

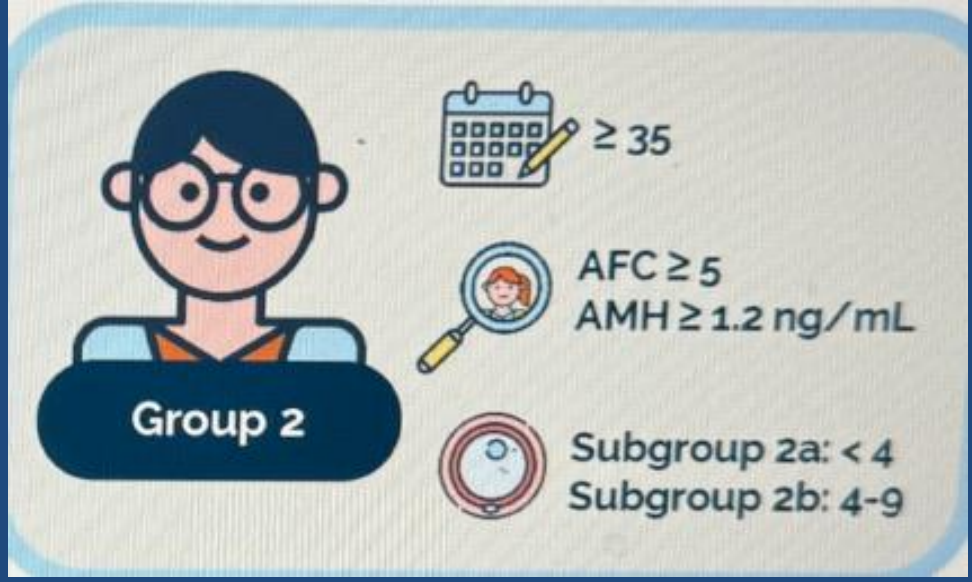
Use of PRP and Growth Hormone in Poor responders in ART

Dr Keya Parashar Jain, *NOVA IVF, AGRA*

Background

Poor ovarian reserve as a cause of infertility/subfertility has significantly increased in today’s scenario. Around 10% women in IVF clinics show POR. There are multiple reasons for POR in females.

- Aging
- Past exposure to cytotoxic / anti cancer drugs
- Radiation therapy
- Genital Tuberculosis (sp in Indian Sub continent)
- Genetic factors
- Lifestyle
- Poor Ovarian reserve is categorised using multiple criteria ie Bologna and Poseidon. In our study we used Poseidon criteria.
- It is important to note that not all women with POR are infertile. Their treatment options vary and that is where Artificial Reproduction specially comes in picture.
- In this race against time ART provides a trusted and reliable solution to the infertile couple.
- Many of these patients need Third party reproduction. Some families do not agree for donor cycles due to many reasons like unacceptability, religious restrictions etc.
- For these cases it is impertinent to workout self cycle protocols.
- PRP combined with Gonadotrophin stimulates with adjuvant Growth Hormone look helpful in these cases.



Objective

To increase chances of self cycle in Poseidon 3 and 4 groups using combined Growth hormone (GH) & Platelet rich plasma (PRP)

Materials and methods

- Nine women over a period of 6 months who were categorised as Poseidon 3 and 4.
- Not willing for third party reproduction.
- Willing for pooling cycles/multiple cycles with PRP and GH
- Followed till Embryo transfer and beta HCG report

Analysis

Table 1: Regression Statistics		
Metric	Value	Interpretation
Multiple R	0.982	Very strong correlation between actual and predicted values.
R Square	0.965	96.5% of the variation in the dependent variable is explained by the independent variables.
Adjusted R ²	0.907	Adjusted for number of predictors, still high—the model fits very well.
Standard Error	0.215	Indicates the average distance that the observed values fall from the regression line. Lower is better.
Observations	9	Only 9 data points — a small sample size, so results should be interpreted with caution.

SNo	Name	Age	AMH	AFC	PRP CYCLES	OPU	GH USED	BLASTS FORMED	ET RESULT
1	GB	32	0.8	5	2	2	YES	NIL	NEG
2	DV	45	0.12	2	2	2	YES	1	NEG
3	BP	42	0.9	4	2	2	YES	2	POS
4	TM	41	0.5	3	3	2	YES	2	POS
5	AM	28	1.1	5	2	1	YES	1	NEG
6	IJK	26	1.0	4	1	1	NO	1	NEG
7	KA	43	0.4	2	1	1	YES	2	POS
8	PS	38	0.7	3	1	1	YES	2	POS
9	PK	30	1.1	4	1	2	NO	1	NEG

ANOVA Table					
Source	df	SS	MS	F	Significance F
Regression	5	3.86	0.772	16.65	0.0213
Residual	3	0.139	0.046		
Total	8	4			

