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Review

Platelet rich plasma in ocular surface☆

A.C. Riestra[a,*], J.M. Alonso-Herreros[b], J. Merayo-Lloves[a]

[a] Instituto Universitario Fernández-Vega, Fundación de Investigación Oftalmológica, Universidad de Oviedo, Oviedo, Spain
[b] Hospital Universitario Los Arcos del Mar Menor, Pozo Aledo, Murcia, Spain

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ABSTRACT

The use of platelet-rich preparations has experienced a significant increase in recent years due to its role in tissue-repair and regeneration. The aim of this study is to examine the available evidence regarding the application of plasma rich in growth factors, and its variations, on the ocular surface. A review is also presented on the effects of platelet-derived growth factors, the implications of the preparation methods, and the existing literature on the safety and efficacy of these therapies in ocular surface diseases. Despite the widespread use of platelet preparations there is no consensus on the most appropriate preparation method, and growth factors concentration vary with different systems. These preparations have been used in the treatment of ocular surface diseases, such as dry eye or persistent epithelial defects, among others, with good safety and efficacy profiles, but further studies are needed to compare to the currently available alternatives.

Plasma rico en plaquetas en superficie ocular

Palabras clave:
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Plasma rico en factores de crecimiento
Derivados hemáticos
Superficie ocular
Córnea

RESUMEN

El uso de los preparados ricos en plaquetas ha experimentado un aumento significativo en los últimos años debido a su papel en la reparación y regeneración tisular. El objetivo del presente estudio es recopilar la evidencia disponible respecto a la aplicación de plasma rico en factores de crecimiento y sus variantes sobre la superficie ocular: el efecto de los factores de crecimiento derivados de plaquetas, las implicaciones de los distintos métodos de preparación, los estudios publicados en patologías de la superficie ocular, así como sus contraindicaciones y reacciones adversas. Pese al uso generalizado de los preparados de plaquetas, no existe un consenso sobre el método de preparación más adecuado, variando

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* *Corresponding author.*
E-mail address: ana.riestra@fio.as (A.C. Riestra).

las concentraciones de factores de crecimiento según el sistema empleado. Estos preparados se han utilizado en el tratamiento de enfermedades de la superficie ocular como del ojo seco o los defectos epiteliales persistentes, entre otras, con un perfil adecuado de eficacia y seguridad, aunque son necesarios más estudios para su posicionamiento terapéutico respecto a las alternativas actualmente disponibles.

Introduction

Role of haematic derivates in ophthalmology. Historical perspective. Use of autologous serum

Tears have a very complex composition, with water being the main component (98.3%), followed by salts (1%), proteins and glucoproteins (0.7%), and hydrocarbons, lipids and others in smaller amounts.[1]

Tears have the following properties:

- Refractive
- Mechanical, as lubricant.
- Antimicrobian, not only due to its barrier and cleansing function but also because it comprises lymphocytes, macrophages and enzymes such as arylsulfatase A, peroxidase, lactoferrin and lysozyme, with bacteriostatic and bactericide effects.
- Nutritive, providing glucose, oxygen, water and essential electrolytes for corneal epithelium metabolism.
- Epitheliotropic, due to its content in proteins comprising growth factors, vitamins, immunoglobulins and neuropeptides that regulate the process of proliferation, migration and differentiation of corneal and conjunctival epithelium cells. Diminished epitheliotropic factors can compromise the integrity of the epithelium and give rise to epithelial defects which persist and progress as the results of poor cicatrization.[1]

The use of haematic derivates in ophthalmology arose out of the need for lacrimal substitutes that, in addition to provide hydration, could provide other essential components for ocular surface maintenance and regeneration.

Going back in history, the Ebers papyrus (1534 b.C.) mentions the application of blood in the eyes. In 1975, Ralph was the first to describe the application of autologous serum[2] and in 1984 Fox et al.[3] demonstrated its beneficial effects in patients with keratoconjunctivitis sicca. Subsequently, Tsubota et al.[4] demonstrated that the application of autologous serum in patients with dry eye associated to the Sjögren syndrome not only improved symptoms but also had a beneficial effect on the epithelium.

However, only in the late 90s of the past century the use of autologous serum gained acceptance and rapidly became widespread.[4,5] Since then, autologous serum has been increasingly utilized for treating ocular surface diseases and was accepted by the British health authority (NHS) in 1997 and the New Zealand counterpart in 2000.[4–9]

The composition of serum is very similar to that of tears. The concentration of several components is comparable, with the exception of more vitamin A, lysozyme, transforming growth factor β (TGF-β) and fibronectin, and less IgA, endothelial growth factor (EGF) and vitamin C in serum than in tears[10] (Table 1).

In recent years, the application of platelet derivates has increased in several areas of medicine including ophthalmology, due to its role on tissue repair and regeneration.

Terminology

There is no agreement on the definition of platelet-rich plasma (PRP). The only definition that is consistently defended in the literature defines PRP as the volume of autologous plasma that contains a platelet concentration above the basal level (150,000–350,000/μl).[11]

PRP preparation methods are highly variable and yield a range of products: plasma rich in growth factors (PRGF), platelet-rich plasma and growth factors (PRPGF), platelet-poor plasma (PPP), leukocyte-rich platelet-rich plasma (LR-PRP), leukocyte-poor, platelet-rich plasma (LP-PRP). In ophthalmology, PRP has been used conventionally, *i.e.*, platelet concentration is achieved with centrifugation, as well as PRGF where, in addition to the platelet concentration, degranulation is induced to release growth factors without containing leukocytes, as described by Anitua et al.[12] However, according to the literature, similar preparations are grouped under different terms. This review respects the terminology used by the authors of referenced studies.

Table 1 – Comparison of tear and serum composition.[11,13,56]

	Tear	Serum
pH	7.4	7.4
Osmolarity (mOsm/l)	298	296
EGF (ng ml^{-1})	0.2–0.3 (13), 1.9–9.7 (4)	0.5
TGF-β (ng ml^{-1})	2–10	6–33
Vitamin A (mg ml^{-1})	0.02	46
Fibronectin (μg ml^{-1})	21	205
Lisozyme (mg ml^{-1})	1.4	6
SIgA (μg ml^{-1})	1190	2
IGF-I (ng ml^{-1})	157	
PS (ng ml^{-1})	0.157	0.071
NGF (pg ml^{-1})	468	54

EGF: epidermic growth factor; IGF-I: insulin-like growth factor; NGF: nerve growth factor; SIgA: surface immunoglobulin A; PS: P substance; TGF-β: transforming growth factor β.