



AMERICAN SOCIETY FOR
REPRODUCTIVE MEDICINE



American Society for Reproductive Medicine 2014 Annual Meeting
October 18 to 22, 2014 • Honolulu, Hawaii

Title:

LETROZOLE AS AN ADJUNCT IN GNRH ANTAGONIST CYCLES IMPROVES IVF OUTCOME IN POOR RESPONDERS

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Objective:

There is a lack of consensus regarding the ideal management of patients with poor response to ovarian stimulation. Letrozole (Lz) increases endogenous gonadotropin (GND) release, without competing with endometrial estradiol (E2) receptors. We seek to elucidate whether adding Lz in the early follicular phase of a GnRH antagonist (GA) stimulation cycle improves IVF outcome in poor responders.

Design:

Retrospective analysis

Materials and Methods:

We included 90 poor responders, comparing baseline characteristics and IVF outcomes from prior GA cycle vs. subsequent GA cycle with added follicular phase Lz (LzGA). Student's T-test and chi-square analysis were used with significance at $p < 0.05$.

Results:

An interval of 0.36 ± 0.5 years passed between GA and subsequent LzGA cycles. Patient age, BMI and basal antral follicle count were similar among both cycles. LzGA had higher Day 3 (D3) FSH (9.1 ± 0.5 vs. 7.6 ± 4.5 , $p < 0.05$) and lower peak E2 levels (515.7 ± 377.7 vs. 917.9 ± 639 , $p < 0.05$). The proportion of follicles reaching >14 mm (53.6% vs. 56.3%) and number of mature oocytes retrieved (232 vs. 216) were comparable between LzGA and GA, respectively. LzGA had a lower fertilization rate (15.2% vs. 24.1%, $p < 0.05$). There was a non-significant trend towards higher implantation rate (25.5% vs. 19.6%) and ongoing pregnancy rate (35.7% vs. 28.1%) in LzGA. LzGA had thicker endometrium at time of embryo transfer (9.8 ± 2.4 mm vs. 8.9 ± 2.11 mm, $p < 0.05$) and yielded greater high quality D3 (132 vs. 69) and Day 5 embryos (D5) (32 vs. 24). LzGA received a mean Lz dose of 22.95 ± 7.2 mg and required less total amounts of FSH (9237.1 ± 3869 vs. 11714 ± 3755 , $p < 0.05$) and HMG (5451.2 ± 3382.1 vs. 6528.7 ± 4232 , $p < 0.05$). 43.3% of LzGA were cancelled vs. 45.6% of GA. Of cancelled GA ($n=41$), 56.1% yielded 115 mature



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oocytes with LzGA stimulation, of which 46.1% fertilized. 21 D3 and 11 D5 embryos were transferred, with 18.8% implantation rate and 15.6% ongoing pregnancy rate.

Conclusions:

LzGA reduced GND requirement and demonstrated a trend towards improved implantation and ongoing pregnancy rates. 56% of the poorest responders (with <4 mature follicles in previously cancelled GA cycles) had oocytes retrieved with LzGA, resulting in 18.8% implantation. While Lz did not improve overall oocyte quality, it may improve oocyte quantity in poorly responding patients without adversely affecting the endometrium.

Support:

None.