Researchers investigate estrogen to prevent depression and cardiovascular disease

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Researchers at the University of North Carolina at Chapel Hill have launched a new clinical trial to determine if estrogen replacement therapy may help prevent depression and cardiovascular illness in women between the ages of 45 and 55.

It's a move that may raise eyebrows in some quarters, given that a Women's Health Initiative (WHI) study was halted in 2004 due to findings that estrogen therapy resulted in an increased risk of stroke and blood clots.

But there's an important difference between the UNC study and the WHI estrogen study, said David Rubinow, MD, UNC's chair of psychiatry and one of two principal investigators of the new 5-year study, which is funded by a $4.5 million grant from the National Institutes of Health. The other principal investigator is Susan Girdler, PhD, professor of psychiatry

"The Women's Health Initiative study led to the mistaken belief that estrogen replacement therapy is bad for all women. And as a result, it has served to deprive some women of a treatment that might greatly and favorably impact their lives. Much of the negative impact of estrogen that they found was related to the fact that most of the women in the Women's Health Initiative study were far past the menopause and up to 79 years old," Dr. Rubinow said.

"There are now a large number of studies that demonstrate what has

been called the timing hypothesis. That is, giving estrogen within a year or two of menopause has beneficial effects, but giving estrogen in women more than five years beyond the menopause can actually be harmful.

"When the women who were close to menopause were looked at separately, the adverse effects on the heart were not seen and in fact some suggestion of beneficial effects was seen. Perimenopausal women in the Women's Health Initiative who received estrogen had significantly lower coronary artery calcification compared to the women who didn't take estrogen.

"That raises the question: Is estrogen potentially beneficial for women in the perimenopause – the years surrounding the menopause? It's really an unanswered question at this point. Our study is an effort to find out what puts an individual woman at risk for heart disease and depression and what predicts beneficial effects of estrogen replacement during the perimenopause on affective well-being and cardiovascular well-being."

The study, which began in August 2010 and will be conducted entirely at UNC, seeks to enroll a total of 320 women ages 45 to 55 who are in the menopause transition. All will be randomized to receive treatment with estradiol (estrogen replacement) skin patches or placebo.

Women in the study will be tested three times: before treatment and then again after 6 months and 12 months of treatment. These laboratory tests will measure their cardiovascular and inflammatory responses to mental stress, indicators of cardiovascular health and metabolic markers such as a glucose tolerance test, waist/hip ratio and lipid profiles. In addition, assessments of their moods, vital signs, side effects and compliance with the treatment regimen will be conducted on each participant.

"Given the mortality and morbidity associated with depression and heart

disease, and the tremendous increase in risk of these disorders during the perimenopause, it is critical that we identify those women who will be helped by estradiol," Dr. Rubinow said.

Provided by University of North Carolina School of Medicine