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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)

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Summary

Purpose: To see if the single injection of one mg of the gonadotropin releasing hormone agonist (GnRHa) leuprolide acetate given in the mid-luteal phase can increase live delivered pregnancy and implantation rates. Furthermore the purpose was to determine if improvement was found, did the mechanism involve increased secretion of human chorionic gonadotropin (hCG). *Materials and Methods:* A prospective study was conducted in women aged ≤ 35 who were undergoing in vitro fertilization-embryo transfer (IVF-ET). They were advised of data from Tesarik *et al.* and a previous pilot study conducted in the present IVF center showing improved pregnancy rates with the injection of a GnRHa three days after embryo transfer. They were offered the option of returning for a one-mg injection s.c. of leuprolide acetate or not. Clinical and live delivered pregnancy rates were compared according to those taking or not the leuprolide acetate one-mg injection. Chi-square analysis was used for statistical comparisons. Serum beta-hCG levels were compared between those conceiving with or without the extra injection of leuprolide. *Results:* There was a non-significant trend for higher live delivered pregnancy rates in those taking leuprolide (47.8%, 64/134) *vs.* those not taking it (38.6%, 76/197). For those pregnant there was no difference in hCG levels according to taking the GnRHa or not. *Conclusions:* The 25% increased live delivered pregnancy rate per transfer was insufficiently powered to detect a significant difference. The results do justify continuing the study. Perhaps the difference could be wider using a slightly older age group whose embryos are frequently less hearty.

Key words: Luteal phase; Gonadotropin releasing hormone agonists; Leuprolide acetate; In vitro fertilization-embryo transfer; Implantation.

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 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 human chorionic gonadotropin (hCG) since higher 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].

Materials and Methods

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

Only controlled ovarian hyperstimulation (COH) regimens using GnRHa 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 would be 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

One hundred thirty-four chose to take one-mg leuprolide acetate. One hundred ninety-seven chose not to take the GnRHa. Chi-square analysis failed to reveal any significant differences in either clinical pregnancy rates ($p = 0.77$) or live delivered pregnancy rates ($p = 0.12$) (Table 1).

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.

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Table 1. — *Effect of GnRHa 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%)

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 in the mid-luteal phase: Tesarik *et al.* – triptorelin [1], Picard *et al.* – buserelin [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 where pregnancy rates are lower.

Conclusion

It would appear 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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