Advances in Research on the Application of Autologous Platelet-Rich Concentrate in Gynecology (Postprint)

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Abstract

Autologous platelet-rich concentrate is a platelet concentrate obtained by centrifuging blood drawn from humans or animals, mainly including the first-generation platelet concentrate, platelet-rich plasma (PRP), and the second-generation platelet concentrate, platelet-rich fibrin (PRF). Due to its role in promoting wound healing and tissue repair, it is widely used in fields such as oral implantology, bone defect repair, and burn and plastic surgery. In recent years, autologous platelet-rich concentrate has begun to be used for improving ovarian function, promoting endometrial hyperplasia and repair, and treating cervical and vulvar-related lesions, achieving significant therapeutic effects, but there is currently a lack of effective integration of research findings on PRP and PRF in the field of gynecology. This article systematically and comprehensively reviews the preparation, biological characteristics, and applications in various gynecological diseases of autologous platelet-rich concentrate, with the aim of providing clinicians with new therapeutic ideas for gynecology-related diseases and offering references for the in-depth development of research and application of autologous platelet-rich concentrate.

Full Text

Advances in the Application of Autologous Platelet Concentrate in the Field of Gynecology

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Abstract

Autologous platelet concentrate (APC) is a platelet concentrate obtained by centrifugation of human or animal blood, primarily including first-generation platelet-rich plasma (PRP) and second-generation platelet-rich fibrin (PRF). Due to its role in promoting wound healing and tissue repair, APC has been widely applied in dental implants, bone defect repair, burn and plastic surgery, and other fields. In recent years, APC has been increasingly used to improve ovarian function, promote endometrial regeneration and repair, and treat cervical and vulvar lesions, achieving significant therapeutic efficacy. However, research findings on PRP and PRF in gynecology have not been comprehensively integrated. This article systematically reviews the preparation methods, biological characteristics, and applications of APC in various gynecological diseases, aiming to provide clinicians with novel therapeutic approaches for gynecological conditions and to serve as a reference for advancing APC research and clinical implementation.

Keywords: Gynecologic diseases; Platelet-rich plasma; Platelet-rich fibrin; Autologous platelet concentrates; Endometrial hyperplasia; Ovarian diseases; Review

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1. Literature Search Strategy

A computerized search was conducted in PubMed, Web of Science, Embase, CNKI, and other databases from inception to February 2023. English search terms included "platelet-rich plasma," "platelet-rich fibrin," "PRP," "PRF," and "Gynecological diseases," while Chinese search terms included "autologous platelet concentrate," "platelet-rich plasma," "platelet-rich fibrin," and "gynecological diseases." Inclusion criteria comprised clinical or basic research studies, reviews, meta-analyses, and case reports addressing the preparation, biological characteristics, or therapeutic applications of autologous platelet concentrate, PRP, or PRF. Exclusion criteria included conference abstracts, commentaries, letters, and literature with unavailable full text or poor methodological quality.

2. PRP Characteristics and Applications

2.1 PRP Preparation Methods Platelet-related products first emerged in the 1970s, and PRP extraction technology in the 1990s drew widespread attention to platelet concentrates. PRP is a high-concentration platelet plasma obtained through centrifugation of autologous whole blood, containing 5–10 times the growth factor concentration of whole blood. PRP is primarily prepared via density gradient centrifugation, including one-step, two-step, and three-step methods. The two-step method is widely used clinically due to its high platelet concentration and growth factor yield. The main procedures are as follows: (1) Draw venous blood and inject it into tubes containing anticoagulants; (2) To prevent platelet activation during centrifugation, a temperature of 21–24°C is recommended. After centrifugation at a specific force, the blood separates into three layers: the bottom red blood cell layer (approximately 1/2 of total volume), a thin white middle layer rich in leukocytes, and the top platelet layer containing few leukocytes appearing yellow; (3) Aspirate the plasma above the red blood cell layer and transfer it to another sterile tube without anticoagulants; (4) After centrifugation, the plasma separates into two layers: the upper 2/3 is platelet-poor plasma, and the lower 1/3 is platelet-rich plasma. Approximately 30 mL of venous blood yields 3–5 mL of PRP; (5) Remove the upper platelet-poor plasma with a pipette, leaving sufficient plasma to resuspend the concentrated platelets, then add bovine thrombin and calcium chloride to activate the platelets for clinical use. With the advancement and clinical application of PRP technology, commercial PRP preparation systems have become available.

