

Topical vs subconjunctival application of regenerative factor-rich plasma for chemical eye burns: a comparative study

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RECEIVED:

14-2-2012

ACCEPTED:

8-8-2012

CONFLICT OF INTEREST:

The authors declare no conflict of interest in relation with the present article.

We assess the efficacy of subconjunctival and topical application of regenerative factor-rich plasma (RFRP) for chemical eye burns. Fifteen eyes with chemical burns in 15 patients distributed in 3 groups were treated. One group received routine care (control group), another received routine care plus topical RFRP application, and another received routine care plus subconjunctival RFRP application. Clinical course and time until definitive cure. Were analyzed times until a definitive cure and corneal and conjunctival epithelization in the groups receiving RFRP application (either topical or subconjunctival) were shorter than the times in the control group. We conclude that RFRP application, whether topical or subconjunctival, is an effective, uncomplicated, and economical treatment for eye burns from caustic chemicals. [Emergencias 2013;25:393-396]

Keywords: Emergency health services. Eye burns. Eye surface. Regenerative factor-rich plasma. Regenerative medicine.

Introduction

Eye burns are a leading causes of emergency care in ophthalmology and chemical eye burn is the most common cause of occupational non-penetrating trauma with great socio-economic impact and morbidity¹. The objective of treatment is to achieve rapid corneal and conjunctival re-epithelization with the least possible permanent damage.

The limited effectiveness of commercial products has led to experimentation with body fluids such as blood² or its derivatives³, and autologous serum, which facilitate epithelial regeneration⁴. Similarly, the application of certain fractions of serum and plasma favors cell growth⁵, and platelet concentrate and plasma rich in growth factors (PRGF) have been used⁶. In addition to platelets, plasma contains other factors favoring migration, growth and cell differentiation, such as fibronectin, vitamin A or neuropeptides⁷. Therefore, previous techniques have been improved with the inclusion of all of these elements to cre-

ate PRGF, with proven effectiveness^{8,9} and advantage over auto-hemotherapy¹⁰. It is unnecessary to activate it to make it effective as with other solutions⁶; it avoids the risks of disease transmission; it can be prepared immediately anywhere; It has antigenic effects and is a very low-cost therapy. Our aim was to confirm the efficacy of treatment with PRGF in eye burns and determine whether there are differences in the various forms of use, such as subconjunctival and topical application.

Method

We studied 15 eyes of 15 men attended in the emergency department (ED) for chemical eye burn, due to accidents at work, with the same degree of injury: corneal limbar involvement at 2-3 o'clock and 20-30% conjunctival lesion. After scheduled treatment, clinical follow-up to complete recovery was performed. Patients were enrolled consecutively and assigned to each group according to order of arrival: first we recruited for

