

به نام آنکه جان را حکمت آموخت

Evaluation of intra-ovarian platelet-rich plasma administration on oocytes-dependent variables in patients with poor ovarian response:

A retrospective study according to POSEIDON criteria

Marzieh Farimani,

Background

- The primordial germ cells originated in the yolk sac.
- Rapid mitotic multiplication of germ cells begins at **6-8 weeks** of pregnancy ,and by 16-18 weeks ,the maximum number of oocytes; is reached a total **of 6-7 millions** in both ovaries.
- The most rapid decrease occurs before birth ,resulting in a decline from 6-7 to **2 million at birth** and **300,000 at puberty**.
- From this large reservoir, about **400 follicle will ovulate** during a woman's reproductive years.

Background

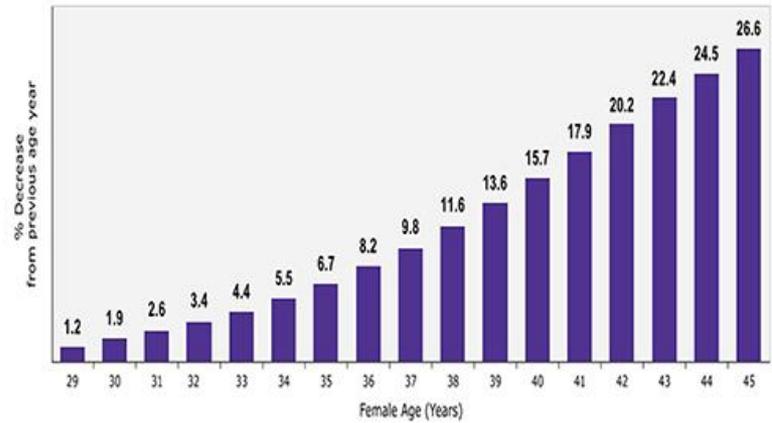
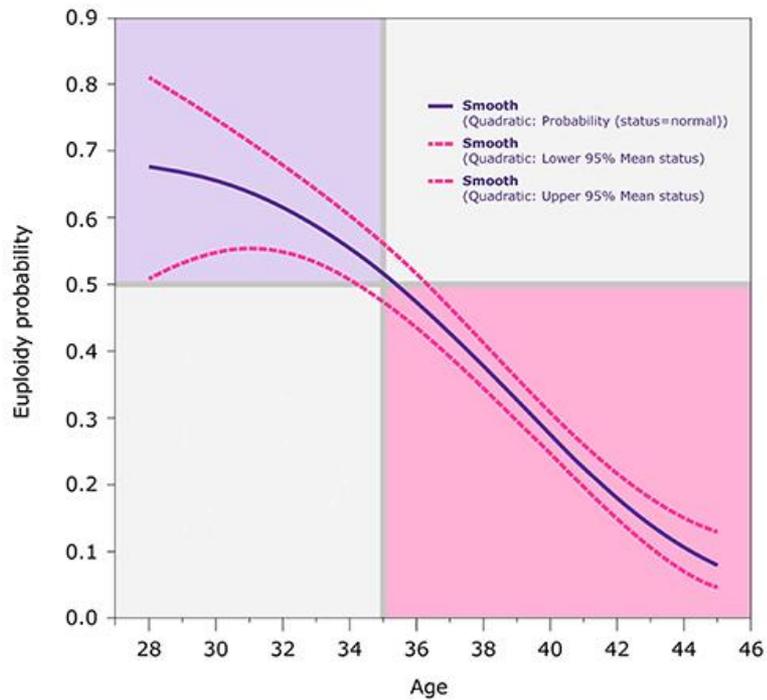
- The **mechanism** for determining which follicles and will start growing during any one cycle is **unknown**.
- It is possible that the follicle that is singled out to play the leading role in particular cycle is the beneficiary of a timely match of follicle readiness (**perhaps prepared by autocrine-paracrine actions** in its microenvironment),and appropriate **tropic hormone stimulation**.
- Unilateral oophorectomy causes the remaining follicle **to redistribute their availability** over time.

