An Imperfect Literature and Evidence-Based Medicine

Two original articles comprise our Focus on Women's Mental Health section this month. In their article, "Selective Serotonin Reuptake Inhibitor Exposure During Early Pregnancy and the Risk of Fetal Major Malformations: Focus on Paroxetine," Gentile and Bellantuono address an important clinical topic that has been the focus of many articles and media attention. A few reports regarding the risks of early antenatal exposure to selective serotonin reuptake inhibitors have raised concerns regarding possible rare malformations, but replication of such findings are generally lacking, and findings of risk are inconsistent and do not as a whole elucidate patterns that would support teratogenic effects. In particular, a registry from GlaxoSmithKline[1–3] suggested an increased risk of cardiovascular malformations with paroxetine use in pregnancy (unpublished data), a finding that not surprisingly raised concerns about its use in pregnancy among health care providers and the public.

Drs. Gentile and Bellantuono conducted a search of the medical literature for data regarding infant outcomes after exposure to paroxetine, in comparison to no antidepressant exposure and other antidepressants in prospective studies, and to the general population in large databases. After careful assessment of 25 studies, the authors found that studies performed to date have utilized heterogeneous designs with substantial limitations, with conflicting conclusions about paroxetine exposure in the first trimester. Another comprehensive analysis by Einarson et al.[4] did not find paroxetine exposure in early pregnancy to be associated with an increase in congenital malformations compared to unexposed pregnancies. Gentile and Bellantuono describe the limitations of the literature to date and propose that large, prospective studies with adequate control groups are necessary to determine the risk of in utero exposure to paroxetine. Adequate studies must take into account the underlying indication for treatment, the risk of nontreatment, and the timing and length of exposure to medication.

Di Scalea et al. also address an important issue related to the risks and benefits of psychotropic medication. In a study of 70 postpartum women, the investigators systematically assessed sexual functioning among women randomly assigned to either sertraline or nortriptyline for postpartum major depressive disorder. From high rates of symptoms of dysfunction at the study onset, treatment with both antidepressants was associated with improved sexual function after treatment, which was associated with remission of major depressive disorder. Sexual dysfunction is associated with untreated depressive symptoms, as well as commonly utilized antidepressants, so the finding that postpartum women experienced improved sexual functioning with remitted mood symptoms in the context of antidepressant therapy informs the analysis of risks and benefits of antidepressant treatment around the topic of sexual function.

The determination of risk from psychotropic medications is challenging. Ethical, financial, and time constraints make it more difficult to fully study potential risks, especially in vulnerable populations. This section's offerings represent important contributions to risk assessment in women's mental health.

As always, we welcome your feedback and suggestions regarding this section and *The Journal of Clinical Psychiatry*. Please e-mail me at mfreeman@psychiatrist.com with comments. Information on the Focus on Women's Mental Health section can be found at psychiatrist.com.

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