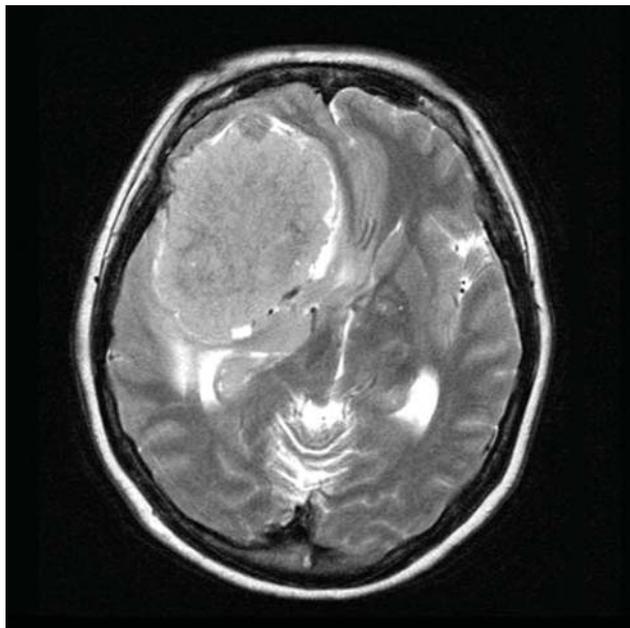


FIGURE 1. T2-Weighted Axial MRI Scan Demonstrating a Large Meningioma With Surrounding Parenchyma Edema Resulting in Ventricular Compression and Midline Shift



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Excretion of Methylphenidate in Breast Milk

TO THE EDITOR: It is unknown to which extent methylphenidate is transferred to breast milk. We therefore present a case of a lactating woman from whom the levels of methylphenidate were measured in serum and breast milk.

A 31-year-old woman with narcolepsy had used methylphenidate regularly before she became pregnant. During pregnancy and the first months postpartum, the drug was discontinued. When she started work after her maternity leave, the need for methylphenidate reappeared. She had a desire to continue breast-feeding, and the question was thus raised as to whether the use of methylphenidate was compatible with breast feeding.

Her daily methylphenidate dose was 5 mg in the morning and 10 mg at noon, using immediate-release tablets (Ritalin, Novartis, Switzerland). After giving written informed consent, maternal serum and breast milk were obtained at the following five points of time: immediately before the morning dose at 8 a.m., just before the dose at noon, and 4, 8, and 21 hours after the dose at noon. The first three samples were from foremilk, whereas the two last samples were from hindmilk. Concentrations of methylphenidate were analyzed by liquid chromatography-

mass spectrometry with a limit of quantification of 0.3 ng/ml.

The maternal serum concentrations in the five samples were <0.3, 2.3, 3.8, 1.7, and <0.3 ng/ml, respectively. The corresponding milk concentrations were <0.3, 2.4, 5.9, 1.4, and <0.3 ng/ml.

Accordingly, in the three samples with measurable concentrations, the mean milk/serum concentration ratio was 1.1, with variations from 0.8 to 1.6. Assuming that the mean milk concentration of 2.5 ng/ml $([0.3+2.4+5.9+1.4] \text{ ng/ml}:4)$ represents the true mean during a 24-hour period and that the infant ingested a standard volume of 150 ml of milk per kilogram of body weight per day, the daily infant dose can be estimated to 0.38 μg per kilogram of body weight. Compared with the maternal daily dose of 234 mg per kilogram of body weight, the infant dose was only 0.16%. This value is far below the 10% notational level of concern for drugs that are not particularly toxic. Three of the samples were foremilk samples, which tend to underestimate the infant exposure to lipid-soluble drugs. However, since the lipophilicity of methylphenidate is low, this factor would not be expected to significantly influence the exposure.

The infant's age was 11 months, and he was only sporadically breastfed. Thus, it was not considered meaningful to measure his methylphenidate plasma concentration, since it would nevertheless not be relevant for the "worst case" scenario—a newborn who is exclusively breastfed. The infant's general health status was excellent, and no possible adverse effects were observed.

Because methylphenidate was not detected in breast milk 20–21 hours after the previous dose, an infant would not be expected to be exposed to methylphenidate if breastfed immediately before the maternal morning dose. This finding is consistent with the short plasma elimination half-life of 2–3 hours. It is, however, important to note that only one patient was studied and that this finding is not necessarily valid in subjects with elimination half-lives that are longer than average, if the last dose is taken in the afternoon, or if a slow-release formulation is used.

