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Olanzapine

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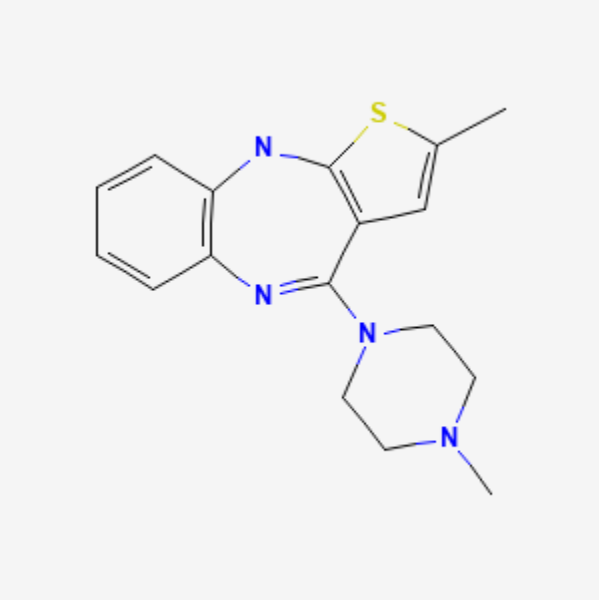

Drug Levels and Effects

Summary of Use during Lactation

Maternal doses of olanzapine up to 20 mg daily produce low levels in milk and undetectable levels in the serum of breastfed infants. In most cases, short-term side effects have not been reported, but sedation has occurred. Limited long-term follow-up of infants exposed to olanzapine indicates that infants generally developed normally. A safety scoring system finds olanzapine to be acceptable during breastfeeding.[1] Systematic reviews of second-generation antipsychotics concluded that olanzapine seems to be a first-line agent during breastfeeding.[2-4]Monitor the infant for drowsiness and developmental milestones, especially if other antipsychotics are used concurrently.

Drug Levels

Maternal Levels. A nursing mother was started on olanzapine 20 mg daily on day 9 postpartum. Numerous milk olanzapine levels collected over the subsequent 8 days ranged from 7.6 to 27.5 mcg/L. The authors calculated that an exclusively breastfed infant would receive 0.011 mg/kg daily or about 4% of the maternal weight-adjusted dosage.[5]

Nine paired serum and milk levels were obtained from 5 mothers who were taking olanzapine. In 2 women taking 10 mg daily, one had a milk level of 21 mcg/L 11 hours after the dose and the other had a milk level of 16 mcg/L 23 hours after the dose. In 3 women taking 2.5 mg daily, milk levels ranged from <1 to 8 mcg/L 11 to 12 hours after the dose, 4 mcg/L at 16 hours after the dose and 2 to 7 mcg/L at 22 to 23 hours after the dose. Using these data, an exclusively breastfed infant would consume an average of 1.6% of the maternal weight-adjusted dosage (range 0 to 2.66%).[6]

Seven mother-infant pairs were studied during maternal olanzapine use. The mean dose was 7.5 mg daily (range 5 to 20 mg daily) and serum levels were at steady state. A median peak serum level of 16 mcg/L occurred 5.2 hours (range 0.7 to 13.2 hours) after the dose. The median infant dosage was 1.12% (range 0.22 to 1.19%) of the maternal weight-adjusted dosage in 6 of the mothers and 1.13% in the seventh.[7]

A woman was taking olanzapine 5 mg orally 3 times daily, amounting to 270 mcg/kg daily. After 11 days on olanzapine, a milk sample was taken just before nursing (time after dose not reported). The concentration of olanzapine was 12 ng per gram of breastmilk. The authors estimated that was 0.3% of the maternal weight-adjusted dosage.[8]

A woman was started on oral olanzapine 5 mg in the morning and 10 mg in the evening daily 3 months postpartum. Two weeks later, the milk concentration (time after dose not stated) was 5 mcg/L. Over a period of 5 months, milk olanzapine concentrations decreased somewhat with time and a reduction in dosage to a concentration of 3 mcg/L with a dosage of 10 mg daily.[9]

