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INNOVATIVE TECHNOLOGIES IN REPRODUCTIVE MEDICINE: PLATELET-RICH PLASMA FOR OVARIAN REJUVENATION AND INFERTILITY - A NARRATIVE REVIEW

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ABSTRACT

Introduction and purpose: Regenerative medicine has introduced new biological strategies to improve ovarian function in women with diminished ovarian reserve (DOR) or premature ovarian insufficiency (POI). Among them, platelet-rich plasma (PRP) - a concentrate of platelets derived from the patient's own blood - has gained interest for its potential to stimulate follicular growth and enhance reproductive capacity. PRP contains various growth factors and cytokines that promote angiogenesis, cell proliferation, and tissue repair. This review summarizes current evidence regarding PRP's mechanisms of action, clinical effects, and safety in the context of ovarian rejuvenation.

State of knowledge: PRP is obtained by centrifuging autologous blood to increase platelet concentration, followed by activation using agents such as calcium chloride or thrombin. Once activated, platelets release growth factors including PDGF, VEGF, EGF, IGF, and TGF-β, which are involved in tissue regeneration and modulation of inflammation. When injected into the ovaries, PRP may stimulate dormant follicles, improve blood flow, and alter the ovarian microenvironment via anti-inflammatory and immunomodulatory effects. Early clinical studies report encouraging outcomes such as improved ovarian reserve markers and pregnancy rates.

Conclusions: PRP therapy is a promising, minimally invasive technique with potential to support ovarian function in selected patients with POI or DOR. Its use is biologically justified by the regenerative properties of platelet-derived factors. Nevertheless, due to limited and low-quality evidence, as well as a lack of standardized preparation and administration protocols, PRP cannot yet be recommended as routine treatment.

KEYWORDS

Platelet-Rich Plasma (PRP), Ovarian Rejuvenation, Premature Ovarian Insufficiency (POI), Diminished Ovarian Reserve (DOR), Infertility

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Introduction

In recent years, regenerative medicine has introduced novel biological approaches to enhance endogenous ovarian function. One such strategy is the use of Platelet-Rich Plasma (PRP)—an autologous concentration of platelets derived from the patient's own blood. Originally utilized in fields like orthopedics, dentistry, and dermatology, PRP has gained attention in reproductive medicine due to its rich content of growth factors and cytokines that support tissue repair, angiogenesis, and cellular proliferation. Preliminary studies suggest that intra-ovarian administration of PRP may stimulate follicular development, enhance hormonal profiles, and potentially restore fertility in women with compromised ovarian function.

This narrative review aims to synthesize the most current evidence regarding the mechanisms of action, clinical efficacy, safety profile, and potential limitations of PRP in the context of ovarian rejuvenation. By drawing from literature published between 2015 and 2025, this review provides an overview of the biological rationale for PRP therapy, summarizes clinical findings to date, and identifies gaps in knowledge that warrant further investigation. The goal is to offer clinicians and researchers a comprehensive yet critical understanding of PRP's role as an experimental adjunct in infertility treatment for women with DOR or POI.

Materials and Methods

This narrative review was conducted to summarize and critically evaluate the current literature on the use of Platelet-Rich Plasma (PRP) in ovarian rejuvenation. A literature search was performed in PubMed, Google Scholar, and ScienceDirect for publications from January 2015 to June 2025. Search terms included combinations of "Platelet-Rich Plasma," "ovarian rejuvenation," "infertility," "poor/diminished ovarian response," and "premature ovarian insufficiency."

Results

What is Platelet-Rich Plasma?

Platelet-rich plasma (PRP) is an autologous blood-derived product obtained by centrifuging whole blood to concentrate platelets in plasma. Initially introduced in transfusion medicine in the 1970s and later applied in maxillofacial and orthopedic surgery, PRP has gained increasing attention in regenerative medicine due to its biological potential and ease of preparation [1,2]. Its use in gynecology has expanded in recent years, driven by a need for less invasive and biologically guided treatment modalities in fertility preservation and tissue repair [3].

The preparation of Platelet-Rich Plasma (PRP) typically involves a series of centrifugation steps from a patient's autologous whole blood, aiming to achieve a supra-physiological concentration of platelets while minimizing erythrocyte and leukocyte contamination, depending on the specific protocol [4]. Although various commercial kits and standardized protocols exist, the general principle involves initial soft centrifugation to separate plasma from red blood cells, followed by a second, harder centrifugation to concentrate platelets from the plasma. The final product should ideally contain a platelet concentration 3 to 7 times higher than baseline levels in peripheral blood [5]. Key variables in PRP preparation include the initial blood volume, centrifugation speed and duration, and the presence or absence of leukocytes in the final product (leukocyte-rich PRP vs. leukocyte-poor PRP), which can influence its biological properties [6]. Activation of PRP, often achieved by adding exogenous activators like calcium chloride or thrombin, or through intrinsic activation upon contact with collagen *in vivo*, leads to the degranulation of platelet alpha-granules and the release of numerous bioactive molecules [7].