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Mirtazapine and Breastfeeding: Maternal and Infant Plasma Levels

TO THE EDITOR: Selective serotonin reuptake inhibitors are the most studied antidepressants in breastfeeding mothers (1). However, to date, there is only one case report regarding mirtazapine and breastfeeding (2). This study found no clinically significant levels of mirtazapine in the milk, and serum concentrations in the infant were below therapeutic concentration. Breastmilk levels, assessed 15 and 22 hours postdose, were higher in hindmilk compared with foremilk. A fully breastfed infant would ingest 0.21%–1.02% of the weight-adjusted maternal dose on a daily basis, suggesting minimal exposure of mirtazapine to the infant. However, infants may be exposed to higher levels, since serum mirtazapine concentrations peak at approximately 4 hours postdose. We report the

case of evaluated mirtazapine levels in breastmilk at the time of expected maximum postdose plasma levels under the assumption that breastmilk levels peak at similar timepoints.

A 35-year-old, 60 kg, primiparous, breastfeeding woman who was prescribed mirtazapine (22.5 mg/day) approached our outpatient service for concerns about her 6-week-old child's possible exposure to mirtazapine through her breastmilk. After description of the study procedure to the patient, written informed consent was obtained for herself and her child. We examined breastmilk levels following 14 days of mirtazapine therapy to ensure that steady state was reached. At the time of assessment, the mother was breastfeeding exclusively. Breastmilk was collected at 4 and 10 hours postdose, foremilk and hindmilk were collected separately. Because of nighttime medication intake, maternal and infant plasma could not be obtained until 12.5 hours postdose. Mirtazapine levels (mass transition, 266 >165) were determined by tandem mass spectrometry, as described previously (2), with an interday imprecision of 12%. Mass transition characterizes the mirtazapine molecule. In tandem mass spectrometry, the mother molecule is broken into fragments, and 165-dalton fragment is taken to characterize and quantify mirtazapine. Although considerably higher levels were found in the milk 4 hours postdose (130 ng/ml foremilk, 145 ng/ml hindmilk) compared with 10 hours postdose (61ng/ml foremilk, 90ng/ml hindmilk), the weight-adjusted maternal dose was still relatively low, ranging from 3.9%–4.4% at 4 hours to 1.8%–2.7% at 10 hours. Infant plasma levels were not detectable at 12.5 hours postdose. Weekly follow-ups showed no abnormalities of the infant, especially regarding sedation or weight gain. The infant's weight at 6 months was 6.3 kg, i.e. consistently below the 25 percentile even before mirtazapine therapy.

Mirtazapine is indeed excreted in breastmilk with slightly higher hindmilk than foremilk levels. Given the minimal infant exposure to the drug and lack of adverse events in our case report, substitution of feeding did not seem necessary at that time. However, because of the scarcity of reports on mirtazapine exposure to nursed infants, interindividual differences are not known. Further research in a larger cohort and a longitudinal design assessing changes in infants' behavior as well as behavioral problems in childhood are needed to confirm the compatibility of mirtazapine treatment during breastfeeding.

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False Positive Phencyclidine Results Caused by Venlafaxine

TO THE EDITOR: We report the case of an unexpected positive result on routine urine drug screening for phencyclidine in a patient who assured that she had never used such substance. Because similar results have recently been reported (1, 2) and in order to avoid inappropriate suspicion by medical caregivers, we performed a blood test that confirmed the absence of phencyclidine and the interpretation of the former urine test as a false positive result.

"Ms. A," a 48-year-old patient with a 31-year history of recurrent depressive disorder, was admitted to the psychiatric hospitalization unit for an acute exacerbation of her mental disorder. She was receiving treatment with venlafaxine 225 mg/day, lamotrigine 100 mg/day, and lormetazepam 2 mg/day. During the prior month she experienced worsening of the depressive symptoms, concurrent with mood-incongruent psychotic symptoms that were not of a clearly depressive nature (thought broadcasting, paranoid and mystic delusions, delusions of control and influence, and grossly disorganized behavior). A routine drug screening by the qualitative immunoassay INSTANT-VIEW Multi-Drug Screen Urine Test (Alpha Laboratories) upon admission was positive for phencyclidine and negative for other drugs. The package insert for the test (3) shows cross-reactivity to methylphenidate, pheniramine, and tenocyclidine, but not for venlafaxine. Given the importance of knowing the origin of the psychotic symptoms, because she would meet DSM-IV criteria for schizoaffective disorder if a toxic etiology was excluded, we performed another urine test 2 weeks later that was also positive for phencyclidine. We then extracted, on the same day, blood and urine samples to check this result by means of a gas chromatography-mass spectrometry analysis. This technique revealed the absence of phencyclidine in blood and in urine (and confirmed that the two prior positive urine tests for phencyclidine were false positives) and confirmed the presence of venlafaxine in blood and of venlafaxine and norvenlafaxine in urine. The urine analysis by gas chromatography-mass spectrometry revealed only prescribed drugs and caffeine. The patient was hospitalized and compliance of the other prescribed drugs was adequate. The diagnosis was changed to schizoaffective disorder, and treatment with amisulpride 100 mg/day yielded a significant improvement of the psychotic symptoms.

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