Background

- The total duration of time to achieve pre-ovulatory status is approximately **85 days**.
- Remember that the very early development of follicles begins continuously and **independently from gonadotropin** influence.
- The **molecular events** that regulate primordial follicle formation involve a variety of factors, all **locally produced** and regulated , including members of transforming growth factor beta (TGF-B),activin ,inhibin, AMH , bone morphogenetic proteins.

Background

- **Oocytes are dependent on adjacent granulosa cells** to metabolize glucose into a usable energy substrate .
- Oocytes are linked to their investment of granulosa cells **via gap junctions** ,which allow passage of small molecules such as ions (**calcium**),metabolites(pyruvate, **inositol**),CAMP,..
- To meet their energy needs, oocytes stimulate glycolysis , amino acid transport , and cholesterol synthesis in granulosa cells via paracrine that promote expression of transcripts involved in metabolic processes.



probability of a blastocyst being euploid
blastocyst euploidy as a function of female age

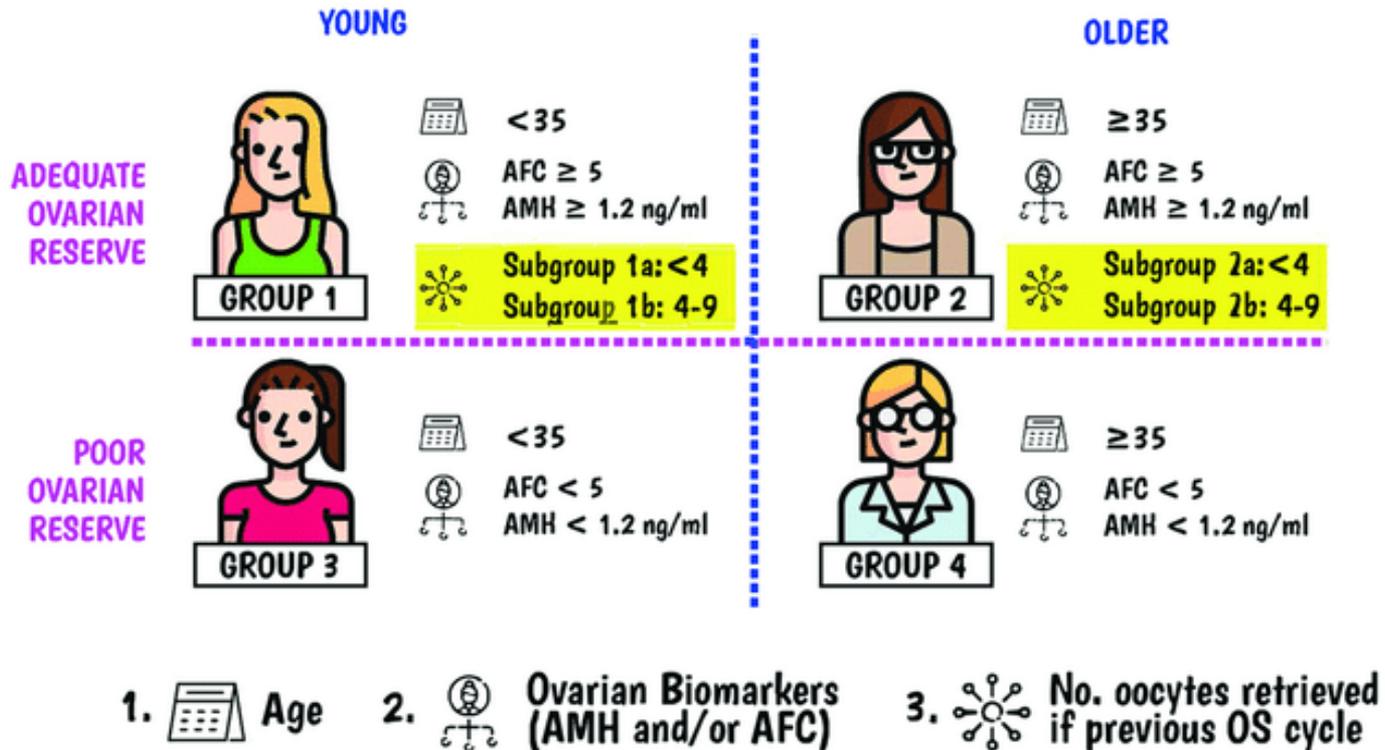
Background

- After the **Bologna criteria** for POR were proposed in 2011 , the universal definition of POR helped investigators enroll **more homogeneous populations** when conducting studies in patients undergoing IVF/intracytoplasmic sperm injection (ICSI
- Although the Bologna criteria were thought initially to characterize a homogeneous population, subsequent research showed that this was not the fact, and that the **Bologna criteria describe a heterogeneous population with different reproductive outcomes**, mainly because the effect of **age on oocyte quality was not taken into consideration)**

Background

- Recently, in an effort to further refine the Bologna criteria, the **Patient-Oriented Strategies Encompassing Individualized Oocyte Number (POSEIDON)** was proposed.
- These criteria stratify patients according to **age** (and therefore the expected euploidy rate), **ovarian biomarkers**, and **ovarian response** if a previous stimulation has been performed.
- The aim of the POSEIDON stratification was not only to **help clinicians** counsel and **set patient expectation**, but also to establish a working plan to **reduce the time to pregnancy**

LOW PROGNOSIS GROUPS



Poseidon Group; Alviggi et al. Fertil Steril. 2016; Humaidan et al. F1000Research 2016

Background

- POSEIDON groups 1 and 2 are characterized by hypo-response to ovarian stimulation, which can be caused by among others **environmental contaminants, polymorphisms, and drugs.**
- The mechanisms are still far from being understood, but studies suggest some genetic causes.
