Psychotropic Drugs May Be Needed in Pregnancy

Maternal psychiatric illness, if inadequately treated or untreated, may result in poor compliance with care.

BY GREG MUIRHEAD
Contributing Writer

KOLOA, HAWAII — Although labeling typically doesn't support the use of psychotropic drugs in pregnant women, the drugs might be needed during pregnancy, according to an observational study done at Emory University, Atlanta.

"What I want you to recognize is that you're going to expose the child to something, be it illness or treatment, and in the context of that, some decisions are far worse than others," Dr. Zachary N. Stowe said at the annual meeting of the American College of Psychiatrists. "Abruptly stopping or changing treatment at knowledge of conception is an effort on your part to reduce your anxiety. It doesn't change outcome. In fact, it probably worsens outcome," Dr. Stowe asserted.

The need for treatment cannot be ignored. A large number of women who become pregnant have a mental health problem.

"We're talking about [400,000] or 500,000 women every year with a neuropsychiatric illness that" begins before family planning, or that might have been treated or needed to be treated during family planning, said Dr. Stowe, who is director of the women's mental health program at Emory University.

And with 4 million U.S. deliveries per year, he pointed out, "over 50% of pregnancies are unplanned."

Studies of antenatal depression and its consequences led the American College of Obstetricians and Gynecologists to issue the following guideline statement in November 2007:

"Maternal psychiatric illness, if inadequately treated or untreated, may result in poor compliance with prenatal care, inadequate nutrition, exposure to additional medications or herbal remedies, increased alcohol and tobacco use, deficits in mother-infant bonding, and disruptions within the family environment."

Other antenatal depression study findings include increases in suicide, postpartum depression, premature birth, low birth weight, neonatal complications, and fetal demise, said Dr. Stowe.

In the observational study that he and his colleagues conducted, pregnant women who had depression decided for themselves whether to discontinue their antidepressant medication.

Of the women who discontinued, 68% became "sick" before delivery, said Dr. Stowe. The other 32% were able to stop taking their antidepressant safely, but 25% who stayed on their antidepressant still became sick.

For women with bipolar disorder who discontinued their mood-stabilizing medication, 85% became sick before delivery.

A big problem, of course, is the typical drug labeling statement that "use in pregnancy is not recommended unless the potential benefits justify the potential risks to the fetus," which Dr. Stowe called "handwashing."

There's no question that psychotropic drugs will reach the fetus. Psychotropic medicines are designed to get past the blood-brain barrier and reach the brain, which means they will likely pass through the placental barrier without any difficulty. His own unpublished research has supported this, but he wondered if it is always harmful.

"You can actually statistically argue that antidepressants reduce your risk of birth defects," he said. "To date, we have no confirmed evidence of increased birth defects on our antidepressants."

In some psychotropic categories, however, some drugs are better than others—or much worse.

"Valproate has consistently the highest placental passage of any medicine we've studied, and it has the worst outcome," said Dr. Stowe. "It is worse than Accutane."

"In my opinion, there is no justification for first-line use of valproic acid in women of reproductive years," he continued. In babies whose mothers used valproic acid during pregnancy, "the mean IQ drop is 15 points. One in 10 children is mentally retarded," he said.

For medication purposes, 'You should treat all women as though they are pregnant, starting at age 9. From 9 to 49, they are pregnant until proven otherwise.'

On the other hand, "lamotrigine is the cleanest anticonvulsant we've seen. It is emerging as the number-one treatment for epilepsy during pregnancy. The overall malformation rate is lower than the national average," he pointed out.

A recent, not-yet-published study of the use of lamotrigine in 26 women with bipolar disorder found that they did well if they continued the drug throughout pregnancy but not if they discontinued.

A higher dosage is needed for treatment of bipolar disorder, just as it is needed for epilepsy, Dr. Stowe said.

Another unpublished study found that pregnant women using olanzapine "failed their blood sugar test, independent of dose," he said. "We should not trade gestational diabetes to treat mental illness during pregnancy, because what you're actually trading is the risk for adult-onset diabetes after pregnancy. Gestational diabetes is a well-known risk factor for that."

Not much is known about the use of atypical antipsychotic drugs during pregnancy, he said.

As for pregnant women using lithium, be aware that dehydration at birth can cause lithium toxicity in the infant, he said (Am. J. Psychiatry 2005;162:2162-70).

