

Treating pain during pregnancy

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ABSTRACT

QUESTION My pregnant patients frequently ask about taking pain medications, sometimes for chronic conditions. What is known about the safety of using analgesics in therapeutic doses for acute or chronic pain during pregnancy?

ANSWER Commonly prescribed pain medications appear to be relatively safe to use during pregnancy. None of the analgesics has been found to increase the risk of major malformations, although caution should be used when prescribing them in late pregnancy.

RÉSUMÉ

QUESTION Mes patientes enceintes me posent souvent des questions sur l'usage des médicaments antidouleur, parfois pour des problèmes chroniques. Que sait-on des risques de l'utilisation d'analgésiques à doses thérapeutiques pour la douleur aiguë ou chronique durant la grossesse?

RÉPONSE Les médicaments contre la douleur couramment prescrits semblent relativement sécuritaires durant la grossesse. Aucun analgésique ne s'est encore avéré causer des risques accrus de malformations importantes, mais il vaut mieux être prudent lorsqu'on les prescrit en fin de grossesse.

Because of fear about use of drugs during pregnancy, some pregnant women would rather suffer than treat their pain. Consequently, it is possible that such women are at risk of undertreatment, or no treatment, for painful conditions. Chronic, severe pain that is ineffectively treated is associated with hypertension, anxiety, and depression—none of which is conducive to a healthy pregnancy.^{1,2}

Analgesics

There are 2 main categories of commonly used analgesics: systemic nonopioid analgesics (eg, acetaminophen, aspirin, nonsteroidal anti-inflammatory drugs [NSAIDs]) and opioid analgesics (eg, morphine, codeine, meperidine).

Acetaminophen. Acetaminophen, a nonsalicylate similar to aspirin in analgesic potency, has demonstrated efficacy and apparent safety at all stages of pregnancy in standard therapeutic doses. Its established safety profile for use has been demonstrated in a recent study of thousands of pregnant women, without increasing risks of congenital anomalies or other adverse pregnancy outcomes.³

Aspirin. Aspirin has potential risks, as it inhibits platelet function and can contribute to maternal and fetal bleeding.⁴ Although aspirin has not been associated with other congenital anomalies, it has been associated with increased risk of vascular disruption, in particular gastroschisis, although this remains unproven.⁵ Overall, large trials demonstrate low-dose aspirin's relative safety and generally positive effects on reproductive outcomes.⁶

Nonsteroidal anti-inflammatory drugs. Nonsalicylate NSAIDs are known to relieve pain through peripheral

inhibition of cyclooxygenase and hence inhibition of prostaglandin synthetase. They include drugs such as ibuprofen, naproxen, and ketorolac. To date, studies have failed to show consistent evidence of increased teratogenic effects in either humans or animals following therapeutic doses during the first trimester. However, even short-term use of NSAIDs in late pregnancy is associated with a substantial increase in the risk of premature ductal closure.⁷

Opioids. These agents include morphine-like agonists (eg, morphine, hydromorphone, hydrocodone, codeine, and oxycodone), meperidine-like agonists, and synthetic opioid analogues (eg, tramadol). Reproductive studies describing the use of narcotic analgesics in human pregnancies are limited, and there are no prospective, comparative studies. However, these drugs have been used in therapeutic doses by pregnant women for many years and have not been linked to elevated risk of major or minor malformations. The Collaborative Perinatal Project identified 448 morphine exposures at various stages of pregnancy and found no evidence of increased teratogenic effects.⁸ The Michigan Medicaid study reported 332 newborns exposed to hydrocodone, 281 exposed to oxycodone, and 7640 exposed to codeine, all in the first trimester. The rate of major birth defects was 4.6% for the oxycodone-exposed group; 4.9% for the codeine-exposed group (consistent with the general population risk); and 7.2% for the hydrocodone group, which could have been influenced by confounding factors (ie, maternal disease severity and concurrent drug use).⁹ A case-control study of 141 infants with cardiac malformations did not report an association with the use of codeine in the first trimester of pregnancy.¹⁰ Neonatal withdrawal has been

observed with use of codeine in late pregnancy, even with therapeutic doses in nonaddicted mothers.^{11,12}

Fentanyl patch

Several forms of fentanyl, including the patch, have been on the market for many years without reports of serious adverse effects, and it is considered effective for all types of chronic pain, including cancer and non-cancer pain.¹³ There is little information on its use in pregnancy, with only 2 case reports in the literature. In one, a high-dose fentanyl patch (ie, 125 µg/h) was used throughout pregnancy, and the newborn infant manifested mild withdrawal symptoms at 24 to 72 hours after birth.¹⁴ In the other, which was from the Motherisk team, a lower dose of the fentanyl patch was used with no apparent adverse effects.¹⁵

Conclusion

Medications used in therapeutic doses for acute and chronic pain appear to be relatively safe in pregnancy. To minimize fetal risk, initiate drug interventions at the lowest effective dose, especially in late pregnancy, and select analgesics only after careful review of a woman's medical or medication history. Women should avoid using NSAIDs after 32 weeks' gestation, owing to the possibility of antiplatelet or prolonged bleeding effects. Opioids should also be used with caution, especially in higher doses in late pregnancy when the infant should be observed carefully in the neonatal period for any signs of withdrawal (neonatal abstinence syndrome). ❁

Competing interests

None declared

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MOTHERISK

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Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at 416 813-7562; they will be addressed in future **Motherisk Updates**.

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