- Regarding **POSEIDON groups 3 and 4**, the low AFC and the expected decrease in the **number of euploid embryos for transfer are the main causes of poor outcomes**

Background

- In **POSEIDON groups 3 and 4**, the reasons for poor response include **poor ovarian reserve**:
- **asynchronous development**,
- and **genetic polymorphisms in FSH receptor**,
- **LH receptor**,
- and the possible presence **of variant LH- β** .
- The clinical management include **down-regulation** with a long GnRH agonist protocol, stimulation with **recombinant FSH** with or without **recombinant LH**, possible pre-treatment with **androgens**, fresh embryo transfer, **or oocyte/embryo accumulation** and frozen embryo transfer

Background

Specifically for **POSEIDON group 4**, **recombinant LH** can be added to **increase circulating androgens** (which are decreased in older patients and play **an important role** for optimal folliculogenesis stimulation).

In POSEIDON groups 1, 2, 3, and 4, the **CLBRs** after one complete cycle were **56.04, 30.85, 14.73, and 6.58%**, respectively.

Background

Aging causes different changes in the physiology of the human body and is associated with increased the risk of infertility in females. •

Over the course of time, ovaries experience a **decrease in their follicular quantity** (ovarian reserve) also knowns as poor ovarian reserve. •

Women in **POSEIDON groups 1 and 2** have **an adequate ovarian reserve**, but unexpectedly the ovarian response to stimulation is either **poor** or **suboptimal**, defined as **<4 oocytes** and **≤9 oocytes**, respectively. •

- So far, platelet-rich plasma (PRP) has been used in many trials for accelerating the healing of **acute and chronic wounds, plastic surgeries, tendinopathies** and other **regenerative goals**.
- Then, we aimed to use this autologous product for women with poor response to gonadotropin stimulation as well.
- Nowadays, PRP is used more widely in reproductive medicine due to its regenerative potentials; however, not enough data is available on this issue .
- One of **the new strategies** for facing primary ovarian insufficiency is PRP therapy.

- A report on 23 women **with primary ovarian insufficiency has shown that PRP could be a proper treatment option** for these patients
- Recently, PRP therapy has been used as a possible treatment for **17 women** diagnosed with poor ovarian response (POR) which seemed **potent enough to be a possible future treatment** according to the obtained results.
- After the **first live birth** following PRP usage in a woman with primary infertility , we aimed to investigate the potential of intra-ovarian PRP injection in women with POR and comparing the obtained results in the groups categorized according to the POSEIDON criteria

› Int J Clin Exp Med. 2015 Jan 15;8(1):1286-90. eCollection 2015.

