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Comparison between Laparoscopic intra-ovarian platelet rich plasma injection alone and with gonadotropins for ovarian rejuvenation

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Abstract
Background: The physiological process of ovarian aging is accompanied by a decrease in oocyte number & quality. **Objectives:** To compare the impact of PRP Injection alone & PRP with gonadotropins on ovarian Reserve in poor ovarian Responders (PORs) patients under laparoscope guidance. **Patients & methods:** This is Prospective controlled research, that had been carried at carried out at the obstetrics & gynecology department at Benha University from March 2023 till September 2023. 60 patients were included from the obstetrics & gynecology department at Benha University Hospital & some private centers. Patients from age 20 to 50 years old with poor ovarian responses participated and were separated into 2 groups, Group A & B. All underwent the laparoscopy for the procedure. Group A consists of thirty studied cases who received PRP Injection, and Group B consists of thirty studied cases who received PRP with gonadotropins. **Results:** There had been a high statistically significant variation among the 2 studied groups regarding FSH in the Sixth month. Also, there had been statistical variation among different periods in group A as regards AMH. There had been a high statistically significant variation between different periods in group B as regards AMH There had been statistically significant variation among 2 studied groups regarding Estradiol in the Sixth month**. Conclusion:** Women with premature ovarian insufficiency, particularly those who have tried unsuccessfully to conceive in the past, may benefit from intra-ovarian PRP injections because they are safe, effective, & all-natural.

Keywords: Platelet-Rich Plasma (PRP); Premature ovarian insufficiency (POI); poor ovarian Responders (PORs)

Introduction

World Health Organization has identified female infertility as a global public health issue, and since 2005, more than 1 million IVF (in vitro fertilization) cycles have been carried out worldwide annually. Endocrine dysfunction, implantation failure, endometriosis, uterine fibroids, in addition to pathologies directly related to the ovary, such as polycystic ovary syndrome, primary ovarian insufficiency, environmental factors, & inflammatory disease, may all contribute to female infertility **(1, 2).**

The physiological process of ovarian aging is accompanied by a decrease in oocyte number & quality. It has significant effects on fertility & is a common cause why women seek out fertility treatment **(3, 4).**

1 recently proposed alternative for ovarian rejuvenation is intraovarian injection of platelet-rich plasma which is being utilized increasingly in clinical settings for several soft tissues, containing to assist wound healing & ligament & muscle repair **(5).**

By centrifuging & separating the various components of whole blood, which contains plasma (fifty-five percent), red blood cells (forty-one percent), platelets, & white blood cells (four percent), platelet-rich plasma is created. Red blood cells are removed throughout the centrifugation & separation process, & plasma is created that has a five–ten times higher concentration of growth factors **(6, 7).**

PRP is a natural substance that has 3 to 5 times more growth factors than plasma and a high concentration of platelets. Growth factors that are stored in granules include platelet-derived growth factors, transforming growth factor-beta, vascular endothelial growth factor, epidermal growth factor, fibroblast growth factor, & insulin growth factor **(8, 9).**

The goal of that research had been to compare the impact of PRP Injection alone and PRP with gonadotropins on ovarian Reserve in poor ovarian Responders (PORs) patients under laparoscope guidance.

Patient & methods

This is Prospective controlled research, that had been carried at carried out at the obstetrics & gynecology department at Benha University from March 2023 till September 2023.

60 patients were included from the obstetrics & gynecology department at Benha University Hospital & some private centers. Patients from age 20 to 50 years old with poor ovarian responses participated and were split into 2 groups, Group A & B. All underwent laparoscopy for the procedure. Group A consists of thirty studied cases who received PRP Injection, and Group B consists of thirty studied cases who received PRP with gonadotropins.

Inclusion criteria: The study included poor ovarian responders (PORs) between 20 to 50 years old who meet at least 2of the following3 Bologna criteria, published by the European Society of Human Reproduction & Embryology.

Exclusion criteria: studied cases with the following criteria should be excluded from this research: ovarian insufficiency brought on by chromosomal abnormalities and gonadal dysgenesis. lack of immunoglobulins. using anticoagulants. drugs with

psychoactive effects. psychiatric conditions. cancers or background of persistent pelvic discomfort. existing infection. platelets less than 150 x 10ʒ/µl or haemoglobin less than 11 g/L.

