Postpartum Psychosis Induced by Bromocriptine and Pseudoephedrine

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Bromocriptine is an ergot-derived dopamine agonist sometimes used for postpartum suppression of lactation. On rare occasions (a total of seven previous reports in the literature), use of the medication has been associated with psychotic symptomatology in postpartum patients. This case report describes a 19-year-old postpartum woman who developed severe psychotic symptoms while taking low doses of bromocriptine and pseudoephedrine. The use of bromocriptine for suppression of lactation is controversial. If prescribed for postpartum patients, bromocriptine alone or in combination with sympathomimetic drugs should be used only with caution.

KEY WORDS. Bromocriptine; pseudoephedrine; lactation; puerperium; psychotic disorders. *(J Fam Pract 1997; 44:164-166)*

Bromocriptine is a semisynthetic ergot alkaloid that acts as a dopamine receptor agonist. Its current uses include the treatment of Parkinson's disease (optimal dosage 40 to 60 mg daily), prolactinomas and acromegaly (usually in dosages of 7.5 to 30 mg per day), and amenorrhea and galactorrhea secondary to neuroleptic use.[1] The prolactin-producing cells of the anterior pituitary appear to be inhibited by dopamine. Randomized clinical trials of bromocriptine vs placebo demonstrating the efficacy of the drug led to the use of bromocriptine at low dosages of 2.5 mg every 12 hours for 14 days for the inhibition of postpartum lactation.[2,3] Although no drug should be routinely used to prevent postpartum lactation, the texbook *Williams Obstetrics*, in its 1993 edition,[4] reported that the use of bromocriptine for this purpose was "widespread." As reported in the next edition of the textbook 4 years later,[5] the *Physicians' Desk Reference* had subsequently removed lactation suppression as an indication for using bromocriptine.

Psychiatric side effects of bromocriptine include hallucinations, delusions, confusion, and mania.[6] These symptoms are thought to result from excess dopamine activity. There have been seven reported cases of psychotic symptoms in patients with no history of psychosis for whom bromocriptine was used for postpartum lactation suppression.[3,7-11] Symptoms described included delusions, hallucinations, and mania. The incidence of postpartum psychosis in primiparous women is about 1 in 500; after a subsequent delivery, the risk is about 1 in 3 for previously affected women.[12] Thus, these cases may represent coincidental occurrence in patients taking bromocriptine. Postpartum psychosis usually develops between the 3rd and 14th day postpartum and may begin with confusion, depersonalization, and insomnia, and then progress rapidly to delirium with prominent hallucinations and delusions. Rapidly changing states of mania and deep depression may occur, as well as outbursts of florid psychosis.

Many sympathomimetic drugs may cause or exacerbate psychotic symptoms, presumably by dopaminergic stimulation. This is seen most commonly with amphetamine and cocaine, but may also occur with several less potent drugs, including over-the-counter sympathomimetics.[13] Psychotic symptoms induced by pseudoephedrine have occurred primarily in patients with an underlying psychiatric disorder or after use of relatively large doses.[14-16]

Case Report

The patient was a 21-year-old white woman, para 0 gravida 1, who gave birth to a healthy male infant without complications. Her prenatal course had

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been uneventful, and her postnatal examinations were reported unremarkable. She was given bromocriptine, 2.5 mg twice daily, which she took without any problem for 9 days. On the 9th day she began taking an over-the-counter preparation of pseudoephedrine, 60 mg four times daily. On the next day she was depressed and cried a large part of the day. She then became hyperactive and delusional, sleeping very little over the next 3 days. She was brought to the hospital by family members, who felt they could not control her. They described her as "talking silly" and impossible to "settle down."

Her past psychiatric history was unremarkable, as was her medical history. She denied using drugs except for rare use of marijuana and beer. There was no family history of psychiatric disorder.

An examination showed her to be alert and hyperactive. Her mood was elevated and expansive. Her speech was pressured. Her thought processes were tangential with flight of ideas. Her thought content was delusional, including an unfounded belief that she could earn $100,000 per year as a beautician and that she had recently bought a new house and a new expensive car. Extremely grandiose ideas about her abilities and future plans were stated repeatedly.

