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Original Articles

Reproductive Biology Section

Mid-luteal phase injection of subcutaneous leuprolide acetate improves live delivered pregnancy and implantation rates in younger women undergoing in vitro fertilization-embryo transfer (IVF-ET)

J.H. Check[1,2], C. Wilson[2], J.K. Choe[1,2]

[1] Cooper Medical School of Rowan University, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ; [2] Cooper Institute For Reproductive Hormonal Disorders, P.C., Mt. Laurel, NJ (USA)

Summary

Purpose: To determine if a single injection of one-mg leuprolide acetate three days after embryo transfer (ET) in younger women causes an increase in pregnancy rates, and if so, is it associated with a higher initial serum hCG level? *Materials and Methods:* A prospective study was initiated where women aged ≤ 35 years were offered the option of taking the leuprolide or not. *Results:* Though a significant difference was not found, there was a trend for higher live delivered pregnancy rates in those taking the leuprolide supplement (47.8%) *vs.* those not taking it (38.6%). There was no difference in the first serum beta hCG level. *Conclusions:* The trends is interesting enough to continue with a higher powered study.

Key words: GnRH agonist; Leuprolide acetate; Embryo implantation rate; Beta hCG levels.

Introduction

A previous study by Tesarik *et al.* found that the single injection during the mid-luteal phase of a gonadotropin releasing hormone agonist (GnRHa) in women undergoing in vitro fertilization-embryo transfer (IVF-ET) and intracytoplasmic sperm injection (ICSI) in both GnRHa and GnRH antagonist cycles improved embryo implantation rates [1].

Tesarik *et al.* suggested that the beneficial effect may have been related to stimulating the embryo to make more hCG since high levels of serum hCG were found in early pregnancies in the women who conceived and took the GnRHa *vs.* those who did not take the GnRHa [1].

The objective of the present study was aimed to determine if some beneficial effect would be found with a single mid-luteal phase injection of a different GnRHa – leuprolide acetate one-mg. Furthermore the aim was to corroborate or refute the mechanism of action related to increased hCG secretion from the fetal-placental unit.

Materials and Methods

Consecutive women who requested IVF-ET age ≤ 35 years or under were given the option of taking 1mg leuprolide acetate three days after ET or not. They were advised of the data from the Tesarik *et al.* study and from a pilot study in the present authors' IVF-ET center.

Only controlled ovarian hyperstimulation (COH) regimens using GnRH antagonists were included. Chi-square analysis was used for comparison of clinical and live delivered pregnancy rates. The average first serum beta-hCG levels in those conceiving were determined.

There were no exclusions for failure to conceive in previous IVF-ET cycles or diminished oocyte reserve. Fertilization requiring ICSI or conventional oocyte insemination were not distinguished. A clinical pregnancy was defined as ultrasound evidence of pregnancy at eight weeks.

Results

There were 134 women who chose to take one mg leuprolide acetate and 197 who chose not to take the GnRHa. The results are seen in Table 1. Chi-square analysis failed to reveal any significant differences in either clinical preg-

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Table 1. — *Effect of GnRH agonist (leuprolide acetate) single injection on pregnancy rates following IVF-ET.*

Leuprolide acetate one mg given	No. transfers	No. clinical pregnancies (%)	No. live delivered pregnancy rates
Yes	134	69 (51.5%	64 (47.8%)
No	197	97 (44.2%)	76 (38.6%)

nancy rates ($p = 0.77$) or live delivered pregnancy rates ($p = 0.12$). The implantation rates for those receiving GnRHa injection was 37.9% (97/256) *vs.* 33.1% (128/387) for those not receiving one-mg leuprolide acetate ($p = 0.24$) with the mean number of embryos transferred at 1.9 *vs.* 2.0. The average first serum beta-hCG level from pregnant women taking leuprolide was 285 mIU/ml and 273 mIU/ml for those pregnant not taking it (p = NS).

Discussion

There have been a few studies suggesting improved benefit from the use of GnRHa's in the mid-luteal phase, e.g., Tesarik *et al.* using triptorelin and Picard *et al.* using buserelin [1, 2]. This is the first study with the GnRHa leuprolide acetate. Although there were no significant differences noted, there was a trend for improved pregnancy outcome by using one mg of leuprolide acetate three days after ET. The possibility is that the younger group has less likelihood of the need to improve embryo implantation compared to women of more advanced reproductive age. Presently the authors are evaluating women under similar circumstances between age 36-39 years, where pregnancy rates are significantly lower without the use of the mid-luteal phase injection of lueprolide acetate.

It would appear that, if indeed, a GnRHa study with more power shows a significant difference, the mechanism does not seem to be related to increasing the beta-hCG output from the fetal-placental unit.

References

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Address reprint requests to:
J.H. CHECK, M.D., Ph.D.
7447 Old York Road
Melrose Park, PA 19027 (USA)
e-mail: laurie@ccivf.com