INTRODUCTION

Controlled ovarian hyperstimulation (COH) seeks to improve IVF-ET results by increasing per-cycle oocyte and embryo availability. Yet, the coexistence of multiple preovulatory follicles engenders compulsory alterations in the endocrine milieu of the follicular phase. The most evident of them is the extremely high estradiol (E2) levels. Incidentally, in breast cancer patients who seek to preserve their fertility through the freezing of multiple oocytes or embryos, this overexposure to estrogens as a result of COH is particularly unwanted. In addition, the co-treatment with aromatase inhibitors, an approach that has been proposed to attenuate E2 levels during COH, is unfortunately not authorized in France.

Therefore, we elaborated and tested an innovative COH protocol that aimed at dissociating E2 production from multiple follicle development. For obtaining this effect, we decided to virtually curtail endogenous LH levels by using strong and sustained GnRH antagonist doses while maintaining standard exogenous FSH-only administration.

MATERIALS AND METHODS

We studied 11 IVF-ET candidates aged 25-38 years who volunteered to undergo NATOS. On day 2 of their menstrual cycle, patients started daily recombinant-FSH paralleled with daily GnRH-antagonist administration. This combined treatment was continued until the day of hCG administration (dhCG). Five patients received GnRH-antagonist 3 mg/day SC and 11 patients received only 1.5 mg/day SC. Ovulation triggering with hCG (10,000 IU, IM) was performed when routine criteria of follicle maturation were met and IVF-ET was done according to our routine procedures. No exogenous E2 supplementation was performed during COH.

RESULTS

On dhCG, serum E2 levels were 343.8 ± 170.8 pg/ml and 317.2 ± 184.2 pg/ml for the 3 mg and 1.5 mg groups, respectively and serum LH levels were undetectable in both groups. Contrasting with the low E2 levels, we obtained 16.2 ± 7.3 and 10.5 ± 6.3 mature oocytes in the two groups, respectively.

The difference in the result between the two groups can be explained by the difference of age and antral follicle count.

Eleven out of sixteen patients achieved a clinical pregnancy (five of them delivered already healthy babies and six currently are normally evolving)

Conclusions

These pilot results indicate that:

1. Profound LH suppression by strong and sustained GnRH antagonist doses in the presence of multiple growing follicles maintains E2 levels serum around the physiological range.

2. NATOS offers a new therapeutic option for stimulating women undergoing IVF-ET, in particular, those with breast cancer seeking fertility preservation or those suffering from repeated failures.