P-225

PROGESTERONE LEVEL ON THE DAY OF HCG TRIGGERING: A NEW TOOL FOR SUCCESSFUL MODIFIED NATURAL IN VITRO FERTILIZATION (MNIVF) CYCLE?

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OBJECTIVE

Determine if progesterone (PG) level on trigger day could predict pregnancy rates (PR) in mnIVF.

METHODS

We retrospectively reviewed 1074 mnIVF cycles including 581 women between January 1, 2012 and June 30, 2013.

STATISTICS

PG level at trigger day is available for 839 cycles. Analyses were performed per cycle, taking correlation within patient into account.

Mixed effects univariate logistic regression analysis to identify PG as factor associated to « no oocyte retrieved at egg collection », biochemical and clinical pregnancies were performed. Patient was included in the model as a random factor.

Receiver operating characteristic (ROC) curve analysis to find a PG threshold for pregnancy prediction was used. ROC curve accuracy was measured by area under an ROC curve (AUC) and Youden Index (Y). Cycle were consider independent and sensitivities analyses were performed.

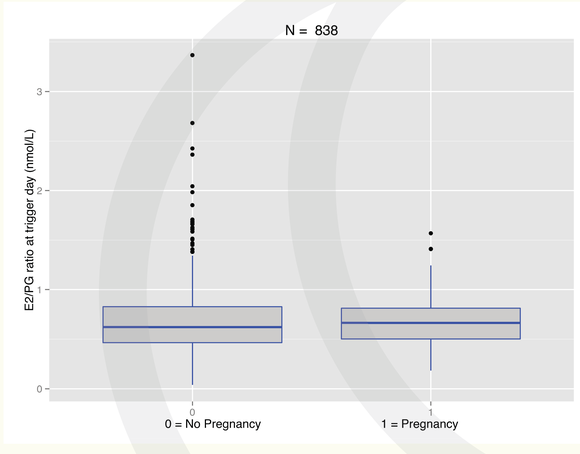
Univariate and multivariate regression analysis were also done to determine association between PG threshold and pregnancy issue.

All statistical analysis was performed using R version 3.2.1.

RESULTS

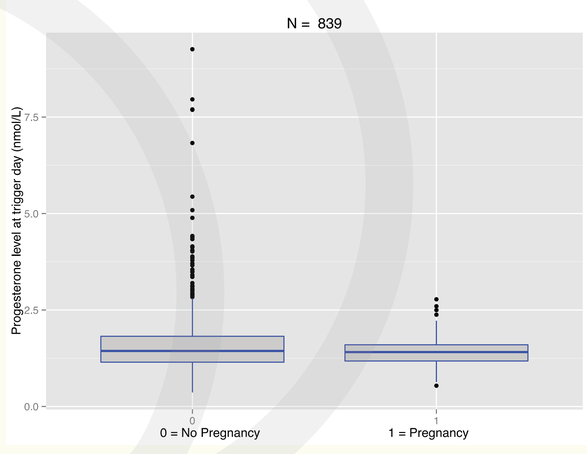
Female were aged 32.4 ± 3.5 years, with AMH, E2 and progesterone levels at 1.7 ± 1.9 ng/mL, 916±303 pmol/L, and 1.6 ± 0.8 nmol/L, respectively. The "no oocyte retrieved at egg collection per cycle" rate was 9.5%. Per egg collection, 94% of oocytes were mature. Biochemical and clinical PR were respectively 17.8% and 16.2% per cycle and 35.9% and 32.8% per embryo transfer. Associations were found between PG level and no oocyte retrieved at egg collection (OR = 1.61 (1.2-2.16); p = 0.001), biochemical PR (OR = 0.62 (0.41-0.93); p = 0.02), and clinical PR (OR = 0.63 (0.42-0.95); p = 0.02).

E2/PG ratio at trigger day and clinical pregnancy outcome



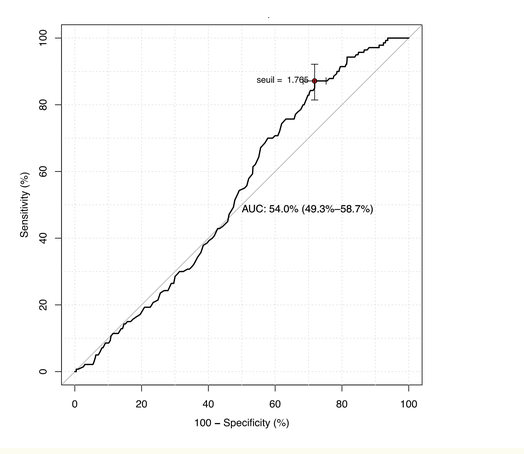
Patients without pregnancy have high E2/PG ratio at trigger day. Boxes display quantiles, with whiskers extending to the most extreme data point.

PG level at trigger day and clinical pregnancy outcome



Patients without pregnancy have high progesterone levels at trigger day. Boxes display quantiles, with whiskers extending to the most extreme data point.

PG level at trigger day to predict clinical pregnancy



ROC curve analysis of PG levels at trigger day.

Best determined PG threshold is 1.765 nmol/L (Se = 87.4% and Sp: 28.1%). Accuracy of ROC curve measured both by Area Under an ROC curve (AUC) = 54% (49.3% - 58.7%) and by Youden Index (Y) = (0.87 + 0.28) -1 = 0.15

1.77 nmol/L PG level threshold: clinical significance

Clinical pregnancy			
	Yes	No	
PG < 1.77 nmol/L	122 (19.6 %)	502 (80.4%)	624
PG≥ 1.77 nmol/L	18 (8.4%)	197 (91.6%)	215
	140	699	

PG < 1.765 vs. PG ≥ 1.765: 11.2% pregnancy rate difference (p=0.0002).

There is no pregnancy with PG ≥ 2.78 nmol/L (n = 44) of 839 nmIVF cycles.

Pregnancy and PG ≥ 1.77 nmol/L threshold

Outcomes	OR (95% CI)	p
Univariate analyses		
Clinical pregnancy	0.35 (0.20-0.62)	0.01*
Multivariate analyses		
Clinical pregnancy	0.29 (0.15-0.55)	0.0002*

Multivariate analyses when adjusting for diagnosis of low ovarian reserve; female age over 35 years; follicle and endometrium sizes, E2/PG ratio.

Lower chance of pregnancy is worse when adjusting for confounding factors (71%) vs. Without adjusting (65%).

* p < 0.05 as significant

CONCLUSIONS

PG appears to have a detrimental effect on egg collection, biochemical and clinical pregnancies in mnIVF.

Using PG threshold by 1.77 nmol/L to predict clinical pregnancy is not statistically significant as demonstrated by AUC and Youden index. However, Its clinical significance cannot be ignored (PG ≥ 1.77 nmol/L vs. < 1.77 nmol/L): Lower chance of pregnancy when adjusting for confounding factors (71%), difference in pregnancy rate (11.2%). There is no pregnancy with PG ≥ 2.78 nmol/L.

Our results need to be validated by other research teams. Regarding these results, our recommandation would be: (1) Cancel cycle if PG ≥ 2.78 nmol/L and discuss cancellation depending on infertility history if PG ≥ 1.77 nmol/L.

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