2.2 PRP Structural Characteristics and Biological Properties PRP appears as a red, viscous liquid macroscopically. Under scanning electron microscopy, platelets aggregate in clusters with overlapping pseudopodia, and some leukocytes are scattered among the platelets. PRP platelets are rich in cytokines and growth factors. Once activated, platelets degranulate and release numerous factors including 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 secrete fibronectin, vitronectin, and sphingosine-1-phosphate, which promote wound repair and tissue regeneration by enhancing cell chemotaxis, adhesion, proliferation, migration, and angiogenesis. PRP has a pH of 6.5–6.7, creating a weakly acidic medium that inhibits microorganisms, while platelets themselves can secrete bactericidal proteins and release antimicrobial peptides upon activation. Thus, PRP exerts antibacterial effects through multiple mechanisms.

2.3 Basic Research on PRP in Gynecological Diseases SUGINAMI et al. used immunohistochemistry to analyze platelet distribution patterns during

the human menstrual cycle, finding that platelets were abundant in the endometrial stroma near the luminal epithelium during menstruation but sparse during the proliferative and secretory phases. When co-cultured with EM-E6/E7/hTERT immortalized endometrial epithelial cells, platelets promoted cell adhesion to Matrigel and increased cell-cell contact by enhancing E-cadherin expression, suggesting that platelets may participate in human endometrial re-epithelialization. AGHAJANOVA et al. found that activated 5% PRP promoted migration of human endometrial stromal fibroblasts, endometrial mesenchymal stem cells, and bone marrow-derived mesenchymal stem cells, while also promoting proliferation of endometrial stromal fibroblasts and endometrial mesenchymal stem cells. These two studies provide in vitro evidence for platelet concentrate-mediated endometrial regeneration. Animal studies have shown that intrauterine PRP injection promotes regeneration of ethanol-induced endometrial injury in rats, reduces fibrosis, and increases endometrial receptivity. ZHANG et al. investigated the synergistic therapeutic effect of PRP and menstrual blood-derived stromal cells on mechanically injured intrauterine adhesions, finding that PRP enhanced the reparative effects of menstrual blood-derived stromal cells on the endometrium. These studies provide evidence supporting PRP' s clinical application for improving endometrial function.

2.3.2 Protecting Ovarian Function from Ischemia-Reperfusion Injury To investigate PRP' s protective effects against ovarian ischemia-reperfusion injury, BAKACAK et al. conducted uterine adnexal torsion experiments in 60 female rats. The experimental group received intraperitoneal PRP injection 30 minutes before torsion. After detorsion, the experimental group showed superior outcomes compared to controls in oxidative stress levels, histopathological changes, and reduction of ovarian ischemia-reperfusion injury, suggesting that PRP can protect ovarian function from such damage.

2.4 Clinical Applications of PRP in Gynecological Diseases

2.4.1 Promoting Postoperative Wound Healing and Reducing Complications Activated PRP platelets release multiple high-concentration growth factors that far exceed the threshold required for wound repair. These factors rapidly initiate wound healing by promoting proliferation and migration of local repair cells, extracellular matrix deposition, and local angiogenesis. PRP demonstrates significant efficacy in healing refractory wounds such as diabetic chronic wounds, pressure ulcers, lower extremity venous ulcers, and radiation-induced skin necrosis. TEHRANIAN et al. studied the effect of autologous PRP on wound healing after cesarean section in high-risk patients, randomly dividing 140 women into two groups: an intervention group receiving postoperative PRP treatment and a control group receiving standard care. Results showed that the PRP group had significantly greater reductions in redness, bruising, and pain compared to controls ($P<0.001$), indicating that PRP can accelerate healing of refractory wounds after cesarean section. Another Phase I/II prospective

