Effect of Platelet rich plasma on healing of corneal wound

Experimental study

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Introduction

Trauma or disease may cause haze in the cornea through myofibroblast-mediated wound healing activity, leading to visual impairment. *

* (Wilson, 2012)
• Corneal lesions present pathological responses usually associated with loss of transparency, especially in the absence of appropriate therapy.*

* Gigler et al, 2007

Corneal wound healing is comprised of a cascade of events.*

Keratocyte apoptosis
Keratocyte proliferation & migration
Myofibroblast Accumulation
Inflammatory cell infiltration
Stromal remodeling
Myofibroblast apoptosis

* Mohan et al, 2001
Introduction

- **Myofibroblast apoptosis** has an important role in the regulation of corneal haze through the removal of the cellular contribution to the opacity.

* (Wilson et al, 2007)

Introduction

**Platelet-rich plasma (PRP)** has been widely used in a variety of clinical applications as:

- Oral and maxillofacial surgery
- Orthopedic surgery
- Soft tissue diseases & burns
- Hard-to-heal wounds

Introduction

- The effectiveness of PRP is based on its high level of growth factors such as:
  - Platelet-derived growth factor (PDGF),
  - Vascular endothelial growth factor (VEGF)
  - Transforming growth factor (TGF), & others.

- These growth factors are important in modulating cell migration and proliferation during the healing process. *

* (Alsousou et al, 2013 and Foster et al, 2009)

Introduction

- **In ophthalmology:**
  Many studies has demonstrated the role of PRP in:
  - Moderate to severe dry eye
  - Persistent epithelial corneal defect
  - Recurrent corneal erosion
  - Neurotrophic keratopathy
  - Superior limbic keratoconjunctivitis
  - Graft–versus–host disease
  - Post–LASIK Ocular surface syndrome
  - Others;

* (Alsousou et al, 2013 and Foster et al, 2009)
Use of PRP in Dry Eye.

In 2007, Alio et al. demonstrated that the use of autologous PRP is very effective in 80% of patients suffering from dry eye symptoms, improving both patient satisfaction and ocular surface syndrome. (on 36 eyes)

Another study (2011) demonstrated that PRP can be used in the treatment of severe dry eye in patients with different etiopathologies such as Sjogren’s Syndrome.

Ribeiro et. al. (2016) analyzed the efficacy of PRP treatment in 12 diabetic patients. The results showed improvement in 100% of patients in relation to symptoms & regarding Schirmer’s test.
In 2017, Another study performed with larger number of subjects (N=368)

Use of PRP in persistent epithelial defect.
The effect of PRP on PEDs was evaluated by means of a prospective study in 20 eyes

Results showed full recovery of the epithelial defect in 85% of cases (17 of 20 eyes). The tolerance to PRGF eye drops treatment was good in 95% of cases (19 of 20). Only one case showed discomfort to PRP treatment showing redness and itching.
Use of PRP in RCE

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Autologous Platelet-rich Plasma Eye Drops in the Treatment of Recurrent Corneal Erosions

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Conclusions
The use of PRP eye drops for the treatment of RCE was shown to be effective in reducing the recurrence rate without any significant complications.

Neurotrophic ulcer

In 2011, a study showed, in a case report, the use of solid PRP associated to Tutopatch® (a biological membrane obtained from bovine pericardium) as a protection in a case of progressive neurotrophic corneal ulcer that did not respond to any treatment including AMT.

Treatment of a neurotrophic corneal ulcer with solid platelet-rich plasma and Tutopatch®

V.J. Ortuno-Prados,* J.L. Alio

ARCH SOC ESP OFTALMOL. 2011;86(4):121-123

DISCUSSION: We found this form of treatment very effective for progressive ulcers. Tutopatch® may constitute an alternative to amniotic membrane transplantation.
Use of PRP post LASIK OSS:

Methods:
This prospective interventional consecutive clinical study include 156 eyes of 80 patients affected by post-LASIK chronic OSS who were treated with autologous E-PRP 6 times a day as monotherapy for 6 weeks.

Conclusion:
Monotherapy with autologous E-PRP is a well-tolerated, safe, and effective treatment for the management of post-LASIK ocular surface syndrome.

