Certain Oral Contraceptives May Pose Health Risks, Study Suggests

ScienceDaily (Mar. 11, 2008) — The widely used synthetic progestin medroxyprogesterone acetate (MPA) decreased endothelial function in premenopausal women in a study done at the University of Oregon. The finding, researchers said, raises concerns about long-term effects of MPA and possibly other synthetic hormones on vascular health in young women.

The vascular endothelium lines the inside of blood vessels. In recent years, it has been found to be a dynamic organ that serves an important role in the prevention of atherosclerosis.

"The logical conclusion of this study is that over a long period of time it would not be good to have exposure to an agent that is reducing blood vessel flexibility, because it could be associated with the development of heart disease or related problems," said co-author Dr. Paul F. Kaplan, a long-time Eugene gynecologist and senior researcher in the UO's human physiology department. He stressed, however, that a longer, larger study is needed.

MPA is the progestin that was used in the Women's Health Initiative (WHI), including a clinical study on hormone-replacement therapy halted because of health concerns in postmenopausal women. MPA is the active ingredient of Provera, which is used to treat abnormal uterine bleeding, induce menstrual cycles and relieve symptoms of the menopause.

It's also a component in Depo/Provera, an injectible long-lasting contraceptive used by many young women. Millions of women use various hormone therapies with a variety of progestin types for contraception. In the U.S. alone, 80 percent of women have used oral contraceptives.

The UO study, appearing online ahead of regular publication by the journal Heart and Circulatory Physiology, is among the first to focus on the impact of MPA in premenopausal women. Fourteen women, 19-27 years old, took part in the study after passing thorough medical exams to screen out numerous health conditions.

The five-member UO team -- led by Jessica R. Meendering, a former UO doctoral student now a professor of exercise science at the University of Nebraska in Omaha -- studied the effects of the sex hormone estradiol by itself and in combination with MPA on endothelial function of the brachial artery. The health of the endothelium in this artery has been shown to be a telling proxy for the coronary arteries and a good predictor of cardiovascular risk.

When researchers gave an oral version of MPA to determine its impact, they found that it wiped out the positive effects on endothelial function that estradiol had provided. MPA reduced the function by reducing the brachial artery's ability to dilate -- grow bigger in diameter -- in response to the stress of changing blood flow, Kaplan said.

UO researchers also found that MPA had an effect on concentrations of endothelin-1, a peptide that promotes cell division and serves as a mediator of inflammation. It also acts as a constricting factor for blood vessels. When peptide levels rise, endothelin-1 is suspected to play a key role in many diseases of the airways, pulmonary circulation, inflammatory lung diseases and vasoconstriction of blood vessels. UO researchers saw levels decline with estradiol alone, but increase substantially with the

addition of MPA, negating the benefits of the estrogen.

"There is an overwhelming amount of evidence to suggest that estrogen is beneficial to arterial vascular health of women," Meendering said. "Since the WHI found either no benefit or a slight increase in adverse cardiovascular events in postmenopausal women taking combination hormone-replacement therapy containing estrogen and MPA, many have questioned the vascular effects MPA and its use in postmenopausal women. This led our group to question how MPA affects the vasculature in young women.

"We need to be taking the time to find out if different synthetic hormones have different effects on vascular health in young women," she said. "It's not a big health concern right now, because there are no obvious short-term effects raising health concerns. But we don't know how these synthetic hormones taken by young women affect their long-term cardiovascular health. Maybe effects aren't being noticed while women are young, but maybe they are adding to the fact that rates of cardiovascular disease are so high in women."

Kaplan stressed that this project was a starting point of "major basic science research, so this study does not say women should change what they are doing."

"We can say that we saw vascular changes in the arteries of the arm that have been shown in previous studies involving coronary arteries," he added. "This study does let us say that whatever changes we are seeing are important not just for the arm but probably for most of the major arteries in the body, and this is important for cardiac disease."

The research was done in the Exercise and Environmental Physiology Laboratories of co-author Christopher T. Minson, a UO professor of human physiology. The study was supported in part by grants from the Medical Research Foundation of Oregon to Minson and by a Eugene and Clarissa Evonuk Graduate Fellowship to Meendering. Additional research is planned under a grant from the National Institutes of Health, Kaplan said.

Other co-authors were doctoral student Britta N. Torgrimson and undergraduate Nicole P. Miller.