

Mirtazapine and Breast-Feeding

TO THE EDITOR: Postpartum depression occurs in approximately 10% of childbearing women, and for many of them, treatment with an antidepressant may be necessary. The benefit of breast-feeding for the infant and the mother is well established; clinicians are therefore asked to make a careful risk-benefit decision on the use of antidepressants. The literature on antidepressants and breast-feeding consists mainly of case series of selective serotonin reuptake inhibitors and tricyclics, whereas information on newer antidepressants is scarce (1). We describe what we believe to be the first reported data on mirtazapine treatment in a breast-feeding woman.

Ms. A, a 27-year-old woman, was admitted to a psychiatric hospital 3 weeks after delivery of her daughter. She was suffering from a severe depressive episode with suicidal thoughts. Ms. A had a history of a first depressive episode at age 18 that was not treated. At the time of admission to the mother-child unit, Ms. A was breast-feeding her child and had so far not received antidepressive treatment. A routine diagnostic assessment, including a physical examination, laboratory studies, and a cerebral computerized tomography scan were normal. Treatment with sertraline, 150 mg/day for 11 weeks, was not effective. Therefore, Ms. A was switched to mirtazapine, 30 mg/day at 9:00 p.m. She fed her infant six times a day. Concentrations of mirtazapine were determined in breast milk and in the serum of mother and infant by using mass spectrometry after Ms. A provided written informed consent and the study was approved by the local ethics committee for measurement of her and her infant's serum levels of the drug. Samples were taken after reaching steady state before breast-feeding, the first time at 7:00 p.m. (22 hours postdose) and a second time at 12:00 a.m. (15 hours postdose).

At 7:00 p.m., the maternal plasma level of mirtazapine was 7 ng/ml (therapeutic range=5–100 ng/ml); the same level was found in the foremilk (the early portion), whereas in the hindmilk (the later portion), a concentration of 18 ng/ml was detected. On the next day at 12:00 a.m., the maternal plasma concentration was 25 ng/ml; in the foremilk, a concentration of 28 ng/ml and in the hindmilk, 34 ng/ml were found. The infant's plasma concentration was 0.2 ng/ml. The body weight of the infant was 6.8 kg at this time.

Ms. A was discharged in remission after 6 weeks of mirtazapine treatment. The psychomotor development of the infant was normal, as rated by an experienced neuropediatrician. No adverse events related to the mother's mirtazapine intake could be detected; especially, there was no sedation or abnormal weight gain.

The results of this case report demonstrate that mirtazapine is excreted into the milk of a nursing mother. No accumulation of mirtazapine in the milk was found. Measured serum concentration in the infant was below therapeutic concentration. We would like to add this information to still incomplete evidence on the safety of antidepressants and breast-feeding.

Reference

1. Burt VK, Suri R, Altshuler L, Stowe Z, Hendrick VC, Muntean E: The use of psychotropic medications during breast-feeding. *Am J Psychiatry* 2001; 158:1001–1009

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Bradycardia at Low Doses of Risperidone

TO THE EDITOR: Risperidone is a selective antagonist of dopamine and serotonin receptors and is widely used for the treatment of schizophrenia. The cardiac side effects of risperidone relate to a prolonged QT interval, orthostatic hypotension, and tachycardia. Recently, an article described a case of symptomatic bradycardia secondary to risperidone in a young man undergoing alcoholic withdrawal (1) but only after increases to moderately high levels of risperidone. We describe here the dramatic finding of acute sinus bradycardia with frequent premature ventricular complexes in a pattern of bigeminy in a geriatric patient taking an initial low starting dose of risperidone. He had normal sinus rhythm before the addition, and the bradycardia and ventricular bigeminy resolved after termination of risperidone, suggesting that risperidone was the etiological agent in the arrhythmia.

Mr. A was an 80-year-old widowed white man with a history of coronary artery disease and cerebrovascular disease who was transferred to our clinic from an outside facility for treatment of dementia not otherwise specified. He was originally hospitalized for an inability to care for himself, with confusion, delusions, and poor orientation. At the outside facility, an ECG revealed a normal sinus rhythm at 74 bpm, a P-R interval of 171, a QRS interval of 81 msec, and a QT/QTc of 362/402. His CBC, liver function tests, thyroid function tests, and basic metabolic panel were all normal. Mr. A was not taking any medication initially; during the stay, the following medications were given to him: risperidone, 0.75 mg/day (for agitation and delusions), and donepezil, 10 mg/day. Five days afterward, Mr. A was admitted to our facility, and a diagnosis of dementia not otherwise specified was made. As part of our evaluation, we also performed an ECG and repeated the tests and studies. All laboratory values and studies, including calcium, phosphate, and magnesium were normal, except for borderline diabetes. Of interest was that his ECG now displayed marked sinus bradycardia with frequent premature ventricular contractions in a bigeminy pattern. His ventricular rate, including bigeminy, was 70 bpm. Discounting the confounding premature ventricular contractions, his heart rate was 38 bpm. His P-R interval was 180 msec, his QRS interval was 80 msec, and his QT/QTc was 481/451 msec. Pending evaluation by the cardiology service and because of Mr. A's increased agitation and delusional status, we increased his risperidone to an oral dose of 1.5 mg at bedtime. Seven days after being admitted to our service and 12 days after drug initiation, we discontinued risperidone. An ECG revealed a normal sinus rhythm, with a rate of 67 bpm within 1 day of discontinuation. Throughout this time, Mr. A reported no syncope or palpitations. All major laboratory values and studies were normal before, during, and after the addition of risperidone.