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Case series on ovarian PRP and its effect on IVF outcomes

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Abstract

Poor ovarian reserve is one of the most challenging causes in IVF. It greatly affects the success rate .PRP (Platelet Rich Plasma) is a component of blood which contains numerous growth factor and cytokines which has shown promising result in regenerative medicine .This case series comprise of three cases with low ovarian reserve who were offered ultrasound guided ovarian PRP(Platelet Rich Plasma) before undergoing IVF stimulation. Case selection was done with strict criteria .Ovarian PRP was done on day 6 or day 7 of cycle preceding IVF stimulation .20 ml of blood sample was taken from patient in BD tube. The sample was centrifuged using soft spin. Supernatant was transferred into another sterile tube and centrifuged at higher concentration. The lower 1/3rd is PRP which was injected into each ovary via ultrasound guidance .Controlled ovarian stimulation was done in next cycle and oocyte retrieval was done under general anesthesia .Number of mature oocyte retrieved and number and grade of embryos formed were compared with previous cycle. Better quality oocyte and embryos were formed post ovarian PRP.

Keywords: Poor Ovarian Reserve, PRP, Oocyte, IVF, Centrifuge.

Introduction

Platelet-rich plasma (PRP) is derived from whole blood, which contains plasma (55%), red blood cells (41%), platelets, and white blood cells (4%), by centrifugation and separation of its different components [1].The centrifugation process separates the RBCs and provides plasma with high concentration of growth factor. This promotes cell growth and angiogenesis and has shown promising result in regenerative medicine. The clinical use of PRP has considerably increased over the last decade, and now include treatments for musculoskeletal injuries [2,3], arthritis [4,5], periorbital rejuvenation [6], regenerative dentistry [7], wound healing [8], alopecia [9], and others.

Recently intraovarian PRP has been used in Assisted Reproductive Technique in case of poor ovaran reserve, previous poor response to ovarian stimulation and even menopause.Low ovarian reserve constitute 9-18% of IVF/embryo transfer cycle (10). Different ovarian stimulation protocol, Increasing the gonadotropin doses, antioxidants, androgen etc have been tried but with little success. Ovarian rejuvenation carried out by injecting platelet rich plasma in each ovary has been shown to not only improve the egg retrieval rates but also better quality oocyte and better quality embryos but very few studies are available to support this claim. Patient selection is also an important factor. Right technique of injection and PRP injection before selection of the dominant follicle have given better results. The given case series was conducted at IVF department in Nowrosjee Wadia Maternity Hospital.

Case Report

Strict Criteria was used for selection of the patients:

1. Previous controlled ovarian stimulation with poor oocyte yield.
2. Age less than 45.
3. Not attained menopause.
4. FSH <15
5. AMH less than 1.5 but more than 0.1

Table 1: Patient distribution with respect to age, S.AMH, S.FSH

Patient	Age (Years)	AMH(ng/ml)	FSH (IU/L)
Case no. 1	44	0.3	13.5
Case no.2	35	0.6	9
Case no. 3	33	1	10

All three patients were stimulated with antagonist protocol in their first controlled ovarian stimulation. High dose gonadotropin was used in view of poor ovarian reserve and advanced age.

Table 2: Patient distribution according to Total dose of gonadotropin, number of oocyte retrieved, number of embryos formed in 1st cycle

Patient	Total dose of gonadotropins (IU)	Number of oocyte retrieved	Number of embryos formed	Pregnancy test
Case no.1	3600	3	1 Day 3(Grade B)	Negative
Case no. 2	3375	7	3Day 3(2B,1C)	Negative
Case no.3	4950	3	1 Day 3(Grade A)	Negative

All three patients were offered ovarian rejuvenation .Ovarian PRP was scheduled on Day 6 or Day 7 of menstrual cycle.

20ml of blood was withdrawn in BD tube from the patient. It was centrifuged at 2000 rpm for 20 mins. Approximately 2 mL of plasma is gathered above the newly formed buffy coat layer from each tube. The plasma was transferred in resuspended tube and centrifuged again at 2000 rpm for 20 mins. Plasma obtained from the tubes is transferred into a single re-suspension tube and gently agitated for 30-60 seconds to prepare the PRP solution for use. 4ml of PRP was obtained, it was divided in half to be injected in each ovary. The procedure was done under conscious sedation. The procedure was carried on with a 35 cm long 17 G needle (oocyte retrieval needle) under transvaginal

ultrasound guidance. 2 mL PRP was injected in the stroma of each ovary. The patients were discharged the same day. Controlled ovarian stimulation was done in the next cycle.