When activated—spontaneously or through exogenous agents such as calcium chloride or thrombin—platelets degranulate, releasing a wide array of growth factors and bioactive molecules stored within their α-granules. These include platelet-derived growth factor (PDGF), which stimulates mitogenesis and angiogenesis; transforming growth factor-beta (TGF-β), known for its role in extracellular matrix remodeling; vascular endothelial growth factor (VEGF), which promotes endothelial proliferation and new vessel formation; epidermal growth factor (EGF), involved in epithelial cell migration; and insulin-like growth factors (IGF-1 and IGF-2), which regulate tissue homeostasis and cell proliferation [8,9]. These mediators play key roles in cellular processes such as cell proliferation, differentiation, chemotaxis, angiogenesis, and tissue remodeling [8]. The application of PRP in ovarian rejuvenation is theoretically predicated on its capacity to stimulate dormant primordial follicles, enhance neovascularization within the ovarian cortex, modulate the ovarian microenvironment, and exert anti-inflammatory effects, thereby potentially reactivating ovarian function and improving oocyte competence in women with compromised ovarian reserve [10,11].

Beyond their regenerative properties, platelets also exhibit immunomodulatory and anti-inflammatory effects. PRP has been shown to downregulate pro-inflammatory cytokines such as interleukin (IL)-1β, IL-6, and tumor necrosis factor-alpha (TNF-α) while promoting the expression of anti-inflammatory mediators including IL-4 and IL-10 [12,13]. These effects contribute to local immune modulation, resolution of chronic inflammation, and improved microenvironmental conditions for tissue repair [13].

Discussion

Infertility and Ovarian Dysfunction

Infertility, defined as the inability to achieve pregnancy after 12 months or more of regular unprotected sexual intercourse, constitutes a significant global health challenge, impacting millions of couples worldwide [14]. A substantial proportion of these cases are attributable to female factor infertility, with diminished/poor ovarian reserve (DOR/POR) and premature ovarian insufficiency (POI) emerging as increasingly prevalent and complex etiologies [15].

Diminished/poor ovarian reserve (DOR/POR) is characterized by a quantitative and qualitative decline in the ovarian follicular pool, often manifesting as reduced Anti-Müllerian Hormone (AMH) levels and elevated Follicle-Stimulating Hormone (FSH) concentrations, particularly impacting reproductive outcomes in older women [16].

Premature Ovarian Insufficiency (POI) is a multifaceted condition in women of childbearing age, distinguished by a decline in ovarian function before the age of 40. While it affects up to 3.7% of women globally, it is noteworthy that over half of these individuals still possess viable follicles in their ovaries. The primary treatment for infertility associated with POI is oocyte donation; however, many patients seek to

achieve pregnancy using their own eggs. While assisted reproductive technologies (ARTs) remain the cornerstone of infertility management, women with DOR or POI frequently exhibit poor ovarian response to controlled ovarian stimulation, resulting in low oocyte yield, diminished embryo quality, and reduced live birth rates [17]. The limitations of conventional ART, coupled with the emotional and financial burden of oocyte donation, underscore the urgent need for innovative therapeutic strategies aimed at restoring or improving endogenous ovarian function. This demand has led to the exploration of several innovative biological treatments, such as Platelet-Rich Plasma (PRP) and others like Exosomes (exos) therapy, In vitro Activation (IVA), Stem Cell therapy, MicroRNAs and Mitochondrial Targeting Therapies. The objective of these experimental strategies is to stimulate oogenesis and folliculogenesis by enhancing the natural biochemical pathways and creating a more favorable ovarian microenvironment [18].

Clinical Evidence and Efficacy of PRP in Ovarian Rejuvenation

In women with DOR, PRP treatment has been explored as a strategy to improve ovarian response to controlled ovarian hyperstimulation and ultimately, pregnancy rates. Several studies report an increase in Anti-Müllerian Hormone (AMH) levels and a decrease in Follicle-Stimulating Hormone (FSH) levels following PRP administration, suggesting an improvement in ovarian reserve markers [18]. Clinically, positive associations between PRP and oocyte quality-related parameters such as maturation and fertilization rates have been observed in some cohorts of DOR patients undergoing *in vitro* fertilization (IVF) cycles subsequent to PRP treatment [18-21].

The studies also showed that intraovarian PRP injection significantly increased oocyte number, M2 oocyte number, antral follicle count (AFC), and AMH levels in women with DOR. Besides, in women with POI, PRP injection improved AFC and serum levels of FSH , AMH and LH [22-24].