Other applications:

- Treatment of macular hole
- Amniotic membrane transplantation combined with clot of platelet-rich plasma in cases of corneal perforation
- In Vivo lamellar keratoplasty using PRP as bioadhesive
Complications:

- Frequent blood extractions, mainly in the groups requiring prolonged treatment.
- Peripheral corneal infiltrate and ulcer
- Eyelid eczema
- Microbial keratitis especially in patients with an epithelial defect
- Increased discomfort or epitheliopathy
- Scleral vasculitis and melting

The above complications are rare.
Aim of the work

- Studying the *histopathological* effect of platelet rich plasma on repair of corneal wound.

Materials & Methods
Study included:

• 10 adult male Albino rabbits, weighing 2.0 – 4.0 Kg.
• The animal procedure was performed in accordance with guidelines for ethical conduct in care and use of animals.

Materials & Methods

The study is Interventional Experimental carried at animal lab of Medical studies & research institute, Alexandria.

Introduction

Experimental design

Rabbits divided into two main groups;

<table>
<thead>
<tr>
<th>Control Group</th>
<th>PRP treated group</th>
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<tbody>
<tr>
<td>Five rabbits</td>
<td>Five rabbits which had corneal wound in left eye*</td>
</tr>
<tr>
<td>Corneal wound, left eye *</td>
<td>single dose of subconjunctival autologous PRP</td>
</tr>
<tr>
<td>Allowed for wound repair</td>
<td></td>
</tr>
<tr>
<td>Received no treatment</td>
<td></td>
</tr>
</tbody>
</table>

* The right eye is kept normal and studied for normal Histology
Materials & Methods

Blood sampling and platelet rich plasma preparation

• Aspiration of 5 ml of rabbit blood through ear central vein, mixed with 3.8% sodium citrate.

* Maria et al, 2010
1. **Marking:**
   The center of the cornea was marked using a 7-mm trepan blue stained Ring.
Surgical procedure

2. De-epithelialization
Corneal epithelium in the marked area was removed using a knife.

Materials & Methods

Surgical procedure

3. Stromal injury:
- 27-gauge needle was used to make four incisions in the central corneal stroma forming crossed pair of parallel horizontal and vertical incisions.
PRP treated group received a single dose of subconjunctival autologous PRP.

A total of 0.5 ml PRP was injected into the superior conjunctival fornix using 1-mL syringe.

Other rabbits received no treatment and assigned as control group.

*Tanidir et al, 2010..
Materials & Methods

Histopathological examination

• Rabbit eye Excised after 7 days and fixed in 10% formalin.
• The paraffin sections were prepared and cut.
• The sections then were stained with H & E and Masson's trichrome and studied for histopathological changes.
• Also electron microscopy was done for each of the groups.

Results
Results

• **Gross Picture**

Naked eye examination of cornea reveals that treated group had clear cornea while control group present central unclearity representing delayed healing

Control Group

PRP Treated Group

Results

**Histological examination**

• **Normal cornea (H&E)**

Close to Human

Intact Epithelium

Uniform arrangement of Collagen

Right eye H & E X 200
Results

Microscopic Picture

- Corneal injury (H&E)

Absence of Epithelium
Stromal Wound

Left eye H & E X 100

Results

Histopathological examination

Healing (H & E)

Control Group
PRP Treated Group

(Both Photos) Left eye H & E X 100
Results

Histopathological examination

**Low Power (H & E)**

Control Group  PRP Treated Group

(Both Photos) Left eye H & E X25

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Results

Histopathological examination

**High Power (H & E)**

Control Group  PRP Treated Group

Left eye H & E X100
Results

Histological examination
Normal cornea (Masson’s Trichrome)

Microscopic Picture
• Corneal injury (Masson)

Absence of Epithelium
Stromal Wound
Results

Histopathological examination

Low Power (Masson)

Control Group  
PRP Treated Group

Left eye Masson’s X 25

Results

Histopathological examination

High Power (Masson)

Control Group  
PRP Treated Group

Left eye Masson’s X 100
Results

Histopathological examination

Control Group  |  EM  |  PRP Treated Group

Conclusion
Conclusion

There is microscopic evidence of improvement of healing of corneal wound with use of PRP in the form of:

- Rapid Regular epithelial healing.
- Better remodeling of stroma with decreased population of cells & uniform arrangement of collagen bundle.