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Role of Platelet Rich Fibrin Glue in Vesicovaginal Fistulas

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Abstract:

Vesicovaginal fistula (VVF) remains one of the most distressing complications of gynecological and obstetric procedures. Traditional surgical repairs, such as the Martius flap, are effective but associated with longer operative time and donor-site morbidity. Platelet-rich fibrin (PRF) glue, a second-generation autologous platelet concentrate, provides a three-dimensional fibrin matrix enriched with platelets and leukocytes, enabling controlled release of growth factors. This enhances tissue regeneration, angiogenesis, and wound healing, making PRF a promising alternative as an interposition layer in VVF repair.

Keywords: Vesicovaginal fistula; Platelet-rich fibrin; Fibrin glue; Martius flap; Regenerative surgery; Vaginal repair.

Introduction

Platelet-rich fibrin (PRF) has recently aroused widespread interest as a biophysical and biochemical milieu that delivers growth factors (GFs), cytokines and immune/stem-like cells for immunomodulation and tissue healing purposes. **(1)**

Platelet-rich fibrin (PRF) is a second-generation technology. It is anteceded by platelet-rich plasma (PRP), which is whole blood centrifuged to remove red blood cells, leaving behind a suspension rich in white blood cells and plasma components that are thought to be important in promoting wound healing. Both PRF and PRP use autologous blood. **(2)**

Both PRF and PRP aim to use blood growth factors to promote the body's own healing process. PRF builds on PRP by preserving the growth factors in a fibrin matrix and can exert its effects days or weeks after the surgery. As opposed to PRP, PRF is prepared without the use of anticoagulation factors, which are known to inhibit wound healing. In comparison to PRP, PRF preparations tend to have higher leukocyte count because of centrifuge technique improvements, a fibrin matrix that promotes healing and allows growth factors to be slowly released over time and comes in moldable forms that improve workability.**(2)**

Brief history about Platelet-rich fibrin

As early as the 1950s, Kingsley used the term PRP to describe a thrombocyte concentrate used for patients with thrombocytopenia. Hematologists started to widely use the term in the 1970s.**(1)**

The study of PRP took off in varying directions in the following decades with varying investigators proposing different protocols and different applications in medicine. These early ways to prepare PRP were sometimes lengthy, and anticoagulants such as bovine thrombin or CaCl2 were part of the preparation to prevent clotting and to keep the concentrate in a liquid form.**(3)**

In the 1970s, Matras **(4)** studied skin healing in rats. He proposed the use of what he called "fibrin glue" in various preparations to enhance healing in rats. The stickier fibrin glue had fewer anticoagulant effects, and he was unable to achieve consistent results. After that, there was a growing number of reports of platelet concentrates in "glue" or "gelatin" in general surgery, neurosurgery, and ophthalmology.

In 2000, Choukroun **(5)** finally coined the term PRF by using a form of platelet-rich concentrate that was firmer in consistency. This form of platelet concentration is widely accepted as the second-generation platelet concentration.

Mechanism of action. (2)

When the body tries to repair itself, it will undergo 3 phases: **inflammatory phase**, **proliferative phase**, and **the remodeling phase**. The first, inflammatory phase, is an acute inflammation reaction to injury. Blood is the vector that brings these inflammatory cells to the site of the injury. In addition to phagocytes that clean the wound, white blood cells and platelets release important cellular mediators that begin the healing process. Important growth factors that are released include TGFB1, PDGF, VEGF, IGF1, which mediate cell migration, proliferation, and differentiation.

After 24 to 48 hours, the proliferative phase takes over by virtue of the presence of the inflammatory mixture of cellular signals created during the inflammatory phase. There can now be proliferation of fibroblasts, leukocytes, macrophages, and mesenchymal stem cells, which begin to lay the first foundations of the new tissue Platelets also secrete coagulation factors that ensure initial hemostasis.

Depending on the extent of the defect along with the immune capabilities of the body, the site will transition to the remodeling phase of healing when there is stability in the first tissues laid.

PRF is formed by dividing autologous blood into components that promote the wound-healing process and components that do not. Components that promote wound healing are suspended in a fibrin matrix for preservation and slow release as the wound heals. The red blood cells ideally are spun out during the centrifuge. process, and what are kept are the white blood cells, platelets, and fibrin. Per volume, these ingredients for wound healing are found at much higher than physiological levels.

The fibrin matrix is the main advantage PRF has over PRP. It acts as a 3-dimensional scaffold for the leukocytes and platelets and their release products. The matrix allows for delayed release of its contents so that the beneficial wound-healing effects are present for a longer time.

The mass effect of the fibrin clot is also advantageous in that it can take up space where PRP cannot. Peripherally proliferating cells can use the scaffold to penetrate the wounded site, which is not possible with the pure liquid preparation of PRP. The scaffold nature of PRF is especially true because the fibrin clot is workable and can be adapted to many tissue defect forms.