Autologous platelet-rich plasma promotes endometrial growth and improves pregnancy outcome during in vitro fertilization

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Affiliations + expand

PMID: 25785127 PMCID: PMC4358582

[Free PMC article](#)

Abstract

Introduction: This study was to evaluate the effectiveness of PRP in the therapy of infertile women with thin endometrium (≤ 7 mm).

Material and methods: Five women undergoing in vitro fertilization (IVF) with poor endometrial response still had thin endometrium (< 7 mm) after standard hormone replacement therapy (HRT) and had to cancel embryo transfer cycle. In addition to HRT, intrauterine infusion of PRP was performed. PRP was prepared from autologous blood by centrifugation, and 0.5-1 ml of PRP was infused into the uterine cavity on the 10(th) day of HRT cycle. If endometrial thickness failed to

In September 2016 we reported intrauterine PRP injection in patients with recurrent implantation failure (RIF) which led to noticeable findings .

JRHS 2016; 16(3): 172-173



JRHS

Journal of Research in Health Sciences

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Letter to the Editor

A New Approach Using Autologous Platelet-Rich Plasma to Treat Infertility and To Improve Population Replacement Rate

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Dear Editor-in-Chief

The total fertility rate (TFR) or the number births over a woman's lifetime, has reached 1.8 in 2012 which is the lowest among Islamic countries, and even below the world average of 2.1 births per woman^{1,2}. This is less than population replacement rate. Furthermore, increasing age of marriage and change in lifestyle such as exposure to environment toxins increased the incidence rate of infertility³. More than three million people and nearly 15% of couples suffer from

further animal and human studies were conducted to demonstrate the efficacy of PDGF administration for infertility.

Chang et al. administered intrauterine infusion of platelet rich plasma (PRP) in infertile women with thin endometrium and reported good results 4 pregnancy from five patients with thin endometrium and poor response to conventional therapy during freeze embryo transfer¹⁰. PRP is quite a new treatment used for the improvement the endometrial thickness in women with thin endometrium. The use of PRP is considered safe because of autologous nature derived from patient's own blood¹¹.

In 2016, for the first time, we performed a single-blind

Successful pregnancy and live birth after intrauterine administration of autologous platelet-rich plasma in a woman with recurrent implantation failure: A case report

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PMID: 29492478 PMCID: PMC5816241

[Free PMC article](#)

Abstract

Background: Platelets contain a significant amount of growth factors that have positive effects on local tissue repair and endometrial receptivity.

Case: Here we present a 45-yr-old woman with primary infertility and two failed in vitro fertilization (IVF) cycles who was candidate to receive donor eggs. Five consecutive frozen-thawed embryo transfer cycles with good quality embryos were performed within 2 yr. With the diagnosis of recurrent implantation failure (RIF), the patient was treated for improving endometrial receptivity with intrauterine administration of autologous platelet-rich plasma (PRP), 24 hr before embryo transfer. The patient gave birth to a healthy baby boy weighing 2350 gr in the cesarean section.

Epub 2018 Aug 22.

A Case Series on Platelet-Rich Plasma Revolutionary Management of Poor Responder Patients

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PMID: 30134239 DOI: [10.1159/000491697](#)

Abstract

Poor responders are described as those In Vitro Fertilization (IVF) patients who are failing to respond to controlled ovarian stimulation protocols. Extensive research has focused on crafting the optimal treatment. However, it appears that each approach fails to be established as effective or guaranteed towards successful management. Platelet-Rich Plasma (PRP) is a novel, highly promising approach that has been successfully applied for an array of medical issues. In this case series, we present 3 poor responder patients with the common denominator of: failed IVF attempts, poor oocyte yield, and poor embryo quality. The option of oocyte donation was rejected. All patients were treated with autologous PRP ovarian infusion following written consent. Within a 3-month interval, follicle-stimulating hormone decreased by 67.33%, while Anti-Müllerian hormone increased by 75.18%. These impressive results on the biochemical infertility markers alone are classified as a complete biological

> *Gynecol Endocrinol.* 2018 Sep;34(9):756-760. doi: 10.1080/09513590.2018.1445219.
Epub 2018 Feb 28.

