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Mirtazapine

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CASRN: 61337-67-5

Drug Levels and Effects

Summary of Use during Lactation

Limited information indicates that maternal doses of up to 120 mg daily produce low levels in milk and would not be expected to cause any adverse effects in breastfed infants, especially if the infant is older than 2 months. If mirtazapine is required by the mother, it is not a reason to discontinue breastfeeding. Exclusively breastfed infants should be monitored for behavioral side effects and adequate growth if this drug is used during lactation.

Drug Levels

Maternal Levels. A woman who was 14 weeks postpartum was started on mirtazapine 30 mg daily. After reaching steady-state (therapy duration not specified), a foremilk level of 7 mcg/L and hindmilk level of 18 mcg/L were measured 22 hours after the previous dose. The next day, a foremilk level of 28 mcg/L and hindmilk level of 34 mcg/L were measured 15 hours after the previous dose.[1]

Eight nursing mothers who averaged 6.3 months postpartum (range 1.5 to 13 months) were taking mirtazapine in an average dosage of 495 mcg/kg daily (30 to 120 mg daily). Mothers provided milk samples every 3 to 4 hours for 24 hours after their daily dose. Using these data, the authors estimated that an exclusively breastfed infant would receive an average of 8 mcg/kg daily of mirtazapine and 3 mcg/kg daily of desmethylmirtazapine. These values averaged 1.5% (range 0.6 to 2.8%) of the maternal weight-adjusted dosage for mirtazapine and 0.4% (range 0.1 to 0.7%) for desmethylmirtazapine. Mirtazapine's concentration in hindmilk averaged 2.3 times the foremilk concentration in 4 of the subjects tested. Desmethylmirtazapine's concentration in hindmilk was only 10% higher than in foremilk.[2]

A woman who was 6 weeks postpartum was taking mirtazapine 22.5 mg daily at night. Foremilk and hind milk levels of mirtazapine were 130 and 145 mcg/L, respectively, at 4 hours after the dose and 61 and 90 mcg/L at 10 hours after the dose.[3]

A woman took mirtazapine 15 to 30 mg daily throughout the second and third trimesters of pregnancy and during breastfeeding. Her postpartum dose was 15 mg daily or 224 mcg/kg daily. In the morning, 12 hours after the dose, the concentration of mirtazapine in her foremilk was 15 mcg/L.[4]

Infant Levels. A woman who was 14 weeks postpartum was started on mirtazapine 30 mg daily. The patient breastfed her 6.8 kg infant 6 times daily during therapy and an infant plasma level of 0.2 mcg/L was found 15 hours after a dose, which was 0.8% of the maternal serum concentration.[1]

Eight infants who averaged 6.3 months of age (range 1.5 to 13 months) were breastfed (extent not stated) by mothers taking mirtazapine in an average dosage of 495 mcg/kg daily for 6 to 129 days. No mirtazapine or desmethylmirtazapine were detected (<1 mcg/L) in the serum of 4 infants whose mothers' doses ranged from 309 to 517 mcg/kg daily. Three others had unquantifiably low levels in milk. One infant, whose mother was taking 1967 mcg/kg daily, had 1.5 mcg/L of mirtazapine in serum, but an unquantifiable serum level of the metabolite.[2]

A 6-week-old infant was exclusively breastfed by a mother who was taking mirtazapine 22.5 mg at daily at night. Mirtazapine was undetectable in the infant's plasma 12.5 hours after the dose.[3]

A 2-month-old infant was breastfed (extent not stated) by a mother who was taking mirtazapine 15 mg (224 mcg/kg) daily at night. The infant's serum mirtazapine concentration at 2 hours after the first morning feeding (14 hours after the previous maternal dose) was 10 mcg/L compared to a maternal serum mirtazapine concentration of 27 mcg/L at 12 hours after the previous dose.[4]

Effects in Breastfed Infants

A 14-week old infant was breastfed 6 times daily during maternal treatment with mirtazapine 30 mg daily. After 6 weeks of therapy, the infant was judged to have normal psychomotor development and no adverse effects, including sedation or abnormal weight gain.[1]