PRF preparation protocol (5)

The classic PRF protocol was suggested by Choukroun. The basic protocol of producing PRF requires around 10 ml of blood to be collected from the patient without anticoagulant tubes. After collecting, the blood is quickly subjected to centrifugation at 2700 rpm for 12 minutes.

After the completion of cycle, the blood in the tube gets separated into three distinct layers; platelet poor plasma at the top, PRF in the middle and a red blood corpuscular base in the bottom. The PRF is then carefully retrieved from the test tube and the RBC base is carefully removed to retain a small part of it in the clot. The clot thus obtained can be used as it is, compressed to form plugs for implantation into the socket.

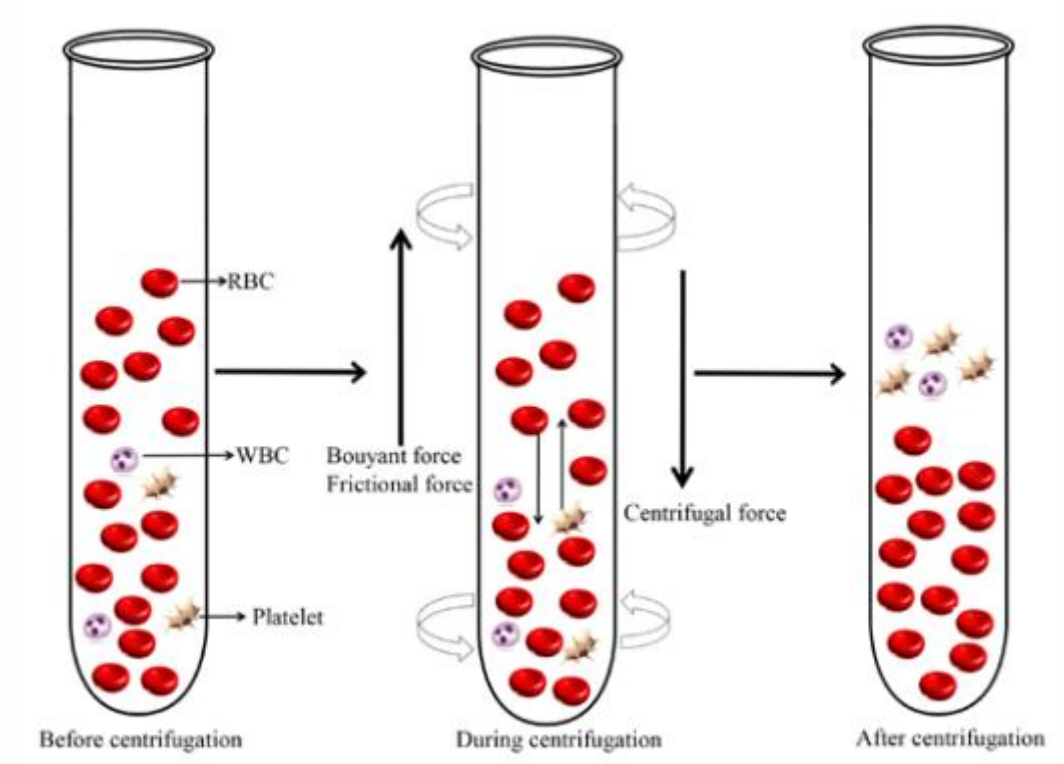

Figure (1) Formation of PRF. Before centrifugation, all cells are mixed. During centrifugation centrifugal force is directed towards the bottom of the tube and buoyant and frictional forces oppose it. There is a net centrifugal force, and this is dependent on the mass of the particles. Hence, the RBC's which have higher mass are pulled towards the bottom of the tube and WBC's and platelets along with plasma which have comparatively lower mass reach the top of the tube. This eventually excludes the RBC's from coagulation and the clot hence formed is PRF. **(6)**

When freshly drawn blood is collected in glass/glass coated plastic tubes without anticoagulant, the coagulation cascade starts immediately. The basic principle is to allow the blood to clot as it would physiologically. Under normal circumstances, the blood would coagulate to form a blood clot.

under the centrifugation force, RBC's, which have relatively higher mass settle towards the bottom of the tube. Whereas WBC's, platelets and plasma along with its clotting factors which have comparatively lower mass are pushed towards the top of the tube While this separation occurs, another process that happens simultaneously is blood coagulation owing to the absence of an anticoagulant. By the time the final steps of coagulation cascade i.e. conversion of prothrombin to thrombin and fibrinogen to fibrin occurs, the factors required for coagulation are all present in the plasma, which is now located at the top of the tube near platelets under the force of centrifugation. Once this separation is achieved, the rest 6-8 minutes of the centrifugation cycle is maintained and let

clotting proceed. Hence, RBC's which do not contribute significantly to healing of a wound are effectively excluded from the blood clot under the centrifugation force, and the clot now consists mainly of platelets and fibrin. The normal time taken for the coagulation to complete is around 8 mins and hence all the protocols to produce the PRF concentrates have a duration like these**. (6)**

