

The 12-month treatment with the oral contraceptive formulation containing dienogest (DNG) and estradiol valerate (E2V) shows beneficial effects on psychological symptoms: results from a prospective comparative study with a formulation containing ethinyl estradiol (EE) and drospirenone (DRSP)

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Summary

The COCs evolution has been obtained with new and different progestinic compounds associated with lower doses of EE (ethinylestradiol). The revolution in the COCs field is the introduction of estradiol valerate (E2V), ester of the natural estrogen, estradiol (E2) instead of EE. Dienogest (DNG) is the progestinic compound of the COC *Klaira*[®] associated with E2V in a multiphase formulation. DNG has a strong antiandrogenic action without the mineralocorticoid and glucocorticoid action and E2V acts in this association improving the subjective sleep quality, somatic complaints, anxiety, vigilance, cognition and numerical memory. The EE/DRSP (drospirenone) association (*Yaz*[®]) has a progestinic compound characterized by antiminerocorticoid

and antiandrogenic properties with a positive effect on psychological symptoms. In this prospective study we evaluated if E2V is able to exert the same psychological symptoms as EE/DRSP formulation. Psychological changes were evaluated with SCL90 for 5 cycles. In comparison with the basal value the score was significantly reduced ($p < 0,001$) during both treatments. This effects observed confirm that DNG and DRSP act with beneficial effects on CNS.

KEY WORDS: dienogest, drospirenone, estradiol valerate, extracontraceptive benefits, psychological effects, contraception.

Introduction

Since the first “pill” the composition of the combined oral contraceptives (COCs) has been changed in order either to reduce side effects dependent on steroid compounds or to magnify extra-contraceptive benefits. This evolution has been obtained with new progestinic compounds, mainly with those with antiandrogenic and antiminerocorticoid properties, associated with lower doses of EE. The introduction of the natural estrogen, estradiol (E2), instead of EE represents the revolution in the COCs field.

The progestinic compound DNG combined with the natural estrogen, E2V, is an innovative multiphase formulation contained in the COC manufactured by Bayer (Germany) and commercially called *Klaira*[®]. In comparison to EE, E2V has a lower action on liver protein induction (SHBG, angiotensinogen and coagulation proteins) without acting like EE on lipoproteins and on tryglicerides synthesis. Dienogest exerts an effective contraceptive action with a strong antiproliferative action both on endometrial tissue and endometriosis implants (1). In addition, DNG has a strong antiandrogenic action without the mineralocorticoid and glucocorticoid action. In postmenopausal women, the addition of DNG to E2V demonstrated to increase the beneficial action of E2V on the activity of some neural centers, with a better improvement compared to E2V alone, on subjective sleep quality, somatic complaints and anxiety, vigilance, cognition and numerical memory (2).

Yaz® is the commercial name of a COC manufactured by Bayer (Germany) containing 20 mcg of EE and DRSP, a progestin compound characterized by antiminer-alcorticoid, antiandrogenic properties (3), associated with a central neural effect and beneficial impact on psychological symptoms (4).

In this prospective study we aimed to evaluate whether E2V/DNG is able to exert the same psychological effects of the formulations containing EE/DRSP.

Thirty seven women with inclusion and without exclusion criteria to COCs assumption, participated in the study: 23 of them were treated with E2V/DNG and 14 with EE/DRSP. Psychological changes were evaluated with the psychometric scale SCL90 before the COCs assumption, and at the first, the third, seventh and the twelfth cycle of treatments.

In comparison to basal values, the total global score of SCL90 was significantly reduced ($p < 0.001$) during both treatments, showing a decrease from the first cycle with a continuous reduction up to the end of the study. No statistical differences between the treatments were calculated with the two way ANOVA analysis.

The similar psychological effects observed with these COCs, confirm that DNG and DRSP exert beneficial effects on central nervous system. Further studies are needed to evaluate whether similarly to the formula-

tions with EE plus DRSP, E2V/DNG can also exert positive effect on body composition.

References

1. Strowitzki T, Faustmann T, Gerlinger C, Seitz C. Dienogest in the treatment of endometriosis-associated pelvic pain: a 12-week, randomized, double-blind, placebo-controlled study. *Eur J Obstet Gynecol Reprod Biol* 2010; 151:193-8.
2. Saletu-Zyhlarz G, Anderer P, Gruber G, Mandl M, Gruber D, Metka M et al. Insomnia related to postmenopausal syndrome and hormone replacement therapy: sleep laboratory studies on baseline differences between patients and controls and double-blind, placebo-controlled investigations on the effects of a novel estrogen-progestogen combination (Climodien, Lafamme) versus estrogen alone. *J Sleep Res* 2003; 12:239-54.
3. Fruzzetti F, Lello S, Lazzarini V, Fratta S, Orrù M, Sorge R et al. The oral contraceptive containing 30 microg of ethinylestradiol plus 3 mg of drospirenone is able to antagonize the increase of extracellular water occurring in healthy young women during the luteal phase of the menstrual cycle: an observational study. *Contraception* 2007; 75:199-203.
4. Paoletti AM, Lello S, Fratta S, Orrù M, Ranuzzi F, Sogliano C et al. Psychological effect of the oral contraceptive formulation containing 3 mg of drospirenone plus 30 microg of ethinyl estradiol. *Fertil Steril* 2004; 81:645-51.