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Title:

DUAL TRIGGER WITH GNRH AGONIST AND LOW DOSE HCG LEADS TO ADEQUATE LUTEINIZATION IN PATIENTS WITH ISOLATED LOW BASAL LH LEVELS

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Background:

The use of a dual ovulation trigger (leuproloide acetate combined with low dose hCG) in patients undergoing controlled ovarian hyperstimulation (COH) with a GnRH antagonist protocol has nearly eliminated the incidence of ovarian hyperstimulation syndrome (OHSS). As the GnRH agonist trigger relies on endogenous stores of LH from the anterior pituitary to luteinize mature follicles, patients who lack a reservoir of pituitary LH and FSH (i.e. hypothalamic hypogonadism) might not realize its full benefit.

Objective:

Our study sought to determine whether when using dual trigger, patients with no history of hypothalamic dysfunction who present with low baseline serum LH levels are at risk of poor luteinization.

Materials and Methods:

This retrospective cohort study included patients with low basal LH levels (<2 mIU/mL) who underwent IVF with the GnRH antagonist protocol for controlled ovarian hyperstimulation (COH) from 2002 to 2017. Patients with a diagnosis of hypothalamic hypogonadism (FSH <2 mIU/mL) and those suppressed with pretreatment OCPs were excluded. Patients were stratified

by whether they received dual trigger (40 U Lupron with low dose hCG) or high dose hCG alone. Student's t-test was used to compare demographic and cycle outcome data and multivariate linear regression analysis was used to assess whether trigger type influenced the degree of luteinization (measured as ratio of estradiol (pg/ml) to the number of eggs retrieved).

Results:

Of the 305 IVF patients with low basal LH levels that underwent COH using the GnRH antagonist protocol, 47 received a dual trigger (hCG dose range: 1000-3000U) vs. 258 who received a high dose of hCG alone (range: 5000-10000U). Patients who received dual trigger were significantly younger (35.9 ± 3.9 vs. 37.7 ± 4.7, p=0.01), with greater ovarian reserve (BAFC 12.4 ± 6.4 vs. 8.6 ± 5.2, p<0.0001), higher serum E2 levels on day of surge (2246.6 ± 946.9 vs. 1541.1 ± 820.1, p<0.0001), higher degree of rise in P4 levels the day after trigger (512.31 ± 275.7 % vs. 328.7 ± 187.3 %, p<0.0001) and had more eggs retrieved (15.4 ± 7.2 vs. 11.7 ± 7.3, p=0.0015).

Patients receiving dual trigger received a significantly lower hCG dose (1255.3 ± 674.6 vs. 7864.3 ± 2345.8, p<0.0001) but had a similar degree of luteinization 166.9 ± 81.8 vs. 159.0 ± 88.3, p=0.6) (Table 1). Controlling for age, day 3 FSH, BAFC and the dose of HCG administered, the degree of luteinization was not significantly modified by trigger type (r^2= 0.05, β = -12.0, p=0.56). No patients experienced luteinization failure (no eggs retrieved) in either cohort.

Conclusion:

Patients with low baseline serum LH levels adequately luteinized when ovulation was triggered with dual administration of Lupron with low dose hCG. Isolated low basal serum LH levels are not necessarily reflective of a functionally hypothalamic state. Dual ovulation trigger can be used in high responding patients with low basal serum LH levels to reduce the incidence of OHSS without compromising clinical outcome.

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References:

None

Table 1:

Patients with low basal LH levels who received dual trigger vs. high does hCG alone: demographic data and cycle characteristics

	Dual Lupron/HCG Trigger	HCG Trigger Only	P value
Age	35.9 ± 3.9	37.7 ± 4.7	**0.01**
Day 3 FSH	3.9 ± 2.0	4.6 ± 2.5	**0.06**
Day 3 LH	1.3 ± 0.6	1.3 ± 0.6	0.99
BAFC	12.4 ± 6.4	8.6 ± 5.2	**<0.0001**
BMI	25.8 ± 5.8	25.6 ± 5.9	0.87
HCG dose administered	1255.3 ± 674.6	7864.3 ± 2345.8	**<0.0001**
E2 at surge	2246.6 ± 946.9	1541.1 ± 820.1	**<0.0001**
P4 at surge	0.8 ± 0.4	0.8 ± 0.5	0.72
E2 rise day after surge	27.2 ± 32.0 %	27.3 ± 27.5 %	0.99
P4 rise day after surge	512.31 ± 275.7 %	328.7 ± 187.3 %	**<0.0001**
Mature follicles	3.8 ± 2.2	3.6 ± 2.1	0.67
Eggs retrieved	15.4 ± 7.2	11.7 ± 7.3	**0.0015**
E2/eggs retrieved ratio	166.9 ± 81.8	159.0 ± 88.3	0.57