

IS AN COMBINED CONTRACEPTIVE PILL CONTAINING ESTRADIOL VALERATE THE OPTIMAL CHOICE FOR PRETREATMENT IN IVF CYCLES?

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Introduction

The study examines the effect of pretreatment with oral contraceptive pills before ovarian stimulation for in vitro fertilization (IVF). This practice, common in reproductive medicine clinics, allows for more precise scheduling of stimulation cycles. However, recent studies have raised doubts about the effectiveness of pretreatment, highlighting possible negative effects such as a lower number of retrieved oocytes, reduced maturation and fertilization rates, decreased endometrial receptivity, longer stimulation cycles, and higher gonadotropin doses. In recent years, interest has grown in the use of luteal phase estradiol in GnRH antagonist protocols for cycle scheduling. Most existing studies have focused on pills containing ethinylestradiol and a progestin, neglecting “natural” pills based on estradiol valerate, which is considered more physiological as it is metabolized into estradiol, similar to the endogenous hormone.

Objective

To evaluate IVF cycle outcomes in women who underwent pretreatment with quadriphasic estradiol valerate (EV) and dienogest (DD) (3mg EV/2days, 2mg EV and 2mg DD/5 days, 2mg EV and 3mg DD/17days, 1mg EV/2 days) versus monophasic 0.02 mg ethinylestradiol (EE) and 0.1 mg levonorgestrel (LNG), with a particular focus on stimulation duration, total medication dosage, and fresh pregnancy rates.

Pretreatment with an EV-based contraceptive pill does not improve key IVF outcomes, which are reportedly negatively associated with estrogen-progestin pretreatment. Despite the use of natural estrogen, as seen with estradiol valerate alone during the luteal phase, and a more physiological hormonal regimen, the expected benefits were not observed. This suggests a likely role of progestin use or exogenous hormonal administration in suppressing the hypothalamic-pituitary-gonadal axis, leading to a decline in subsequent IVF cycle parameters. If we consider pill pretreatment as an unfavorable factor for IVF cycles, further research is needed to clarify its specific impact, particularly in relation to endometrial receptivity and ovarian response.

Results

A total of 184 patients underwent ovarian stimulation following pretreatment with quadriphasic estradiol valerate and dienogest, while 207 patients received pretreatment with monophasic ethinylestradiol and levonorgestrel. At baseline, 15.2% of patients in the quadriphasic group and 12.1% in the monophasic group presented with functional ovarian cysts. Cycle discontinuation rates due to inadequate ovarian response were similar between the two groups (23.9% for EV-DD and 22.7% for EE-LNG). Among the fresh embryo transfers, 31.8% of cycles in the quadriphasic group and 38.67% in the monophasic group resulted in positive β -hCG tests, with biochemical pregnancies occurring in 5 and 9 cycles, respectively. The cumulative live birth rate was higher in the monophasic group (40%) compared to the quadriphasic group (21.7%). There were no significant differences between the groups in the mean duration of ovarian stimulation or total gonadotropin dosage ($p > 0.05$). At the end of the observation period, 26 patients in the EV-DD and 83 in the EE-LNG had remaining blastocysts available for future transfers, with an average of 2.4 blastocysts per patient.