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Lower Risk of Cardiovascular Events in Postmenopausal Women Taking Oral Estradiol Compared With Oral Conjugated Equine Estrogens.

Smith NL, Blondon M, Wiggins KL, Harrington LB, van Hylckama Vlieg A, Floyd JS, Hwang M, Bis JC, McKnight B, Rice KM, Lumley T, Rosendaal FR, Heckbert SR, Psaty BM.

Department of Epidemiology, University of Washington, Seattle2Group Health Research Institute, Group Health Cooperative, Seattle, Washington3Seattle Epidemiologic Research and Information Center, Department of Veterans Affairs Office of Research and Development, Seattle, Washington.

Abstract

IMPORTANCE Little is known about the comparative cardiovascular safety of oral hormone therapy products, which impedes women from making informed safety decisions about hormone therapy to treat menopausal symptoms. OBJECTIVE **To compare the relative clinical cardiovascular safety of 2 commonly used oral estrogen drugs-conjugated equine estrogens (CEEs) and estradiol**. DESIGN, SETTING, AND PARTICIPANTS Population-based, case-control study from January 1, 2003, to December 31, 2009, comparing cardiovascular event risk associated with current CEEs and estradiol use in a large health maintenance organization in which the preferred formulary estrogen changed from CEEs to estradiol during the course of data collection. Participants were 384 postmenopausal women aged 30 to 79 years using oral hormone therapy. MAIN OUTCOMES AND MEASURES Incident venous thrombosis was the primary clinical outcome, and incident myocardial infarction and ischemic stroke were secondary outcomes. As validation, an intermediate clotting phenotype, the endogenous thrombin potential-based normalized activated protein C sensitivity ratio, was measured in plasma of controls. RESULTS **We studied 68 venous thrombosis, 67 myocardial infarction, and 48 ischemic stroke cases, with 201 matched controls; all participants were current users of oral CEEs or estradiol. In adjusted analyses, current oral CEEs use compared with current oral estradiol use was associated with an increased venous thrombosis risk** (odds ratio, 2.08; 95% CI, 1.02-4.27; P = .045) **and an increased myocardial infarction risk that did not reach statistical significance** (odds ratio, 1.87; 95% CI, 0.91-3.84; P = .09) and was not associated with ischemic stroke risk (odds ratio, 1.13; 95% CI, 0.55-2.31; P = .74). **Among 140 controls, CEEs users compared with estradiol users had higher endogenous thrombin potential-based normalized activated protein C sensitivity ratios (P < .001), indicating a stronger clotting propensity**. CONCLUSIONS AND RELEVANCE In an observational study of oral hormone therapy users, CEEs use was associated with a higher risk of incident venous thrombosis and possibly myocardial infarction than estradiol use. This risk differential was supported by biologic data. These findings need replication and suggest that various oral estrogen drugs may be associated with different levels of cardiovascular risk.