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Estradiol Valerate/Dienogest
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Therapeutic options for postmenopausal women with indications for some form of sex steroid therapy have increased significantly in recent years. This is fortunate, as clinicians will find that tolerance and response to different products often vary widely within and between different patients. Unfortunately, the scientific literature is less than helpful in predicting the anticipated individual response to therapy because of a general lack of head-to-head (direct product comparison) studies.

Estradiol valerate, an oral esterified estrogen, has been long available and widely tested. In the reviewed product, 2mg of estradiol valerate is combined with either 2mg or 3mg of the hybrid progestogen, dienogest.

The key studies cited in the accompanying paper report on the effects of these combination products on endometrial response, bleeding, symptom response, and certain metabolic parameters. Except for effects on climacteric symptoms and bleeding profiles, no data are given for actual outcomes such as myocardial infarction or osteoporotic fractures, although inference is made to biological markers. This remains a weakness in the knowledge regarding most of the sex steroids.

It is unfortunate that these studies continue to utilise and rely on the discredited and invalidated Kupperman index, rather than utilising modern acceptable tools for symptom and quality of life evaluation. Nonetheless, the vasomotor response is satisfactory at all doses tested.

The endometrial and bleeding responses are slightly more difficult to evaluate. The lower rates of bleeding in the lower dose of estradiol valerate/dienogest, as compared to the higher dose estradiol valerate/dienogest or to the estradiol valerate/norethisterone acetate could be anticipated, given the general trend to lower dose combination therapy with sex steroid products.[1-3] The dose-ranging studies with estradiol valerate/dienogest suggest that this might be so, but would have been enhanced by testing lower doses of estradiol valerate as well.

Finally, the question of whether the attenuation of the effects of estradiol valerate on certain parameters such as estradiol-induced serotonin production or thromboxane formation by the addition of the progestogen dienogest, remains unanswered. Clearly, there is an urgent need for adequately powered, long-term, randomised and blinded clinical studies utilising these products with proper outcome factors as endpoints, such as the incidence of myocardial infarction and venous thromboembolism. ▲

References

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