affecting patient safety is the impact of missed methadone doses.

FIVE POINTS TO CONSIDER:

1. WHY THE CONCERN ABOUT PATIENTS WHO MISS DOSES?

Pharmacists, as part of their daily practice, motivate all their patients to take medication as prescribed. This takes on special significance with methadone maintenance treatment.

Tolerance to opioids, including methadone, is lost rapidly. If the regular dose of methadone is given after a period of missed doses, there is risk of overdose and death. Missed doses are an important indicator of patient instability and may be a symptom of a variety of problems, including relapse to alcohol or other drug use. (4)

The pharmacist is usually the first member of the interprofessional team to become aware that a patient has missed doses.

2. PHARMACISTS MUST BE ABLE TO EASILY TRACK MISSED DOSES.

All pharmacy dispensary staff need to be able to easily retrieve information to accurately determine if a patient has missed doses. Communication tools (e.g. patient calendars, other patient alerts, etc.) should be in place within each pharmacy to track patients' missed doses. The OCP Methadone Policy (5) requires that the time and date of methadone dose ingestion be recorded.

Even though patients may be in a hurry, and the pharmacy may be busy, pharmacists should always take the necessary time to check for missed doses and verify that it is safe to give the methadone dose. It's useful for pharmacists to advise patients at the outset of treatment, that time will be needed in the dispensary to medicate them safely.

3A. IN THE 1ST 2 WEEKS OF TREATMENT (EARLY STABILIZATION PHASE), THE DOSE SHOULD NOT BE INCREASED UNLESS THE PATIENT HAS BEEN ON THE SAME DOSE FOR 3 CONSECUTIVE DAYS (4).

Whether or not indicated on the prescription, it needs to be cancelled if 2 or more consecutive doses are missed. No dose increase should be implemented until the patient has been on the same dose for at least 3 consecutive days prior to the dose increase. This early stabilization phase is a critical period associated with high risk for overdose.

3B. FOR PATIENTS AT A STABLE DOSE, A CLINICALLY SIGNIFICANT LOSS OF TOLERANCE TO OPIOIDS MAY OCCUR WITHIN AS LITTLE AS 3 DAYS WITHOUT METHADONE (4)

Whether or not indicated on the prescription, it needs to be cancelled if 3 or more consecutive doses are missed.

Implementation of a dose increase on the day after a dose has been missed is not recommended. A consultation with the prescriber is best practice in this situation.

AFTER ANY PERIOD OF MISSED DOSES, THE METHADONE DOSE SHOULD BE ADJUSTED BY THE PRESCRIBER ACCORDING TO INFORMATION OUTLINED IN THE TABLE BELOW FROM THE CPSO MMT PROGRAM STANDARDS AND CLINICAL GUIDELINES (4).

TABLE 08: MANAGEMENT OF MISSED DOSES

PHASE OF TREATMENT	MISSED DOSES	ACTION	DOSE CHANGE
Early Stabilization (0-2) weeks	1 day missed	No dose increase	◦ Resume same dose. ◦ Do not increase dose until 3 consecutive days at the same dose.
	2 consecutive days missed	◦ Reassess patient in person ◦ Cancel remainder of prescription	◦ Restart at initial dose (10-30 mg) for at least 3 days ◦ Reassess after 3rd consecutive dose.
Late Stabilization/ Maintenance	1-2 days missed	◦ Provide usual prescribed dose if patient is not intoxicated. ◦ Assess patient in 1-2 weeks to determine clinical stability	◦ No change
Late Stabilization/ Maintenance	3 consecutive days missed	◦ Reassess patient in person ◦ Cancel remainder of prescription ◦ Reassess every 3-4 days if dose is increased daily	◦ Restarted at 50% of regular dose or decrease to 30 mg ◦ Then increase dose to no more than 10 mg daily for maximum of 3 days, then reassess by day 3-4. ◦ There after, dose increase of 10- 15 mg every 3 -5 days until 80 mg ◦ Then 10 mg every 5-7 days for dose increases above 80 mg
Late Stabilization/ Maintenance	4 or more consecutive days missed	◦ Re-assess patient in person ◦ Cancel remainder of prescription	◦ Restart at 30 mg or less ◦ Then increase dose no more than 10-15 mg every 3-4 days until 80 mg ◦ Then increase 10 mg every 5-7 days for dose increases above 80 mg.

4. ALL MISSED METHADONE DOSES NEED TO BE COMMUNICATED TO THE MMT PRESCRIBER IN A TIMELY FASHION

It is good practice for pharmacists who provide MMT services, to report missed doses to the prescriber, whether or not this is specified on the prescription. Prescribers who do not have timely access to this information may make clinical decisions which may jeopardize patient safety.

This has many benefits, including the opportunity for the team to intervene early when doses are beginning to be missed. Although typically a prescription for a patient on a stable dose is cancelled after 3 consecutive missed doses, some patients never miss 3 days in a row. Some miss 1 or 2 days very frequently –some may miss 3 to 4 doses per week and cannot be considered as being stable.

At times, even one missed dose has clinical significance, e.g., early in treatment (see above) or in someone with "full carries". For the latter, a missed dose can be a very meaningful indicator of loss of stability, especially if it happens frequently.

5. PHARMACISTS PROVIDING MMT WORK COLLABORATIVELY WITH THE PHYSICIAN TO PROVIDE METHADONE IN A SAFE MANNER TO THEIR PATIENTS.

Pharmacists receiving a prescription which is not in accordance with the CPSO MMT Standards and Guidelines are encouraged to follow up to discuss appropriate dosing with the MMT prescriber. This may need to include a discussion about whether the prescriber has had the opportunity to review missed dose information.

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4. CPSO Methadone Program, Methadone Maintenance Treatment, Program Standards and Clinical Guidelines, 4th Edition February 2011 http://www.cpso.on.ca/uploadedFiles/members/MMT-Guidelines.pdf
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