Methadone exposure during lactation

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ABSTRACT

QUESTION One of my patients is currently using methadone for maintenance of opioid dependence. She wants to breastfeed. Is breastfeeding safe for her infant?

ANSWER The exposure of infants to methadone through their mothers' breast milk is minimal. Women using methadone for treatment of opioid dependence should not be discouraged from breastfeeding. The benefits of breastfeeding largely outweigh any theoretical minimal risks.

RÉSUMÉ

QUESTION Une de mes patientes prend présentement de la méthadone pour la prise en charge de la dépendance aux opiacés. Elle souhaite allaiter son bébé. Est-ce sans danger pour le nourrisson?

RÉPONSE L'exposition des nourrissons à la méthadone dans le lait maternel est minime. Il ne faudrait pas décourager l'allaitement par les femmes qui prennent de la méthadone pour le traitement d'une dépendance aux opiacés. Les avantages de l'allaitement compensent largement les risques théoriques minimes.

Methadone is an opioid analgesic used in the treatment of narcotic dependency.[1] Its usefulness is related to its long serum half-life, slow onset of action, and lower rate of euphoric effects compared with other opiates. The long elimination half-life of methadone allows gradual decrease in dose. Methadone has been shown to reduce the illicit use of opiates and associated crime,[2] and maintenance programs have been shown to reduce the risk of acquiring sexually transmitted infections, including HIV.[2] Methadone can be prescribed and legally dispensed for outpatient use, facilitating management of these patients.[3]

Although chemically different from morphine, methadone has similar clinical analgesic effects. It is well absorbed from the gastrointestinal tract, and therapeutic concentrations are evident in plasma 30 minutes after ingestion.[4] Peak plasma concentrations are reached 2 to 4 hours after therapeutic doses. Typically, the elimination half-life ranges between 10 and 18 hours.[5] Metabolism and clearance rate of methadone are highly variable. Liver metabolism by cytochrome P450 isoenzymes CYP 3A4 and CYP 2B6[6] is the main route of elimination.

There is sparse published evidence of exposure of infants to methadone through breast milk. Concentrations of methadone in breast milk are low and remain stable over time.[7-9] Methadone doses of 25 to 180 mg/d produce concentrations in milk ranging from 27 to 260 ng/mL, leading to an average daily methadone ingestion of 0.05 mg (based on an infant's estimated milk intake of approximately 500 mL/d).[10] This ingested amount would be equal, in a 5-kg baby, to the ingestion of less than 1% of the maternal weight–adjusted dose (typical adult dose is 40 to 180 mg/d).[10] Even after correcting for slower clearance rate of methadone in neonates as compared with adults, the relative infant dose would not exceed 5% of the maternal weight–adjusted dose.

Methadone offers important therapeutic benefits to the population of opiate-dependent pregnant women that far outweigh the theoretical small risk posed by minimal excretion of the drug into breast milk.[11] For 18 years, the American Academy of Pediatrics recommended that methadone was only compatible with breastfeeding at maternal doses below 20 mg/d[12]; in September 2001, based on the evidence available, the American Academy of Pediatrics lifted this dose restriction. The new statement considers methadone compatible with breastfeeding at any maternal dose.[13]

Infants born to women using methadone for maintenance can develop neonatal abstinence syndrome (NAS), attributable to methadone withdrawal in the first days of life.[14] The commonly observed delay between delivery and appearance of NAS, compared with other opiates, can be explained by the fact that in the early neonatal period the concentrations of methadone in the infant and in the mother are similar. Thereafter, methadone levels decline slowly in the infant according to its long elimination half-life. Malpas et al have suggested that breastfeeding might be beneficial in the treatment of NAS,[15,16] although it is not clear if this is because of the beneficial effects of breastfeeding itself or because of the low concentrations of methadone present in breast milk mitigating the withdrawal.

Conclusion

The very low concentrations of methadone in beast milk reported in the literature support the recommendation to

not discourage breastfeeding women from using methadone treatment, regardless of the dose.

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Competing interests

None declared

MOTHERISK

Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. **Drs Glatstein, Garcia-Bournissen,** and **Finkelstein** are members and **Dr Koren** is Director of the Motherisk Program. **Dr Koren** is supported by the Research Leadership for Better Pharmacotherapy during Pregnancy and Lactation. He holds the Ivey Chair in Molecular Toxicology in the Department of Medicine at the University of Western Ontario in London.

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