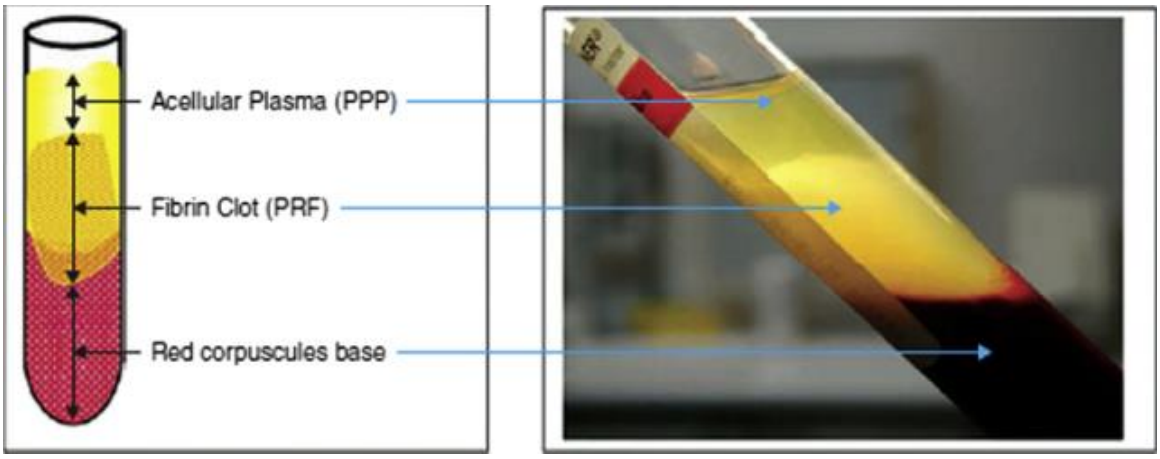

figure (2) Solid PRF after centrifugation. The bottom layer is predominantly red blood cells and is discarded. The solid middle layer is clotted solid PRF. The top layer is uncloted plasma. Both the middle and the top layers have useable growth factors.**(2)**

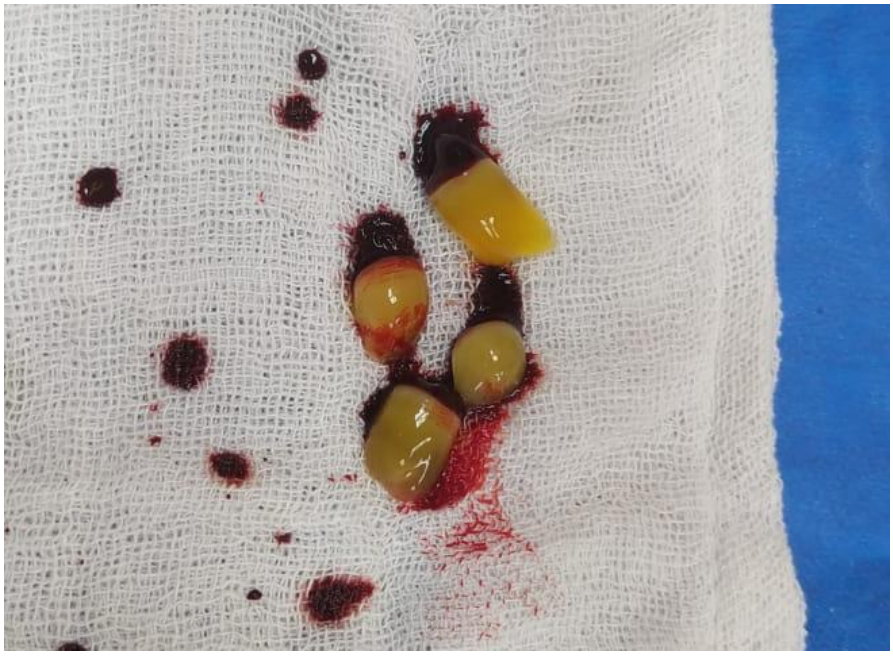

Figure (3) After extraction of the middle layer of PRF

Uses of PRF in urological surgeries

VVF treatment only with PRP injection and platelet-rich fibrin glue without any other additional surgical procedure on 12 patients Platelet rich plasma was injected around the fistula into the tissue and platelet rich fibrin glue was interposition in the tract, in a fistula diameter Less than 5mm which the fistula close in about 6 months, No complications were observed during and after the

injection. There for PRP considered a safe material in healing small VVF without any remarkable complications. **(7)**

PRP was used as an adjuvant therapy for recurrent vesicovaginal fistulas. It was injected at four to five points around the fistula's edges of 16 patients, allowing for proper neovascularization and remodeling of surrounding tissues between six and eight weeks prior to the Latzko procedure for VVF repair. One patient was cured by PRP injection without the need for surgery.**(8)**

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