Title
ANEUPLOIDY RATES ARE UNAFFECTED BY CHOICE OF TRIGGER MEDICATION IN HUMAN IVF-ET CYCLES

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Objective
Clinicians have a variety of medication choices available for triggering final maturation of oocytes prior to egg retrieval. GnRH agonists with or without low doses of hCG has been increasingly popular due to its advantage of minimizing the risk of ovarian hyperstimulation syndrome (OHSS). An IVF study using GnRH agonist demonstrated an increased incidence of meiotic aberrations in non-fertilized oocytes, although the rate of aneuploidy was not significantly enhanced (Nogueira D, 2006, Hodes Wertz B, 2015). This study sought to explore the relationship between varying trigger strategies and ploidy outcomes in assisted reproduction technology (ART) treatment cycles.

Design
Retrospective cohort analysis

Materials and Methods
The study consisted of patients who underwent an IVF cycle(s) with preimplantation genetic screening (PGS) between January 2012 and February 2017. Only GnRH antagonist stimulation protocol cycles and patients categorized as normal responders (AMH ≥1pmol/L; basal antral follicular count ≥10; basal FSH ≤10IU/mL) were included. Oocyte donation cycles were excluded. Cycles were segregated into 4 groups (Group A: GnRh antagonist (leuprolide acetate 2mg); Group B: Dual trigger(leuprolide acetate 2mg + 1000 IU rhCG); Group C: RhCG,(250 µg); and Group D: P-hCG(10000 IU)). Data was analyzed by ANOVA and Brown Forsythe's tests for unequal variances, significance set at $p < 0.05$. Multivariate logistic regression analysis was performed to observe variability in clinical factors and ploidy outcomes.

Results

A total of 704 cycles were included in the study (Group A: 62 cycles (8.8%); Group B: 1172 cycles (65.7%); Group C: 498 cycles (15.34%); and Group D: 201 cycles (10.1%)). Cycle demographics, stimulation, post retrieval metrics, and ploidy outcomes are shown in Table 1. Overall 53.06 % of screened embryos were found to be euploid (Group A: 58.9%; Group B: 53.48%; Group C: 44.59%; and Group D: 49.2%). Significant differences in age, number of eggs retrieved, MII oocytes and embryos biopsied between the groups ($p < 0.0001$) were observed, albeit ploidy outcome(s) were similar (Figure 1). After adjusting for age, BMI, total number of mature oocytes and blastocysts biopsied per cycle, no association between the trigger type and ploidy outcome was observed (Table 2).

Conclusions

The type of trigger medication used during an IVF GnRH antagonist protocol cycles does not appear to influence ploidy outcome regardless of patient age, oocyte retrieval count, or embryos available for biopsy. The opportunity to choose triggers allows clinicians to offer patients personalized treatment approach and minimize risks of treatment including OHSS.

Support

None.

Table 1

Comparison of Cycle demographics, stimulation and post retrieval metrics.					
Variable	GnRHa Trigger (n=62)	Dual trigger GnRHa + hCG(n=1172)	R-hCG (n=498)	P-hCG (n=201)	P value
Age mean	35.4 (±3.6)	35.7 (±3.7)	37.9 (±3.9)	37.8 (±4.3)	**< 0.0001**
BMI mean	22.8 (±3.9)	23.4 (±3.9)	24.1 (±4.3)	24.5 (±5.5)	NS
Day 3 FSH (IU/mL) mean	5.26 (±2.3)	5.57 (±3.9)	6.0 (±2.2)	6.1 (±2.2)	NS
BAFC	17.5 (±7.6)	15.7 (±5.4)	13.2 (±3.4)	13.8 (±5.0)	NS
AMH	6.6 (±6.0)	5.0 (±4.3)	2.8 (±2.4)	3.8 (±4.6)	NS
Eggs retrieved mean	24.1 (±13.1)	19.0 (±8.9)	14.3 (±6.1)	14.6 (±8.4)	**< 0.0001**
MII oocytes mean	18.8 (±10.2)	14.7 (±6.9)	10.2 (±5.0)	10.2 (±6.5)	**< 0.0001**
Mean blastocysts biopsied	8.3 (±4.6)	6.7 (±4.3)	3.8 (±2.7)	4.6 (±3.8)	**< 0.0001**
Euploidy rate %	58.9	53.4	44.5	49.4	NS
Aneuploidy rate %	34.8	38.5	47.9	45.6	NS
Others rate %	6.1	8.0	7.9	4.9	NS

Table 2.