Ethical considerations: - Written consent was obtained from all studied cases after a full explanation of the hazards & benefits of the management procedure that had been performed for each studied case before getting them involved in research (carried out by the researcher). The management procedure used in the present study has no harmful effects. studied case's right to decline participation will not have any bearing on the expected level of medical treatment for her. privacy of all study participants' data had been maintained.

Statistical Analysis: Gathered data was cleared and filtered using Microsoft Excel program edition 2013 then was statistically analyzed by using SPSS version22 (SPSS Inc., Chicago, IL, USA) and AP info programs. Studying the significant data will be done by the Chi-Square test for categorical data & by the Student T test for numerical data.

Results

Table (1): Comparing both groups as regards demographic data

		Group A (n=thirty)	Group B (n=thirty)	P value
Age	Mean ± SD	30.2 ± 3.1	29.8 ± 3.5	0.87
	Median (Minimum-Maximum)	31 (25 - 35)	31 (25 - 35)	
Infertility period (years)	Mean ± SD	2.67 ± 1.4	2.8 ± 1.2	0.45
	Median (Minimum-Maximum)	3 (1 - 5)	3 (1 - 5)	

T: Two-Sample Independent t-Test, p-value >0.05: nonsignificant, p-value <0.05 significant, Data are presented as frequency (%) unless otherwise mentioned, Median (Minimum-Maximum)

There had been no statistically significant variation among the 2 studied groups regarding age, & infertility period as shown in **Table 1**.

Table (2): Comparing both groups as regards HAQ.

		Group A (n=thirty)	Group B (n=thirty)	P value
The HAQ Disability Index	Mean ± SD	1.5 ± 0.7	1.57 ± 0.71	0.86
	Median (Minimum-Maximum)	1 (0 - 3)	1 (0 - 3)	
The HAQ VAS Pain Scale	Mean ± SD	1.4 ± 0.65	1.45 ± 0.62	0.87
	Median (Minimum-Maximum)	1 (0 - 3)	1 (0 - 3)	

T: Two-Sample Independent t-Test, p-value >0.05: nonsignificant, p-value <0.05 significant, Data are presented as frequency (%) unless otherwise mentioned, Median (Minimum-Maximum)

There had been no statistically significant variation among the 2 studied groups regarding The HAQ Disability Index or The HAQ VAS Pain Scale as shown in **Table 2**.

Table (3): Comparing both groups as regards CBC.

		Group A (n=thirty)	Group B (n=thirty)	P value
Hb	Mean ± SD	11.4 ± 1.1	11.5 ± 1.2	0.78
	Median (Minimum-Maximum)	12 (10 - 14)	12 (10 - 14)	
Platelet	Mean ± SD	220 ± 18	225± 17	0.88
	Median (Minimum-Maximum)	225 (200 - 240)	229 (200 - 240)	
WBCs	Mean ± SD	6.5 ± 1	6.7 ± 1.1	0.79
	Median (Minimum-Maximum)	7 (5 - 8)	7 (5 - 8)	

T: Two-Sample Independent t-Test, p-value >0.05: nonsignificant, p-value <0.05 significant, Data are presented as frequency (%) unless otherwise mentioned, Median (Minimum-Maximum)

There had been no statistically significant variation among the 2 studied groups regarding Hb, Platelet, or WBCs as shown in **Table 3**.

Table (4): Comparing both groups as regards kidney and liver function tests.

