Hormone Therapy Raises Lung Cancer Death Risk

BY MARY JO M. DALES

ORLANDO — Hormone therapy with estrogen plus progestin for more than 5 years increased the risk of death in women diagnosed with non–small cell lung cancer, based on secondary analyses from the Women's Health Initiative reported at the annual meeting of the American Society of Clinical Oncology.

The increased risk was most notable in women who were current smokers. One in 100 current smokers using combined hormone therapy (HT) in the trial experienced an avoidable death from non–small cell lung cancer during the 8 years of this study, said Dr. Rowan Chlebowski, a medical oncologist at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center and the study's lead author.

The findings "should influence discussions between physicians and women considering hormone therapy use, especially for those with a smoking history," Dr. Chlebowski said. Women who smoke and are seeking or already receiving hormone therapy should be strongly advised to quit smoking.

The incidence and mortality of non–small cell lung cancer (NSCLC) were examined during 5.6 years of intervention with HT or placebo and 2.4 additional years of follow-up.

While the incidence of NSCLC diagnosis was not significantly different for controls and women on HT, survival after diagnosis was significantly lower in the hormone therapy group. There were 67 deaths among 96 women on HT and 39 deaths in 72 cases in the control group. Further, median survival was 9.4 months in the hormone therapy group and 16.1 months in the control group.

The HT and control groups were evenly matched for smoking history with 50% never smokers, 40% former smokers, and 10% current smokers. But when the data on NSCLC deaths were analyzed by tobacco use, the risk was higher in current smokers and considerably higher in smokers also taking HT.

Of the 67 NSCLC deaths in the hormone therapy group, 27 occurred in 800 current smokers. The other 38 deaths occurred in 9 of 4,178 never smokers and in 29 of 3,362 former smokers. Of the 39 NSCLC deaths in the control group, 19 occurred in 838 current smokers. The other 20 deaths occurred in 5 of 3,999 never smokers and in 15 of 3,157 past smokers.

Dr. Chlebowski disclosed that he is a consultant and adviser to numerous pharmaceutical companies. These disclosures were not relevant to the WHI analysis. ■

Metoclopramide Does Not Appear to Raise Risks to Fetus

BY MARY ANN MOON

The use of metoclopramide to control nausea and vomiting in the first trimester does not increase the risk for congenital malformations, low birth weight, or perinatal death, according to a recent report.

These findings from a large retrospective cohort study "provide reassurance about the safety of metoclopramide," which has not been convincingly established until now, wrote Ilan Matok of Ben-Gurion University of the Negev, Beer-Sheva, Israel, and associates.

"Despite its extensive use, only a few studies have assessed the safety to the fetus of maternal exposure to metoclopramide during the first trimester, and the relatively small sizes of these studies limited their power," they noted.

The researchers assessed singleton deliveries between 1998 and 2007 at the largest HMO in Israel, where metoclopramide is the antiemetic drug of choice during pregnancy. Approximately half of the 81,703 infants in the study were born to Jewish parents and half to Bedouin Muslim parents.

A total of 3,458 (4%) of these infants were exposed to metoclopramide during the first trimester. The mean duration of exposure was 1 week.

The rate of major congenital malformations was 5.3% among exposed infants and 4.9% among unexposed infants, a nonsignificant difference.

The rates of minor congenital malformations (3.8% vs. 3.5%) and of multiple malformations (2.5% vs. 2.3%) also were similar between exposed and nonexposed infants. There also were no significant associations between subclasses of congenital malformations and metoclopramide exposure, nor was there any clustering of anomalies among exposed infants.

When the data were analyzed according to subjects' ethnic backgrounds, the drug did not raise risks to infants of either Jewish or Bedouin Muslim parents (N. Engl. J. Med. 2009;360:2528-35).

Metoclopramide also was not associated with an increased risk of preterm birth, low Apgar scores, perinatal death, or low birth weight.