Mechanism of Action in Ovarian Rejuvenation

The proposed mechanisms by which PRP exerts its effects on ovarian function are multifaceted, primarily stemming from the growth factors and cytokines released upon platelet activation. These factors interact synergistically to influence various cellular processes within the ovarian microenvironment.

Table 1. A summary of key bioactive molecules in Platelet-Rich Plasma (PRP) and their proposed mechanisms of action:

Molecule in PRP	Primary Function	Mechanism of Action in the Ovary
Platelet-Derived Growth Factor (PDGF)	Cell growth, proliferation, differentiation, angiogenesis	Activates membrane receptors to trigger cellular activities like mitosis, angiogenesis, and macrophage activation, contributing to tissue regeneration.
Transforming Growth Factor beta (TGF-β)	Anti-proliferation, ECM remodeling, tissue repair	Acts as an anti-proliferative factor in epithelial cells, while targeting fibroblasts, bone marrow stem cells, and preosteoblasts. Also involved in ECM synthesis and degradation.
Vascular Endothelial Growth Factor (VEGF)	Angiogenesis (formation of new blood vessels)	As a signal transduction protein, it stimulates the formation of new blood vessels to improve blood supply and deliver nutrients to the ovarian microenvironment.
Epidermal Growth Factor (EGF)	Cell growth, proliferation, and differentiation	Acts as a mitogen to stimulate the proliferation and growth of ovarian cells and potentially reactivate dormant primordial follicles.
Hepatocyte Growth Factor (HGF)	Cell migration, growth, angiogenesis	Involved in cell proliferation, migration, differentiation, and angiogenesis, contributing to tissue regeneration and repair.

Fibroblast Growth Factor (FGF)	Cell proliferation, angiogenesis, tissue repair	Enhances cell growth, proliferation, and differentiation, while promoting angiogenesis and tissue regeneration.
Insulin-like Growth Factor-1 (IGF-1)	Cell growth and metabolism	Works synergistically with other growth factors to stimulate cell proliferation and contribute to the growth and maturation of follicles.
Other Bioactive Molecules	Anti-inflammatory and immunomodulatory effects	Reduces chronic inflammation, inhibits apoptosis, and extends cell growth, creating a more favorable environment for follicular development.

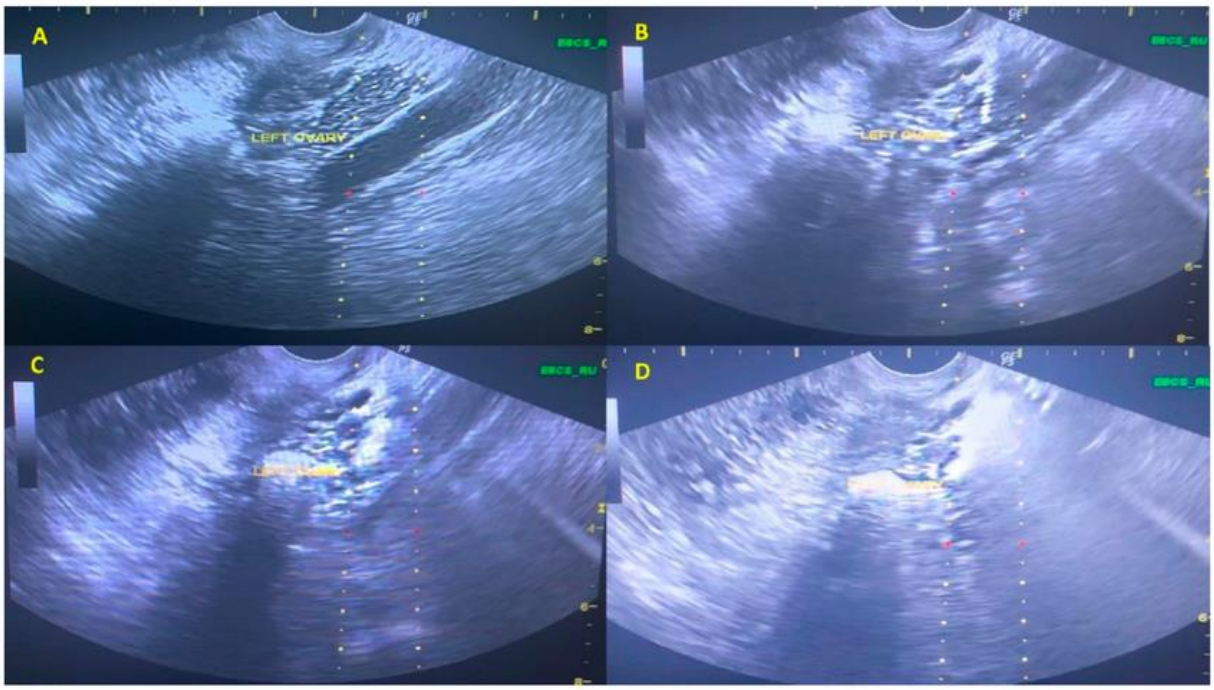
Source: Adapted from: [25-30].

