Drugs 1998 Nov; 56 (5): 834-835
0012-6667/98/0011-0834/$02.00/0

Dienogest

A Viewpoint by Herbert Kuhl

Department of Obstetrics and Gynecology, Johann Wolfgang Goethe University of Frankfurt, Frankfurt am Main, Germany

Although dienogest has been used in Germany since 1991, it is relatively unknown outside Germany. At the dose of 2mg, dienogest is used as an ovulation inhibitor and oral contraceptive (in combination with ethinylestradiol 30μg) and for hormone replacement therapy (in combination with estradiol valerate 2mg).

Dienogest represents a new progestogen that combines some properties of the 19-nortestosterone derivatives with some effects of progesterone derivatives.

A unique feature of dienogest is that it is the only 19-nortestosterone derivative that contains no ethinyl group, but instead has a cyanomethyl group at position C17α. This might be the reason for its relatively short half-life, lack of androgenic activity, remarkable antiandrogenic properties, relatively low binding affinity to the progesterone receptor and lack of binding to sex-hormone binding globulin. Despite this, its oral bioavailability is high (90%) and the peak concentration after intake of 2mg is approximately 50 μg/L, of which 10% is nonprotein-bound. Consequently, transitorily high local concentrations of dienogest within the target cells may be present, even though no accumulation occurs.

Dienogest is an interesting compound from a scientific point of view, and it may contribute to understanding some actions of synthetic progestogens. The ovulation inhibiting dose of dienogest (1mg) is in the range of that of progesterone derivatives and much higher than that of levonorgestrel (0.06mg) and some other 19-nortestosterone derivatives. In contrast to this, the transformation dose of dienogest (6.3mg) is in the range of that of levonorgestrel (3.5mg) and some other 19-nortestosterone derivatives but lower than that of progesterone derivatives such as cyproterone acetate (12mg) and chlormadinone acetate (25mg). The explanation for this phenomenon may be found in the role of the ethinyl group present in other 19-nortestosterone derivatives, but not dienogest.

The direct inhibitory effect of 19-nortestosterone derivatives on ovarian activity may be partly mediated by a pharmacological interaction of the ethinyl group, which after oxidative activation can react with the catalytic centre of cytochrome P450-dependent enzymes, resulting in an irreversible inhibition. Cytochrome P450 enzymes are not only involved in the metabolism of steroid hormones but also in the biosynthesis of endogenous sex steroids. By means of this mechanism, the inactivation of ethinylated progestogens is slowed down (reflected by longer half-lives) and the ovulation inhibiting dose is very low. Dienogest, which has no ethinyl group, is therefore much less potent with respect to ovulation inhibition. On the other hand, the similar potency between dienogest and 19-nortestosterone derivatives such as levonorgestrel in terms of effects on the endometrium may be explained by high intracellular concentrations of dienogest. ▲