One woman was taking olanzapine 15 mg daily at 11 pm. She avoided breastfeeding from 11 pm to 7 am each day. Breastmilk samples were collected at 4 am, 8 am and 11 pm daily for 26 days. The average olanzapine concentrations in her breastmilk were 15.8 mcg/L, at 4 am, 15.1 mcg/L at 8 am, and 7.8 mcg/L at 11 pm. The authors estimated that her infant would receive a maximum of 0.78 mg/kg daily and a median dosage of 0.21 mg/kg daily, which would translate to 0.47% and 0.13% of the weight-adjusted maternal dosage, respectively.[10]

Three women were taking olanzapine while breastfeeding. Dosages and corresponding milk olanzapine levels were as follows: 0.18 mg/kg daily with a level of 30 mcg/L on day 11 postpartum; 0.26 mg/kg daily with a milk level of 35 mcg/L on day 10 postpartum; and 0.26 mg/kg daily with 8 milk levels were taken at 2 weeks postpartum. Levels ranged from 11 mcg/L at 23 hours after a dose to 21 mcg/L at 9 hours after the following dose.[11]

A woman with bipolar disorder who delivered twins and was taking sodium valproate was started on olanzapine 15 mg and quetiapine 200 mg at 11 pm daily after 20 days postpartum. She withheld breastfeeding during the night and discarded milk pumped at 7 am. She then breastfed her infants until 11 pm. After 7 days of therapy, milk samples were obtained at 4 am, 8 am and 11 pm for 27 of the next 45 days. The median average daily olanzapine milk concentration was 10.2 mcg/L. Median milk concentrations were 12.7 mcg/L at 4 am, 10 mg/L at 8 am and 7.6 mg/L at 11 pm. The authors calculated that if the infants had been fully breastfed, they would have received a daily dosage of 1.29 mcg/kg or 0.74% of the maternal weight-adjusted dosage. By withholding nursing during the night, the infants' quetiapine dosage was reduced by 36% compared to the dose they would have received if they had been breastfed around the clock.[12]

A woman with psychosis began treatment with long-acting olanzapine injection during pregnancy. The drug was continued postpartum at a dose of 210 mg every 2 weeks. Four milk samples were obtained at 6 weeks and 7 months postpartum. Milk olanzapine levels ranged from 14.4 to 23.7 mcg/L (46 to 76 nmol/L), which correspond to 0.7 to 1% of the maternal weight-adjusted dosage.[13]

Infant Levels. At birth, the infant of one mother who was taking olanzapine 10 mg daily orally had an olanzapine serum level of about one-third that of the mother. The infant was breastfed (extent not stated) and had undetectable serum levels (<2 mcg/L) at 2 and 6 weeks of age.[14]

In one 4-month-old infant, olanzapine was undetectable (<1 mcg/L) in serum 15 hours after the mother's dose (dose unstated).[6]

Olanzapine was undetectable (<0.1 to 0.5 mcg/L) in the serum of 5 breastfed infants with an average age 2.4 months (range 0.1 to 4.3 months) whose mothers were taking a mean dose of 7.5 mg daily (range 2.5 to 20 mg daily).[7]

A 5-month-old infant was breastfed (extent not stated) by a mother who had been taking olanzapine 5 mg 3 times daily for 11 days. After an overnight fast, the infant's serum olanzapine concentration was <5 mcg/L.[8]

The mother of a 3 month-old breastfed (extent not stated) infant was started on olanzapine 5 mg in the morning and 10 mg in the evening daily by mouth. Two weeks later, the infant's olanzapine serum concentration (time stated) was 11 mcg/L. At 5 and 6 months of age, the serum concentration was 0 and 0.8 mcg/L, respectively. At 7 months of age, the serum concentration was 1.3 mcg/L with a maternal dose of 10 mg daily. At 8 months of age, the serum concentration was 0.02 mcg/L with a maternal dose of 5 mg daily. At 9 months of age, the serum concentration was 0.8 mcg/L with a maternal dose of 10 mg daily. Whether the variability in infant concentrations was caused by variable sampling times or by changes in maternal dosage, infant metabolism, or extent of breastfeeding cannot be determined from the report.[9]

