Making the Switch

Opioid Dependence in Pregnancy

Alice Ordean, MD, CCFP; and Meldon Kahan, MD, CCFP, FCFP, FRCPC

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How is opioid abuse recognized?

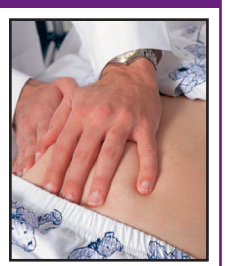
After a thorough assessment has been completed (Table 1), the diagnosis of opiate abuse versus dependence can be confirmed. According to the Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) criteria,[1] opiate dependence is a maladaptive pattern of substance use, leading to clinically significant impairment or distress, as manifested by three or more symptoms occurring at any time in the same 12-month period (Table 2).[2] Opiate abuse refers primarily to the consequences of opiate use.[2] For patients using opioids for chronic pain, the guidelines developed by the College of Physicians and Surgeons of Ontario should be followed for methadone management.

What is methadone maintenance therapy?

Methadone acts on mu-opioid receptors; therefore it relieves drug cravings and withdrawal symptoms. A methadone drink is dispensed in solution mixed with orange juice to prevent injection use. Methadone is a long-acting opioid with a half-life of 24 to 36 hours. It is well-absorbed through the gastrointestinal tract and, thus, provides a steady concentration in maternal blood.

Heroin, and other opioid abuse, have been associated with numerous adverse effects in pregnancy, such as intrauterine growth retardation and premature labour. These effects have been reduced with methadone use. There is no evidence of any significant toxic effects of methadone; however, neonatal withdrawal syndome may occur.

Susan's case



Susan, 24, presents complaining of nausea, vomiting, diarrhea, and myalgias. She admits to a five-year history of injection drug use and the use of oxycocet, which she obtained from the street. Her last menstrual period is unknown, as she has been amenorrheic for the past three years. She smokes 20 cigarettes daily, and also uses marijuana and cocaine on the weekends.

For a followup on Susan, go to page 66.

Table 1
Assessment for opioid dependence

Symptom, sign, or behaviour	Background
Withdrawal symptoms	Myalgias are most reliable; typically occur 4-6 hours after short-acting opioid use. Patients also report marked dysphoria, and a marked intensification of their underlying pain condition (withdrawal-mediated pain). Additional symptoms include nausea, abdominal cramps, diarrhea, and chills.
Rapid escalation of opioid dose	Tolerance develops slowly to the analgesic effects of opioids, but rapidly to its psychoactive effects.
Binge use	While scheduled dosing provides more consistent analgesia, binge dosing creates more of a euphoric effect. Corroboration from a family member might be needed to confirm binge use.
Dramatic or inconsistent response to pain rating scale	With each dose increase, the analgesia should last longer, and the pain intensity should decrease by 1-2 points on 10-point scale. Patients who use opioids for euphoria only will give implausible responses to this question.
Preference for short-acting opioids	This is a "soft" sign, but warrants further evaluation. Long-acting opioids, while better for analgesia, have a less euphoric effect because of slower entry into the CNS (unless at high doses, or if the tablet is crushed or injected).
Report of pleasurable psychoactive effect from opioid	The effect may be subtle (*e.g.*, a mild mood-levelling effect).
Drug-seeking behaviours	These include acquiring opioids from friends or from "the street," consistently running out early, and losing scripts. Sometimes corroboration from friend or family member is needed to confirm these behaviours.
Elevated GGT, MCV, or ALT	GGT and MCV are elevated by excessive alcohol use (usually at least four drinks/day). ALT elevation may indicate hepatitis C, which is common in injection drug users.
Non-compliance with prenatal care	The lives of opioid-dependent patients are often too chaotic to keep up with medical appointments.
Social and psychiatric problems	Common social problems include financial problems, unemployment or homelessness, substance-using or physically abusive partner, involvement with child protection agency, and criminal involvement. Psychiatric problems include depression, anxiety, psychosis, and suicide attempts. While none of these are diagnostic, they warrant careful assessment for substance abuse.
Poor weight gain, slow fetal growth	Heavy, daily opioid use, or use of other drugs (such as alcohol and cocaine), are associated with low birth weight due to fetal malnutrition and direct drug effects.
Current or past history of dependence on opioids, alcohol, benzodiazepines, cocaine, or other drugs	Patients who become dependent on prescription opioids often have a history of abuse or dependence on other drugs.
Urine drug screen positive for non-prescribed opioids, cocaine, benzodiazepines, or cannabis	Positive UDS results do not prove opioid dependence, but indicate the need for further assessment.
Concerns expressed by spouse or family	Close family members are the first to observe changes in personality and deterioration in functional status caused by opioid dependence.

CNS: Central nervous system
GGT: Gamma-glutamyl transferase
MCV: Mean cell volume
ALT: Alanine aminotransferase
UDS: Ultra-Doppler sonography

Can MMT be used in pregnancy?

The standard of care for opioid dependence is methadone maintenance treatment (MMT). However, there are no formal guidelines for the management of pregnant women on methadone.

Women who are on MMT prior to pregnancy can be maintained on their pre-pregnancy dose until the third trimester. Women using heroin or other opioids should be started on methadone. Methadone initiation during pregnancy requires hospital admission to determine the adequate dose. Dose may range from 20 mg to 200 mg or more.