		Group A (n=thirty)	Group B (n=thirty)	P value
Creatinine	Mean ± SD	0.8 ± 0.1	0.79 ± 0.12	0.78
	Median (Minimum-Maximum)	0.9 (0.7 - 1.2)	0.9 (0.7 - 1.2)	
BUN	Mean ± SD	37 ± 2.5	38 ± 2.4	0.89
	Median (Minimum-Maximum)	39 (33 - 42)	39 (33 - 42)	
AST	Mean ± SD	25± 3.1	26.2± 3.5	0.68
	Median (Minimum-Maximum)	26 (20 - 30)	27 (20 - 30)	
ALT	Mean ± SD	29± 4.5	30± 4.1	0.75
	Median	30 (25 -	30 (25 -	

	(Minimum-Maximum)	40)	40)	

T: Two-Sample Independent t-Test, p-value >0.05: nonsignificant, p-value <0.05 significant, Data are presented as frequency (%) unless otherwise mentioned, Median (Minimum-Maximum)

There had been no statistically significant variation among the 2 studied groups regarding creatinine, BUN AST, or ALT as shown in **Table 4.**

Table (5): Comparing both groups as regards FSH Levels

FSH (mIU/ml)		**Group A (n=thirty)**	**Group B (n=thirty)**	**P value**
Baseline	Median (Minimum-Maximum)	41.9(19.8-57.0)	45.7(23.4-67.9)	**<0.001**
First month	Median (Minimum-Maximum)	25.6(14.7-38.3)	54.7(20.4-68.7)	**<0.001**
Second month	Median (Minimum-Maximum)	20.1(10.7-32.3)	42.8(20.4-56.6)	**<0.001**
Third	Median (Minimum-Maximum)	12(8.3-21.2)	37.6(21.5-62.2)	**<0.001**
Sixth	Median (Minimum-Maximum)	13.7(6.8-24.0)	48.1(20.4-62.4)	**<0.001**
P value		**<0.001**	**0.04**	

T: Two-Sample Independent t-Test, p-value >0.05: nonsignificant, p-value <0.05 significant, Data are presented as frequency (%) unless otherwise mentioned, Median (Minimum-Maximum)

There was a high statistically significant variation among the 2 studied groups regarding FSH in the Sixth month as shown in **Table 5**.

Table (6): Comparing both groups as regards AMH Levels

AMH (ng/ml)		**Group A (n=thirty)**	**Group B (n=thirty)**	**P value**
Baseline	Mean ± SD	0.39 ± 0.09	0.41 ± 0.08	0.89
	Median (Minimum-Maximum)	0.4 (0.3 - 0.45)	0.4 (0.3 - 0.45)	
First month	Mean ± SD	0.63 ± 0.1	0.67 ± 0.15	0.44
	Median (Minimum-Maximum)	0.65 (0.5 - 0.75)	0.7 (0.5 - 0.75)	
Second month	Mean ± SD	0.71± 0.13	0.76± 0.17	0.35
	Median (Minimum-Maximum)	0.75 (0.6 - 0.8)	0.78 (0.6 - 0.8)	
Third	Mean ± SD	0.8 ± 0.1	0.88 ± 0.17	0.38
	Median (Minimum-Maximum)	0.85 (0.75 - 0.95)	0.9 (0.75 - 1)	
Sixth	Mean ± SD	0.85 ± 0.2	0.92 ± 0.3	0.07
	Median (Minimum-Maximum)	0.9 (0.5 - 1.1)	0.99 (0.5 - 1.1)	
P value		**0.04**	**<0.001**	

T: Two-Sample Independent t-Test, p-value >0.05: nonsignificant, p-value <0.05 significant, Data are presented as frequency (%) unless otherwise mentioned, Median (Minimum-Maximum)

There had been statistical variation among different periods in group A as regards AMH. There had been a high statistically significant variation between different periods in group B as regards AMH. as shown in **table 6**.

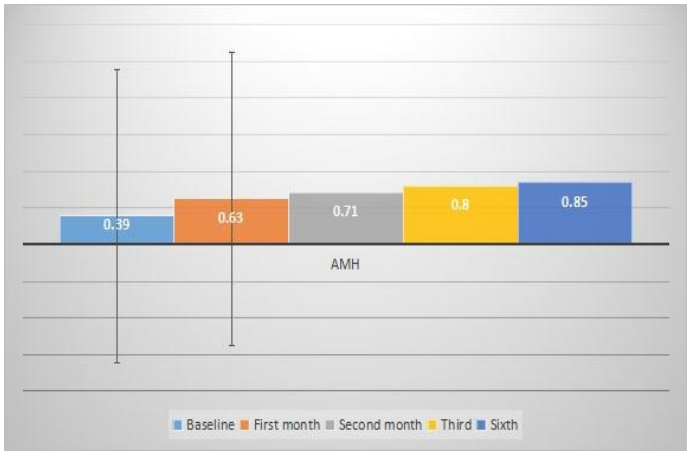

Fig. (1): Comparison between both different periods in group A as regards AMH.

