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Ethinylestradiol/ Chlormadinone Acetate

A Viewpoint by Herbert Kuhl

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The combination of ethinylestradiol 30μg and chlormadinone acetate 2mg (EE/CMA) is not only a reliable oral contraceptive, but may also improve acne vulgaris. The latter effect is frequently ascribed to the antiandrogenic effect of CMA which has been demonstrated in animal experiments.

Antiandrogens are defined as compounds that bind to the androgen receptor without exerting androgenic effects. Instead, they compete with testosterone and the more potent androgen dihydrotestosterone (DHT) for binding to the androgen receptor and, hence, reduce the effectiveness of both endogenous androgens. Considering the low binding affinities of CMA to the androgen receptor (3% of that of DHT), high local CMA concentration must be present within the hair follicles to reduce the interaction of DHT with the androgen receptor. The serum level of DHT in normal women is 0.6 ng/mL, but can reach much higher local levels in women with hyperandrogenic disorders due to the conversion of dehydroepiandrosterone, androstenedione and testosterone to DHT within the pilosebaceous units.

It is known that, in patients with idiopathic acne or hirsutism, the effect of oral contraceptives, such as EE 35μg plus cyproterone 2mg (CPA), is mostly not satisfactory. An improvement can generally be achieved only after an elevation of the CPA dose to 10–100 mg/day. This clearly demonstrates that a true antiandrogenic effect of the progestin via occupation of the androgen receptor is only possible with high local concentrations. In the face of the relatively low serum concentrations of CMA (peak concentration about 2 ng/mL) during use of EE/CMA, a notable antiandrogenic effect of CMA is rather improbable. In women with mild-to-moderate acne or seborrhoea with elevated serum levels of total or free testosterone or androgen precursors, estrogen-predominant oral contraceptives like EE/CMA will improve the disorder efficiently. Their therapeutic effect is mainly based on a strong increase in the serum levels of sex-hormone binding globulin and a more or less pronounced decrease in testosterone, resulting in a profound decrease of free testosterone.

This effect was exemplified by a randomised study in 183 women with acne. Treatment with either EE 35μg plus CPA 2mg or a biphasic combination with EE and desogestrel revealed a similar reduction in the number of lesions and the degree of severity, even in grade 3 and 4 acne. As desogestrel is a nortestosterone derivative with a slight androgenic activity, the lack of any difference in the therapeutic effect of both preparations indicates that there is no contribution of the antiandrogenic activity of CPA.

Nevertheless, EE/CMA is an efficient low-dose oral contraceptive which is well tolerated and may, in addition, improve mild-to-moderate androgenic disorders in patients with hyperandrogenaemia. ▲