Safety and efficacy of a combined oral contraceptive: gestodene 75 μg plus ethinyl estradiol 30 μg in Mexican women

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Abstract

An open prospective clinical trial designed to evaluate the efficacy and safety of the combined hormonal oral contraceptive (OC) containing 75 μg gestodene plus 30 μg ethinyl estradiol was undertaken in a Mexican population. Sixty-nine healthy women of reproductive age took part in the study for a total of 627 woman-months of observation. The combination of gestodene and ethinyl estradiol proved its effectiveness in preventing pregnancy during the study. Side-effects were minimal and regular endometrial bleeding patterns were observed during one year of continuous use of this OC preparation. The discontinuation rate for medical reasons was 11.6% at one year. Among a sample of 10 women, the gestodene/ethinyl estradiol combination did not induce significant changes in the serum concentration of total cholesterol and LDL cholesterol after 12 months of continuous administration. An increase in serum triglycerides and HDL cholesterol was observed; this effect could be attributed to a lack of androgenic and/or the intrinsic estrogenic behavior of gestodene.

It can be concluded that this preparation is highly effective as a combined oral contraceptive; it is well tolerated and might offer some advantages with respect to other oral contraceptive combinations in its short- and medium-term impact on lipid metabolism.

Introduction

For more than 25 years hormonal oral contraception has been considered a fertility regulating method that combines the criteria of safety, efficacy, reversibility and acceptability. The results of recent evaluations show that the risk–benefit balance for
OCs is much more favorable than had been previously thought [1].

With the aim of reducing the doses and thus minimizing side-effects and metabolic changes, research in the field of hormonal oral contraceptives has focused on the development of new strategies to reduce the doses of existing progestins as well as the synthesis of new more potent steroids.

Research was focused for many years on the estrogenic component of the formulation, which suggested that ethinyl estradiol as used in commercial preparations of combined OCs is the most suitable and effective estrogen at doses of 30 µg or even less.

In recent years pharmacologic investigations were focused on the development of new progestins allowing reduction of the doses without compromising their efficacy.

Until recently, levonorgestrel (LNG) was probably the most potent progestin used in oral combined contraceptives, even though it has, besides its progestational activity, intrinsic androgenic properties. Modification of the molecular structure of LNG led to the synthesis of the third generation of 19-nor progestins, or gonane-type progestogens: norgestimate, desogestrel and, recently, gestodene. The synthesis of gestodene by Hoffmeister et al. [2] in the research laboratories of Schering (Berlin) has resulted in the most potent progestogen currently available.

Gestodene has a structure very similar to levonorgestrel and only differs from it by the presence of a double bond between carbon 15 and 16, thus transforming it to delta 15-levonorgestrel. The evaluation of the progestational activity of gestodene in a number of biological tests [3], has shown that this progestin is 2 to 10 times as potent as levonorgestrel. Furthermore, in vivo and in vitro studies [4,5] have demonstrated that the antigonadotropic potency of gestodene is 2–3 times greater than levonorgestrel.

In general, the 19-nortestosterone derivatives exhibit some degree of androgenic activity. In recent studies [6], gestodene was found to have progestational activity but was not accompanied by great androgenic activity.

Information on the efficacy of gestodene in combination with ethinyl estradiol has been accumulated in more than 200 000 cycles in almost 38 000 women from different countries [7]. The reported pregnancy rate is less than 0.1 per 100 woman-years [8]. Good cycle control has also been demonstrated during gestodene/ethinyl estradiol use.

Epidemiologic studies have demonstrated an association between cardiovascular disease and combined OC use. In previous studies with gestodene/ethinyl estradiol, no significant changes in HDL-cholesterol and LDL-cholesterol serum levels have been found, although a moderate rise in total cholesterol and triglycerides was reported [8–11].

The present study was undertaken to evaluate both efficacy and metabolic effects of 75 µg of gestodene in combination with 30 µg of ethinyl estradiol in a Mexican population. In addition, changes in serum lipids and lipoproteins were prospectively evaluated at 0, 4, 8 and 12 months of use.