In three case reports, mothers taking dosages of olanzapine of 0.17, 0.18 and 0.26 mg/kg daily breastfed their newborn infants (extent: one full, one partial and the other not clearly stated). All infants had undetectable (<5 mcg/L) olanzapine plasma levels after 4 days to 2 weeks of nursing.[11]

A woman with psychosis began treatment with long-acting olanzapine injection during pregnancy. The drug was continued postpartum at a dose of 210 mg every 2 weeks. Four plasma samples were obtained at 6 weeks and 7 months postpartum. Serum concentrations in breastfed (extent not stated) were less than the limit of detection in all samples (<2.3 mcg/L [<7.5 nmol/L]).[13]

Effects in Breastfed Infants

The manufacturer compiled reports of adverse effects reported in breastfed infants whose mothers were taking olanzapine.[15] Reports were compiled from spontaneous reports from physicians and mothers, clinical trials and published papers. Details of the exposures were not provided. Some of the infants reported appear to be the same as those reported in references [6-9] below. Overall, 102 breastfed infants were identified whose mothers were taking olanzapine. Of these, 62 reported dosages taken during pregnancy that averaged 7.4 mg daily by mouth. The duration of exposure to olanzapine was reported in 30 nursing mothers with a median of 30 days and mean of 74 days. Of the infants exposed to olanzapine via breastmilk, 15.6% reportedly experienced adverse effects, primarily somnolence, irritability, tremor and insomnia.[15] It appears that at least some of the adverse effects may have been a result of prenatal exposure to olanzapine.

One infant was breastfed for 2 months during maternal intake of olanzapine 10 mg daily. No abnormalities were found in growth and development during 11 months of follow-up.[14]

Five infants aged 3 weeks to 6 months were breastfed during maternal olanzapine 2.5 to 10 mg daily. No adverse health or developmental effects were noted during the observation period of 5 days to 8 weeks.[6]

One infant was breastfed from birth during maternal use of olanzapine 5 mg daily orally. The infant was healthy at 6 months of age.[16]

Six breastfed infants with an average age 2.4 months (range 0.1 to 4.3 months) whose mothers were taking olanzapine 2.5 to 20 mg daily had no adverse effects reported by their mothers or found on detailed medical testing. Development was deemed normal in 4 infants after extensive testing. A fifth had a somewhat decreased intellectual development on testing, but her mother had also taken clonazepam, droperidol, sertraline, thioridazine and valproic acid while breastfeeding. Four of the infants' body weight were maintained, one fell slightly and one dropped from the 97th percentile at birth to the 50th percentile upon later measurement. One of the infants reportedly had drowsiness during maternal intake of 10 mg daily, but it was not evident 3 weeks after reducing the dose to 5 mg daily. The drowsiness was possibly related to olanzapine in milk.[7]

A 5-month-old infant was breastfed (extent not stated) by a mother who took olanzapine 5 mg 3 times daily for 13 days, then 5 mg twice daily. The infant was followed up after 2 months. The infant gained weight steadily and no jaundice or motor function impairment were noted.[8]

A case-control study compared mothers who took olanzapine 2.5 to 10 mg daily during breastfeeding to those who took the drug and did not breastfeed, and nursing mothers who took acetaminophen which is thought to be safe during breastfeeding. Mothers filled out a questionnaire regarding adverse infant outcomes at 1 to 2 years postpartum. The percentage of adverse outcomes in the breastfed infants who were exposed to olanzapine in breastmilk (n = 22) was greater (14%), than those in the nonbreastfed (n = 15; 7%) and breastfed infants without olanzapine exposure (n = 51; 8%), but these differences were not statistically significant. Long-term adverse outcomes seen included speech delay in 1 infant, motor development delay in 1 infant and failure to gain weight in 2 infants (one infant experienced 2 adverse outcomes).[17]

A woman took 10 mg of olanzapine (0.18 mg/kg) daily during pregnancy and postpartum She began breastfeeding at 7 days postpartum and continued to breastfeed for an unstated period. At 12 weeks of age, a pediatric examination was normal. Another woman who took olanzapine throughout pregnancy was taking olanzapine 0.17 mg/kg daily while she partially breastfed her infant. The total duration of breastfeeding was not stated, but the infant had developed normally at 20 months of age.[11]