Table 3: Distribution of patients with respect to dose of gonadotropins, mature oocyte retrieved, embryos formed in second cycle

Patient	Total dose of gonadtropins used (IU)	Number of oocte retrieved and maturity	Number of embryos formed
Case no. 1	3375	4(2M2,2M1)	2 Blastocyst(5AA,5AB) 1Day 3 embryo(Grade B)
Case no. 2	3000	14 (10 M2,2M1,2GV)	7 Day 3 embryos (5 Grade A,2 Grade B)
Case no. 3	3300	4(2 M2,1M1,1GV)	3 Day 3 embryos(2 Grade A,1Grade B)

Case series 1

The 44 year old patient was stimulated with 3600 IU of total gonadotropin in 1st attempt, 3 oocytes were obtained of which 1 Day 3 embryo (Grade B) was formed . Embryo transfer was done followed by a pregnancy test 12 days later which was negative. Ovarian PRP was done in the cycle preceding the second stimulation. Post ovarian PRP ,in the second stimulation total 3375IU of gonadotropin was given ,4 oocyte was obtained and 2 Day 5 embryos were formed and 1 Day 3 embryo was formed.

Case series 2

35 year old patient was stimulated with 3000 IU of gonadotropin in 1st cycle, 7 oocyte were obtained of which 3 Day 3 embryos (2 Grade B, 1 Grade C) were formed .Embryo transfer was done, pregnancy test was unsuccessful .In controlled ovarian stimulation cycle following ovarian PRP, 3000 IU of gonadotropin was given.14 oocyte were retrieved which resulted in 7 day 3 embryos (5 Grade A, 2 Grade B).

Case Series 3

33 year old patient was stimulated with 3300 IU of gonadotropin in 1st cycle 3 oocytes were obtained and 1 Day 3 embryo was formed which gave a negative pregnancy. Ovarian PRP was followed by second stimulation with 3300 IU of gonadotropin, 4 oocyte were retrieved which gave 3 Day 3 embryos (2 Grade A, 1 Grade B)

Discussion

This case series of 3 cases show a significant improvement in number of ooctyte retrieved, number and grade of embryos formed. It was observed that lesser dose of gonadotropin was required indicating better response. The possible mechanism of action could be the regenerative action by cytokines produced by the platelets leading to improvement in ovarian microenvironment and improved vascularity which may lead to denovo development from precursor cell (11, 12, 13).The optimal time of controlled ovarian stimulation following ovarian PRP is not known but stimulation within 90 days of ovarian PRP is considered optimal. Although there is no quantification of the ovarian reserve, lesser requirement of gonadotropin with better response suggest improved ovarian response and better sensitivity to gonadotropins.

PRP has shown to hasten the process of shift from primary to pre Antral follicle with the help of increased concentration of TGF (Tumour Growth Factor). A study showed that after PRP treatment, follicle-stimulating hormone (FSH) significantly decreased, while anti-Mullerian hormone (AMH) and luteinizing hormone (LH) significantly increased in patients with poor ovarian response (POR).

The number of antral follicles increased, leading to a significant increase in the number of obtained eggs and mature oocytes.

Additionally, the number of Metaphase II oocytes, 2PN (two pronuclei) embryos, and high-quality embryos also significantly increased

IVF Outcomes

Another study found that PRP treatment resulted in:
Higher Antral follicle count (AFC)
Higher serum AMH (anti-Müllerian hormone)
Lower serum FSH (follicle-stimulating hormone)
A higher number of mature oocytes, cleavage-stage embryos, and blastocyst-stage embryos.
Some women even conceived spontaneously after PRP injection.

Clinical Potential

Pooled results suggest that intra-ovarian injection of PRP can promote ovarian regeneration and improve reproductive outcomes in patients with ovarian dysfunction.

This therapy may have significant clinical potential in improving sex hormone levels, increasing AFC, oocyte count, and embryo count (14)

Conclusion

Poor ovarian reserve is the biggest challenge faced by infertility specialist. Ovarian PRP by improving the sensitivity of ovarian tissue to gonadotropins, improving ovarian vascularity, providing mature oocytes resulting in better quality embryos provides a very promising and a comparatively judicious option for women with poor ovarian reserve. However more studies are needed to support the claim.

Abbreviations

POR-Poor ovarian Reserve
IVF-In vitro Fertilisation
PRP-Platelet Rich Plasma
M2-Meosis 2
M1-Meosis 1
GV- Germinal Vesicle

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