Reliability of leuprolide ovulation trigger assessed by contemporaneous urinary and blood testing for improved patient access to care

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Introduction and Objectives

The use of leuprolide (GnRH agonist) for follicular/oocyte maturation has become widespread with proven reliability and advantages. The rise in serum levels of LH and progesterone (P4) ~12 hours after trigger are markers of pituitary response.

Serum testing, however, requires patient travel, phlebotomy services, and endocrine laboratory with same-day turnaround. These factors add inconveniences and costs that pose additional impediments to access to care for both metropolitan and dispersed, underserved populations.

A natural and intuitive alternative lies in the application of commercially available urinary LH kits to confirm a rise in serum/urine LH (uLH) after trigger. While described by various individuals and programs, data demonstrating the efficacy and reliability for this approach in a routine clinical population are lacking. This study sought to retrieve data to assess this reliability of this approach.

Methods

Data Source: medical records from ART patients, ages 21-45, who had received leuprolide triggering for egg retrieval and had contemporaneous urinary LH assessment

Sample Size: 164 IVF cycles in 153 subjects

Intervention: contemporaneous urinary LH testing following ovulation trigger injection by leuprolide (4mg subcutaneously)

Data Collection:

- uLH kits (Ovuquick One-Step, Vitrolife, Inc. Threshold Sensitivity = 40mIU/mL) were performed on the day of trigger and 10-14 hours after trigger at the time of sampling for serum LH and P4, measured by ELISA (Cobas e411, Roche Diagnostics, Inc).
- Data were also captured for peak estrogen, post-trigger P4, total and mature oocytes, fertilization, cleavage and blastulation rates.

Outcome Measure:
A positive correlation was anticipated to be a conversion from negative to a positive uLH and serum LH >15 and/or P4 > 3.0 after trigger.

Statistical Analysis: Wilcoxon-Mann-Whitney and Fisher's exact tests were used to compare cases of correlation and failure.

Results

- Change in uLH test agreed with serum LH in 157 of 164 (95.7%) of cases (p=0.025)
- uLH did not convert in one case, agreeing with a low post-trigger serum LH
- 7 Discrepant Cases:
  - 5 cases: (+) uLH before and after trigger with a satisfactory rise of serum LH
  - 1 false negative: persistent (-) uLH despite adequate serum LH
  - 1 false positive: (-) uLH changed to (+) uLH but inadequate serum LH
- Discrepant cases did not differ from correlating cases by factors such as age, and ART lab outcomes, except fertilization rate being higher in discrepant cases (93% vs 77%, p=0.008).
- PCOS diagnosis was present in 38 (23.3%) of concordant cases and 3 (42.9%) of the 7 discrepant cases.
- Of the 5 (3%) cases reporting premature +uLH (before trigger), 1 patient had diagnoses of PCOS. However, these small numbers preclude drawing meaningful analyses or conclusions.

Discussion

Based on these findings, the intuitive application of serial uLH testing appears to have high correlation with serum LH in the assessment of effective leuprolide triggering. Acting solely on a post-trigger uLH test, management errors might occur in 1-2% of cases.

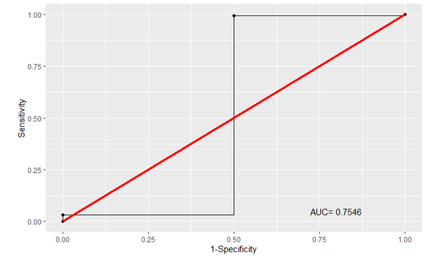
uLH testing to determine efficacy of leuprolide triggering showed high reliability.

Implementing uLH testing should portend improved patient convenience, access to care, and cost savings.

Results

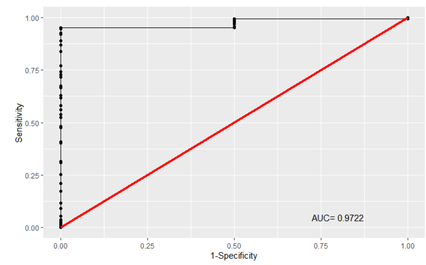
Data Set 1.
Logistic regression for serum LH and P4 results

Variable (Intercept) uLH Trigger	Paired Changes in uLH	Coefficient (Odds Ratio)	95% Confidence Interval		P - value
			2.5%	97.5%	
(Intercept)		1.00	0.04	25.29	
uLH assessment of trigger	Neg. → Pos. vs. Neg.→ Neg.	156,00	4.30	7871.79	0.0036
	Pos. → Pos. vs. Neg.→ Neg.	115,648,792.73	0.00	N/A	0.9949



Data Set 2.
Logistic regression for serum LH and P4 results with the inclusion of variables

Variable (Intercept) uLH Trigger	Paired Changes in uLH	Coefficient (Odds Ratio)	95% Confidence Interval		P - value
			2.5%	97.5%	
(Intercept)		0.04	0.00	8702.69	0.5328
uLH assessment of trigger	Neg. → Pos. vs. Neg.→ Neg.	90.91	2.14	5224.49	0.0125
	Pos. → Pos. vs. Neg.→ Neg.	202,380,347.87	0.00	N/A	0.9968
Dx of PCOS/Anovulation?		0.39	0.01	20.27	0.5883
Patient's Age		1.13	0.76	1.53	0.463



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References

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