The key growth factors within PRP play a central role in folliculogenesis. They positively influence the transition of follicles from the primordial to the pre-antral stage. Furthermore, TGF-β is particularly important as it can enhance the expression of both FSH and LH receptors, which provides survival stimuli for antral follicles and inhibits follicular apoptosis. The administration of these exogenous growth factors via intraovarian PRP injection is thus proposed as a therapeutic strategy to enhance follicular growth, maturation, and survival, ultimately improving the potential for pregnancy [31].

Intra-Ovarian PRP Administration

The primary clinical application of PRP in ovarian rejuvenation involves direct intra-ovarian injection, typically guided by transvaginal ultrasound. This minimally invasive procedure aims to deliver concentrated growth factors directly to the ovarian cortex, where primordial and developing follicles reside [32].

Figure 2. Sequence of images (A–D), illustrating the steps during PRP procedure on the left ovary. (A): Transvaginal Ultrasound Scan Image of the left ovary and the needle guide viewed prior to needle insertion. (B): Transvaginal Ultrasound Scan Image of the left ovary while the needle is fully inserted into cortex of the ovary. (C): Transvaginal Ultrasound Scan Image of the left ovary during PRP injection. (D): Transvaginal Ultrasound Scan Image of the left ovary aligned with the needle guide, following PRP injection.



Source: Sfakianoudis, K., Simopoulou, M., Grigoriadis, S., Pantou, A., Tsioulou, P., Maziotis, E., Rapani, A., Giannelou, P., Nitsos, N., Kokkali, G., Koutsilieris, M., & Pantos, K. (2020). Reactivating ovarian function through autologous platelet-rich plasma intraovarian infusion: Pilot data on premature ovarian insufficiency, perimenopausal, menopausal, and poor responder women. *Journal of Clinical Medicine, 9*(6), 1809. https://doi.org/10.3390/jcm9061809

Safety Profile

The safety profile of intra-ovarian Platelet-Rich Plasma (PRP) administration is generally considered favorable, primarily due to its autologous nature, which minimizes the risk of immunological reactions or disease transmission [33]. The advantages of PRP as an intervention also include low or no risk of infection, cross-contamination, and transmission of microbial diseases or immune reactions. Mild side effects of PRP, such as pain, swelling, and bleeding, are reported in 2% to 5% people treated. Reported adverse events are typically mild and transient, largely associated with the transvaginal ultrasound-guided injection procedure itself rather than the PRP product [34]. These may include temporary pelvic pain, mild discomfort, or transient spotting, consistent with any invasive gynecological procedure. Serious complications such as infection, significant hemorrhage, or damage to surrounding organs are exceedingly rare but remain theoretical concerns for any transvaginal ovarian intervention [35]. Long-term safety data, particularly concerning the potential for sustained effects on ovarian function, tumorigenesis, or systemic implications, are still limited and require further investigation [36].

Conclusions

Platelet-Rich Plasma (PRP) has emerged as a novel and promising autologous biological therapy for improving ovarian function in women with premature ovarian insufficiency (POI) and poor ovarian response (POR). The therapeutic potential of PRP is attributed to its rich concentration of growth factors, including PDGF, TGF-β, VEGF, and IGF-1, which collectively promote cellular proliferation, angiogenesis, tissue repair, and anti-inflammatory effects within the ovarian microenvironment.

Clinical evidence, although largely from observational studies and initial systematic reviews, suggests that intra-ovarian PRP administration can lead to improvements in ovarian reserve markers and fertility outcomes in these challenging patient populations. However, the field is still in its nascent stages, and the definitive efficacy and safety of PRP have yet to be established. The significant heterogeneity in PRP preparation methods and the lack of large-scale randomized controlled trials pose considerable challenges to drawing firm conclusions. Until such data are available, the use of PRP should be considered experimental and offered only within ethically approved investigational frameworks or fertility clinics with expertise in advanced reproductive technologies.

Disclosure

Author Contributions:
Conceptualization: EB
Methodology: EB, KD-K
Software: JB, WZ
Formal analysis: PB, JB
Investigation: ID, MK, EB
Resources: JP, WZ, ID
Check: ID, PB, AD
Writing - rough preparation: EB, WZ
Writing - review and editing: WZ, JP, MB, AD
Supervision: PB, MB
Visualization: KD-K, MK

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