Serum Bupropion Levels in 2 Breastfeeding Mother-Infant Pairs

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Background: These are the first reported data on bupropion and hydroxybupropion levels in infants whose treated mothers were breastfeeding. The information will assist physicians and parents in the risk-benefit decision-making process for bupropion treatment during breastfeeding.

Method: Serum samples were obtained by venipuncture from 2 mother-infant pairs. The serum was assayed for levels of bupropion and its most active metabolite, hydroxybupropion.

Results: Neither infant had quantifiable serum levels of bupropion or its metabolite at steady state. Neither infant had medical problems during the time of maternal therapy.

Conclusion: We recommend obtaining and publishing additional serum level findings for breastfeeding mother-infant pairs since data for bupropion are favorable but limited.

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Postpartum depression occurs in 10% to 15% of women,[1] and an affective episode occurs in 40% to 70% of postpartum bipolar women.[2–4] The benefits of breastfeeding have been established[5]; therefore, information to inform risk-benefit decision making for drug treatment during breastfeeding is critical.

Bupropion is an antidepressant of the aminoketone class that differs from other antidepressants. The chemical structure of bupropion is unrelated to that of the tricyclics, tetracyclics, selective serotonin reuptake inhibitors (SSRIs), and other antidepressants.[6,7] After chronic dosing with bupropion, metabolite concentrations in the brain and plasma begin to approach those needed for inhibition of norepinephrine reuptake in vitro, which contributes to antidepressant activity.[8] Hydroxybupropion is the major metabolite of bupropion. The half-life of hydroxybupropion is about 20 hours in adults, compared with the short half-life of bupropion.[8] Bupropion undergoes extensive hepatic metabolism with elimination being primarily through the kidney.[6] Because of its unique mechanism of action, bupropion may be useful for patients who have not responded to or have intolerable side effects from other classes of antidepressants.

Although data for mother-infant plasma levels exist for many of the tricyclic and SSRI antidepressants,[9] only 1 case report for bupropion has been published.[10] A 37-year-old lactating woman was treated with bupropion (100 mg t.i.d.). She breastfed her son (aged 14 months) twice a day. Serum was obtained from her child 3.7 hours after breastfeeding and 9.5 hours after the mother's last dose of bupropion. There was no measurable amount of the drug or metabolites in the toddler's serum. The level of quantifiability for bupropion was 5 ng/mL and 200 ng/mL for metabolites (hydroxybupropion and threohydrobupropion). The mother and pediatrician noted no adverse effects in the toddler.

In this article, we present infant serum levels of bupropion and hydroxybupropion in 2 cases of mother-infant pairs.

METHOD

Each subject gave consent following a risk-benefit discussion and agreed to have her infant's serum sampled when her drug levels were at steady state. The infants' pediatricians monitored them during bupropion treatment. Mother and infant blood was obtained by antecubital venipuncture, and serum levels of bupropion and its major metabolite, hydroxybupropion, were analyzed by Medtox Laboratory, St. Paul, Minn. Levels of reliable quantifiability were from < 5 to < 10 ng/mL for bupropion and < 100 to < 200 ng/mL for hydroxybupropion. The volume of infant serum determined the level of test quantifiability; 0.5 mL of serum is needed for optimum quantifiability.

Table 1. Serum Concentrations of Bupropion and Hydroxybupropion in Breastfeeding Mother-Infant Pairs[a]

Case	Infant Sex	Infant Age (wk)	Maternal Bupropion Dose (mg/d)	Bupropion Serum Level		Hydroxybupropion Serum Level		Elapsed Time Since Both Bupropion Dose and Breastfeeding (h)
				Maternal (ng/mL)	Infant (ng/mL)	Maternal (ng/mL)	Infant (ng/mL)	
1	Male	17.0	150 (non-SR)	55	< 5	1780	< 100	2.00
2	Female	39.5	150 (SR)	44	< 10[b]	998	< 200[b]	3.25

[a]Abbreviation: SR = sustained release.
[b]The level of quantifiability was restricted by sample volume.

RESULTS

Case 1

Ms. A was a 28-year-old Hispanic woman. Her diagnosis was bipolar I disorder according to DSM-IV criteria with onset occurring during adolescence. Prior to the pregnancy, she had 2 years of mood stability while taking a combination of valproate and bupropion. She delivered a healthy full-term boy. At 15 weeks postpartum, Ms. A became depressed. She was taking valproate (750 mg) and verapamil (360 mg) at the time. The infant was thriving at 20 lb and Ms. A was committed to full breastfeeding. She chose to start bupropion 75 mg b.i.d.[11] At 17 weeks postpartum, 2-hour post-dose and 2-hour post-breastfeeding mother-infant serum levels were obtained (Table 1). No levels of bupropion or hydroxybupropion were quantifiable in the infant's serum. Ms. A and the pediatrician reported no adverse effects in the infant.