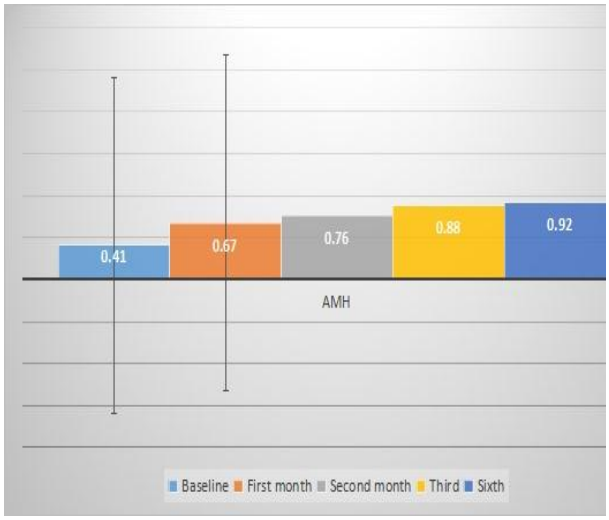

Fig. (2): Comparison between both different periods in group B as regards AMH.

Table (7): Comparison between both groups as regards Estradiol Levels

Estradiol (pg/mL)		Group A (n=thirty)	Group B (n=thirty)	P value
Baseline	Mean ± SD	18.05 ± 2.32	18.1 ± 2.1	0.79
	Median (Minimum-Maximum)	18.5 (14 - 25)	18.5 (14 - 25)	
First month	Mean ± SD	18.55 ± 2.65	18.7 ± 2.8	0.88
	Median (Minimum-Maximum)	19 (15 - 25)	19 (15 - 25)	
Second month	Mean ± SD	18.7 ± 2.8	18.9 ± 2.95	0.75
	Median (Minimum-Maximum)	19.5 (15 - 25)	19.5 (15 - 25)	
Third	Mean ± SD	19.5 ± 3.1	19.9± 3.4	0.5
	Median (Minimum-Maximum)	20 (16 - 26)	21 (16 - 26)	
Sixth	Mean ± SD	19.7 ± 3.2	20.7 ± 4.5	**0.04**
	Median (Minimum-Maximum)	20 (16 - 26)	22 (15 - 28)	
P value		**0.02**	**<0.001**	

T: Two-Sample Independent t-Test, p-value >0.05: nonsignificant, p-value <0.05 significant, Data are presented as frequency (%) unless otherwise mentioned, Median (Minimum-Maximum)

There had been statistically significant variation among the 2 studied groups regarding Estradiol in the Sixth month as shown in **table 7.**

Discussion

In the present investigation, we discovered that there had been no statistically significant variation in age or duration of infertility among the 2 analyzed groups. This was by **Machura et al. (10)** reported that the studied cases evaluated ranged in years from twenty-four to thirty-eight, with an average age of 31.1 (±4.48 SD) and an average infertile time of 2.66 (±1.33 SD) with a range of one to five years,

These results were compatible with **Maciejewska-Jeske et al. (11)** who stated that 1st research, compared the live birth rate of twenty poor responders to twenty control participants after they received three to five mL of autologous PRP while being monitored by transvaginal ultrasound. When all known confounders had been considered, multivariable analysis could not detect any statistical variation even though other fundamental factors like age & baseline FSH had been balanced in both groups.

In the present research, we showed that there had been no statistically significant variation among the two studied groups regarding The HAQ Disability Index or The HAQ VAS Pain Scale. There had been no statistically significant variation among the 2 studied groups regarding Hb, Platelet, or WBCs. There had been no statistically significant variation among two studied groups regarding creatinine, BUN AST, or ALT.