First data on in vitro fertilization and blastocyst formation after intraovarian injection of calcium gluconate-activated autologous platelet rich plasma

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Abstract

Platelets modulate clinically relevant yet incompletely understood tissue regeneration processes, and platelet rich plasma (PRP) has been previously used with some success in various non-reproductive medical contexts. Here, we extended PRP application to ovarian tissue with a view to document impact on ovarian reserve among women attending for infertility treatment. PRP was freshly isolated from patients (n= 4) with diminished ovarian reserve as determined by at least one prior IVF cycle canceled for poor follicular recruitment response or estimated by serum AMH and/or FSH, no menses for ≥ 1 year. Immediately following substrate isolation and activation with calcium gluconate, approximately 5 mL of autologous PRP was injected into each ovary under direct transvaginal sonogram guidance. For each study subject, AMH, FSH, and serum estradiol data were recorded at two-week intervals post-PRP and compared to baseline (pre-PRP) values. In this pilot group, mean

Epub 2019 Feb 5.

A report on three live births in women with poor ovarian response following intra-ovarian injection of platelet-rich plasma (PRP)

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PMID: 30725347 DOI: 10.1007/s11033-019-04609-w

Abstract

The prevalence of poor response to gonadotropin stimulation is approximately 9-24% in women undergoing in vitro fertilization. Interestingly, due to containing a variety of growth factors, platelet-rich plasma (PRP) can play an important role in oocyte maturation and healing. Thus, in this research, we aimed to investigate the intra-ovarian injection of PRP in women with poor ovarian response. To this goal, 23 poor responders constituted the study population, from among whom 19 women were enrolled. These patients underwent ovarian stimulation according to the Shanghai protocol.

Immediately after the first follicular puncture, 2 mL of PRP was injected into each ovary. 1 day after the first puncture and PRP injection, the second stimulation was initiated. Then, oocyte retrieval was followed. About 2-3 months after the first cycle, the patients underwent another treatment with ovarian stimulation according to the Shanghai protocol and then, follicular puncture was performed.

Autologous Platelet-Rich Plasma Treatment Enables Pregnancy for a Woman in Premature Menopause

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Original Article | [Published: 08 March 2021](#)

Effects of Intraovarian Injection of Autologous Platelet-Rich Plasma on Ovarian Rejuvenation in Poor Responders and Women with Primary Ovarian Insufficiency

[Abbas Aflatoonian](#), [Marzieh Lotfi](#) , [Lida Saeed](#)  & [Nasim Tabibnejad](#)

[Reproductive Sciences](#) **28**, 2050–2059 (2021) | [Cite this article](#)

315 Accesses | **1** Citations | [Metrics](#)

Abstract

Injection of intraovarian platelet-rich plasma (PRP) was recently presented in terms of improvement ovarian function in women with a poor ovarian response (POR) or primary ovarian insufficiency (POI). In a before and after study, 17 poor responder women and 9 women with the diagnosis of POI were recruited. The multifocal intramedullary infusion of 1.5

Research | [Open Access](#) | Published: 08 September 2021

Evaluation of intra-ovarian platelet-rich plasma administration on oocytes-dependent variables in patients with poor ovarian response: A retrospective study according to the POSEIDON criteria

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Reproductive Biology and Endocrinology **19**, Article number: 137 (2021) | [Cite this article](#)

322 Accesses | **2** Altmetric | [Metrics](#)

Abstract

Background

Poor ovarian response (POR) is among the common findings in infertile women with no significant underlying condition. The aim of this study was to investigate the intra-ovarian potential of platelet-rich plasma (PRP) administration on oocytes-dependent variables in the POR women grouped according to the POSEIDON criteria.