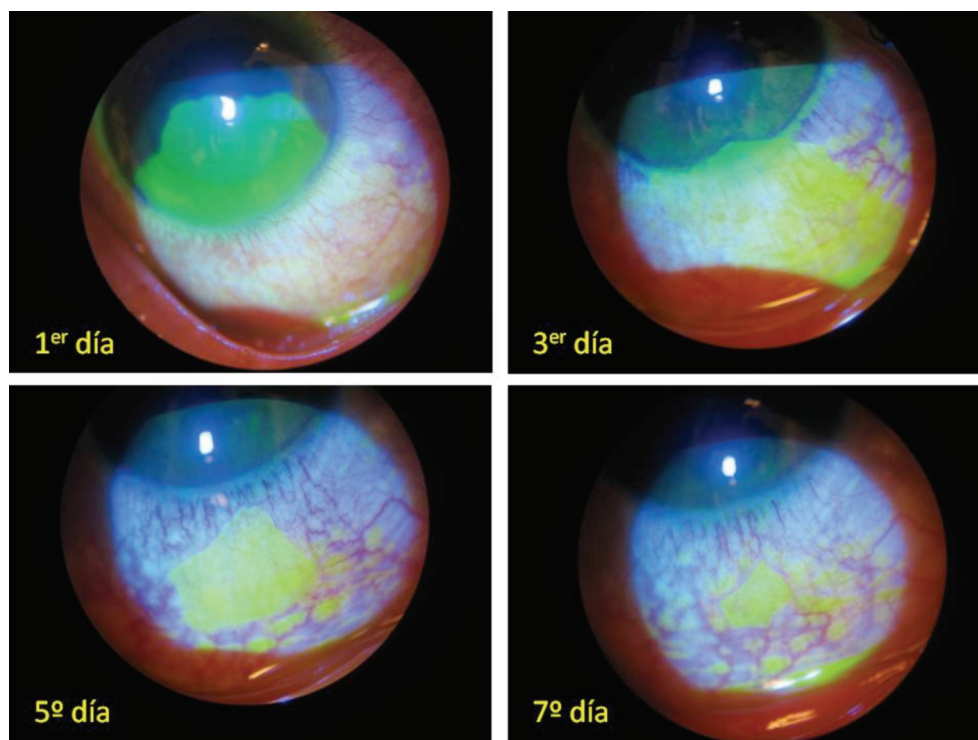


Figure 1. Alkaline chemical burn of the cornea and conjunctiva, treated with topical regenerative plasma rich in growth factors.

the classical treatment group, then for the classical plus topical PRGF treatment group and, finally, for the classical plus subconjunctival treatment group. The results were analyzed only after the last patient concluded the study treatment. The study was approved by the Clinical Ethics Commission and was conducted in accordance with the Helsinki protocol.

The patients were divided into three groups according to treatment received: to) Group 1 or control: 5 patients with conventional medical treatment; (b) Group 2: 5 patients with conventional medical treatment plus topical PRGF; (c) Group 3: 5 patients with conventional medical treatment plus subconjunctival PRGF infiltration.

We performed a prospective comparative study including duration of attention time, time to corneal and conjunctival healing, keratitis, healing time of the process (TC), complications and sequelae. All patients had had an eye wash with water within a minute after the accident.

Conventional medical treatment was: washing with physiological saline and cleaning with a swab, eye drops of 1 mg dexamethasone and 1 drop/6 h 3 mg tobramycin; 10,000 IU retinol + gentamycin ointment, sulfate 3 mg + DL-methionine 5 mg/6 h.

The following protocol was used in both

groups treated with PRGF: first detailed information was given and signed informed consent obtained; second, RFRP was obtained, after extraction of 20 cc peripheral blood in 4.5 ml test tubes with 3.5 ml sodium citrate. In addition, blood was extracted for blood count and complete biochemistry, hepatitis B, C and HIV tests. The tubes were centrifuged (at 2,100 rpm and 7') and the plasma was separated into fractions.

For the subconjunctival treatment we used fraction I of plasma, 200-500 MI (0.2-0.5 cc) immediately above the red series. After application of 1 anesthetic eye drop/3'/3 times, 1 cc of PRGF was infiltrated under the bulbar conjunctiva. Antibiotic ointment + anti-inflammatory eye drops were applied followed by 24 h occlusion. For topical treatment we used the 3 fractions of plasma placed in 5cc opaque sterile bottles, handed to the patient with indications on form of conservation, manipulation and application (1 drop/6 times a day).

For clinical evaluation we used slit-lamp biomicroscopy with or without fluorescein staining and the subjective description of symptoms by the patient. To quantify the degree of burn, Dua classification was used¹¹, with the eye divided into sectors. The patients were reviewed periodically until complete recovery.

Data were recorded on an Excel sheet and

statistical analysis was performed using IBM-SPSS version 19. The results are expressed as means and standard deviation; Shapiro-Wilk test was used to assess distribution, and parametric tests (Mann-Whitney U and Kruskal-Wallis) were used to compare non-normally distributed variables.

Results

The results are summarized in Tables 1 and 2. All patients were similar in terms of sex, type of chemical, degree of injury and initial cleaning time (Table 1).

On analyzing the three groups together there were no statistical differences regarding age, eye, and time taken to reach the hospital, but the rest of the variables showed differences. Studied two by two, there were statistical differences in all the variables between the classic treatment and the subconjunctival groups, except for keratitis. There were statistical differences between the classical and the topical treatment groups for all the variables and between the subconjunctival and topical treatment groups. The subconjunctival group showed faster healing time, but not significantly so (Table 2).

In all 5 eyes treated with subconjunctival PRGF, chemosis had disappeared within 24 hours; three patients (60%) reported transient itching after infiltration; two (40%) had a small subconjunctival deposit at the point of infiltration which disappeared at 6 days. In terms of sequelae, only one control group patient showed slight astigmatism (0.75 dp) which resolved at 6 months.

