

HT Thrombosis Risk Tied to Coagulation Factors

BY FRAN LOWRY
Orlando Bureau

ATLANTA — Women who opt for hormone therapy to ease their discomfort from hot flashes and other menopausal symptoms often do so without knowing their risk of developing adverse effects.

Now, data from the Women's Health Initiative trials of hormone therapy (HT) may help women make more informed decisions about their risk for venous thromboembolism, should they choose to resume or start hormones.

A nested case-control study from the WHI presented at the annual meeting of the American Society of Hematology has found that excessively high levels of the coagulation factor D-dimer, in the presence



'This type of information might be helpful to women deciding for or against' hormone therapy.

DR. CUSHMAN

of HT, significantly increases a woman's risk of developing venous thrombosis.

"If your D-dimer was in the top quarter of population distribution and you were assigned to HT, your relative risk of deep vein thrombosis was increased sixfold, compared to women whose D-dimer was low and who were assigned placebo," principal investigator Dr. Mary Cushman, professor of medicine at the University of Vermont, Burlington, said. "This means that you go from a one or two per thousand annual risk to about a 6-12 per thousand annual risk. This type of information might be helpful to women deciding for or against HT."

Other factors that were found to be associated with an elevated venous thrombosis risk in the presence of HT included lower free protein S and plasmin-antiplasmin complex (PAP), a research-based test.

Dr. Cushman and her colleagues measured baseline levels of potential coagulation risk factors to see if they could pinpoint women at higher risk of venous thrombosis with hormones. They did a nested case-control study that measured baseline levels of these factors in 215 participants of the WHI who developed venous thrombosis, and 867 age-matched controls.

The women were all participants of two placebo-controlled double-blind randomized WHI trials evaluating the following regimens: conjugated equine estrogens alone, or estrogen plus medroxyprogesterone acetate. The mean age of the women in the analysis was 66 and ranged from 50 to 79 years.

The investigators studied procoagulant, anticoagulant, and fibrinolytic markers in blood samples that were taken at the time the women entered the WHI studies.

They found that women who had low levels of protein C, free protein S, and antithrombin, and high levels of D-dimer, PAP, and prothrombin fragment 1-2 had an elevated risk of venous thromboembolism. The highest risk was associated

with women who had D-dimer in the top quartile and who were taking HT.

In an interview, Dr. Cushman cautioned that testing for D-dimer is not yet ready for prime time because there are currently no standardized tests specifically designed to gauge venous thrombosis risk.

"There are various D-dimer assays commercially available, but choosing a proper threshold and so forth among all the different commercially available assays is a challenge," she said. "We used a

particular assay in our analysis, and studies would be needed assessing other assays before using this in clinical practice."

Nevertheless, D-dimer is a biomarker with the potential to identify 25% of women at risk for venous thromboembolism. Being able to tell those women their risk should they choose to go on HT would be very useful in helping them think carefully about the treatment, Dr. Cushman said.

She is doubtful that her results will be

replicated in other studies. "In terms of confirming the findings, it's difficult because there's probably not going to be another large study like this. But this is definitely something that could be tested further. The most important take home is the translation about what we are beginning to understand about the pathophysiology and the additive nature of these coagulation factor abnormalities. The potential for clinical applicability is potentially there." ■

Activate the immune cascade


Aldara Cream is indicated for the treatment of external genital and perianal warts/condyloma acuminata in individuals 12 years old or older.


Most local skin reactions were mild to moderate and included erythema, erosion, flaking, edema, scabbing, and induration at the external genital wart (EGW) site. The most common application-site reactions were itching (26%), burning (16%), and pain (4%) at the wart site. Application-site pigmentation changes have also been reported. New EGWs may develop during treatment.

Aldara Cream has not been evaluated for the treatment of urethral, intra-vaginal, cervical, rectal, or intra-anal human papilloma viral disease and is not recommended for those conditions.

The effect of Aldara Cream on the transmission of EGWs is unknown. Aldara Cream may weaken condoms and diaphragms. Sexual contact should be avoided while the cream is on the skin.

Please see brief summary of Prescribing Information on adjacent pages.

 **Aldara**[®]
(IMIQUMOD)
Cream, 5%
CLEARANCE FROM WITHIN

Distributed by:  GRACEWAY[™] PHARMACEUTICALS

©2007 Graceway Pharmaceuticals, LLC, Bristol, TN www.gracewaypharma.com www.aldara.com ALD070703