Odds ratio estimates and profile – likelihood confidence intervals			
Variable	Odds ratio estimates	95% Wald confidence limits	P value
Age	0.791	$0.75 - 0.82$	**<0.0001**
BMI	0.984	$0.95 - 1.01$	NS
MII oocyte count	1.02	$1.02 - 1.05$	**<0.0001**
Biopsied blastocysts	0.61	$0.5 - 0.65$	**<0.0001**
Dual trigger vs P-hCG	0.83	$0.49 - 1.39$	NS
GnRH agonist vs P-hCG	1.04	$0.52 - 2.08$	NS
R-hCG vs P-hCG	0.82	$0.45 - 1.52$	NS

Figure 1.

Distribution of BxAneuploidCount

Figure 2.

Odds Ratios with 95% Wald Confidence Limits
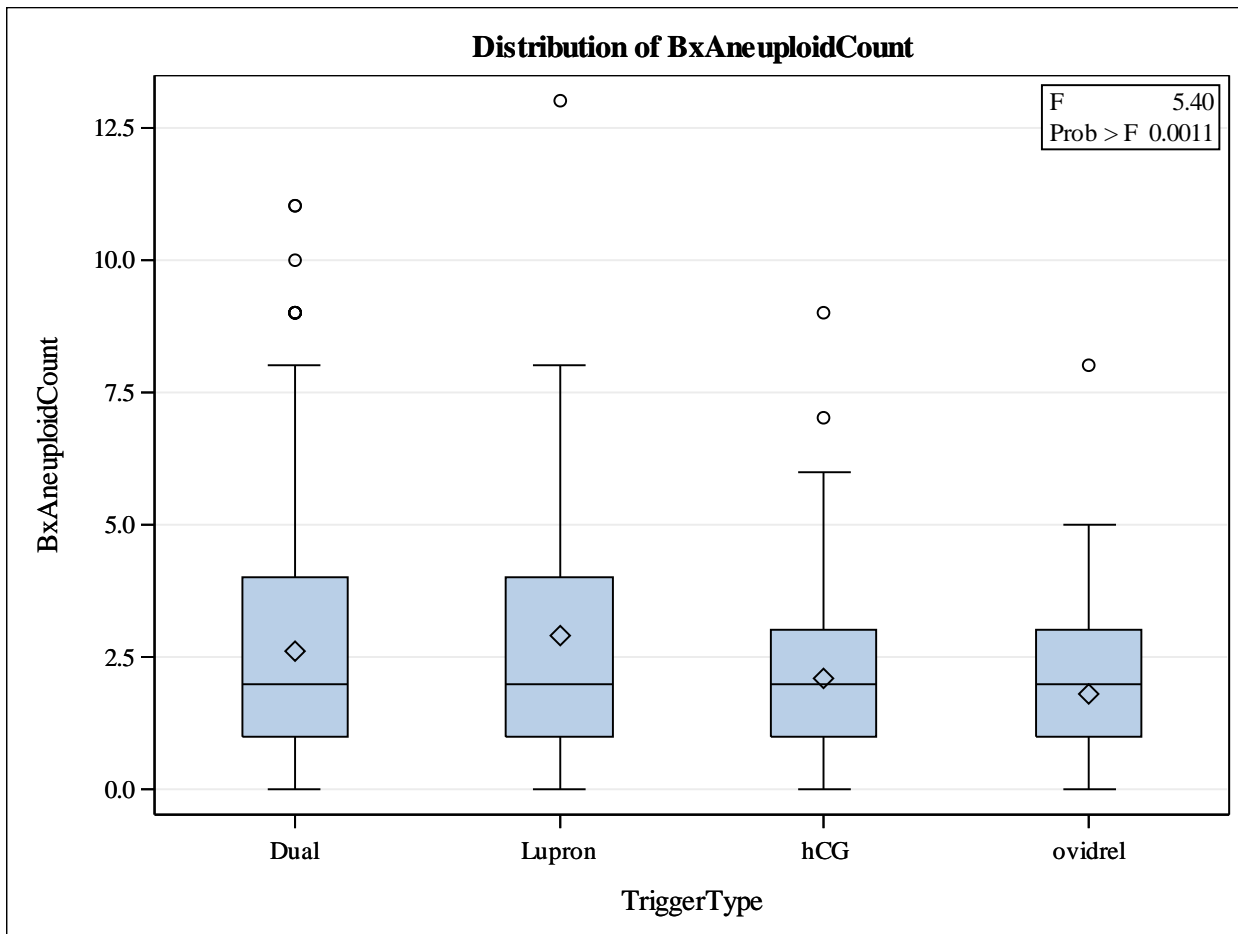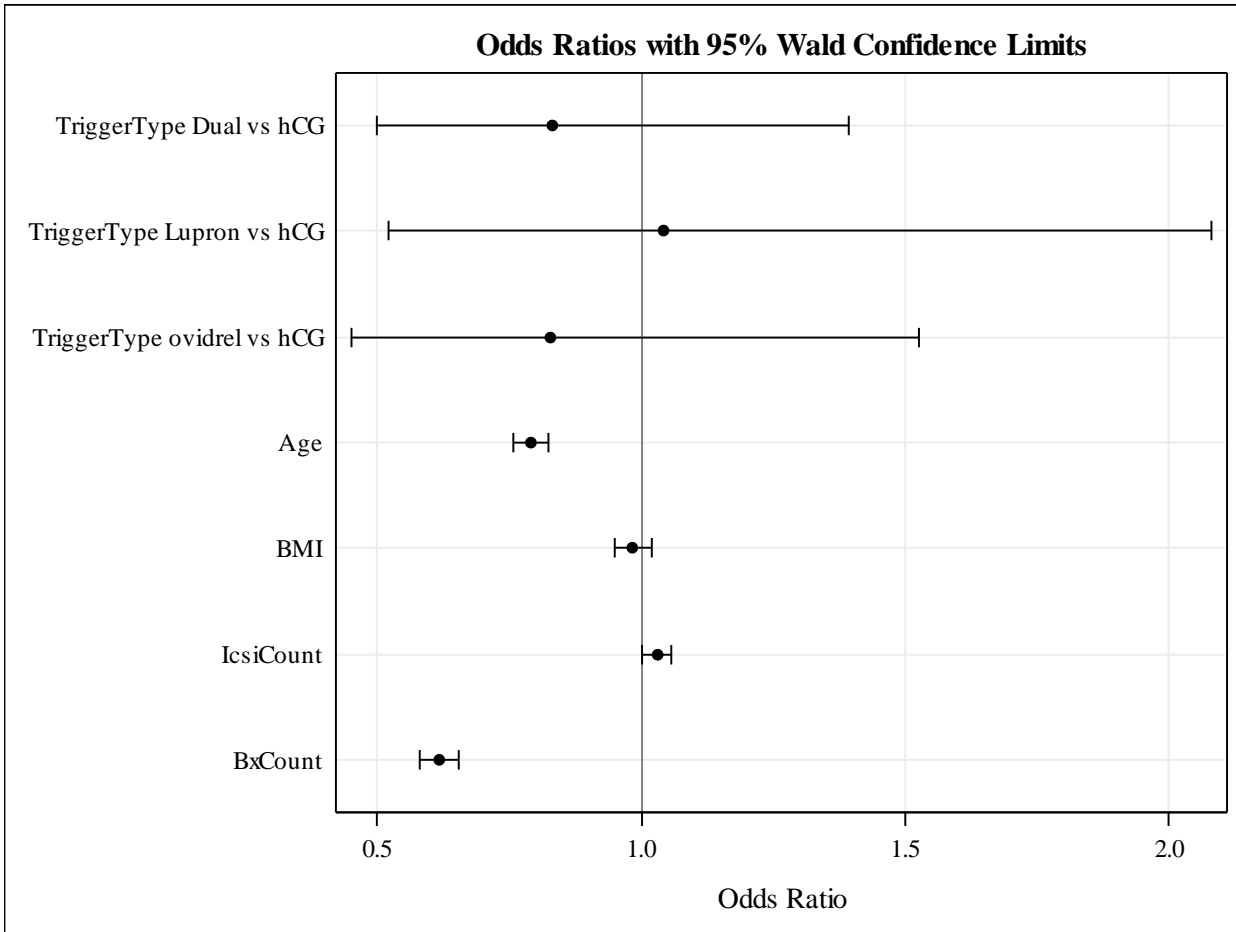
Reference: Fert and Steril Vol. 90, No. 4, October 2008 Can pregnancy rate be improved in gonadotropinreleasing hormone (GnRH) antagonist cycles by administering GnRH agonist before oocyte retrieval? A prospective, randomized study. Morey Schachter, M.D., Shevach Friedler, M.D., Raphael Ron-El, M.D., Ariel L. Zimmerman, M.D., Deborah Strassburger, Ph.D., Orna Bern, Ph.D., and Arieh Raziel, M.D.