Expert: Be More Alert To H1N1 in Pregnancy

BY KATE JOHNSON

MONTREAL — Prenatal care providers need to take a frontline attitude about novel influenza A (H1N1) because pregnant women are among those at highest risk for infection and serious complications.

"We need to get the message out to the practitioners in the field that they've really got to be thinking about this. They need to recognize that influenza in pregnancy is not trivial, and they should consider early treatment," said Dr. Deborah Money, president-elect of the Infectious Diseases Society for Obstetrics and Gynecology.

Speaking after chairing an urgent update session on novel H1N1 influenza at the society's annual meeting, Dr. Money said the latest figures on the infection in pregnancy, published in Lancet (doi:10.1016/S0140-6736[09]61304-0) paint a worrisome picture of practitioner's reaction time.

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DR. MONEY

Of 34 pregnant women who contracted the virus, only 50% were treated with oseltamivir, and just 8 (24%) received treatment within 48 hours of symptom onset.

"Antivirals have the best impact within the first 48 hours of treatment and the latest deaths in this population had late starts with oseltamivir treatment," she said in an interview. Among the six women who died, the earliest initiation of oseltamivir was 6 days after symptom onset, and the latest was 15 days.

The most common presentation was a febrile, influenzalike illness (94% of the patients), which included fever plus cough or sore throat. Vomiting and diarrhea occurred in only 18% and 12% of pregnant patients. Pregnant women were more likely to report shortness of breath (41%) than patients in the general population (15%). Rhinorrhea occurred in 59% of pregnant patients.

Patient awareness also may be an issue, since many pregnant women might not think to call their obstetricians when they come down with the sniffles, she acknowledged.

Dr. Money, an associate professor of obstetrics and gynecology at the University of British Columbia, Vancouver, said prenatal care providers must now make new plans, not only to include influenza patients in their daily schedules, but to ensure that these patients do not put their other patients at risk.

"If the woman really needs to be seen, [providers] need to orchestrate this in a way that is safe for their other patients—either at the end of the day, or in a place with a negative pressure room, or by getting them to wear a mask on entry."

The drug of choice is oseltamivir, at a dosage of 75 mg twice per day for 5 days (www.cdc.gov/h1n1flu/).

"We already have a poor track record with the seasonal influenza. U.S. guidelines have recommended the seasonal influenza vaccine for pregnant women for some time, but despite those recommendations the uptake in studies has been in the 14% range. So given that poor track record, how are we going to manage immunizing women against both seasonal and H1N1 influenza?"

In the Lancet study, 56% of the pregnant women with novel H1N1 influenza had not received the seasonal influenza vaccine, 9% had been vaccinated, and vaccination status was unknown for the remaining 35%.

"The H1N1 vaccine might turn out to be two doses, although that is still to be determined. So, with the addition of the seasonal vaccine we're looking potentially at three doses through the fall and winter of all pregnant women going to care providers, and the logistics start to boggle the mind."

Discussion at the meeting explored the possibility of setting up influenza vaccination clinics at teaching hospitals to relieve small clinics and private practitioners. However, this plan would still rely on vaccination recommendations from private practitioners.

"Our experience anecdotally is that care providers have been advising against vaccination in pregnancy because they misunderstand which ones you can give in pregnancy and which ones you can't. Our anxiety is that they won't give oseltamivir, and they won't give the vaccine because they are in that mind set. But generally speaking, those of us in academic centers that see complications, end up seeing more complications related to undertreatment rather than overtreatment," Dr. Money said. ■

DRUGS, PREGNANCY, AND LACTATION

Treating Morning Sickness

Currently, no drug approved by the Food and Drug Administration is available for treating morning sickness. Bendectin, the combination of the antihistamine doxylamine with pyridoxine (vitamin B_6)—used in the United States and Canada in the 1960s and 1970s for treating nausea and vomiting of pregnancy—was pulled from the market because of litigious claims. But this combination has been shown to be safe in large studies conducted since that time, and has been approved and available continuously as Diclectin in Canada.