Qin et al. (12) reported that in comparison to levels in whole blood, the platelet count had been boosted by four times, the WBC count by ~2.6 times, & the RBC & hematocrit by about ~40 percent. quantities of hemoglobin found in activated sample supernatants.

Moreover, the results of **Sfakianoudis et al. (13)** noted that before the procedure & twenty-four & forty-eight hours later, measurements of hemoglobin (mg/dL) & hematocrit (percent) did not reveal any significant variations among groups ($p > 0.05$). At twenty-four hours, forty-eight hours, 1 week, 3 weeks, & 2 months following surgery, a group that received platelet-rich plasma exhibited benefit on verbal pain score ($p < 0.05$).

In the present research, we showed that there had been a high statistically significant variation among the 2 studied groups regarding FSH in the Sixth month. There had been statistically significant variation among different periods in group A as regards FSH. There had been a high statistically significant variation between different periods in group B as regards FSH. There had been no statistically significant variation among the 2 studied groups regarding AMH in the Sixth month. There had been statistically significant variation among different periods in group A as regards AMH. There had been a high statistically significant variation between different periods in group B as regards AMH.

In agreement with our findings, **Mazerbourg et al. (14)** found that it is noteworthy that levels of FSH & LH dropped in a month & stayed significantly lower for almost the entire research for the second, third, sixth-, & twelfth months following the introduction of PRP, compared with the group before treatment ($p< 0.0007$-0.00004), suggesting that PRP is likely to demonstrate its regulatory & immunomodulatory abilities.

In agreement with our findings, **Revelli et al. (15)** noted that the chart below shows that due to the dynamics of AMH, we were unable to determine the advantages of PRP. In contrast to data obtained before treatment, the statistical analysis provided support for an increase in AMH level after twelve months following rejuvenation ($p <0.000023$). AMH levels in several women have dramatically improved, up to 1.1 ng/ml from 0.08 ng/ml before ovarian rejuvenation. Contrarily, some women had low AMH throughout the trial, but this did not stop them from becoming pregnant or at the very least allowed for retrieval of their eggs.

In the current research, we showed that there had been a statistically significant variation among the 2 studied groups regarding Estradiol in the Sixth month. There had been statistically significant variation among different periods in group A as regards Estradiol. There had been a high statistically significant variation between different periods in group B as regards Estradiol. There had been no statistically significant variation among the 2 studied groups regarding the Total number of follicles. There had been statistically significant variation among different periods in group A as regards the Total number of follicles. There had been high statistical variation among different periods in group B as regards the Total number of follicles.

This agreed with **Matsuda et al. (16)** stated that After PRP therapy, the level of estradiol gradually rises from the first to sixth month. After a year, it then started to decline gradually. highest amounts of estradiol, when compared to data from before rejuvenation, had been attained at months six & twelve ($p <0.0003$ & <0.0005, respectively). These findings might suggest that platelet-derived growth factors enhance the microenvironment of dormant follicles.

Moreover, the results of **Pavlovic et al. (17)** noted that We extracted & cultivated sixty primordial follicles altogether. PRP alone group demonstrated the greatest changes in size ($p <0.001$) & viability ($p <0.05$); viability had been evaluated under a stereomicroscope using trypan blue staining; follicles with dead oocytes or with > fifty percent dead granulosa cells had been stained blue & had been therefore classified as non-viable. Even though the size of follicles significantly increased ($p <0.001$) after ten days in all groups.

Conclusion

An alternative treatment strategy for those who don't respond well might be intraovarian injection of autologous PRP. However, more thorough research is required before this novel therapy approach may be used in patients to determine its safety, efficacy, & any short- & long-term negative effects. Women had the opportunity to use their eggs when PRP was injected into their ovaries. They were able to lessen the severity of early menopause symptoms thanks to it. increased levels of FSH, LH, estradiol, & AMH hormones, plus obtaining intended pregnancy & giving birth to healthy children, provided evidence supporting facts. Therefore, PRP may be used alone or in conjunction with hormone therapy to treat women whose infertility is caused by poor ovarian reserve. Women with POI (premature ovarian insufficiency), particularly those who have tried unsuccessfully to conceive in the past, may benefit from intra-ovarian PRP injections because they are safe, effective, & all-natural.

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