Discussion

Although endogenous growth factors act in ocular cell repair processes, the exogenous application of these factors can accelerate healing of the cornea¹², although with technical difficulties and costs¹³. The PRGF technique aims to circumvent these limitations.

In our study, the duration of healing time and epithelialization of the cornea and the conjunctiva was halved using subconjunctival PRGF treatment; and in keratitis when we used the topical treatment. While topical treatment seemed more effective than subconjunctival PRGF for keratitis, the opposite occurred for the remaining variables, although not significantly so. This could be due to limited duration of the effect of subconjunctival PRGF infiltration, estimated at one week. Therefore we would recommend repeated infiltration after a week or complement the infiltration with topical application of PRGF^{12,14}. The presence of a small conjunctival elevation following subconjunctival treatment is due to PRGF deposits that should prolong the effect of such treatment. In addition, chemosis after infiltration promotes conjunctival distention and prevents symblepharon.

Both topical and subconjunctival PRGF improves epithelialization of corneal-conjunctival lesions⁸ and eye burns⁹ and accelerates the integration of eye transplants⁸, among other effects.

The present study confirmed that topical and subconjunctival PRGF treatment accelerates healing of corneal and conjunctival lesions in cases of eye burn, and that PRGF is a simple, economical, effective treatment without any undesirable side effects.

Table 1. Characteristics of the patients studied

Nº	Age	Sex	Eye	Caustic agent	Treat (minutes)	TH (hours)	t PRGF (days)	CHt (days)	CJHt (days)	KHt (days)	LHt
1º	47	V	I	cement	CLA	60	---	6	6	6	8
2º	28	V	D	degreaser	CLA	30	---	7	7	0	9
3º	28	V	I	chalk	CLA	50	---	4	8	8	13
4º	30	V	D	caustic soda	CLA	35	---	7	7	10	7
5º	19	V	I	solvent	CLA	60	---	11	12	12	11
6º	26	V	I	stucco	SUB	60	24	3	6	0	6
7º	27	V	I	solvent	SUB	180	2	4	4	0	4
8º	32	V	I	cement	SUB	60	10	2	4	5	7
9º	35	V	D	caustic soda	SUB	35	2	3	6	7	6
10º	41	V	D	detergent	SUB	35	1	1	2	0	3
11º	42	V	D	chalk	TOP	60	3	5	6	5	6
12º	30	V	D	plaster	TOP	60	3	3	4	5	3
13º	34	V	I	caustic	TOP	60	12	3	4	4	5
14º	49	V	I	caustic	TOP	60	20	5	4	5	9
15º	33	V	D	detergent	TOP	35	1	4	6	0	7

M: male; R: right; L: left; Treat: type of treatment applied in hospital; CLA: classical treatment; SUB: subconjunctival treatment with plasma rich in growth factors (PRGF); TOP: topical PRGF treatment; T-t: time to first hospital treatment and initiation of classical medical treatment; t PRGF: time elapsed until initiating treatment with PRGF; CHt: corneal healing time; CJHt: conjunctiva healing time; KHt: keratitis healing time; LHt: lesion healing time.

Table 2. Descriptive results and statistical comparison between groups

Groups	Age Mean (SD)	FHt Mean (SD)	COR Mean (SD)	Cjep Mean (SD)	KHt Mean (SD)	t-H (minutes) Median (25-75)
Total patients	32 (8)	6.93 (2.7)	4.5 (2.4)	5.29 (1.63)	6.70 (2.58)	
Patients of G 1	26 (5)	9.60 (2.4)	7 (2.5)	7 (0.81)	9 (2.58)	50 (32-60)
Patients of G 2	38 (8)	6 (2.2)*	4 (1)*	4.8 (1.09)*	4.75 (0.5)*	60 (35-120)
Patients of G 3	32 (6)	5.20 (1.6)*	2.6 (1.1)*	4.40 (1.67)*	6 (1.41)	60 (47-60)

G 1: Conventional treatment group; G 2: topical PRGF group; G 3: subconjunctival PRGF group; FHt: final healing time; SD: standard deviation; COR: corneal epithelialization time (days); CJ: conjunctiva epithelialization time (days); KHt: keratitis healing time (days) time; t-H: time to hospital arrival [median (P25-75)], in minutes.

