

MOTHERISK UPDATE

Which drugs are contraindicated during breastfeeding?

Practice guidelines

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abstract

QUESTION Many breastfeeding mothers are concerned about taking medications that might affect their babies. Are there any guidelines on which drugs are safe?

ANSWER Only a few drugs pose a clinically significant risk to breastfed babies. In general, antineoplastics, drugs of abuse, some anticonvulsants, ergot alkaloids, and radiopharmaceuticals should not be taken, and levels of amiodarone, cyclosporine, and lithium should be monitored.

résumé

QUESTION Plusieurs femmes qui allaitent sont inquiètes de prendre des médicaments qui pourraient être néfastes pour leur nourrisson. Existe-t-il des lignes directrices au sujet de l'innocuité des médicaments dans un tel cas?

RÉPONSE Il n'existe que quelques médicaments qui posent des risques cliniquement significatifs chez les enfants nourris au sein. En général, les cytotoxiques, les stupéfiants, certains anticonvulsifs, les alcaloïdes de l'ergot et les agents radiopharmaceutiques sont à proscrire et les concentrations d'amiodarone, de cyclosporine et de lithium devraient être surveillées.

There is no question that breastfeeding is best for providing all necessary nutrients to infants for the first 6 months of life. Use of medication while lactating, however, complicates the decision to breastfeed. Fortunately, most drugs are compatible with breastfeeding and do not pose a risk to infants. While certain drugs are traditionally contraindicated for nursing mothers, many of these restrictions are based on theoretical concerns only rather than on evidence or clinical observation. In this update we discuss these contraindicated drugs in light of the practice guidelines of the Motherisk Program.

Drugs generally considered incompatible with breastfeeding

Antineoplastics. Anti-cancer drugs used in chemotherapy are generally

considered incompatible with breastfeeding because even very low levels of exposure can prove toxic. If breastfeeding is continued, drug levels in milk and infant plasma, and infant hematologic parameters, must be monitored. Much research is still required in this area, and only limited information is available on some of these agents.

Nine cases of infants breastfed by mothers taking azathioprine (25 to 100 mg/d) appear in the current literature. All infants thrived and had no reported adverse effects.¹⁻³

Breastfeeding might be possible provided infants are closely monitored. Two cases of cisplatin excretion into milk indicated that patients excrete this drug in varying amounts into milk.^{4,5} The outcome of infants exposed to cisplatin through milk are not known. Adverse events, including neutropenia⁶ and leukopenia,⁷ are reported in two infants whose mothers used cyclophosphamide while breastfeeding.

In a single report, low levels of doxorubicin were found in breast milk⁵ although infant outcome was

not known. Methotrexate is excreted into milk in minimal amounts,⁸ and single weekly doses, such as those used for rheumatoid arthritis maintenance therapy, are unlikely to pose substantial risk to babies. Use of methotrexate for cancer chemotherapy is not

Do you have questions about the safety 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. Published Motherisk Updates are available on the College of Family Physicians of Canada website (www.cfpc.ca). Some articles are published in *The Motherisk Newsletter* and Motherisk website (www.motherisk.org) also.

Motherisk questions are prepared by the **Motherisk Team** at the Hospital for Sick Children in Toronto. **Ms Moretti, Ms Lee, and Dr Ito** are members of the Motherisk Team.

recommended for lactating mothers because we do not know how it affects suckling infants.

Anticonvulsants. Only a few anti-convulsants are excreted in high concentrations in breast milk. Phenobarbital, ethosuximide, and primidone might result in substantial infant exposure.⁹ Close monitoring of infants exposed to phenobarbital is warranted because their blood levels might approach therapeutic levels. Sedation has been observed, and there is potential for withdrawal upon weaning.

Drugs of abuse. Generally speaking, all drugs of abuse should be avoided by nursing women. In addition to unnecessary infant exposure, mothers' ability to care for their babies while under the influence of such substances becomes an issue.

Heavy alcohol consumption was associated with pseudo-Cushing's syndrome in a 4-month-old baby.¹⁰ Ethanol was also associated with decreased milk intake by infants,¹¹ altered sleep patterns,¹² and slower neurologic development.¹³ If mothers drink alcohol, breastfeeding could be withheld temporarily (about 2 to 3 hours per drink) to ensure alcohol levels in the milk have diminished.