Eight infants who averaged 6.3 months of age (range 1.5 to 13 months) were breastfed by mothers taking mirtazapine in an average dosage of 495 mcg/kg daily for 6 to 129 days. At the time they were studied, the average Denver developmental age in the 7 infants studied averaged 101% of normal. No adverse effects were noted in any of the infants.[2]

A 6-week-old infant was exclusively breastfed by a mother who was taking mirtazapine 22.5 mg at daily at night beginning at 4 weeks postpartum. Weekly follow-ups of the infant found no sedation or alterations in weight gain, although the infant's weight was consistently below the 25th percentile even before mirtazapine was begun.[3]

A 2-month-old infant was breastfed (extent not stated) by a mother taking 15 mg of mirtazapine daily during pregnancy and lactation. The mother stated that the infant had a higher birthweight and gained weight more rapidly than her previous 3 infants, and that unlike her other infants, this infant slept through the night at this age. The authors noted that these observations cannot necessarily be attributed to mirtazapine.[4]

In a case series of 55 women who took mirtazapine during pregnancy and postpartum, 24 of their 56 infants were exclusively breastfed and 20 were partially breastfed. Of the infants who were exposed in utero during the third trimester, those who were breastfed either partially or exclusively had a lower frequency of poor neonatal adaptation syndrome than those who were exclusively formula fed. No sleeping or feeding problems were seen in any of the infants.[5]

A case series reported 8 women who received paroxetine 20 mg and mirtazapine 15 mg daily for various psychiatric disorders. The women breastfed (extent not stated) their infants who averaged 4.3 weeks of age. Follow-up of the infants after 3 to 6 weeks when mirtazapine was discontinued found one infant who experienced restlessness after 5 days of therapy according to the mother. Discontinuation of mirtazapine had no effect, but the symptoms disappeared when paroxetine was discontinued. No other infants had other adverse effects observed.[6]

Effects on Lactation and Breastmilk

Gynecomastia, hyperprolactinemia and galactorrhea were reported in an 89-year-old man after 21 months of therapy with mirtazapine 30 mg daily. Symptoms regressed 1 month after discontinuation and prolactin levels normalized.[7]

A 28-year-old female inpatient developed galactorrhea, mastodynia, fatigue, and extended subcutaneous edema of the trunk and extremities 4 weeks after adjusting her mirtazapine dose to 30 mg daily. At this time her morning serum prolactin level was not elevated; however, 12 days later, morning serum prolactin was 32.1 mcg/L (normal range 4.79-23.3 mcg/L). Serum prolactin normalized, and edema and galactorrhea remitted within 1 week after discontinuing mirtazapine and starting escitalopram. Pituitary tumor was ruled out. Mirtazapine was probably the cause of the patient's symptoms.[8] The clinical relevance of these findings in nursing mothers is not known. The prolactin level in a mother with established lactation may not affect her ability to breastfeed.

An observational study looked at outcomes of 2859 women who took an antidepressant during the 2 years prior to pregnancy. Compared to women who did not take an antidepressant during pregnancy, mothers who took an antidepressant during all 3 trimesters of pregnancy were 37% less likely to be breastfeeding upon hospital discharge. Mothers who took an antidepressant only during the third trimester were 75% less likely to be breastfeeding at discharge. Those who took an antidepressant only during the first and second trimesters did not have a reduced likelihood of breastfeeding at discharge.[9] The antidepressants used by the mothers were not specified.

A retrospective cohort study of hospital electronic medical records from 2001 to 2008 compared women who had been dispensed an antidepressant during late gestation (n = 575; mirtazapine n = 12) to those who had a psychiatric illness but did not receive an antidepressant (n = 1552) and mothers who did not have a psychiatric diagnosis (n = 30,535). Women who received an antidepressant were 37% less likely to be breastfeeding at discharge than women without a psychiatric diagnosis, but no less likely to be breastfeeding than untreated mothers with a psychiatric diagnosis.[10]

Alternate Drugs to Consider

Nortriptyline, Paroxetine, Sertraline

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Substance Identification

Substance Name

Mirtazapine

CAS Registry Number

61337-67-5

Drug Class

Breast Feeding

Lactation

Antidepressive Agents

Antidepressive Agents, Second-Generation