Regression model				
Variable	Coefficient	p-value	Significance	Interpretation
Intercept	-1.767	0.213	Not significant	Base value when all predictors = 0
Age	0.0952	0.026	Yes	As age increases by 1 unit, the outcome increases by 0.095 (holding others constant)
AMH	3.586	0.009	Yes	Strong positive influence; increase in AMH significantly increases the outcome.
AFC	-0.823	0.023	Yes	Negative influence, more AFC linked with lower outcome
PRP Cycle	0.541	0.048	Yes	PRP treatment cycles are positively related to the outcome
OPO	-0.612	0.045	Yes	Negative relationship; as OPO increases, outcome decreases

Results

The model yielded a Multiple R of 0.982, and an R² value of 0.965, indicating that 96.5% of the variation in the dependent variable is explained by these predictors. The adjusted R² of 0.907 further supports the model’s strong explanatory power even after accounting for the number of predictors. The ANOVA F-test result (F = 16.65, p = 0.021) indicates that the model is statistically significant at the 5% level, implying that at least one independent variable significantly affects the outcome.

Out of all the predictors, the following variables were statistically significant:

- Age (p = 0.026): Positively associated with the outcome.
- AFC (p = 0.023): Significant negative influence.
- OPU (p = 0.045): Negative and significant.
- AMH (p = 0.009): Strong positive influence.
- PRP Cycle (p = 0.048): Positive and significant.

Only the Intercept (p = 0.213) was not statistically significant. The regression model significantly predicts the outcome variable, with very high explanatory power (R² = 0.965). AMH, Age, PRP Cycle contribute positively, while AFC and OPO show negative associations. All these predictors were statistically significant, suggesting they have meaningful impacts on the outcome. Given the small sample size (n = 9), these findings should be interpreted with some caution, but they provide strong initial evidence of which factors most influence the response variable. Further analysis with a larger dataset is recommended to validate and generalize these results.

Discussion

Platelet rich plasma (PRP) is used in many situations in infertility. It is used for

- Ovarian rejuvenation
- Improving endometrial thickness and blood flow
- Improving oocyte numbers
- Improving oocyte quality
- Multiple regimens have been tried for POR cases opting for self cycles. Use of recombinant gonadotrophin increased dosages, addition of Letrozole or Clomiphene, anti oxidants but we are far from ideal protocol.
- PRP is rich with around 700 proteins, hormones, Growth factor with biological activity. These factors stimulate angiogenesis, anabolic processes cell migration, cell differentiation and tissue proliferation at the site of autologous grafting.
- Present studies do give a possible short term benefit in cases of POI and POR but further studies are needed to define a definite protocol.

GROWTH HORMONE

- GH is a pleiotropic, multifunctional hormone with multiple effects. Its chief secretion is by pituitary but in females small quantities are secreted by ovaries. It helps in follicular growth particularly mono follicular growth.
- It binds to GH receptors on Granulosa cell, theca cell and luteal cells promoting steroidogenesis and gametogenesis
- GH also improves Ovarian sensitivity to Gn stimulation and along with IGF-1 & IGF-2 affects follicular maturation by inhibiting apoptosis. When given along with Gonadotropins it improves follicular survival and cell proliferation by strengthening LH action.
- Studies shows oocytes with normal GH concentration have better cytoplasmic and nuclear maturation. Thus co treatment with HMG and HCG improves dose requirement and duration for stimulation leading to a better result, but patient selection criteria should be defined.
- Hypogonadotrophic hypogonadism patients, patients with long standing infertility definitely benefit from GH but its indiscriminate use is to be avoided.

Conclusion

Though more tests are required PRP with GH use in POR patients unwilling for Donor cycle do have a hope to look forward to. The most potive correlation does turn out to be with number of blasts formed but number of blasts formed does increase with PRP and GH.

References

1. Garcia JE Jones et al., JR Human Menopausal Gonadotrophin/HCG follicular maturation for oocyte aspiration. Ph ! Fertil Syeril 1981.
2. Keay SD et al Assisted conception following poor ovarian response to Gn Stimulation. Br J Obstetrics Gynecol 1997; 104:521-7.
3. DK Kesharwani Fertility with early reduction of Ovarian reserve., PMC 2022 October 15;14(10):e30326.
4. N Magon, Sonia Malik et al., Growth Hormone in Management of female infertility. Indian J Endocrinology Metbol 2011 Sep;15(Suppl3);S246-S247
5. Chia Wei Chang et al., Growth hormone in fertility and infertility; Front. Endocrine., 14 Nov 2022.
6. Irina Pacu et al PMID: PMC8524761 OCT 2022.
7. Fady I Sharara., A narrative review of PRP IN REPRODUCTIVE MEDICINE. J Assist Reprod Genert 2021 Mar15;38(5):1003-1012