Mood in Pregnancy May Impact Birth Outcomes

BY PATRICE WENDLING
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PITTSBURGH — Pregnant women with anxiety or depression have higher levels of α-amylase, a measure of adrenergic system activity, and lower morning cortisol levels, preliminary results from a longitudinal study demonstrated.

The findings suggest the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis may be affected in opposite directions by stress during pregnancy, Alison Shea, Ph.D. candidate, and her associates reported in a poster at the International Congress of Neuroendocrinology.

Birth length was smaller for babies born to women with anxiety or depression compared with those born to controls and women on antidepressants.

The analysis included 60 women who were among the first of 250 pregnant women to be recruited as part of the multicenter Maternal Adversity, Vulnerability, and Neurodevelopment (MAVAN) study led by Dr. Meir Steiner, of McMaster University, Hamilton, Ont. The women were divided into three groups: those presenting with symptoms of depression or anxiety who chose psychotherapy only, those with symptoms who chose antidepressants, and a control group with no current or past psychiatric illness.

A battery of psychological tests was performed at baseline (gestational age 14-24 weeks), and morning salivary samples were collected daily to measure stress indicators such as cortisol, dehydroepiandrosterone (DHEA), and α-amylase. A follow-up assessment was performed at 24-30 weeks and included psychological testing, salivary samples, and a 24-hour Holter ECG. Infants are being followed during the postpartum period until 3 years of age.

The results indicate that depression and anxiety scores during pregnancy are positively correlated with α-amylase levels and negatively correlated with morning cortisol levels. Both associations were statistically significant, reported Ms. Shea, of the Women's Health Concerns Clinic, St. Joseph's Healthcare, Hamilton.

Compared with controls, both the cortisol response to awakening and the 24-hour heart rate variability were lower for mothers with anxiety and depression, particularly among those not taking antidepressants. Reduced heart rate variability indicates the body's inability to respond to stress in a changing environment, and is thought to improve with the use of antidepressants, Ms. Shea said in an interview. The study found that the greater the mother's heart rate variability, the longer the gestation. "It makes sense, but it's never been looked at in pregnant women," she said.

Head circumference at birth was strongly correlated with maternal 24-hour mean heart rate during pregnancy, even after controlling for birth weight and gestational age. Among women with depression and anxiety, the higher the heart rate during pregnancy, the smaller the head circumference. Head circumference is purported to be a measure of brain volume and has been found to be smaller among babies born to women with posttraumatic stress disorder, she said.

Birth length was significantly smaller for babies born to women with anxiety or depression (49.64 cm), compared with those born to women treated with antidepressants (50.91 cm) and controls (53.01 cm).

Ponderal index, which is an indicator of infant body mass index, also was significantly higher among babies of women suffering from anxiety and depression (2.65 g/cm^3), compared with those of women treated with antidepressants (2.55 g/cm^3) and of controls (2.3 g/cm^3). The lower the maternal cortisol levels during pregnancy, the higher the ponderal index, which suggests some type of modulation of the HPA axis that would impact birth outcomes and growth, Ms. Shea said. ■

Research Consortium Launched

The National Institutes of Health has launched a national consortium focused on transforming how clinical research is conducted in the hopes of providing patients with new treatments more quickly and effectively. Twelve institutions have received funding thus far. The goal is to have about 60 linked institutions by 2012. For more information, go to www.ncrr.nih. gov/clinicaldiscipline.asp. ■

Drugs, Pregnancy, And Lactation

Accumulating Data on Prenatal Exposure to SSRIs

BY LEE COHEN, M.D.

Over the last year, several studies on possible neonatal effects of prenatal exposure to SSRIs have been reviewed in this column. These studies have raised concerns about potential risks, including congenital malformations—as may be the case with paroxetine (associated with a putative increased risk for cardiovascular malformations, prompting a change in the pregnancy risk category label from C to D)—and perinatal distress and pulmonary complications, as noted in two recent studies (Family Practice News, February 1, May 1, 2006). Other studies discussed here have highlighted the high risk of depressive relapse associated with discontinuation of antidepressants during pregnancy.