References

- Nicaeus T, Erb C, Rohrbach M, Thiel HJ. An Analysis of 148 outpatient treated occupational accidents. *Klin Monatsbl Augenheilkd*. 1996;209:A7-11.
- Lenkiewicz E, Ferencowa A, Szewczykowa E. Subconjunctival autologous serum application in the treatment of neurotrophic keratopathy. *Ophthalmology*. 2004;111:1115-20.
- Hartwig D, Herminghaus P, Wedel T, Liu L, Schlenke P, Dibbelt L, et al. Topical treatment of ocular surface defects: comparison of epithelialization capacity of fresh frozen plasma and serum on corneal epithelial cells in an in vitro cell culture model. *Transfus Med*. 2005;15:107-13.
- Alio JL, Pastor S, Ruiz-Colecha J, Rodríguez A, Artola A. Treatment of ocular surface syndrome after LASIK with autologous platelet-rich plasma. *J Refract Surg*. 2007;23:617-9.
- Nakamura M, Kawahara M, Morishige N, Chikama T, Nakata K, Nishida T, et al. Promotion of corneal epithelial wound healing in diabetic rats by the combination of a substance P-derived peptide with (FGLM-NH2) and insulin-like growth factor-1. *Diabetologia*. 2003;46:839-42.
- Márquez de Aracena R, Montero de Espinosa I, Muñoz M, Pereira G, Martín F. Tratamiento con concentrado plaquetario plasmático subconjuntival y tópico en el trasplante de limbo. *Mapfre Medicina*. 2006;17:280-5.
- Márquez de Aracena R, Montero de Espinosa I, Muñoz M, Pereira G. Aplicación subconjuntival de concentrado de plaquetas plasmáticas en el tratamiento de quemaduras oculares. Resultados preliminares. *Arch Soc Esp Oftalmol*. 2007;82:475-82.
- Márquez de Aracena R, Montero de Espinosa I. Subconjunctival application of regenerative factor-rich plasma for the treatment of ocular alkali burns. *Eur J Ophthalmol*. 2009;19:909-15.
- Dua HS, King AJ, Joseph A. A new classification of ocular surface burns. *Br J Ophthalmol*. 2001;85:1379-83.
- Liu L, Li YP, Huang SQ, Lin JX, Zhang WX. Mechanism of keratinocyte growth factor-2 accelerating corneal epithelial wound healing on rabbit alkali burned cornea. *Zhonghua Yan Ke Za Zhi*. 2005;41:364-8.
- Daniele S, Gilbard JP, Schepens CL. Treatment of persistent epithelial defects in neurotrophic keratitis with epidermal growth factor: a preliminary open study. *Graefes Arch Clin Exp Ophthalmol*. 1992;30:314-7.
- Mathers WD, Sherman M, Fryczkowski A, Jester JV. Dose-dependent effects of epidermal growth factor on corneal wound healing. *Invest Ophthalmol Vis Sci*. 1989;30:2403-6.

Tratamiento de las quemaduras oculares por productos químicos mediante aplicación tópica y subconjuntival de plasma rico en factores regeneradores. Estudio comparativo

Márquez de Aracena R

Estudio de la aplicación subconjuntival y tópica de plasma rico en factores regeneradores (PRFR) en pacientes con quemaduras oculares por productos químicos. Se analizaron 15 ojos de 15 pacientes con quemaduras químicas oculares. Se dividieron en tres grupos: uno de control con tratamiento médico clásico; otro con tratamiento médico clásico y tópico de PRFR y un tercero, con tratamiento médico clásico e infiltración subconjuntival de PRFR. Se estudió la evolución clínica de las lesiones y tiempo hasta su curación final. En los grupos con PRFR tópico y subconjuntival hubo un acortamiento de los días de curación frente al grupo control, que fueron significativos para las variables tiempo de curación final, epitelización de córnea y conjuntiva. Podemos considerar la aplicación tópica y subconjuntival de PRFR como un tratamiento eficaz, sencillo y económico en el tratamiento de las causticaciones de la superficie ocular. [Emergencias 2013;25:393-396]

Palabras clave: Urgencias. Quemaduras oculares. Plasma. Medicina regenerativa. Superficie ocular. Plasma rico en factores regeneradores.