Menstrual irregularities with hyperandrogenism in 9 (10.5%) of 86 women treated with valproate (Biol. Psychiatry 2006;59:1078-86). Only 2 (1.4%) of 144 women on lithium or an anticonvulsant other than valproate developed these symptoms of polycystic ovary syndrome (PCOS).

In all cases, oligomenorrhea began within a year of the patient’s starting valproate use. The investigators calculated the relative risk as 7.5 for women with bipolar disorder using valproate as a mood stabilizer.

Dr. Hadine Joffe, the lead author, is director of endocrine studies in the perinatal and reproductive psychiatry clinical research program at Massachusetts General Hospital in Boston. She and her colleagues recommended warning women of PCOS risk before starting them on valproate.

Further, women on valproate should be evaluated for PCOS if they develop menstrual irregularities with hyperandrogenic symptoms. Along with PCOS treatment, the investigators suggested that “it may also be appropriate to consider alternative mood stabilizers if PCOS features develop on valproate.”

In an address at a psychiatric symposium sponsored by the University of Arizona, Dr. Gary Sachs, senior author and principal investigator of STEP-BD, emphasized the need for vigilance during the first year a patient is on valproate.

“Before you start women on valproate, you absolutely have to warn them this is a risk,” Dr. Sachs, founder and director of the bipolar clinic and research program at Massachusetts General Hospital, told psychiatrists at the Santa Fe, N.M., symposium.

Sponsored by the National Institute of Mental Health, STEP-BD enrolled 4,361 patients in the largest clinical study to date on the treatment of bipolar disorder. Dr. Sachs said that Abbott Laboratories, which sells valproate under the brand name Depakote, was among the drug companies that supported the trial.

“They were very confident the risk wasn’t there,” he said. “It turned out that was wrong. There really was a risk. The risks are there and published.”

To study the relationship in a nonneoplastic population, the investigators sought out women aged 18-45 years in STEP-BD who were taking at least one mood stabilizer for at least 3 months. Participants who had discontinued another mood stabilizer within the previous 3 months were not included in the sub-study.

Of the 300 identified eligible women, 14 patients previously diagnosed with PCOS and three others with disorders involving oligomenorrhea were among those excluded from the sample. All told, 230 women were available for the analysis.

Of the valproate users, 12 developed oligomenorrhea, and 9 of them also had hirsutism, according to the report.

Among all patients with oligomenorrhea, valproate users had fewer menstrual cycles (median of 5 vs. 8.5 per year) than did nonusers.

Some had elevated total or free testosterone, moderate to severe acne, or male-pattern alopecia.

The valproate users who developed oligomenorrhea with hyperandrogenism had a higher median body mass index (kg/m²) of 36 vs. 26—as well as a higher median homeostatic model assessment for insulin resistance (3.1 vs. 1.7)—than did valproate users who did not take PCOS features.

“Our study raises the possibility that increased body weight, insulin resistance, PCO morphology, younger age of first valproate use, and polyspharmacy may predispose to the development of PCOS features on valproate,” the investigators concluded.

Because of the difficulty of performing continuous glucose monitoring in nondiabetic women with a normal pregnancy, the study did not involve a specific cohort of patients but instead mostly included doctors’ wives, midwives, and nurses.

The women’s overall mean blood glucose (79.3 mg/dL) and mean fasting blood glucose levels (75 mg/dL) were “much, much lower than was previously reported by others,” Dr. Yogev said.

Mean nighttime blood glucose levels (66 mg/dL) “almost represented hypoglycemia,” but such values may actually represent “normal physiology during the first trimester in nondiabetic patients,” he said.

The postprandial glycemic profile of the women was the same after each meal. Mean blood glucose values started at 79 mg/dL, just before a meal and rose to 106 mg/dL 60 minutes after the meal; it reached a high of 112 mg/dL 74 minutes after the meal. The values reached 99 mg/dL at 2 hours and 82 mg/dL at 3 hours.

The fasting and overall mean blood glucose levels were similar in 18 obese (defined as a body mass index greater than 27.3 kg/m²) and 44 nonobese women. Compared with nonobese women, however, those who were obese had significantly higher mean preprandial blood glucose levels (73 mg/dL vs. 88 mg/dL) and significantly lower mean fasting blood glucose concentrations (69 mg/dL vs. 60 mg/dL).

The obese patients were characterized by a higher postprandial peak value, a longer time interval to reach the postprandial peak value, and higher mean blood glucose levels during the 3 hours after each meal, Dr. Yogev said.

Women taking valproate for bipolar disorder are at significantly increased risk of developing features of polycystic ovary syndrome, according to a published study of 230 female patients in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD) trial.

Investigators reported finding new-onset oligomenorrhea with hyperandrogenism in 9 (10.5%) of 86 women treated with valproate (Biol. Psychiatry 2006;59:1078-86). Only 2 (1.4%) of 144 women on lithium or an anticonvulsant other than valproate developed these symptoms of polycystic ovary syndrome (PCOS).

In all cases, oligomenorrhea began within a year of the patient’s starting valproate use. The investigators calculated the relative risk as 7.5 for women with bipolar disorder using valproate as a mood stabilizer.

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