

THE ROLE OF PLATELET-RICH PLASMA INJECTIONS INTO THE OVARY IN IMPROVING OVULATIONMais Hassan*¹, Ahmad Abd el Rahman² and Lina Ramadan³¹Postgraduate Student (PhD), Department of Obstetrics and Gynecology, Faculty of Human Medicine, Tishreen University, Latakia, Syria.²Professor, Department of Obstetrics and Gynecology, Faculty of Human Medicine, Tishreen University, Latakia, Syria.³Assistant Professor, Department of Obstetrics and Gynecology, Faculty of Human Medicine, Tishreen University, Latakia, Syria.***Corresponding Author: Mais Hassan**

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ABSTRACT

The research aimed to evaluate the effectiveness of intraovarian platelet-rich plasma injections in improving ovulation in infertility patients who suffer from ovarian insufficiency (high FSH value), decreased ovarian reserve (low AMH value), or polycystic ovaries (high AMH value). (40) female patients of reproductive age were admitted to the women's clinic at Tishreen University Hospital, who were suffering from infertility due to premature ovarian insufficiency, low ovarian reserve, or dysovulation due to polycystic ovary syndrome. The necessary general and hormonal analyses were performed, as well as ultrasound imaging of the uterus and appendages to diagnose the condition, and a semen analysis of the husband was performed (provided that it was normal). The patient was prepared for laparoscopy in order to inject platelet-rich plasma after the end of the menstrual cycle in the first phase of the cycle. (10) ml of platelet-rich plasma was prepared from the blood of the concerned patient, and (5) ml was injected into each ovary through one puncture, and the improvement of ovulation was monitored by ultrasound imaging and hormonal analyses three months after the injection. The research results showed that platelet-rich plasma injections are a promising treatment for infertility patients, as this treatment can help improve fertility and women's general health. The evidence for this is that (69.23%) of the patients suffering from ovarian insufficiency had an improvement in ovulation after the injection procedure, and the significance of the FSH values three months after the injection indicates its return to normal values compared to its values before the injection, which indicates an increase beyond the limits Natural. Also, (53.33%) of the patients with low ovarian reserve had an improvement in ovulation after the injection procedure, and the significance of the average AMH value after the injection indicates that it has increased and returned to normal values compared to its values before the injection, which indicates that it is outside the normal limits. In addition, (58.33%) of the total patients who had polycystic ovaries had an improvement in ovulation after the injection, and the significance of the AMH value after the injection indicates its decrease and return to normal values.

KEYWORDS: Platelet-rich plasma, ovarian insufficiency, low ovarian reserve, polycystic ovary.**INTRODUCTION**

In clinical infertility practice, one intractable problem is reduced (or absent) ovarian reserve which in turn reflects the depletion of normal oocytes associated with advanced maternal age.^[1]

Global experimental studies are currently being conducted on the role of platelet-rich plasma in restoring ovarian function. Which summarizes the interaction of platelet-derived growth factors with adult ovarian tissue, and the outcome of human reproductive potential after PRP treatment.^[1]

PRP is a biological product defined as a fraction of plasma from autologous blood with a platelet concentration higher than baseline (prepared by centrifugation).^[2] As such, PRP contains not only a high level of platelets, but also a full complement of clotting factors, which usually remain at their normal physiological levels.^[3] It is enriched with a range of GFs, chemokines, cytokines, and other plasma proteins.^[4]

The autologous PRP sample generates an enriched platelet (PLT) substrate that is collected via peripheral venipuncture. The combination of PLT with calcium gluconate achieves the activation of α -granules, which

subsequently initiate the release of at least three classes of molecular mediators. These include chemical compounds such as Interleukin-1 β (IL-1 β), Interleukin-8 (IL-8), and Platelet Factor 4 (PF4).^[5]

Injecting platelet-rich plasma into the ovary helps regulate hormonal interactions, improves the capabilities of the ovary, and contributes to the formation of follicles through molecular mediators released by the combination of platelets with calcium gluconate within the plasma.^[6,7]

2- MATERIALS AND METHODS

The study was conducted on (40) female patients of reproductive age who were patients attending the women's clinic at Tishreen University Hospital, and who were suffering from infertility due to ovarian insufficiency, low ovarian reserve, or polycystic ovaries. The necessary general and hormonal analyzes were performed (follicle-stimulating hormone and anti-Müllerian hormone). Provided that there is a normal semen analysis for the partner after several failed attempts at ovulation induction.

The study period extends over two full years, 2021 and 2023 AD.

20 ml of the patient's venous blood was drawn and placed in a tube containing an anticoagulant, and platelet-rich plasma was prepared by placing this tube in a centrifuge.

Hich zentri higen at 3500 cycles for 10 minutes.

The platelet layer is then mixed with 0.5-1 ml of supernatant to obtain the final PRP sample.

A laparoscopy was performed for the patient after the end of her menstrual cycle in the first phase of the cycle. Platelet-rich plasma, amounting to 5 ml, was injected into each ovary under the ovarian cortex through only one puncture away from the navel of the ovary using a 25 G needle. Then ovulation was monitored with ultrasound and hormonal analyzes were monitored 3 months after the injection.

2.3. Statistics

All data were analysed by the unpaired t test both for equal and unequal variance using the variance ratio function of the Stata software to determine the appropriate use of Satterthwaite's correction for the degrees of freedom. The level of statistical significance was at $p < 0.05$ for all the analyses.

3- RESULTS AND DISCUSSION

The effect of injecting platelet-rich plasma into the ovary in improving ovulation was studied, by monitoring the cases of (40) female patients, before plasma injection, and three months after plasma injection, for the following cases:

The first case: ovarian insufficiency (high FSH values).

The second case: decreased ovarian reserve (low AMH values).