Case 2

Ms. B was a 34-year-old white woman with a diagnosis of recurrent major depression according to DSM-IV criteria. She had been euthymic while taking bupropion sustained-release tablets (bupropion SR)[12] for 6 months prior to pregnancy and discontinued bupropion therapy after learning she was pregnant. She delivered a healthy full-term girl. Because of postpartum depression, she began treatment with sertraline. Ms. B found sertraline only partially effective and decided to resume bupropion SR 150 mg/day at 29 weeks postpartum. A mother-infant bupropion level was obtained when the infant was 39.5 weeks of age. The infant received over 80% of its nourishment from breast milk. The infant had no quantifiable levels of bupropion or hydroxybupropion in the serum (Table 1). Ms. B and the pediatrician reported no adverse effects in the infant.

DISCUSSION

This is the first published report on bupropion and hydroxybupropion in the sera of infants who received the majority of their nourishment from breast milk. The finding of nonquantifiable infant serum levels is encouraging. However, areas of uncertainty in the use of bupropion during breastfeeding remain. Nonquantifiable is not the same as absent, so that trace amounts could be present but not quantified. The "no-effect" level, at which there is no biological activity, for bupropion (or any drug) has not been determined in infants. The decision to use bupropion during breastfeeding requires a case-specific risk-benefit assessment by the mother and her physician. The many benefits of nursing have been established,[5] but must be weighed against the possibility of adverse effects from small amounts of drug exposure. The risk to the mother and family of an untreated depression must also be weighed against exposure.

In the cases presented in this article, each of the mothers had demonstrated prior response to bupropion, and this was also considered in the risk-benefit discussion, which followed the model of Wisner et al.[13] The infants studied in this report were healthy and several months of age; therefore, the results from these 2 cases cannot be generalized to newborns or infants with medical problems. Data for bupropion are favorable but limited, and we recommend obtaining and publishing additional serum level findings for breastfeeding women and their infants.

Drug names: bupropion (Wellbutrin and others), sertraline (Zoloft), verapamil (Covera, Isoptin, and others).

REFERENCES

1. O'Hara MW. Social support, life events, and depression during pregnancy and the puerperium. Arch Gen Psychiatry 1986;43:569–573
2. Bratfos O, Haug JO. Puerperal mental disorders in manic-depressive females. Acta Psychiatr Scand 1966;42:285–294
3. Reich T, Winokur G. Postpartum psychosis in patients with manic depressive disease. J Nerv Ment Dis 1970;151:60–68
4. vanGent EM, Verhoeven WM. Bipolar illness, lithium prophylaxis, and pregnancy. Pharmacopsychiatry 1992;25:187–191
5. US Dept Health and Human Services. Report on the Surgeon General's Workshop on Breastfeeding and Human Lactation. Washington, DC: US Dept Health and Human Services; 1984. Publication HRS-D-MC 84-82
6. Weintraub M, Evan P. Bupropion: a chemically and pharmacologically unique antidepressant. Hospital Formulary 1989;24:254–259
7. Lai AA, Shroeder DH. Clinical pharmacokinetics of bupropion: a review. J Clin Psychiatry 1983;44(5 pt 2):82–84
8. Ascher JA, Cole JO, Colin J-N, et al. Bupropion: a review of its mechanism of antidepressant activity. J Clin Psychiatry 1995;56:395–401
9. Wisner KL, Perel JM, Findling RL. Antidepressant treatment during breast-feeding. Am J Psychiatry 1996;153:1132–1137
10. Briggs GG, Samson JH, Ambrose PJ, et al. Excretion of bupropion in breast milk. Ann Pharmacother 1993;27:431–433
11. Wellbutrin tablets (bupropion). Physicians' Desk Reference. Montvale, NJ: Medical Economics; 2002:1680–1684
12. Wellbutrin SR (bupropion sustained-release tablets). Physicians' Desk Reference. Montvale, NJ: Medical Economics; 2002:1684–1688
13. Wisner KL, Zarin DA, Holmboe ES, et al. Risk-benefit decision making for treatment of depression during pregnancy. Am J Psychiatry 2000;157:1933–1940