Recent studies performed in the United Kingdom (1, 2) and the United States (3, 4) have shown that the current use of oral estrogen as hormonal replacement therapy (HRT) was associated with a two- to threefold increased risk of venous thromboembolism (VTE). Transdermal estrogen is widely used in European countries, but little relevant information is available as regards the route of estrogen administration.

In a recent issue of the Journal, Varas-Lorenzo et al. (5) reported the results of a population-based case-control study conducted in Italy. The aim was to evaluate the risk of VTE among predominant users of transdermal estrogen replacement therapy. The authors analyzed 171 cases of idiopathic VTE and a random sample of 10,000 controls among whom, respectively, six and 232 women were current users of HRT. The authors reported that 79 percent of users had undergone transdermal therapy. They found an overall increased risk of VTE (adjusted odds ratio = 2.3, 95 percent confidence interval 1.0-5.3). However, crude and adjusted odds ratios according to the route of estrogen administration were not shown. Raw data would have been helpful to pool these results with those of the other two available studies which have provided data on transdermal preparations (1, 2). In their report, Daly et al. (1) and Perez-Gutthann et al. (2) suggested that there were no major differences between oral and transdermal routes of estrogen administration, but these results were based, respectively, on only five and seven cases who used transdermal estrogen, and the odds ratios did not significantly differ from one.

From our point of view, the study by Varas-Lorenzo et al. (5), and the two previous studies (1, 2), provided insufficient data to allow a firm conclusion concerning the risk of VTE associated with transdermal estrogen use (6). A study designed to investigate the safety of this latter route of administration with respect to VTE is needed.

REFERENCES

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THE AUTHORS REPLY

We thank Drs. Oger and Scarabin (1) for their interest in our study on the risk of hospitalization for venous thromboembolism (VTE) associated with hormone replacement therapy (HRT) (2). In their letter, Drs. Oger and Scarabin point out that the results from our study and two other recent studies (3, 4) do not allow a firm conclusion concerning the risk of VTE associated with transdermal estrogen use. In our population-based case-control study conducted in Italy, the prevalence of HRT use was very low (2.3 percent among controls). However, 79 percent of users used transdermal therapy. The small number of women exposed to oral replacement therapy did not allow us to estimate the risk according to different routes of administration.

A review of the recent epidemiologic studies of the association between HRT and VTE has also been published by Castellague et al. (5). Table 2 in that publication shows relative risks estimated in each of the individual studies (2-4, 6, 7) and the overall estimators according to type of HRT among current users. Overall estimators were calculated pooling the results from the individual studies and weighting each of them by the inverse of the variance of the log relative risk (8). The overall relative risk of VTE for users of transdermal therapy was estimated to be 2.1 (95 percent confidence interval 1.0-4.7).

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