study evaluated PRP' s safety and analgesic efficacy in gynecologic surgery, enrolling 55 consecutive patients undergoing gynecologic procedures who received 20 mL PRP directly at the surgical site postoperatively. Compared with controls, the PRP group had lower pain scores (2.7 vs. 6.7, $P<0.001$) and lower morphine consumption (17 mg vs. 26 mg, $P<0.05$), with no adverse reactions. MORELLI et al. found that using platelet gel before vulvar reconstruction is an effective strategy to prevent wound dehiscence after surgery for locally advanced vulvar cancer. In their study, patients undergoing vulvar cancer surgery (radical vulvectomy) were divided into Group A (n=10) and Group B (n=15). Group A received platelet gel placement at the vaginal incision during reconstructive surgery, while Group B underwent surgery only. Group A showed significantly lower rates of wound infection, vaginal necrosis, and wound dehiscence compared to Group B ($P<0.05$), with significantly reduced postoperative fever, shorter hospital stays, and faster wound healing ($P<0.05$).

2.4.2 Treating Vulvar and Cervical Lesions BEHNIA-WILLISON et al. investigated PRP' s therapeutic effect on steroid-resistant vulvar lichen sclerosus, with patients receiving three vulvar PRP injections at 4–6 week intervals, followed by another treatment after 12 months. All 28 patients showed clinical improvement in lesion size, with 28.6% achieving complete resolution. HUA et al. conducted a randomized clinical study comparing PRP and laser therapy for benign cervical lesions, finding that the PRP group had significantly shorter re-epithelialization time and lower adverse reaction rates than the laser group.

2.4.3 Improving Ovarian Function and IVF Response Ovarian reserve function is a critical indicator of female fertility, and age-related poor ovarian response and low fertilization rates remain challenges in fertility preservation. WHITE et al. demonstrated that intraovarian injection of growth factor-containing platelets may promote oocyte rejuvenation. CAKIROGLU et al. performed intraovarian PRP injections in 311 women aged 24–40 with primary ovarian insufficiency, finding that PRP increased serum anti-Müllerian hormone levels and improved fertility. After PRP injection, 7.4% of women conceived naturally, 64.8% developed dominant follicles and attempted IVF, with 82 cases (26.4%) achieving successful pregnancy. Subsequently, CAKIROGLU et al. treated 474 women aged 30–45 with poor ovarian response (POR) history using intraovarian PRP injection, with 65.8% achieving successful IVF and embryo transfer. Abundant blood supply and platelet-derived factors are essential for normal ovarian function, and the high concentration of cytokines in PRP may promote intraovarian neovascularization and cell activation, thereby improving ovarian response and female fertility.

2.4.4 Promoting Endometrial Regeneration and Improving Pregnancy Outcomes The endometrium is crucial for embryo implantation and pregnancy maintenance. Damage to the endometrial basal layer leading to impaired

repair is a major cause of uterine infertility and pregnancy complications. Current treatments for endometrial regeneration, including estrogen therapy and stem cell therapy, have limitations. CHANG et al. studied five IVF patients with poor endometrial response whose endometrial thickness remained <7 mm after standard hormone replacement therapy. After intrauterine injection of 0.5–1.0 mL PRP on day 10 of menstruation alongside conventional hormone therapy, PRP promoted endometrial growth and all five patients achieved pregnancy. COLOMBO et al. applied PRP in patients whose endometrial thickness remained <6 mm despite three classic drug regimens, resulting in cycle cancellation. They found that 87% of patients showed significant endometrial thickness increase (average 6.9 mm) before progesterone injection and embryo transfer. Studies by CHANG et al. and DOGRA et al. both found that PRP groups had superior endometrial thickness, clinical pregnancy rates, and cycle cancellation rates compared to controls. NAZARI et al. reported on 18 patients with previous repeated implantation failure who received 0.5 mL intrauterine PRP injection 48 hours before embryo transfer. Sixteen patients achieved successful pregnancy with normal development (visible fetal heartbeat on ultrasound), while two had early miscarriage. A subsequent randomized controlled study enrolled 138 patients who failed to conceive after three or more high-quality embryo transfers. The experimental group received 0.5 mL intrauterine PRP injection 48 hours before blastocyst transfer, while the control group received standard treatment. The PRP group had significantly higher clinical pregnancy rates (44.89% vs. 16.66%, P<0.05). These findings demonstrate PRP' s significant efficacy in treating thin endometrium, repeated implantation failure due to uterine factors, and intrauterine adhesions, offering a new therapeutic approach in reproductive medicine by increasing endometrial thickness and improving endometrial function.