The researchers reported having no relevant conflicts of interest. ■

DRUGS, PREGNANCY, AND LACTATION

H1N1 Virus Infection

Novel H1N1 flu virus can cause acute respiratory illness with rapidly progressive severe pneumonia. Since April 15, 2009, when the Centers for Disease Control and Prevention confirmed by laboratory testing the first case of 2009-H1N1 flu in the United States, the infection has spread to all 50 states, the District of Columbia, and Puerto Rico. Although the overall influenza activity is decreasing in this country, outbreaks of the infection continue to occur, in some cases with intense activity (www.cdc.gov/H1N1FLU).

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Several important factors remain uncertain, such as how many infected people will develop severe morbidity, how many will die, and how the new virus will affect the United States during the fall/winter flu season. It is also unclear how the virus will affect most pregnancies, although pregnancy is thought to be a risk factor for worsening complications of H1N1 infection. Seasonal flu is known to increase the chance of a pregnant woman getting sick or having serious problems, including preterm labor and severe pneumonia. The big question is, will H1N1 cause the same problems?

The CDC has published information on three recent cases of H1N1 virus infection in pregnancy (MMWR 2009;58:497-500). The first case involved a 33-year-old, relatively healthy woman at 35 weeks' gestation who had a history of psoriasis and mild asthma. She presented at her obstetrician's office with a 1-day history of myalgias, dry cough, and low-grade fever. She had not recently traveled to Mexico. A rapid influenza diagnostic test in the physician's office was positive. About 4 days later, she developed worsening shortness of breath, fever, and productive cough.

An emergency cesarean was performed to deliver a female infant with Apgar scores of 4 and 6 at 1 and 5 minutes. Currently, the infant is healthy. Two days after birth, the mother developed acute respiratory distress syndrome and 1 week later was started on oseltamivir (Tamiflu). The woman died about a week later. Testing by the CDC of a nasopharyngeal specimen was positive for H1N1 virus.

The second case involved a previously healthy 35-year-old woman at 32 weeks' gestation. She had been in Mexico for 3 days preceding her presentation with a 1-day history of shortness of breath, fever, cough, diarrhea, headache, myalgias, sore throat, and respiratory chest pain. Rapid influenza diagnostic testing was negative. Several members of her family in Mexico and the United States had recently been ill with influenzalike illness.

The following day, she was seen in her obstetrician's office and a nasopharyngeal swab sample was collected and sent for virus testing. She was treated with antibiotics, antiemetics, acetaminophen, and inhaled corticosteroid. The patient recovered fully and her pregnancy was proceeding normally. Testing of the sample by the CDC confirmed infection with H1N1 virus.

The third case was a 29-year-old woman at 23 weeks' gestation who had a history of asthma but was not taking asthma medications. She presented with her 7-year-old son at a family practice clinic. Both had a 1-day history of cough, sore throat, chills, fever, and weakness. The mother had not traveled to Mexico, but a 10-year-old son had similar symptoms in the previous week. Rapid influenza diagnostic testing of the mother was positive and was later confirmed to be H1N1 virus. The mother and her son were prescribed oseltamivir.

The mother's symptoms are resolving without complications (no information was provided about the son), and her pregnancy was proceeding normally. The clinic physician who evaluated the mother also was pregnant (13 weeks' gestation). She began oseltamivir and has remained asymptomatic.

The antiviral treatment of choice for H1N1 virus infection is oral oseltamivir or oral inhaled zanamivir (Relenza). Treatment should be started within 2 days of the onset of symptoms, but can be started after 48 hours for very sick or pregnant patients, and continued for 5 days. For prophylaxis, treatment should be continued for 10 days. These antivirals have no published information in human pregnancy. Both probably cross the placenta, but based on animal data and experience with most other antiviral agents, appear to be low risk. Moreover, the maternal benefit far outweighs any risk to the embryo or fetus.

Both agents are excreted into milk but probably present no risk to a nursing infant. In fact, the CDC Web site recommends that mothers with H1N1 virus infection continue to breastfeed because of the advantages of breast milk for the infant's immature immune system.

The CDC Web site has an informational page on what pregnant women should know about H1N1 virus (www.cdc.gov/h1n1flu/guidance/pregnant.htm). You may want to print the answers to common questions and provide them to patients as a handout.

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