• • • • •

Method & Material

- This **retrospective study** (on original data) has been performed **in Omid Clinic (Hamedan, Iran)** from **April 2018 to April 2020**.
- The current study was approved by the Medical Ethics Committee of Hamedan University of Medical Sciences (Hamedan, Iran) with the IRB number of **IR.UMSHA.REC.1399.725**.
- The **inclusion criteria** for this study was considered as any POR (according to the **Bologna criteria**) woman undergone intra-ovarian PRP injection.

Method & Material

- **Lack of follow-ups** and **incomplete laboratory results** were considered as the primary exclusion criteria.
- In order to **reduce any bias due to possible differences in kits/devices/operators**, a single laboratory with the **highest number of cases** was selected and cases with results from elsewhere were excluded from the study.
- **Diseases/disorders affecting the chance of fertility** were also among the exclusion criteria but since they were already checked at the time of admission (by the clinic), no further checking was done by the current study.

Method & Material

- All files were explored and data such as **age** and **history of POR** as well as laboratory results for levels of **AMH, FSH, LH, and estradiol** were gathered from each patient's files.
- According to the POSEIDON criteria [3], each case fell under one of the following fourth groups (subgroups were not evaluated): Group 1: Age < 35 years, AMH \geq 1.2 ng/mL; Group 2: Age \geq 35 years, AMH \geq 1.2 ng/mL; Group 3: Age < 35 years, AMH < 1.2 ng/mL; Group 4: Age \geq 35 years, AMH < 1.2 ng/mL.
- The **number of total oocytes** was investigated by ultrasound evaluation and the type of oocytes (**MI, MII, and GV**) were assessed by an expert embryologist.

Result

- **From 383 cases**, a total number of **96** women were enrolled in this study. According to the POSEIDON criteria,
- **group 4** (Age ≥ 35 years, AMH < 1.2 ng/mL) with the ratio of 56/96 (**58.3%**) had the highest prevalence among others.
- As the analyses showed, **changes in the laboratory variables (LH, FSH, AMH, and estradiol) were not significant** in almost all the groups following the intervention.
- Regarding the total oocytes number, PRP administration **caused a significant increase in the total number in all the groups** (all $P < 0.05$).
- Also, the **number of MII oocytes was significantly increased** following the treatment in **all groups except for group 2** (Age ≥ 35 years, AMH ≥ 1.2 ng/mL; all $P < 0.05$).

Result

- The current study investigated the possible potentials of **intra-ovarian PRP administration** on the POR patients.
- According to the results and following single session of the intervention, total **oocytes count showed a statistically significant increase in all POSEIDON groups with more notable changes in group 4.**
- For the MI, MII, and GV oocytes, **only MII ones experienced a significant increase in their count** following PRP administration (but not in the group 2; Age \geq 35 years, AMH \geq 1.2).

Table 1 Laboratory and oocyte-dependent characteristics before and after treatment with platelet-rich plasma (PRP) in the whole population

From: [Evaluation of intra-ovarian platelet-rich plasma administration on oocytes-dependent variables in patients with poor ovarian response: A reirospective study according to the POSEIDON criteria](#)

Variables	Before PRP (Median \pm IQR)	After PRP (Median \pm IQR)	P-value
LH	2.80 \pm 1.93	2.88 \pm 1.76	0.962
FSH	6.21 \pm 4.48	6.41 \pm 3.72	0.059
Estradiol	51.00 \pm 34.10	50.00 \pm 32.68	0.771
AMH	0.72 \pm 0.87	0.73 \pm 1.04	0.905
Total ovocyte number	2.00 \pm 3.00	3.00 \pm 6.00	< 0.001
GV ovocyte number	0.00 \pm 0.00	0.00 \pm 0.00	0.604
MII ovocyte number	0.00 \pm 0.00	0.00 \pm 0.00	0.210
MIII ovocyte number	1.00 \pm 3.00	3.00 \pm 5.00	< 0.001

LH Luteinizing hormone, FSH Follicle-stimulating hormone, AMH Anti-Mullerian hormone