Amphetamines have been detected in infant urine following maternal therapy.¹⁴ Nothing is known about maternal amphetamine abuse and its potential effect on nursing infants. Cocaine is excreted into breast milk in notable concentrations; infants might accumulate the drug because they are less able than adults to metabolize it. Cocaine has been detected in infant serum, and toxicity has been reported in some infants.^{15,16} Infants exposed to marijuana through breast milk showed a delay in motor development at 1 year

old.¹⁷ Heroin toxicity has been observed in infants breastfed by mothers abusing heroin, but at therapeutic doses, most opioids, such as morphine, meperidine, methadone, and codeine, are excreted into milk in only minimal amounts^{18,19} and are compatible with breastfeeding. Phencyclidine, a potent hallucinogen, has been found in breast milk several weeks after maternal dosing.²⁰ This is attributable to its long half-life; nursing mothers should be encouraged to avoid it.

Ergot alkaloids. Ergotamine therapy during lactation was associated with ergotism (vomiting, diarrhea, occasional convulsions) in a 1934 publication²¹ but not in a more recent study.²² We do not know how much of this drug is excreted into milk. Until more data are available, other therapies should be considered for patients requiring headache treatment. Ergonovine is known to reduce serum prolactin levels and might inhibit lactation.²³

Methylergonovine, used for uterine involution, does not influence milk supply. It is not found in clinically significant amounts in breast milk²⁴ and can be used safely. Bromocriptine effectively suppresses lactation and, hence, is not compatible with breastfeeding. Also, it could be hazardous to mothers.²⁵

Others. Although the drugs listed below can be used with caution, safer alternative drugs should be considered first if they exist for the particular indication.

Amiodarone excretion into milk varies from person to person. Nursing infants might ingest up to 50% of the maternal dose (on the basis of weight).²⁶ Also, amiodarone contains large amounts of iodine that could affect infants' thyroid glands. If the decision is made to

continue therapy while breastfeeding, the drug should be monitored in breast milk and infant plasma, as should the infant's thyroid function.

Cyclosporine has been used successfully for several lactating mothers.^{3,27,28} Breast-milk levels ranged widely, although infant plasma levels, when detectable, were low. Because cyclosporine is a potent immunosuppressant, however, it should be continued during breastfeeding only if levels in milk and infant serum are monitored.

Similar to amiodarone, lithium concentrations vary greatly in milk. Although amiodarone is contraindicated by many authorities because infant plasma levels can reach one third to half of maternal levels,²⁹ the only reported adverse event could not rule out possible effects of in utero exposure.³⁰ Lithium is an excellent example of a drug that requires monitoring and case-by-case assessment so nursing mothers can be successfully treated.

Cigarette smoking should be minimized while breastfeeding. While second-hand smoke exposure is probably the greater concern, smoking might decrease milk supply and nicotine can be measured in breast milk.³¹

Estrogens found in oral contraceptives have been shown to reduce milk production in some mothers. On the other hand, progestin-only contraceptives are unlikely to affect milk supply. If estrogen-containing contraceptives are to be used, therapy should commence only after maternal milk supply is well established, about 6 weeks after delivery.³² Infant weight gain can be monitored to ensure sufficient milk is produced.

Radiopharmaceuticals might require temporary cessation of breastfeeding because radioactivity sometimes persists in breast milk for

hours or even days. Before procedures, breast milk may be pumped and frozen to be given to infants while breastfeeding is temporarily withheld. In addition, mothers should pump and discard their breast milk while the isotope is still present in order to preserve milk production. Recommendations to patients should be individualized to particular agents. Consultation with a nuclear medicine physician and reading the various literature resources available^{33,34} will assist in determining the length of breastfeeding interruption.

Conclusion

As experience with lactating women's use of drugs increases, we are realizing that only a few drugs pose a clinically significant risk to infants. This is reassuring for both patients and health care providers faced with the risk-benefit dilemma. To make an informed decision, it is critical that appropriate and the most up-to-date sources be consulted when making recommendations to patients requiring drug therapy while lactating. Contact the Motherisk Program for specific information. ❖

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