Results of a physical examination were within normal limits. Findings from laboratory studies, including complete blood count, chemistry survey, and thyroid function, were also within normal limits. A rapid plasma reagin test was nonreactive. A urine drug screening test was negative.

Bromocriptine and pseudoephedrine were discontinued. She was treated with orally administered haloperidol, 5 mg twice daily, and benztropine, 1 mg twice daily. Her symptoms improved slowly and she was discharged 3 days later, still taking these medications. They were discontinued after complete resolution of her symptoms during the following week. Subsequently, she had no recurrence of symptoms. Twenty months later she gave birth to another healthy infant. Bromocriptine was not prescribed. No psychiatric symptoms occurred during that postpartum period.

Discussion

In this case, the patient appears to have developed psychosis secondary to the combination of low-dose bromocriptine and pseudoephedrine. No symptoms were noted until pseudoephedrine was added to the regimen, 2 days after which her symptoms became marked. Some bromocriptine psychoses, however, have had their onset as late as 8 to 10 days postpartum. It is conceivable that, since the puerperium is a period associated with an increased incidence of psychosis, some such cases may represent postpartum psychosis in patients coincidentally taking bromocriptine. It is clear, however, that bromocriptine can cause psychosis when given in larger doses for pituitary adenoma and Parkinson's disease.

The above and other such reports suggest that bromocriptine may cause psychosis even when given in low doses. The mechanism by which this occurs is probably dopaminergic stimulation. We postulate that the psychotic symptoms in this patient were secondary to the synergistic effects of both bromocriptine and pseudoephedrine on the dopaminergic system. It is also likely that the increased vulnerability of certain patients to psychosis in the puerperium increases the likelihood of their developing psychosis when exposed to bromocriptine or other sympathomimetic medications during that period. Why certain patients are more vulnerable to psychosis during the postpartum period remains unknown, but may be related to fluctuations in hormonal and neurotransmitter levels.

Because postpartum psychosis is a psychiatric emergency that may endanger the mother and her infant, hospitalization and aggressive treatment, sometimes with electroconvulsive therapy, are often necessary. Clinicians should be aware of the potential for medication-induced psychosis so that more conservative treatment, ie, discontinuation of the offending medication, observation, and possibly administration of an antipsychotic agent, may be used before resorting to more aggressive measures.

It should be stressed that bromocriptine is no longer recommended for routine use in the suppression of postpartum lactation. In 1994, the Sandoz Corporation voluntarily withdrew the use of bromocriptine (Parlodel) for this purpose because of concern about reports associating the drug with strokes, myocardial infarction, seizures, and psychiatric disturbances during the puerperium.[17,18] While it is not totally clear whether these complications were due to bromocriptine or to the increased incidence of such events during the puerperium, the withdrawal was undertaken out of concern that the ablactation issue might have a negative impact on the prescription of bromocriptine for the treatment of other

medical problems such as Parkinson's disease, hyperprolactinema, infertility, and certain tumors.[18] It is also important to be aware that an advisory committee of the Food and Drug Administration (FDA) recommended that medications should no longer be used for lactation suppression, but expressed no opinion on the safety of bromocriptine for lactation suppression.[19]

The simplest method of lactation suppression consists of support with a comfortable binder, and application of cold packs and mild analgesics for pain. Bromocriptine should be considered only if severe mammary engorgement develops in spite of conservative treatment.[4,5] If bromocriptine is used, clinicians should be aware of potential psychiatric complications that may occur even at low doses. The potential medicolegal dangers of using a medication for a purpose not approved by the FDA should be seriously considered in the risks-vs-benefits assessment of whether to use bromocriptine for lactation suppression. Clinicians should also be cautious in using combinations of bromocriptine and sympathomimetics in postpartum cases. Bromocriptine alone, or in combination with sympathomimetic drugs, should be used only with extreme caution in patients with a past history of psychosis or mania, as such patients would be at a higher risk for psychiatric complications.

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