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3. PRF Characteristics and Applications

3.1 PRF Characteristics PRF is a second-generation autologous platelet concentrate obtained through specific centrifugation of venous blood, first described by DOHAN et al. in 2006. It requires no exogenous anticoagulants or activators, forming a gel through slow polymerization by its own coagulation factors, with platelet content similar to PRP. PRF offers several advantages over PRP: (1) Simplified and rapid preparation requiring only one centrifugation step without anticoagulants or pre-use thrombin activation; (2) A three-dimensional, loose, mesh-like structure that entraps platelets and growth factors, enabling slow release over up to 10 days; (3) Rich fibrin content that can cover wounds and promote healing. Studies report that PRF matrix contains glycosaminoglycans (heparin, hyaluronic acid) that strongly bind circulating small peptides, while the fibrin matrix stimulates integrin αv$ $3 expression, conferring robust capacity to support cell migration and healing.

3.2 PRF Clinical Applications in Gynecological Diseases While PRF has demonstrated significant efficacy in promoting alveolar bone regeneration, cranial repair, and corneal repair, its application in gynecology remains limited. In pelvic reconstructive surgery, vaginal grafts (both absorbable and non-absorbable) carry serious adverse effects. GORLERO et al. conducted a prospective observational study evaluating PRF in vaginal prolapse repair surgery. Ten patients with high-risk recurrence factors (grade II or higher) receiving surgical repair and PRF treatment at the surgical site showed 80% anatomic restoration rate, 100% improvement in prolapse symptoms, 20% increase in sexual activity, and no dyspareunia, with no intraoperative or postoperative complications. SHIRVAN et al. found that autologous PRP combined with PRF is a novel minimally invasive treatment for genital fistulas. In 12 patients receiving PRP injection around the fistula tract and PRF gel placement within the fistula, 11 achieved clinical cure with normal findings on vaginal examination and cystography after 6 months of follow-up. WANG et al. treated infertile patients with intrauterine adhesions using PRF, finding that the PRF group had significantly higher pregnancy rates than the untreated group, with significantly reduced adhesion scores, indicating PRF' s effectiveness in promoting endometrial repair and preventing adhesion reformation. YANG et al. analyzed endometrial tissue from patients with intrauterine adhesions after PRF treatment, finding increased numbers of endometrial glands and expression of Ki67, cytokeratin 18, and vimentin, with significantly reduced fibrotic area compared to pre-treatment. This suggests PRF promotes wound healing by stimulating endometrial gland hyperplasia and inhibiting fibrosis.

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4. Summary and Outlook

Autologous platelet concentrate is derived from the patient's own blood, avoiding allergic reactions, cross-infection, and immune rejection. Its high concentration of growth factors offers broad application prospects for promoting wound healing and tissue regeneration. PRP and PRF have shown remarkable efficacy in gynecology, particularly in promoting endometrial regeneration and repair in intrauterine adhesions, improving pregnancy outcomes, and enhancing ovarian function and response during IVF. These applications address two major challenges affecting female fertility, demonstrating powerful fertility preservation potential.

However, research on autologous platelet concentrate in gynecology faces several challenges: (1) The mechanisms underlying PRP and PRF promotion of wound healing and tissue regeneration require more in-depth basic research for clarification; (2) PRP and PRF applications in gynecology remain in early stages, with current evidence primarily from case reports and retrospective studies of low quality. Large-scale, multicenter, high-quality randomized controlled trials are needed to further verify the short-term and long-term safety and efficacy; (3) Standardized protocols for PRP and PRF application, including prepara-

tion methods, application procedures, quality control, and dosing, are urgently needed to better serve clinical practice.

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Note: Figure translations are in progress. See original paper for figures.