Blood clot risk lower for estrogen-only, transdermal, and vaginal estrogen at menopause

March 30 2016

A Swedish population study is helping answer lingering questions about hormone therapy safety. Published online today in *Menopause*, the journal of The North American Menopause Society, the study shows that estrogen-only therapy carries a lower risk of blood clots than combined estrogen-progestogen therapy, but there is no significantly increased risk of clots with combination therapy when the estrogen is transdermal, and vaginal estrogen doesn't raise the risk at all.

Blood clots, or "venous thromboembolism" (VTE), can have serious consequences, such as pulmonary embolism (blood clots to the lung). The risk of having them is known to be higher in women who use hormone therapy. In 2002, the Women's Health Initiative (WHI) showed that oral hormone therapy at a standard dose, whether estrogen alone or estrogen combined with progestogen, increased the risk of both VTE and pulmonary embolism. And the WHI confirmed that the greatest risk of VTE occurs during the first year of treatment. Since that time, various studies have tried to address the question of whether lower doses or transdermal doses (through the skin) might carry lower risk, but the answers have not been clear. This large population study of more than 800 Swedish women who had VTEs and nearly 900 age-matched controls who took no hormones is helping answer those questions.

In this study, risk of having VTE was almost twofold higher (OR 1.72) in the women who took hormones than in those who took no hormones,

which is similar to other studies, including the WHI. What's more, women who took combined estrogen-progestogen therapy had nearly three times the VTE risk of those who took no hormones. Women who took estrogen only (because they had had hysterectomies and didn't need a progestogen) had a much lower overall increase in their odds of VTE—a little less than one and half times higher (OR 1.31) compared with those who took no hormones. Women using combined estrogen-progestogen had a twofold higher risk of VTE than those taking estrogen only.

However, this study had good news about the way estrogen is delivered. There was no increased risk of VTE in this study for women who used transdermal estrogen (such as patches), either alone or in combination with a progestogen. And women who used vaginal estrogen alone to ease vaginal dryness and other symptoms of genitourinary syndrome of menopause (GSM) also had no increased risk of VTE. Many menopause experts don't expect vaginal estrogen to raise the risk because absorption into the bloodstream is small and results in levels similar to those in postmenopausal women who use no hormones. But studies on this question have been rare, noted the authors, so this finding is a big help for decision making.

Whether the type of progestogen makes a difference in risk has also been an important question for women and clinicians, and there haven't been many studies on this. Some imply that the VTE risk is higher with medroxyprogesterone acetate (the progestogen used in the WHI) than with norgestrel. But this study didn't show any statistically significant difference in risk between the two synthetic progestins. What it did show was that having a uterus and taking both oral estrogen and a synthetic progestin increased the risk of VTE the most, particularly compared with estrogen only.

"This study adds to our knowledge that transdermal estrogen therapies

are safer than oral, and that different estrogen or progestogen combinations may have different risks," says NAMS Executive Director JoAnn V. Pinkerton, MD, NCMP. "The lack of blood clots with transdermal estrogen and with vaginal estrogen is very reassuring for women who need to continue taking hormones as they age when risk of blood clots increases."

Provided by The North American Menopause Society