A woman with bipolar disorder who delivered twins and was taking sodium valproate in a therapeutic dosage was started on olanzapine 15 mg and quetiapine 200 mg at 11 pm daily after 20 days postpartum. She withheld breastfeeding during the night and discarded milk pumped at 7 am. She then breastfed her infants until 11 pm. The mother continued feeding the infants on this schedule for 15 months. Monthly follow-up of the infants indicated normal growth and neither the pediatricians nor the parents noted any adverse effects in the infants.[12]

A woman with bipolar disorder was treated with olanzapine 10 mg and haloperidol 5 mg daily at the end of pregnancy and during breastfeeding (extent not stated). Follow-up of the breastfed infant for 11 months found no adverse effects and normal development of the infant.[18]

A woman with bipolar disorder was treated with olanzapine 10 mg and haloperidol 5 mg daily at the end of pregnancy and during breastfeeding (extent not stated). Follow-up of the breastfed infant for 11 months found no adverse effects and normal development of the infant.[16] The same author reported 5 infants who were breastfed (extent not stated) during postpartum maternal treatment for bipolar disorder. Olanzapine dosages were 5 or 10 mg daily. None of the mothers reported any adverse effects in their infants.[19]

A prospective cohort study of infants breastfed by mothers in an inpatient mother-baby psychiatric unit in India followed 8 infants who were exposed to olanzapine in breastmilk; most received partial supplementation. Two

infants developed sedation, although the mother of one was also taking chlorpromazine. One infant whose mother was taking olanzapine 20 mg, ranitidine 300 mg, and cough syrup developed constipation. Infants were followed for 1 to 3 months after discharge. Two infants had delayed weight development, although one had also been exposed to phenytoin in utero. One infant who weighed 2 kg at birth had delay in height and a third infant had motor and mental delay.[20]

Patients enlisted in the National Pregnancy Registry for Atypical Antipsychotics who were taking a second-generation antipsychotic drug while breastfeeding (n = 576) were compared to control breastfeeding patients who were not treated with a second-generation antipsychotic (n = 818). Of the patients who were taking a second-generation antipsychotic drug, 60.4% were on more than one psychotropic. A review of the pediatric medical records, no adverse effects were noted among infants exposed or not exposed to second-generation antipsychotic monotherapy or to polytherapy.[21] The number of women taking olanzapine was not reported.

Effects on Lactation and Breastmilk

Unlike the phenothiazines, olanzapine has a minimal effect on serum prolactin levels.[22-26] However, olanzapine-induced hyperprolactinemia and galactorrhea have been reported.[27] One patient was also taking venlafaxine and interferon beta-1b which can increase serum prolactin; however, galactorrhea began only after olanzapine was started.[28]

In 2 studies, some patients who were taking a conventional antipsychotic agent or risperidone had their medication changed to olanzapine. Previously elevated prolactin levels normalized and galactorrhea diminished or stopped.[26,29]

The maternal prolactin level in a mother with established lactation may not affect her ability to breastfeed.

Patients enlisted in the National Pregnancy Registry for Atypical Antipsychotics who were taking a second-generation antipsychotic drug while breastfeeding (n = 576) were compared to control breastfeeding patients who had primarily diagnoses of major depressive disorder and anxiety disorders, most often treated with SSRI or SNRI antidepressants, but not with a second-generation antipsychotic (n = 818). Among women on a second-generation antipsychotic, 60.4% were on more than one psychotropic compared with 24.4% among women in the control group. Of the women on a second-generation antipsychotic, 59.3% reported "ever breastfeeding" compared to 88.2% of women in the control group. At 3 months postpartum, 23% of women on a second-generation antipsychotic were exclusively breastfeeding compared to 47% of women in the control group.[21] The number of women taking olanzapine was not reported.

Alternate Drugs to Consider

(Antipsychotic) Haloperidol, Quetiapine, Risperidone; (Bipolar Disorder) Divalproex, Lithium, Quetiapine, Risperidone, Valproic Acid

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Substance Identification

Substance Name

Olanzapine

CAS Registry Number

132539-06-1

Drug Class

Breast Feeding

Lactation

Milk, Human

Antipsychotic Agents