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▶ Treating pregnant women dependent on opioids is not the same as treating pregnancy and opioid dependence: a knowledge synthesis for better treatment for women and neonates.

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Addiction: 2008, 103, p. 1429–1440.

New guidance on managing pregnant women dependent on heroin and allied drugs emphasises that maintenance prescribing is the core treatment but holistic, individualised care is essential; its warnings about the dangers of detoxification are not universally accepted.

Abstract Unlike alcohol, cocaine and benzodiazepines, opioid use during pregnancy does not cause birth defects or damage foetal cells. Nevertheless, fluctuating levels of opioids in the mother's blood may lead to withdrawal symptoms or overdose in the foetus. Expectant mothers who are actively misusing substances are also at high risk of violence, poor nutrition, and inadequate obstetric care. Those continuing to inject are at heightened risk of medical complications such as infectious diseases, endocarditis, abscesses and sexually transmitted diseases. Pregnant women are typically excluded from clinical trials of medications, limiting the adequacy of the evidence base for their treatment, and the response to these women is often complicated by psychological problems and their use of other substances. To develop recommendations to improve patient management from conception to postnatal follow-up it was decided to synthesise available research with the authors' extensive clinical experience.

Broadly their advice was that in the short and longer term, mother and child do best if multi-disciplinary treatment is initiated as soon as possible, maintenance prescribing is permitted, and there is regular monitoring. Opioid maintenance therapy is the recommended approach during pregnancy. Treatment must take account of the full clinical picture, particularly the frequent complications arising from psychiatric problems and the use of other substances. Babies born to mothers maintained on opioid medication frequently suffer withdrawal symptoms which may require treatment.

Selected further details below.

From whichever of the varied gateways women enter prenatal care, it is essential that the whole healthcare team from receptionist to physician offer assessment, triage, case coordination and referral services in a supportive, culturally sensitive, and non-judgemental environment. Case management is crucial to coordinate care of the women and their families. Ideally, a case conference and referral to appropriate services should be managed by one healthcare professional who oversees the multi-disciplinary team. This team should include an outreach worker to (if required) visit the woman at home.

A comprehensive examination of the multiple problems of this population and standardised documentation and evaluation of all prescribed therapies are very important. Special attention should be given to psychiatric problems, and appropriate treatment initiated. In particular, an opioid-maintained patient with untreated depression may relapse and could be difficult to stabilise. Treatment planning and management should include the woman's partner. If they too are opiate dependent, preferably the same treatment should be provided for both partners. Throughout the woman should be closely monitored, checking psychiatric condition, urinalysis for non-prescribed drugs, and uptake of nutritional supplements.

Health care providers need to be vigilant about drug interactions. For example, enzyme induction may affect levels of opioids in the blood, requiring dose adjustments to avoid destabilising the mother-to-be or her foetus. Screening (and if tests are negative, later rescreening) for HIV and hepatitis infections are recommended to minimise dangers for the foetus.

Detoxification or maintenance using opioid medications should follow established procedures. Detoxification should be undertaken only if the patient is stable and clearly committed to abstinence, and not after 32 weeks of pregnancy. The recommended procedure is a slow, medically supervised taper of a substitute opiate-type medication. Well-controlled medication is safer than continued use of street drugs and improves antenatal monitoring in cases otherwise difficult to engage. To avoid additional use of non-prescribed drugs, doses should be set individually rather than reduced to a set minimum. The 'gold standard' for treating pregnant opioid-dependent women is methadone, though buprenorphine seems equally effective and safe. Opioid antagonist treatment is contraindicated because of the risk to the foetus.

If required, detoxification from benzodiazepines should be gradual to reduce risk of pre-term labour or psychiatric symptoms. Psychosocial therapies are the first line option for mild depression; medication and inpatient care are indicated for major depression with suicide risk. If antidepressants are used, the case management team should be briefed to look for drug interactions, and neonates should be monitored carefully for complications after birth. Obstetricians should be alerted that the patient's maintenance opioid is insufficient for perinatal analgesia, and advised to select opioid analgesics with a view to avoiding precipitated withdrawal.

Mothers should stay in hospital for 5–8 days while the baby is monitored for signs of the neonatal abstinence syndrome. Even if they are maintained on methadone or buprenorphine, those who want to breastfeed should be encouraged to do so, provided they are seronegative for HIV, not misusing other substances, and there are no other contraindications. Where relapse is likely, opioid maintenance should continue after delivery. If the mother is on opioid medication, weaning the baby must be carried out under medical care to avoid withdrawal. It is important to discuss contraception to avoid early unplanned consecutive pregnancy. Finally, the team should focus on stabilising the home environment for the developing child and arranging health service assistance.