Pregnant women on MMT need some adjustment in dosage during the third trimester of their pregnancy. Modifications in methadone dosing during pregnancy would require an increase of 5 mg to 10 mg for optimal control of withdrawal in opioid-dependent women.

If women on MMT experience withdrawal symptoms as pregnancy progresses, the oral dose must be elevated to maintain the same plasma level. Alternatively, if symptoms develop toward the end of the dosing interval, methadone must be administered in divided doses.

What is split dosing?

Studies have shown that twice-daily dosing of methadone is associated with more sustained plasma methadone levels, fewer withdrawal symptoms, and improved compliance with MMT regimens and urine toxicology. Women entering a methadone program later in pregnancy have decreased program compliance as manifested by higher levels of opiate and cocaine use.[3] In these cases, split dosing of methadone should be considered.

Single dosing also influences fetal behaviour, leading to decreased body movements and respiratory activity, and increased inactive period duration. As a result, split dosing is recommended for pregnant women when single dosing treatment produces maternal withdrawal symptoms or abnormal fetal activity patterns.

What is methadone detoxification?

Detoxification is not advised prior to week 14 of pregnancy because of potential risk for spontaneous abortion induction. Detoxification should not be performed after week 32 due to possible

Dr. Ordean is a medical director and staff member, Toronto Centre for Substance Use in Pregnancy, St. Joseph's Health Centre, Toronto, Ontario.

Dr. Kahan is an associate professor, family and community medicine, University of Toronto, and a staff member, St. Joseph's Health Centre, Toronto, Ontario.

A followup on Susan

Susan is found to be eight weeks pregnant. She is referred to an addiction medicine specialist, and is admitted for methadone initiation.

After one week, Susan is stabilized on methadone, 80 mg once daily in the morning. She also agrees to attend an in-patient treatment program. Susan also decides to remain abstinent from marijuana and cocaine. A Nicoderm® patch is started while Susan remains an in-patient.

Upon discharge, Susan is connected to both prenatal care and addiction medicine services.

withdrawal-induced fetal stress causing fetal death or preterm delivery. Therefore, if attempted, a tapered cessation of methadone is safest during the second trimester.

Various reports regarding the safety of antepartum opioid detoxification have been published. Women who were slowly detoxified during pregnancy were followed for the duration of their term.[3] Results indicated that 33% of women resumed antenatal opioid use, whereas 12% could not complete detoxification and opted for continued MMT. There was no evidence of fetal distress, fetal death, or delivery before 36 weeks.[4] Compared to women using street drugs, women with successful prepartal detoxification showed a longer course of pregnancy, normalized birth weight, head circumference, and respiratory status of neonates.[5] Based on these preliminary studies, no adverse outcomes were documented with methadone detoxification during pregnancy.

Table 2

Opioid dependence (DSM IV criteria)

Manifestation of ≥ 3 of the following within a 12-month period:

- Tolerance, as defined by either of the following:
  a) The need for markedly increased amounts of the substance to achieve intoxication or desired effect
  b) Markedly diminished effect with continued use of the same substance amount
- Withdrawal, as manifested by either of the following:
  a) The characteristic withdrawal syndrome
  b) The same substance is taken to relieve or avoid withdrawal symptoms
- Substance is taken in larger amounts or over a longer period than intended
- Persistent desire or unsuccessful efforts to cut down or control substance use
- Much time spent on activities necessary to obtain, use, or recover from effects of substance
- Important social, occupational, or recreational activities given up or reduced due to substance use
- Substance use is continued despite knowledge of having persistent/recurrent physical or psychological problems likely caused or exacerbated by substance

What should be done in each stage of pregnancy?

Antenatal stage

Women on MMT are considered to have high-risk pregnancies, and, therefore, these women require frequent monitoring during the last trimester. Recommended fetal monitoring includes non-stress tests weekly from 32 weeks, and biophysical profiles on a weekly basis from 36 weeks gestational age.

Intrapartum stage

During labour and delivery, women should receive their usual daily dose of methadone. However, methadone does not provide adequate pain relief from labour pains. Narcotics for pain management should be administered, as needed, in addition to methadone.

Postpartum stage

Postpartum women should continue with the usual daily dose of methadone. Shortly after delivery, women may require a dose reduction of 5 mg to 10 mg. Breastfeeding is not contraindicated in women on MMT, although it is contraindicated in the presence of active opioid use.

What is the GP's role?

The family physician:

- Is responsible for diagnosing a woman's pregnancy, and for discovering her opioid dependence.
- Should be a resource for opioid-dependent patients.
- May follow these women and infants in the long-term and, thus, should be aware of the possible short-term and long-term complications.

Methadone-exempt physicians should consult a specialist knowledgeable in methadone dosing in pregnancy to ensure adequate management of methadone-maintained pregnant women. Dx

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1. American Psychiatric Association: Diagnostic and Statistical Manual of Mental Disorders. Fourth Edition, 1994.
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5. Maas U, Kattner E, Weingart-Jesse B, et al: Infrequent neonatal opiate withdrawal following maternal methadone detoxification during pregnancy. Journal of Perinat Med 1990; 18(2):111-8.

Further references available—
contact *The Canadian Jounal of Diagnosis* at **diagnosis@sta.ca**.