

Platelet-rich Plasma in Gynecological Cases and Female Infertility

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Journal of South Asian Federation of Obstetrics and Gynaecology (2020): 10.5005/jp-journals-10006-1767

INTRODUCTION

Platelet-rich plasma (PRP) is an innovative treatment designed to stimulate cellular regeneration, neovascularization, and healthy cell formation.

Autologous PRP is derived from an individual's whole blood and then centrifuged to remove red blood cells. The remaining plasma has a 5- to 10-fold higher concentration of growth factors than whole blood. These growth factors have been found to promote natural healing responses by researchers across multiple specialties, such as dentistry, dermatology, urology, and gynecology.^{1,2}

The theory underlying this treatment modality was derived from natural healing processes, as the body's first response to tissue injury is to deliver platelets to the injured area. Platelets promote healing and attract stem cells to the site of the injury.

PHYSIOLOGICAL ROLE OF PRP

Platelets contain high concentrations of cytokines and growth factors stored within α -granules.³ These growth factors include platelet-derived growth factor, insulin-like growth factor, vascular endothelial growth factor, platelet-derived angiogenic factor, transforming growth factor β , fibroblast growth factor, epidermal growth factor, connective tissue growth factor, and interleukin 8. In addition to growth factors, platelets contain other substances, such as fibronectin, vitronectin, and sphingosine 1-phosphate, that initiate wound healing⁴ (Flowchart 1 and Fig. 1).

Growth factors promote wound healing by initiating the following stages:

- Tissue necrosis resolution
- Chemotaxis
- Cell regeneration
- Cell proliferation and migration
- Extracellular matrix synthesis
- Remodeling
- Angiogenesis
- Epithelialization⁵

PREPARATION

The following steps present a representative method of preparing PRP:

- Venous blood (15–50 mL) is drawn from the patient's arm in anticoagulant-containing tubes.
- The recommended temperature during processing is 21°C to 24°C to prevent platelet activation during centrifugation of the blood.
- The blood is centrifuged at 1,200 rpm for 12 minutes.

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How to cite this article: Garg R, Malhotra N, Rawat A. Platelet-rich Plasma in Gynecological Cases and Female Infertility. J South Asian Feder Obst Gynae 2020;12(3):119–121.

Source of support: Nil

Conflict of interest: None

- The blood separates into three layers: an upper layer that contains platelets and white blood cells, an intermediate thin layer (the buffy coat) that is rich in white blood cells, and a bottom layer that contains red blood cells (Fig. 2).
- The upper and intermediate buffy layers are transferred to an empty sterile tube. The plasma is centrifuged again at 3,300 rpm for 7 minutes to help with the formation of soft pellets (erythrocytes and platelets) at the bottom of the tube.
- The upper two-thirds of the plasma is discarded because it is platelet-poor plasma.
- Pellets are homogenized in the lower third (5 mL) of the plasma to create the PRP.
- The PRP is now ready for injection.

The stages of this process can be outlined in the following order:

- Step 1–Collection of blood from the patient
- Step 2–Separation of platelet-rich plasma
- Step 3–Processing the separated autologous plasma
- Step 4–Injecting the patient with PRP