FINDINGS Around the same time as this team from the Medical University of Vienna published their recommendations, so too did a largely US team which included one of the authors from Vienna. Their more restricted focus was on the appropriate use of methadone and buprenorphine in the treatment of opioid-dependent pregnant women prior to and during delivery, based partly on their experiences in the first large-scale,

controlled comparative trial of these medications with opioid-dependent pregnant women. Usefully they provide a North American perspective and much more detailed guidance on the opioid maintenance therapies which the featured review sees as the primary response. Guidelines are offered on induction, stabilisation, preventing and managing relapse, medication during labour and delivery, pain relief, breastfeeding, the interactions of methadone and buprenorphine with other medications, and managing psychiatric conditions. Throughout the emphasis is on a flexible, non-judgemental stance.

British addiction treatment guidelines agree with the reviewers that substitute prescribing is preferable to continued illicit substance use. By facilitating engagement with health services, this treatment also enables health and social needs to be identified and advice given to improve outcomes. Because of the risk of spontaneous abortion or foetal distress, detoxification is generally considered advisable only in the second trimester in the form of a gradual taper, and the guidelines emphasise that maintenance prescribing should be strongly encouraged if illicit drug use continues or recurs. Though buprenorphine is not licensed for this purpose, the guidelines say that pregnant women who are stable on buprenorphine may best continue on this medication rather than switch to methadone. The authors agree with the reviewers that research shows buprenorphine is as safe as methadone. Breastfeeding is encouraged even if the mother is on methadone (though the dose should be kept as low as possible) and/or continues to use drugs, except for cocaine or a very high dose of benzodiazepines.

The review's and the guidelines' clear preference for maintenance prescribing and, if undertaken, only gradual detoxification and then only in certain phases of pregnancy, is not universally accepted. Though early case reports of foetal distress associated with withdrawal raised alarm, more recent studies with larger samples have not found adverse foetal consequences. Experienced British clinicians argue (1 2 3) that the theoretical risk to the foetus is not borne out in practice. Their advice is that as long as the woman can tolerate withdrawal and is willing to try it, and it is unlikely to lead to uncontrolled substance use, withdrawal can occur at any speed and at any stage of pregnancy. In particular, experience in Britain suggests that given these conditions, there is no reason to discourage women who want to withdraw late in pregnancy in order to avoid their baby suffering withdrawal symptoms. Relevant research is summarised below.

Early concerns were eased when in 1998 a study systematically monitored foetuses for signs of distress during the mothers' detoxification. There were none, and neither were there any miscarriages, despite the fact that some of the mothers were prescribed only clonidine to relieve their withdrawal symptoms and half were detoxified during the last third of pregnancy. One of the few studies to test different regimens took advantage of the switch at a specialist US centre for drug dependent pregnant women from a three-day to a seven-day methadone detoxification; in both phases, other women were prescribed methadone on a maintenance basis. The briefer detoxifications were conducted throughout pregnancy yet none of the 140 women suffered a miscarriage. There was one such event among 70 patients withdrawn more slowly and three among the 116 methadone-maintained patients. Measures of neonatal welfare revealed no adverse effects of withdrawal, or of brief withdrawal in particular. Where maintenance prescribing did win out was in retaining patients at the centre both for the births and for their addiction treatments, with possible longer term benefits. Even when conducted in the last third of pregnancy, hospital records in London revealed no elevated risk of miscarriage due to methadone detoxification, though in this study the reduction schedule was spread over three weeks in an inpatient unit. Similarly in Birmingham, a specialist mother and baby unit in a hospital addiction treatment centre noted no particular problems among the many opiate-dependent women who opted to slowly withdraw during pregnancy. In Glasgow, even abrupt 'cold turkey' withdrawal has not been found to cause elevated rates

of miscarriage.

The recommendation for particularly slow withdrawal of benzodiazepines was based on the desire to avoid precipitating premature labour or exacerbating psychiatric symptoms. Set against this is the need to minimise foetal exposure to drugs which can cause birth defects and withdrawal symptoms in the neonate. Experience at a specialist unit in Glasgow is that inpatients can safely be withdrawn over about a week depending on the woman's ability to cope, though outpatient withdrawal may best be slower.

Opinions in Britain differ too on whether, as the featured review suggests, continued non-medical substance use means breastfeeding is inadvisable. Instead it has been argued that the vulnerability of the baby is such that breastfeeding should be encouraged, regardless of the type of drugs being used by the woman or their dosage (1 2). A major benefit is that by delivering small amounts of the drugs to which the foetus had been exposed during pregnancy, breastfeeding substantially reduces the risk of withdrawal symptoms.

A review for the Cochrane collaboration tentatively supported both opiates and phenobarbitone for the treatment of withdrawal in babies born to opiate-dependent mothers.

Thanks for their comments on this entry in draft to Mary Hepburn of the Glasgow Royal Maternity Hospital. Commentators bear no responsibility for the text including the interpretations and any remaining errors.

Last revised 18 August 2009

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