These and further studies reported over the last few years reflect the heightened interest in perinatal psychopharmacology and have provided a more refined scientific focus on the relative risks of prenatal SSRI exposure vs. the potential risks of untreated mood disorder during pregnancy. These are relative risks that physicians need to discuss with patients, making the best clinical decision possible based on the patient's individual clinical situation.

Until recently, few studies have attempted to parse out the neonatal effects of untreated depression and prenatal SSRI exposure. Most of the available data have been in women treated with an SSRI for underlying depression, and have not included a comparison group of unmedicated women suffering from depression.

However, a study published in August by investigators at the University of British Columbia, Vancouver, using population-based health data in British Columbia and linking records of neonatal birth outcomes with hospital records of psychiatric diagnoses at maternal discharge and prenatal SSRI prescriptions, provides an opportunity to tease apart these two potentially important predictors of neonatal outcomes (Arch. Gen. Psychiatry 2006;63:898-906).

The study compared outcomes of babies born to women diagnosed with depression and treated with an SSRI to outcomes of babies born to women diagnosed with depression who were not treated with medication, and to a control group of babies whose mothers were neither depressed nor on antidepressant medication, between 1998 and 2001.

Among babies exposed to SSRIs, birth weights were lower, hospital stays were longer, and gestational ages were shorter, compared with babies in the control group. A similar pattern was seen when the SSRI-exposed babies were compared with those of depressed mothers who were not treated, except for birth weight for gestational age. In addition, significantly more of the infants of medicated women had respiratory distress and jaundice, compared with babies in the other two groups. Feeding problems were significantly more common among SSRI-exposed infants than among infants of unmedicated women with depression. The rate of convulsions was not significantly different between the groups.

Using propensity scores to match severity of depression in untreated and treated women, the investigators attempted to match women by degree of depression in the year before and during pregnancy, essentially controlling for illness severity while looking at neonatal outcomes. When they compared birth outcomes in these two groups, the associations between prenatal SSRI exposure and feeding problems and jaundice were no longer present. What remained significant was a greater rate of respiratory distress among infants of SSRI-treated mothers and the incidence of birth weight below the 10th percentile. These findings suggest that the effect on respiratory distress may be due to SSRI exposure, rather than maternal depression.

The authors appropriately acknowledge the limitations of using claims data and discharge diagnoses as proxies for real diagnostic assessments. They also note that alcohol or illicit drug use, smoking, or socioeconomic conditions beyond income—all of which can affect neonatal well-being—could not be ascertained. Not factored into the study is another critical issue, the risk of postpartum depression, which is strongly associated with depression during pregnancy. In many respects, postpartum depression may have more enduring long-term outcome than other types of fetal exposures. Also unknown is the nature of respiratory distress, and whether it persisted. In one recent study, for example, symptoms of a "neonatal abstinence syndrome" were transient and did not require clinical intervention (Arch. Pediatr. Adolesc. Med. 2006;16:173-6).

The conclusion from the Canadian study, considering its limitations, is that there may be an independent effect of maternal depression on neonatal outcome and an independent effect of medication exposure, and that these effects may be additive. Confirming this finding may only be possible with a prospective study that more accurately assesses maternal diagnosis and severity over time and where medication exposure is confirmed prospectively.

During consideration of the increasing amount of data on both sides of this relative risk equation, it is critical for clinicians to discuss with patients the range of issues, from the potential neonatal effects of these medicines, to the high risk for relapse when antidepressants are discontinued, to the impact of untreated illness on the baby and mother.

Our own research and clinical experience with this population suggest that patients presented with the same information, including women with extremely similar clinical illness histories, will make very different decisions about medication use during pregnancy. So, there is our task: to present this information and to let patients make decisions consistent with their wishes. With the backdrop of continually evolving data, patient decisions will also evolve, decisions not driven by the clinician, but by collaboration between the clinician and patient.

Dr. Cohen *directs the perinatal psychiatry program at Massachusetts General Hospital, Boston, which provides information about pregnancy and mental health at www.womensmentalhealth.org. He serves as a consultant to manufacturers of several antidepressants, including SSRIs.*