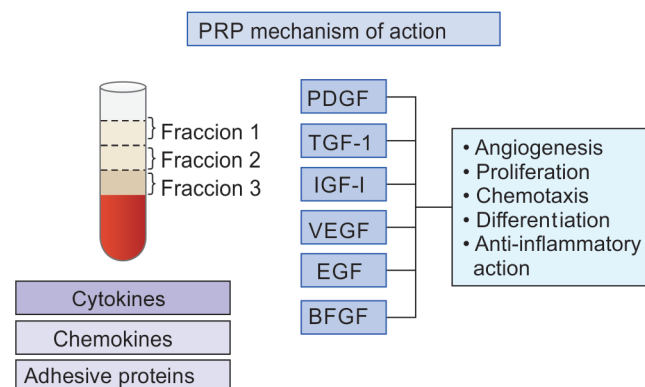


Fig. 1: Mechanism of action of PRP in the body

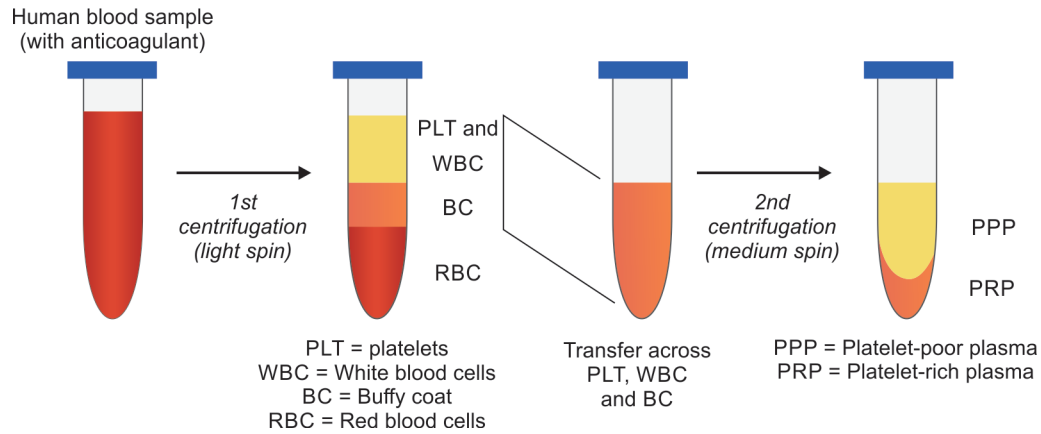
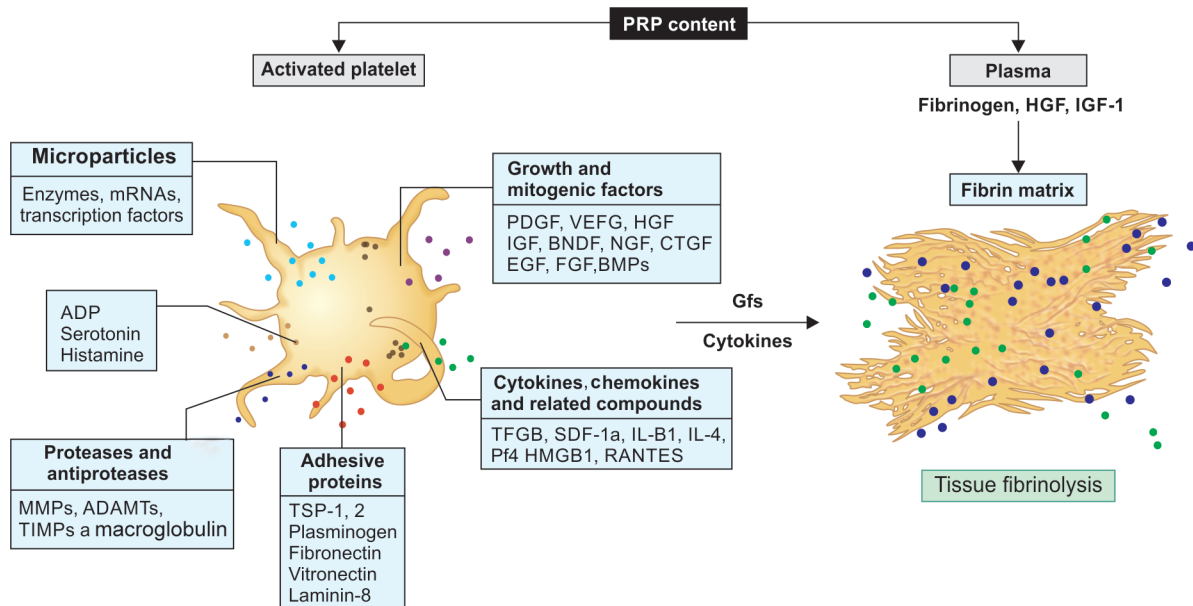


Fig. 2: Stepwise preparation of PRP

Flowchart 1: Physiological role of PRP



TYPES OF PRP

PRP preparations can be classified according to the preparation method, the content of the sample, and the proposed application. Preparations vary in terms of centrifugation speed, centrifugation time, and anticoagulant use, while the content varies depending on the predominant constituent (e.g., platelets, leukocytes, or growth factors).⁶

