SOUTHWESTERN NEWS

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## STUDY CONFIRMS REPLACING ESTROGEN BY SKIN PATCH DECREASES NERVE ACTIVITY, BLOOD PRESSURE IN POSTMENOPAUSAL WOMEN

DALLAS – June 19, 2001 – Researchers at UT Southwestern Medical Center at Dallas report that administering replacement estrogen via a skin patch is superior to oral estrogen replacement therapy in lowering blood pressure and sympathetic nerve activity – the neural control of blood pressure – in postmenopausal women.

The study, published in today's issue of *Circulation,* is the first to compare the effectiveness of oral and transdermal replacement therapies on sympathetic nerve activity in humans.

These findings suggest that how estrogen is administered is the key in optimizing the beneficial effects of estrogen replacement therapy on blood pressure, said Dr. Wanpen Vongpatanasin, assistant professor of internal medicine in hypertension and lead author of the study.

"Prevalence of hypertension is very low in young pre-menopausal women but increases markedly after menopause, suggesting a protective role of estrogen on blood pressure. Knowledge from this study may lead to an effective therapy to treat or prevent hypertension after menopause," she said.

Vongpatanasin and her colleagues reported that transdermal estrogen, or the estrogen patch, decreased nerve activity in postmenopausal women with normal blood pressure by 30 percent. The researchers also reported a small, but statistically significant, decrease in blood pressure in patients taking transdermal estrogen.

Both nerve activity and blood pressure were unaffected in patients taking oral estrogen.

"This is an initial step that leads us to think that all estrogen preparations are not the same," Vongpantanasin said.

"This may be one of the reasons why large clinical trials failed to show a benefit of estrogen replacement therapy on blood pressure or any cardiovascular outcomes. It could very well be because only oral estrogen, the most popular preparation in the United States, has been used rather than transdermal estrogen."

Postmenopausal women have an excessive increase in nerve activity in the sympathetic nervous system. Increased nerve activity in this system causes blood vessels to constrict. An excessive increase may cause hypertension – one of the leading causes of death in women in the

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United States.

Transdermal estrogen replacement therapy has been shown to decrease nerve activity and blood pressure in female laboratory animals.

"In some female rats, removal of the ovaries leads to an increase in nerve activity and blood pressure. Estrogen replacement in the form of an implant under the skin (the effect of which is similar to transdermal estrogen in humans) reverses this problem," Vongpatanasin said.

The 12 study participants randomly received transdermal estrogen replacement therapy for eight weeks, then switched to oral estrogen replacement therapy for eight weeks and a placebo for another eight weeks. The researchers used microelectrodes, which are similar to acupuncture needles, to record sympathetic nerve activity and ambulatory blood pressure readings. The researchers recorded about 50 blood pressure readings during a 24-hour period before and after each eight-week therapy.

In a second portion of the study, the researchers evaluated the effectiveness of intravenous estrogen on blood pressure and sympathetic nerve discharge and found no effect.

When given orally, Vongpatanasin said, estrogen is transported to the liver, which converts the most active form of estrogen, called estradiol, into the weakest form of estrogen, called estrone.

"In order to have similar blood estradiol levels to those seen with transdermal estrogen, a much higher dose of oral estrogen is needed," she said. "This increases the side effects related to the production of a coagulation protein in the liver, which causes blood clots to form in the legs. Other proteins in the liver may also interfere with the ability of estrogen to reduce blood pressure.

"This side effect is much less likely to occur in women on transdermal estrogen replacement therapy because estrogen is absorbed directly into the bloodstream through the skin before it goes through the liver; therefore, the most active form of estrogen remains intact."

Other researchers involved in the study included Debbie Arbique, a senior registered nurse in internal medicine; Dr. Yasser Mansour, a former research fellow; Dr. Meryem Tuncel Kara, a research fellow in internal medicine; and Dr. Ronald Victor, chief of hypertension.

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