Hormone Therapy and Venous Thromboembolism: Early Results from the E3N Prospective Study

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Oral estrogen therapy increases the risk of venous thromboembolism (VTE) among postmenopausal women. Although recent data have shown that transdermal estrogen may be safe with respect to thrombotic risk, the impact of the route of estrogen administration is not fully established. In addition, data on the role of combined progestogens are scarce. We used the data from the E3N Study, a French prospective cohort of 85943 postmenopausal women born between 1925 and 1950 and followed by biannually questionnaires sent from 1990 (mean duration: 10.4 years). We identified 984 women with a first documented VTE (199 pulmonary embolisms and 785 deep vein thrombosis). The relative risks (RR) and 95% confidence intervals (CI) were estimated using a multivariate Cox proportional hazards models after adjustment for obesity, parity, education level and time-period. Compared with non-users, the RR for VTE in current users of oral and transdermal estrogen therapy was 1.6 (95% CI: 1.3–2.0) and 1.0 (95%CI: 0.8 –1.2), respectively. Among oral estrogens users, there was no significant difference in VTE risk across all progestogen subgroups. Transdermal estrogen alone or combined with either micronised progesterone or pregnane derivatives was not significantly associated with VTE risk (RR_0.9; 95%CI: 0.6 –1.3, RR_0.9; 95%CI: 0.7–1.1 and RR_1.0; 95% CI: 0.7–1.3, respectively) whereas transdermal estrogen combined with either norpregnane derivatives or nortestosterone derivatives significantly increased VTE risk (RR_1.4; 95%CI: 1.1–1.8 and RR_3.0; 95%CI: 1.3–7.3, respectively). In conclusion, these data confirm that the route of estrogen administration as well as the type of progestogen may be important determinants of the VTE risk among postmenopausal women who use hormone therapy. Transdermal estrogen alone or combined with either micronised progesterone or pregnane derivatives may be safe with respect to VTE risk.