After centrifugation of whole blood, four types of preparations can be obtained as shown in Table 1. This classification was proposed by Dohan Ehrenfest et al.,⁷ and is based on cell content and fibrin density. This classification was recommended by a multidisciplinary consensus committee.⁸

PRP in Gynecology and Reproductology

Platelet-rich plasma therapy has slowly started to replace antibiotics as a main form of treatment in these two fields. The reason for this is that antibiotics can only block infection triggers, while PRP can also eliminate the consequences that were brought upon a patient by an infection. Because of that, PRP can be used for the treatment of chronic gynecological and reproductive diseases. Also, the results

Table 1: PRP classification was proposed by Dohan Ehrenfest et al.⁷

Preparation	Acronym	Leukocytes	Fibrin density
Pure platelet-rich plasma	P-PRP	Poor	Low
Leukocyte- and platelet-rich plasma	L-PRP	Rich	Low
Pure platelet-rich fibrin	P-PRP	Poor	High
Leukocyte- and platelet-rich fibrin	L-PRP	Rich	High

of the therapy kick in quicker and last longer. Platelets can have a positive effect on patients suffering from the following conditions:

- Lichen sclerosis
- Vulvodynia
- Vaginismus
- Chronic endometritis
- Vaginal dryness
- Lichen planus
- Vestibulitis
- Leukoplakia of the cervix

- Kraurosis vulvae
- Gynecologic inflammations
- Chronic endocervicitis and exocervicitis
- Cervical erosion
- As an alternative therapeutic method in the cases of chronic endometritis and endometriosis. These diseases can initiate inflammation processes that can make embryo implantation difficult in both natural pregnancy and *in vitro* fertilization (IVF) cycles. Application of the PRP injections helps to eliminate inflammation processes in the uterus as well as enhance the activity of the progesterone receptors that stimulates proper growth of the endometrium and, in turn, help to the implantation of the embryos. After this therapy, it is possible to continue IVF treatment with better results.
- In the cases of ovarian failure syndrome, PRP treatment fosters ovarian rejuvenation. If to inject PRP into the ovaries of menopausal and perimenopausal women, it is possible to restart menstrual cycle, which makes it possible to receive and then fertilize the eggs that produced women's ovaries.
- Role in infertility—PRP is used in a number of fertility treatments including intrauterine injection and IVF to assist with and improve egg quantity/quality and improve uterine lining thickness/enhance endometrial receptivity during an embryo transfer. It is most often used in those who have undergone multiple IVF cycles with a history of recurrent implantation failure (RIF), a condition in which multiple IVF transfers do not result in pregnancy, despite high-quality embryos being transferred on multiple occasions. PRP is usually tried before turning to donor egg IVF but may be used alongside donor egg cycles along with other supporting treatments focusing on reproductive immunology.
- Innovative PRP treatment of the testicles helps those men who are diagnosed with infertility to have their own children. Indications:
 - Oligozoospermia <10 million/mL
 - FSH > 10, normal or low testosterone level
 - Testicular ultrasound—normal or diffusely altered echogenicity, not including patients with local formations or diffuse microcalcinoses.
 - Negative tumor markers (LDH), alpha-fetoprotein, free HCG
 - Normal karyotype, negative microdeletions of the Y chromosome (oligozoospermia <5 million/mL).

PRP in Cervical Ectopy

Hua et al.⁹ conducted a randomized clinical study to compare the effectiveness of autologous PRP application to that of laser treatment for benign cervical ectopy. They applied PRP twice on the area of cervical erosion with a 1-week interval in 60 patients, while laser treatment was used in the other 60 patients. They found that the complete cure rate was 93.7% in the PRP group and 92.4% in the

laser group (p value > 0.05). The mean time to re-epithelialization was significantly shorter in the PRP group (p value < 0.01). The rate of adverse treatment effects (i.e., vaginal discharge or vaginal bleeding) was much lower in the PRP group than in the laser group (p value < 0.01). They concluded that autologous PRP application appeared promising for the treatment of cervical ectopy in symptomatic women, as it yielded a shorter tissue healing time and milder adverse effects than laser treatment.

CONCLUSION

Platelets are foundational in many of the body's functions, especially where the mucosa or skin is concerned. PRP is the ultimate "body's own" physiological product because it comes from the patient herself, it is safer, and more natural than animal-derived or human donated products.

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