Pathology study tracks uterine changes with mifepristone

March 7 2011

Research continues to show that the controversial abortion drug mifepristone might have another use, as a therapeutic option besides hysterectomy for women who suffer from severe symptoms associated with uterine fibroids.

The University of Rochester Medical Center in 2004 began investigating mifepristone, in a class of drugs known as progesterone receptor modulators (PRMs), to treat fibroids, which affect roughly half of all women younger than 50. Results showed the drug shrank the fibroids and greatly improved the quality of life for the women involved in the clinical trial.

But concern over whether PRMs could cause tissue changes that signal uterine cancer dampened a growing interest in the drug. The latest URMC study demonstrates that PRMs do not appear to trigger cancerous or pre-cancerous lesions in the lining of the uterus, at least in the short term, according to an article in the journal *Human Pathology*.

"Our biggest concern was cancer, and although we saw significant changes in the endometrial tissue specific to the action of PRMs, all of the changes were benign and well characterized in the laboratory," said lead investigator Julietta Fiscella, M.D., clinical assistant professor of Pathology and Laboratory Medicine at URMC and Director of Pathology at Highland Hospital, an affiliate of URMC.

Fiscella analyzed 152 tissue samples from 53 premenopausal women in

the Rochester, N.Y., area, who volunteered to take mifepristone at very low doses for up to 18 months to alleviate miserable symptoms such as pain and heavy bleeding. She compared samples of unexposed endometrial tissue to samples from women who took the drug in 2.5 mg or 5 mg dosages. (To end an unwanted pregnancy, mifepristone is given in a single-day dose of 200 to 600 mg.)

The changes most evident in the drug-exposed tissue included fluid-filled glands that appeared as scattered, benign cysts of varying size, and some abnormal blood vessels. These features were consistent in 86 percent of the drug-exposed samples, with no statistical differences between the two doses, the study said.

An international panel of pathology experts also conducted a blind review of the 152 samples and confirmed Fiscella's findings, she said. The results suggest that if mifepristone or PRMs with similar properties are eventually approved for treatment of uterine fibroids, pathologists will have a reliable way to track and compare the effects of different doses and treatment schedules (weekly versus daily) on patients during their childbearing years.

The National Institute for Child Health and Human Development funded the study.

Fiscella said larger studies with longer follow-up are needed to more fully characterize the low-dose effect of mifeprisone, and to confirm that changes in the uterus resolve after a woman stops taking the drug.

The Food and Drug Administration approved mifepristone in 2000 for the sole purpose of ending unwanted pregnancies, and has since issued warnings due to a small number of deaths that occurred at the highest doses. Distribution of the drug is strictly controlled, although the FDA does allow it to be studied by qualified physicians. In addition to

research into its effect on common gynecological conditions, scientists in California reported in the journal Science in 2006 that mifepristone blocked the formation of breast tumors in mice, suggesting a potential new path to interfere with the hormone progesterone's role in breast cancer. Since then mifepristone has been actively studied by other scientists as a potential cancer treatment.

Leiomyoma, the medical term for uterine fibroids, routinely causes iron-deficiency anemia due to excessive menstrual bleeding. Thousands of women annually opt for hysterectomies, a major surgery, or have the fibroids removed through minimally invasive embolization because no other medical treatment has been proven effective.

Provided by University of Rochester Medical Center