

Treating Mood Disorders: No Easy Decisions

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MADRID – There are no easy choices for women who present with mood disorders during pregnancy – or for the physicians who treat them.

The decision to treat prenatal depression or anxiety is not to be taken lightly, but often must be considered, despite a relative dearth of data supporting or refuting drug safety during pregnancy, Dr. Shari I. Lusskin said at the conference.

“There are data, but not great data,” said Dr. Lusskin, director of reproductive psychiatry at the NYU Langone Medical Center, New York. “We will never have 10,000 patients taking medication compared to 10,000 not taking it, compared to a control group that is not depressed or anxious, nor will we have years of follow-up data on their children.”

The data that do exist are mostly comprised of case series, which are small and lack controls. “When you see a negative study [about the effect of treating mental disorders in a pregnant woman], keep in mind that there is often a lack of information about the mother’s diagnosis. Reports of smoking and substance abuse are notoriously unreliable,” and can’t be accounted for in the results, she said. “We also know nothing about the mother’s body mass index, which is associated with many fetal complications that have nothing to do with drug exposure. And different studies use different comparison scales – you can’t compare apples and oranges.”

The biggest exception is sodium valproate, an anticonvulsant also used to treat mood disorders, Dr. Lusskin said. The ongoing Neurodevelopmental Effects of Antiepileptic Drugs (NEAD) study has found in utero exposure to be associated with an increase in birth defects, and with cognitive problems in 3-year-olds whose mothers took it during pregnancy.

The uncertainty of treatment leaves pregnant women and their physicians to weigh the risks of psychotropic medications against the risks of untreated mood disorders. “There is no such thing as non-exposure,” Dr. Lusskin said. If the mother is not treated, “the fetus is going to be exposed to the mother’s illness, which can create phenotypic changes with life-long effects. If the mother is treated inadequately, the fetus will be exposed to both the effects of the illness and the medication. And if the mother is treated to remission, with the medication titrated to her response, medication exposure can be at least limited,” while the new mother becomes healthy enough to give her baby the best possible care.

The biggest barrier to treating mental illness during pregnancy is fear of fetal harm: teratogenicity, neonatal complications from drug exposure, and long-term neurodevelopmental effects. But these risks must be considered in light of real world experience – not just based on numbers from a study, Dr. Lusskin said. “Any risk of impairment has to be compared to the

background risk of a birth defect, which is 2%-4%. If a drug increases this risk in a clinically meaningful way, it has to be over and above this background rate.”

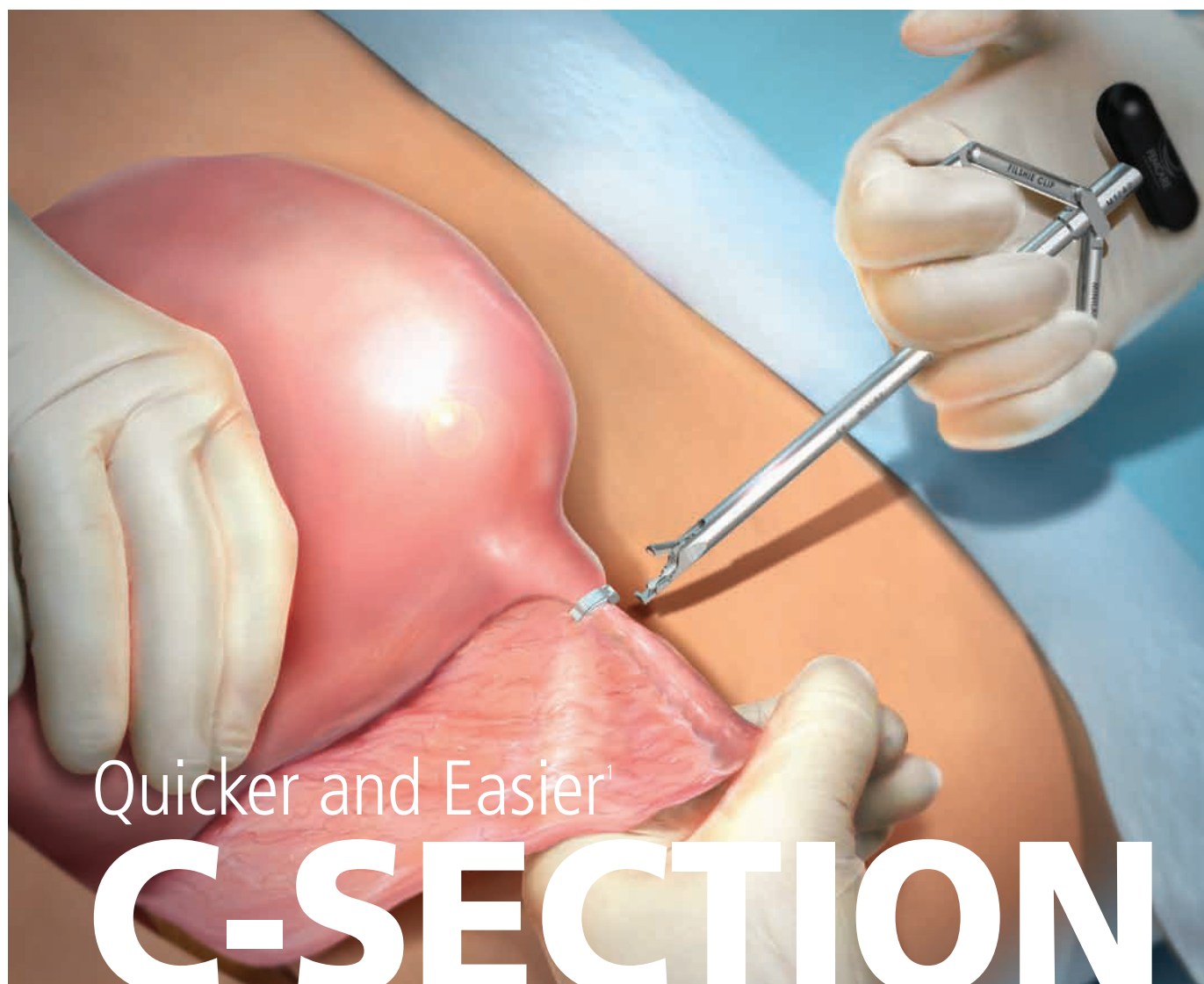
Even a substantial increase in a rare birth defect can be misleading. For instance, Ebstein’s anomaly is a heart defect that occurs in 1 in 20,000 births. “Lithium is said to increase this rate to about 1 in 2,000 births. But this is still way below the expected background rate of birth

defects. Risks are relevant in terms of their relativity – the absolute risk is just quoting a figure,” she said.

But untreated mental illness poses its own risk. Babies exposed in utero to the chronic stress hormones associated with anxiety and depressive disorders might become phenotypically programmed, prone themselves to early childhood behavioral problems and, in later life, to mental illness. “The fetal programming

hypothesis is the interaction between the baby’s genetics and the environmental exposure in utero, and it’s mediated by the sex of the fetus and the timing of exposure,” Dr. Lusskin said.

Dr. Lusskin said she consults for the nonprofit drug safety database www.reprotox.org and has authored a chapter in uptodate.com, an Internet-based textbook on the use of medication in pregnancy and lactation. ■



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