Journal of Assisted Reproduction and Genetics (2021) 38:1013–1014
https://doi.org/10.1007/s10815-021-02195-0

COMMENTARY

Will PRP therapy find a niche in reproductive medicine? Not ready for prime time

Paolo Rinaudo[1] · David Albertini[2]

Received: 7 April 2021 / Accepted: 14 April 2021 / Published online: 23 April 2021

The degranulation and secretion of the platelets' alpha granules initiate the seemingly impossible repair that occurs during wound healing. Widely divergent areas of medicine have been exploiting this and other regenerative and reparative effects of platelets; this trend is making inroads, for better or worse, in reproductive medicine.

The recent review of Sharara and colleagues analyzes the available evidence on potential uses for platelet-rich plasma (PRP) as a treatment for thin endometrial lining (<7 mm), recurrent implantation failure, and poor ovarian reserve ("A narrative review of platelet-rich plasma (PRP) in reproductive medicine"; 10.1007/s10815-021-02146-9). The authors found some marginal benefit for their use but suggest that PRP should still be used under experimental protocols.

PRP (also known as platelet-rich growth factors (GFs), platelet-rich fibrin (PRF) matrix, and platelet concentrate) is an admixture of bioactive molecules that has a relatively long history of utility in medicine. Hematologists were the first to use PRP in the 1970s to treat patients with thrombocytopenia. In the 1980s, PRP-based therapies were used mainly by maxillofacial surgeons to improve healing; in the following decades, widespread adoption of PRP by professional athletes to treat sports injuries made the product well known to the public [1].

As summarized by Sharara, PRP started to be used in reproductive medicine only in the past 3–5 years. However, "therapeutic" applications of PRP are not new to gynecology. Among the more sordid examples, some maverick gynecologists injected PRP into the vagina, in a procedure called "O-shot" or "orgasm shot" with the alleged benefit of improving orgasm.

✉ Paolo Rinaudo
Paolo.Rinaudo@ucsf.edu

[1] University of California San Francisco, San Francisco, CA, USA

[2] Bedford Research Foundation, Bedford, MA, USA

So, what is the magic composition of PRP and why could its use be beneficial for infertility management? And specifically, could direct ovarian injection restore follicular growth especially in older patients?

Platelet alpha granules contain multiple factors including at least 7 critical growth factors: 3 isomers of platelet-derived growth factor, 2 of transforming growth factor β, vascular endothelial growth factor, and epithelial growth factor [2]. In addition, since platelets are bathed in plasma, 3 adhesion molecules are also present: fibrin, fibronectin, and vitronectin. Given this payload of growth-promoting factors, there is good cause to believe these powerful biological components may play a role in activating dormant follicles or stem cells, resulting in their assumed therapeutic role in the wide arrays of pathologies for which they are proposed.

But why are the results of studies utilizing PRP treatments of a controversial or inconsistent nature? And why, when a benefit is observed, this applies only to a subgroup of patients?

The fact that PRP consists of many growth factors, with their exact concentrations unknown and potentially varying from patient to patient (could composition change in different phases of the cycle? with advancing age? with different disease states?) raises doubts about the uniformity of each PRP preparation. In addition, the quality of PRP preparations is often unpredictable, since different devices used to extract PRP have different efficiency with some being consistently less "bioactive" than others [2]. Moreover, since secretion of growth factors begins 10 minutes after blood clotting and more than 95% of growth factors are secreted within 1 hour of clotting, in theory at least, PRP should be used rapidly after clot activation. Studies that fail to use anticoagulated whole blood are therefore not using PRP. Finally, since secretion of the alpha granules requires activation of the growth factor proteins by the addition of carbohydrate side chains and intact plasma membranes, any damage to platelets during the isolation procedure will result in the final PRP product most likely becoming inactive [2].

These limitations alone make clear that PRP preparations are yet not ready for prime time usage. Therapeutic options for PRP are highly promising, but like herbal concoctions, their compositional status remains too close to an alchemic mix to be widely prescribed in medicine. We need to detail the exact compositions and precise concentrations for each growth factor or protein present in PRP to design reproducible experiments and derive meaningful conclusions. This undertaking alone represents a fruitful area of research that could lead to important therapeutic improvements. A deeper scientific understanding of PRP might, rather than asking the philosopher stone to convert lead into gold, transforms PRP components into powerful medications.

References

1. Alves R, Grimalt R. A review of platelet-rich plasma: history, biology, mechanism of action, and classification. Skin appendage disorders. 2018;4:18–24.
2. Marx RE. Platelet-rich plasma: evidence to support its use. Journal of oral and maxillofacial surgery : official journal of the American Association of Oral and Maxillofacial Surgeons. 2004;62:489–96.