BY GIDEON KOREN, M.D.

Doxylamine is an older antihistamine and has central nervous system effects, including sedation, and Diclectin is not yet approved in the United States. Therefore, there is room for alternatives for treating nausea and vomiting in pregnancy (NVP). Currently, trials are being conducted in the United States in a process aimed at reintroducing the combination of doxylamine and pyridoxine to the U.S. market, in view of its impressive safety record.

Metoclopramide, a prokinetic drug used for more than 40 years to treat nausea and vomiting due to various causes, is one alternative to the doxylamine-pyridoxine combination. Because metoclopramide acts mostly through the gut, not the CNS, it has a physiologic advantage in terms of potential side effects and is the drug of choice for NVP in some countries, but not in North America, where it is usually used only for severe cases. It can be associated with extrapyramidal symptoms, which tend to be self-limited and have rarely been reported in the context of morning sickness.

To date, the safety data on the use of metoclopramide during pregnancy have been limited, based on studies involving about 800 pregnancies in the literature. But a large, retrospective cohort study published in June, conducted by investigators at Ben-Gurion University of the Negev, Beer-Sheva, Israel, in collaboration with the Motherisk program in Toronto, provided reassuring data regarding its safety during the first trimester of pregnancy.

The study linked medication database records for females aged 15-49 years who were members of a health maintenance organization in Southern Israel, with databases containing maternal and infant records for the medical center that serves the area. Of the 81,703 infants born to these women between Jan. 1, 1998, and March 31, 2007, a remarkable 3,458 (4.2%) had been exposed to metoclopramide during the first trimester.

This number exceeded what we expected and created a rare opportunity to analyze the reproductive safety of this drug in a large study with good quality data and the ability to adjust for confounding factors, including parity, maternal age, and smoking status. The mean number of daily doses was about seven, and the mean age of the women was almost 28 years.

When compared with the infants of the 78,245 women in the HMO who had not taken metoclopramide during the first trimester, there was no increased risk of major or minor congenital malformations, low birth weight, preterm delivery, or perinatal death among the infants whose mothers had taken metoclopramide during the first trimester, after adjustment for confounding factors (N. Engl. J. Med. 2009;360:2528-35). The results did not change when pregnancy terminations were included.

Metoclopramide is another option for treating nausea and vomiting, the most common condition in pregnancy, which often receives inadequate attention from clinicians, despite studies showing NVP causes significant social and psychological morbidity. Clinicians who may be hesitant to prescribe an antiemetic for patients who are suffering from NVP should be able to prescribe with confidence a treatment for which more data are now available to support its safety.

An important consideration when treating women who have NVP is the impact that heartburn and reflux can have on the severity of these symptoms. Quite a few women who call the dedicated NVP line at Motherisk (800-436-8477) reported also having acid reflux symptoms, along with nausea and vomiting, which led to a study that demonstrated for the first time that heartburn and acid reflux can exacerbate the severity of nausea and vomiting.

The prospective study, published in the Canadian Journal of Gastroenterology in April, compared 194 women with NVP and heartburn, reflux, or both, with 188 women with NVP without heartburn or reflux. We found that the women with heartburn and reflux had significantly higher scores on scales that measured the degree of emesis and nausea, and significantly lower well-being scores, which our analysis determined was related to heartburn and reflux, not to preexisting GI conditions or symptoms, hyperemesis gravidarum in previous pregnancies, or other confounding factors (Can. J. Gastroenterol. 2009;23:270-2).

In another study that is in press, we also found that treating women who have reflux and heartburn associated with NVP with an H_2 receptor blocker or a proton pump inhibitor decreased nausea and vomiting dramatically, without the need for increasing the dose of the antiemetic. The results of this study support managing acid reflux in women with these symptoms to help control nausea and vomiting—a strategy that has not received much consideration previously. Recent meta-analyses by Motherisk have shown that both H_2 blockers and proton pump inhibitors are safe during pregnancy, further supporting the management of reflux.

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