P-values have been calculated by Wilcoxon rank test

Table 2 Laboratory characteristics before and after treatment with platelet-rich plasma (PRP) in for POSEIDON groups

From: [Evaluation of intra-ovarian platelet-rich plasma administration on oocytes-dependent variables in patients with poor ovarian response: A retrospective study according to the POSEIDON criteria](#)

Variables		POSEIDON 1 Median ± IQR	POSEIDON 2 Median ± IQR	POSEIDON 3 Median ± IQR	POSEIDON 4 Median ± IQR	P-value
Age (years)		32.00 ± 3.00	37.00 ± 8.00	33.00 ± 2.00	40.00 ± 5.00	< 0.001
Poor responder (%)		2/7 (28.6%)	8/17 (47.1%)	12/16 (75%)	47/56 (83.9%)	0.002
Number of previous punctures		3 ± 2	3 ± 1	2.5 ± 1	2.00 ± 2.00	0.755
LH (IU/L)	Before PRP	1.87 ± 1.50	2.35 ± 2.82	2.51 ± 1.30	3.02 ± 1.75	0.160
	After PRP	2.08 ± 1.43	2.98 ± 1.68	2.82 ± 2.20	3.05 ± 2.29	0.198
FSH (IU/mL)	Before PRP	4.27 ± 1.73	5.79 ± 2.65	6.08 ± 5.19	6.66 ± 5.11	0.054
	After PRP	5.15 ± 1.63	5.60 ± 3.20	6.85 ± 4.23	7.21 ± 4.04	0.028
Estradiol (pg/mL)	Before PRP	31.00 ± 55.9	46.00 ± 16.65	57.15 ± 40.10	51.60 ± 34.10	0.576
	After PRP	55.80 ± 20.30	51.70 ± 23.30	62.00 ± 45.68	45.00 ± 33.38	0.342
AMH (ng/mL)	Before PRP	1.75 ± 2.07	1.68 ± 0.98	0.6 ± 0.45	0.46 ± 0.51	< 0.001
	After PRP	1.85 ± 2.56	1.53 ± 1.03 *	0.64 ± 0.68	0.50 ± 0.56	< 0.001

IQR Interquartile range, *LH* Luteinizing hormone, *FSH* Follicle-stimulating hormone, *AMH* Anti-Mullerian hormone

*: *p*-value < 0.05, **: *p*-value < 0.01, and ***: *p*-value < 0.001 all compare to the before level

Table 3 Oocytes characteristic features before and after treatment with platelet-rich plasma (PRP) in for POSEIDON groups

From: [Evaluation of intra-ovarian platelet-rich plasma administration on oocytes-dependent variables in patients with poor ovarian response: A retrospective study according to the POSEIDON criteria](#)

Variables		POSEIDON 1 Median ± IQR	POSEIDON 2 Median ± IQR	POSEIDON 3 Median ± IQR	POSEIDON 4 Median ± IQR	P-value
Total Ovocyte number	Before PRP	4.00 ± 2.00	2.00 ± 3.00	1.00 ± 3.00	1.00 ± 1.00	0.003 [‡]
	After PRP	9.00 ± 5.00 *	5.00 ± 5.00 *	2.00 ± 7.00 *	3.00 ± 4.00 ***	< 0.001 [‡]
GV Ovocyte number	Before PRP	1.00 ± 2.00	0.00 ± 0.5	0.00 ± 1.00	0.00 ± 0.00	0.003 [‡]
	After PRP	0.00 ± 0.00	0.00 ± 1.00	0.00 ± 0.75	0.00 ± 0.00	0.085 [†]
MI Ovocyte number	Before PRP	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00	0.175 [†]
	After PRP	1.00 ± 1.00	0.00 ± 1.00	0.00 ± 0.00	0.00 ± 0.00	0.007 [†]
MII Ovocyte number	Before PRP	2.00 ± 3.00	2.00 ± 3.00	1.00 ± 3.00	1.00 ± 2.00	0.052 [†]
	After PRP	8.00 ± 3.00 *	4.00 ± 3.50	2.00 ± 6.50 *	2.00 ± 3.75 ***	0.001 [‡]
Fetus number		17.00 ± 13.00	4.00 ± 5.00	3.00 ± 8.75	2.00 ± 6.00	0.005 [‡]
Pregnancy		5/7 (71.42%)	2/17 (11.76%)	1/16 (6.25%)	6/56 (10.71%)	0.002 [†]