The third case: polycystic ovary (PCO) (high AMH values).

1 - The first case: ovarian insufficiency (high FSH value):

A t-test was performed. test for the difference in FSH values for patients before and three months after injection, as shown in the following table:

Table 1: T-test results. Test for the difference in fsh values for patients before and three months after injection. Paired Samples Statistics.

FSH	N	Mean	Std. Deviation	Std. Error Mean
Before injection	13	15.3308	.78463	.21762
Three months after injection	13	8.3846	3.96229	1.09894

Paired Samples Test

t	df	Sig. (2-tailed)	Mean	Std. Deviation	95% Confidence Interval of the Difference	
					Lower	Upper
6.204	12	.000	6.94615	4.03683	4.50672	9.38559

Table (1) shows that the average FSH values for patients suffering from ovarian insufficiency as a result of high FSH before the injection reached (15.3308) international units/liter, which is outside the normal limits (greater than 12.5 international units/liter), and the average FSH values after the injection reached three Months (8.3846 international units/liter), which is within normal limits, and observing the value of the probability of significance $P=.000 < 0.05$, we find that it is less than the significance level of 0.05, and this indicates that there is a statistically significant difference in favor of three months after the injection, and this indicates the role of plasma injection.

Platelet-rich cells in the ovary resulted in lower FSH values three months after injection.

2 - The second case: decreased ovarian reserve (low AMH value)

A t-test was performed. test for the difference in AMH values for patients before and three months after injection, as the following table shows:

Table 2: t-test results. test for the difference in AMH values for patients before and three months after injection. Paired Samples Statistics.

AMH	N	Mean	Std. Deviation	Std. Error Mean
Before injection	15	.4780	.10652	.02750
Three months after injection	15	1.4747	.88323	.22805

Paired Samples Test

t	df	Sig. (2-tailed)	Mean	Std. Deviation	95% Confidence Interval of the Difference	
					Lower	Upper
-4.650	14	.000	-.99667	.83013	-1.45638	-.53696

Table (2) shows that the average AMH values for patients who suffered from decreased ovarian reserve before the injection reached 0.478 ng/ml, which is outside the normal limits (below the minimum), and the average AMH values three months after the injection reached (1.4747 ng/ml), which is within The normal limits, and observing the significance probability value $P=.000<0.05$, we find it less than the significance level of 0.05, and this indicates that there is a statistically significant difference in favor three months after the

injection, and this indicates the role of platelet-rich plasma injection into the ovaries in increasing the AMH values three months after the injection.

3- The third case: polycystic ovary (PCO) (high AMH)

A t-test was performed. test for the difference in AMH values for patients before and three months after injection, according to the following table:

Table 3: t-test results. test for the difference in AMH values for patients before and three months after injection. Paired Samples Statistics.

AMH	N	Mean	Std. Deviation	Std. Error Mean
Before injection	12	4.9583	.69734	.20131
Three months after injection	12	3.2500	1.35008	.38974

Independent Samples Test

t	df	Sig. (2-tailed)	Mean	Std. Deviation	95% Confidence Interval of the Difference	
					Lower	Upper
5.959	11	.000	1.70833	.99312	1.07733	2.33933

Table (3) shows that the average AMH values for patients suffering from polycystic ovaries before the injection reached 4.9583 ng/ml, which is outside the normal limits (greater than the upper limit), and the average AMH values three months after the injection reached (3.2 ng/ml), which is Within normal limits, and observing the probability value of significance $P=.000<0.05$, we find it less than the significance level of 0.05, and this indicates that there is a statistically significant difference in favor three months after the injection, and this indicates the role of injection of platelet-rich plasma into the ovaries in decreasing the AMH values after three months of injection.

cases resulting from poor ovulation, as this treatment can help improve fertility and women's general health.

The research results are consistent with the findings of a study (Fraidakis et al, 2023), which was conducted on (469) women with a history of infertility, hormonal abnormalities, absence of menstruation, and premature ovarian failure. Which revealed that PRP intervention has significant effects on FSH concentration, as increases in normal values were observed three months and four months after the PRP procedure. Therefore, these results confirm that PRP injection into the ovary is associated with improving ovarian tissue and function.^[8]

CONCLUSIONS

1. Ovulation improved in ovarian insufficiency patients after intraovarian injection of platelet-rich plasma by 69.23%.
2. Ovulation improved in patients with low ovarian reserve by 53.33%.
3. Ovulation improved in polycystic ovary patients by 58.33%.

Therefore, the research results show that platelet-rich plasma injections are a promising treatment for infertility

The results of the research are also consistent with the findings of a study (Atkinson et al, 2021), in which the benefit of platelet-rich plasma (PRP) was studied in a group of regenerative medicine, as it was proven that it stimulates differentiation between a group of cell types, and it is assumed that this Through the action of cytokines and growth factors.^[9]

It is also consistent with the findings of a study (Kawamura, et al, 2021), which showed that intra-ovarian injection of platelet-rich plasma led to an improvement in the state of the hormonal profile and an increase in the

number of eggs retrieved in patients suffering from poor ovulation.^[10]

It also agrees with the study (Navali, etal, 2022) that was conducted on (35) women with an average age of (40.68) years, with a significant increase in the number of eggs as well as in the levels of anti-Mullerian hormone (AMH), and it reached the conclusion that injections of platelet-rich plasma (PRP) once can be effective in improving the chances of conceiving eggs in women with polycystic ovary syndrome.^[11]

Recommendations

1. The use of platelet-rich plasma injections as a treatment for ovarian insufficiency, low ovarian reserve, and polycystic ovaries.
2. Conduct further studies to confirm the effectiveness and safety of this treatment on a larger scale.
3. Expanding the scope of the study to include a larger number of women of different ages. This will help increase the power of the study and give more accurate results.

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