Switching drugs during the course of pregnancy with the thought that drug B has more safety data than drug A is entering "the world of the unknown," Dr. Stowe said, "because all the data for medicine B were not derived from babies that first got medicine A. Everything we know about teratology says two medicines are worse than one. And please remember, the later trimesters can be just as important as the first trimester."

Given the uncertainties of sexual behavior and the possibility of undetected pregnancy in female patients, "you should treat all women as though they are pregnant, starting at age 9. From 9 to 49, they are pregnant until proven otherwise," he said.

Regarding the possibility of passing medications to infants during breast-feeding, "the dose in pregnancy is huge compared to the dose in lactation. Worrying about the medicine in lactation, if you used it in pregnancy, is really a waste of time. Our medicines in the bloodstream for antidepressants are nanograms per milliliter; for anticonvulsants they are in micrograms per milliliter. That's what gets into breast milk," he said.

Dr. Stowe is on advisory boards for Bristol-Myers Squibb Co. and GlaxoSmithKline Inc. He has received grants from GlaxoSmithKline, Pfizer Inc., and Wyeth Pharmaceuticals. He is on the speakers bureaus of Eli Lilly, GlaxoSmithKline, Pfizer, and Wyeth Pharmaceuticals. ■

Induction Protocol Fails to Avert C-Sections, but Aids Outcomes

BY PATRICE WENDLING
Chicago Bureau

DALLAS — Use of the AMOR-IPAT protocol did not significantly reduce cesarean deliveries in a prospective randomized trial of 270 women.

AMOR-IPAT (Active Management of Risk in Pregnancy at Term), a controversial approach, involves prostaglandin-assisted preventive labor induction based on a risk-scoring system, Dr. James Nicholson reported at the annual meeting of the Society for Maternal-Fetal Medicine.

The women enrolled in the study had at least one of six specific risk factors for delivery and were randomized at 37 weeks, 4 days' gestation to either AMOR-IPAT (n = 136) or usual care (n = 134). Their mean age was 23 years.

As expected, the AMOR-IPAT group experienced significantly higher rates of labor induction (60% vs. 22%) and prostaglandin usage (40% vs. 16%), and were delivered, on average, 1 week earlier than the usual-care group.

In an intent-to-treat analysis, the rate of cesarean delivery was not significantly different between the AMOR-IPAT and usual-care groups (10% vs. 15%).

However, the AMOR-IPAT group had a significantly lower neonatal intensive care unit admission rate of 1.5% compared with 6.7%.

In addition, two composite outcomes—uncomplicated vaginal birth (74% vs. 63%) and adverse outcome index (AOI) scores (mean 1.4 vs. 8.6)—were significantly improved in the AMOR-IPAT group.

"AMOR-IPAT may represent a legitimate response to our nation's increasing rates of adverse term outcomes," said Dr. Nicholson of the department of family medicine and community health, University of Pennsylvania, Philadelphia.

'Clearly there is a conflict between our current methods of care and this method of care, so there would need to be changes … for structure and process.'

Audience members were quick to point out that the study failed to achieve its primary goal of lowering cesarean delivery rates and that some of the deliveries went against the current American College of Obstetricians and Gynecologists' recommendation to avoid delivery before 39 weeks' gestation.

Dr. Nicholson responded that the study included only women with very good ultrasound-based dating, and that while a significant number of women were delivered during their 38th week, the protocol actually led to fewer infants going to the neonatal intensive care unit.

"Clearly there is a conflict between our current methods of care and this method of care, so there would need to be changes in labor and delivery for structure and process if this method were to be used," he said.

"During this conference I've heard a lot about the AOI scores … and I would suggest that if the AOI scores are really improved to the level seen in this study that we might take a look at our processes of care and consider some significant changes," Dr. Nicholson commented.

Two previous retrospective, nonrandomized studies showed a significant decrease in cesarean deliveries with the AMOR-IPAT protocol (Ann. Fam. Med. 2007;5:310-9; Am. J. Obstet. Gynecol. 2004;191:1516-28).

The study was funded jointly by the National Institutes of Health and the First Hospital Foundation.

Dr. Nicholson disclosed that Forest Pharmaceuticals provided free samples of its dinoprostone cervical-ripening product to the university's hospital, but that none of the samples were used during the study. ■

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