*: p-value < 0.05, **: p-value < 0.01, and ***: p-value < 0.001 all compare to the before level. †: Fisher exact test. ‡: Kruskal Wallis

Result

- Interestingly, this study showed that **9.75%** of women with no ART got pregnant following a single session of PRP injection. However, it was less than 14.75% for those cases undergone ART.
- On the other hand, **except for AMH in group 2 POSEIDON (17 patients), none of the other laboratory variables experienced a significant change in any of the POSEIDON groups.**
- This result showed that the changes observed in the outcomes of patients are more likely achieved through a non-hormonal pathway(s)..

Discussion

- The current study investigated the possible potentials of intra-ovarian PRP administration on the POR patients.
- According to the results and following single session of the intervention, **total oocytes count showed a statistically significant increase in all POSEIDON groups with more notable changes in group 4' For the MI, MII, and GV oocytes**
- **only MII ones experienced a significant increase in their count following PRP administration (but not in the group 2; Age \geq 35 years, AMH \geq 1.2**

discussion

- PRP is an autologous product and has a notable amount of **α -granules** releasing their many growth factors following their degradation.
- These factors are **basic fibroblast growth factor (bFGF), fibroblast growth factor (FGF), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), insulin-like growth factor-1 (IGF-1), platelet-derived growth factors (PDGF-AA, PDGF-AB, and PDGF-BB), and transforming growth factors β 1 and 2 (TGF- β 1 and 2)** which are the key role players of **angiogenesis and regeneration.**
- **growth factors in the PRP** could affect different characteristic features of **rate o oocytes to eventually increase survival f follicles compared to the controls**

Discussion

- Other than the mentioned applications of PRP, it has been a rather long-used product in the field of infertility as well.
- PRP is also been suggested administration in some endometrial and ovarian complications .
- Cakiroglu et al., investigated the results of intra-ovarian PRP administration on primary ovarian insufficiency.
- They found that PRP treatment could lead to **increased antral follicle count as well as AMH but not FSH**. As they have stated, 201 of 311 (64.8%) PRP treated women developed antral follicle(s).
- Finally, they have concluded their observation as **improved ovarian function after the PRP treatment**.

Discussion

Also, recently, a retrospective study evaluated the effects of **growth hormone (GH)** treatment on cases with POR candidates for intracytoplasmic sperm injection (ICS)/IVF according to **the POSEIDON groups (only those aged > 35 years)**.

They have shown that number of oocytes retrieved, transferrable embryos, and good quality embryos were not significantly different in GH treated and control groups.

According to their results, **only individuals treated with GH in group 4 of POSEIDON had significantly higher good-quality embryos compared to the non-treated group**.

This study has included **notable numbers of women** with the diagnosis of POR which is much higher than similar studies.

Also, **one of the strength points of this study** was the assessment of all laboratory results **with a single kit, device, and operator** which greatly limits possible errors.

Conclusion

- An intra-ovarian injection of PRP in women diagnosed with POR showed results in favor of **improved ovarian function including total oocyte number and especially MII oocytes.**
- On the other hand, **AMH** (other than POSEIDON group 2), **FSH, LH, and estradiol did not significantly change.**
- This might be a clue to how PRP therapy in these patients **did not exploited the hormonal pathways** and there might be other mechanisms involved such as **angiogenesis.**

Conclusion

All and all, it seems **that PRP could be a proper treatment candidate for the patients with POR** who show resistance to the other treatments such as hormonal therapies.

The **authors of this study** strongly suggest further investigations on this hot topic to clarify the potential of intra-ovarian PRP therapy as well as its exact mechanism(s).