

Reproductive Biology Section

A study to determine the efficacy of controlled ovarian hyperstimulation regimen using a gonadotropin releasing hormone agonist versus antagonist in women of advanced reproductive age with varying degrees of oocyte reserve on outcome following in vitro fertilization-embryo transfer

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Summary

Purpose: To determine if the use of gonadotropin releasing hormone (GnRH) agonists (a) or antagonists (ant) allow better pregnancy rates when used in controlled ovarian hyperstimulation protocols in women of advanced reproductive age. Furthermore the study aimed to determine if the status of ovarian oocyte reserve has a confounding effect. **Materials and Methods:** A 12-year retrospective review was performed on all in vitro fertilization-embryo transfer (IVF-ET) cycles in women aged 40-44. Pregnancy rates were determined according to whether a GnRH-a or GnRH-ant was used. The data were also stratified according to normal or low oocyte reserve. **Results:** There was no significant difference in pregnancy rates according to whether a GnRH-a or GnRH-ant was used in women with normal oocyte reserve. Though a large majority of the women used a GnRH-ant, there was a 9% live pregnancy rate vs 0% in the women using a GnRH-a. **Conclusion:** Since it is unlikely that a larger study will ever be conducted, it is probably wise to use a GnRH-ant for the controlled ovarian hyperstimulation regimen in women aged 40-44 with diminished oocyte reserve.

Key words: Gonadotropin releasing hormone (GnRH) agonist; GnRH antagonist; Advanced reproductive age; Diminished oocyte reserve.

Introduction

There is a general consensus that after a learning curve, at least in women of a younger reproductive age, pregnancy rates are similar following in vitro fertilization-embryo transfer (IVF-ET) whether one uses gonadotropin releasing hormone (GnRH) agonists (a) or antagonists (ant) in the controlled ovarian hyperstimulation (COH) protocol [1].

The objective of the present study was to compare the effect of COH protocols using GnRH-a vs GnRH-ant in women of advanced reproductive age (age 40-44). Furthermore the study compared these two protocols according to whether there was diminished oocyte reserve or not.

Materials and Methods

A 12-year retrospective review was performed on IVF-ET cycles in women age 40-44. All cycles were used so that a couple could be utilized more than one time. Pregnancy rates and implantation rates were determined according to whether a GnRH-a or GnRH-ant was used.

Furthermore the data were stratified according to whether day 3 serum FSH was ≤ 10 mIU/ml or > 10 mIU/ml (normal oocyte reserve vs diminished oocyte reserve). For inclusion the women had to be 40-44 years old. Women whose serum FSH was ≤ 10 mIU/ml but whose day 3 serum estradiol was > 50 pg/ml were placed in the diminished oocyte reserve group.

Results

A comparison of clinical and live delivered pregnancy rates per transfer in women aged 40-44, with adequate oocyte reserve as determined by a day 3 serum FSH ≤ 10 mIU/ml is shown in Table 1. Though the clinical and live delivered rates were 25-35% higher with the use of GnRH agonists vs antagonists, the differences were not significant.

A comparison of clinical and live delivered pregnancy rates per transfer in women with diminished oocyte reserve as determined by a day 3 serum FSH > 10 mIU/ml is shown in Table 2. For the diminished oocyte group there were no live pregnancies with GnRH-a but the group was small ($n = 9$) vs a 9% live delivered pregnancy rate with GnRH-ant.

Table 1. — Pregnancy rates following in vitro fertilization-embryo transfer in women aged 40-44 with normal day 3 serum FSH.

	Normal oocyte reserve group		Chi-square analysis
	GnRH-ant	GnRH-a	
No. of IVF-ET cycles	193	138	
No. of clin. preg.	42	39	
Clin. preg. rate/transfer	21.7%	28.0%	$p = 0.22$
No. live delivered	29	29	
Live del. preg. rate/transfer	15.0%	21.0%	$p = 0.21$

Table 2. — Pregnancy rates following IVF-ET in women aged 40-44 with day 3 serum FSH > 10 mIU/ml.

	Diminished oocyte reserve group		Chi-square analysis
	GnRH-ant	GnRH-a	
No. of IVF-ET cycles	101	9	
No. of clin. preg.	17	1	
Clin. preg. rate/transfer	16.8%	11.1%	$p = 0.66$
No. live delivered	9	0	
Live del. preg. rate/transfer	8.9%	0%	$p = 0.76$

Discussion

Though the study included 294 IVF-ET cycles in women aged 40-44, there was still insufficient power to

determine if the 25-35% reduction in pregnancy rates in women with normal oocyte reserve using GnRH-ant compared to GnRH-a was merely by chance alone or whether a larger study eventually show statistical differences?

Similarly the same question applies for women with diminished oocyte reserve. There was a 9% live delivered rate with GnRH-ant but zero with GnRH-a. Since it is not likely that a study with more power will be forthcoming in the near future, it would probably be prudent, at least in the older reproductive group with diminished oocyte reserve, to use a GnRH-ant protocol.

References

- [1] Check M.L., Check J.H., Choe J.K., Davies E., Kiefer D.: "Effect of antagonists vs agonists on in vitro fertilization outcome". *Clin. Exp. Obstet. Gynecol.*, 2004, 31, 257.

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