Long-Term Effects of Prenatal SSRI Exposure on Child Growth: Weighing the Evidence

To the Editor: We read with interest the article by Wisner et al. (1) evaluating the effect of in utero exposure to selective serotonin reuptake inhibitors (SSRIs) or maternal depression on infant growth in the first year of life. While this study represents an important contribution to the literature, we feel that several issues warrant further clarification to improve interpretation of the results.

First, a previously identified issue relates to the potential for sex-specific differences when investigating long-term outcomes (2). There is strong evidence that prenatal exposure to both SSRIs and maternal depression is associated with a variety of sex-specific outcomes, including postnatal growth (2). We have previously investigated the effect of prenatal SSRI exposure on risk for children who are overweight at 4–5 years old. In this study, we observed that girls of SSRI-exposed mothers were less likely to be overweight compared with girls of mothers with an untreated psychiatric illness (adjusted prevalence ratio, 0.23; 95% confidence interval [CI]=0.05–0.98) and girls of unexposed mothers (adjusted prevalence ratio, 0.27; 95% CI=0.07–0.99). In contrast, no association with being overweight was observed among boys of exposed mothers compared with boys of mothers with an untreated psychiatric illness (adjusted prevalence ratio, 1.17; 95% CI=0.54–2.51) and boys of unexposed mothers (adjusted prevalence ratio, 0.93; 95% CI=0.52–1.67) (3). It would be useful to know whether any analyses were undertaken to examine potential interactions between exposure and the child's sex and if so, if any differences were observed.

Second, much like percentiles are standardized for age and sex, it may be beneficial to assess patterns of growth in childhood by taking into account the relationship between a child's height and weight (4). It would be useful to know whether the use of weight-for-length or body mass index-for-age-adjusted percentiles were considered and whether any assessments were undertaken using well-defined international cutoffs to examine growth at either extreme.

While studies such as this emphasize the need for looking beyond birth outcomes and considering long-term effects of prenatal exposure on child development and well-being, an often understudied aspect of medication use in pregnancy, addressing the issues outlined above would enable us to more appropriately weigh the evidence.

References

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Response to Grzeskowiak and Morrison

To the Editor: Drs. Grzeskowiak and Morrison suggested conducting sex-specific analyses to augment our findings (1). These investigators reported that fetal exposure to selective serotonin reuptake inhibitors (SSRIs) was associated with a significantly lower risk for girls who were overweight at ages 4 or 5 years compared with girls exposed prenatally to maternal psychiatric illness or to neither illness nor SSRI (2).

Were any sex differences observed with respect to the impact of SSRI exposure on growth? The impact of fetal exposure to SSRI, major depressive disorder, or neither was modeled for male and female infants with longitudinal mixed-effect regression analyses. No significant associations were found in male infants (weight, p=0.37; length, p=0.27; or head circumference, p=0.63) or in female infants (weight, p=0.53; length, p=0.07; or head circumference, p=0.54).

Did weight-for-length-adjusted percentiles from international standards for growth at either extreme differ by sex? We evaluated the proportion of male and female infants at the <15th and >85th percentiles for weight-for-recumbent length according to both Centers for Disease Control and Prevention (CDC) and World Health Organization (WHO) standards. In 2010, the CDC convened with representatives from NIH and the American Association of Pediatrics and recommended WHO standards for children from birth through 2 years (http://www.cdc.gov/growthcharts/who_charts.htm). The WHO standards reflect growth patterns among predominantly breastfed children and were designed specifically to create growth standards for children under optimal conditions.

Utilizing the CDC standards, the proportions of male infants at the <15th percentile or the >85th percentile did not differ by exposure. Similarly, no difference by exposure was observed for female infants. According to WHO standards, the proportions of male infants at the <15th and the >85th percentiles did not differ by exposure. However, a significant difference was identified for female infants at the <15th percentile. At birth, female infants exposed prenatally to major depressive disorder were more likely to be at the <15th percentile for weight-for-length (p=0.039) than female infants exposed to either SSRI or neither (58% compared with 17% compared with 36%, respectively). However, by 12 weeks old, the proportions of female infants in all groups were approximately 15%. No difference in female infants for the >85th percentile was observed.