

***ROLE OF PLATELET DERIVED GROWTH
FACTOR IN CORNEAL
HEALING***

Thesis

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In Ophthalmology**

By

**Tamer Hassan El-Sersy
(M.B.,B.Ch.,M.Sc.)**

Under The Supervision Of

***Professor Dr. Amira Mohammed Mounir*
Professor of Ophthalmology
Ain Shams University**

***Professor Dr. Mamdouh Hamdy El-Kafrawy*
Professor of Ophthalmology
Ain Shams University**

***Professor Dr. Rafik Mohammed El- Ghazzawy*
Professor of Ophthalmology
Ain Shams University**

***Professor Dr. Sanaa Abd El-Maged Sammour*
Professor of Histopathology
Ain Shams University**

***Dr. Manal Fawzy Ghazlan*
Assistant Professor of Clinical Pathology
Ain Shams University**

**Faculty of Medicine
Ain Shams University
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الطبيب/ تامر حسن السرسى
تحت اشراف

الاستاذ الدكتور/ اميره محمد منير
استاذ طب و جراحة العيون
كلية الطب- جامعة عين شمس

الاستاذ الدكتور/ ممدوح حمدى الكفراوى
استاذ طب و جراحة العيون
كلية الطب- جامعة عين شمس

الاستاذ الدكتور/ رفيق محمد الغزاوى
استاذ طب و جراحة العيون
كلية الطب- جامعة عين شمس

الاستاذ الدكتور/ سناء عبد الماجد سمور
استاذ الباثولوجى
كلية الطب- جامعة عين شمس

دكتور/ منال فوزى غزلان
استاذ مساعد الباثولوجيا الاكلينيكيه
كلية الطب- جامعة عين شمس

كلية الطب
جامعة عين شمس
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LIST OF ABBREVIATIONS

bFGF	basic Fibroblast growth factor
BMP	Bone morphogenic protein
C3	Complement type 3
cAMP	cyclic Adenosine mono phosphate
CCLRU	Cornea and Contact lens Research
CNS	Central nervous system
CSF-1	Colony stimulating factor-1
EGF	Epidermal growth factor
FN	Fibronectin
GC	Glucocorticoid
HGF	Hepatocyte growth factor
HSV	Herpes Simplex Virus
HZO	Herpes Zoster Ophthalmicus
Ig	Immunoglobulin
IGF	Insulin Growth Factor
IL-1	Interleukin-1
IL-6	Interleukin-6
KGF	Keratinocyte growth factor
MALT	Mucosal Associated Lymphoid
MMP	Matrix metalloproteinases
PAP	PDGF-associated protein
PDGF	Platelet derived growth factor
PKC	Protein kinase C
	proteinases
SCF	Stem cell factor
SPE	Sis proximal element
TGF	Transforming growth factor
TIMP	Tissue inhibitors of metallo-
	Tissue
TNF	Tumour necrosis factor
	Unit
US	United States
VEGF	Vascular endothelial growth factor
VZV	Varicella-Zoster Virus

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AIM OF WORK

AIM OF WORK

Clinical evaluation of the rate of corneal healing under the effect of Platelet Derived Growth Factor, together with histopathological examination of the corneal tissues of the experimental animals.

CONCLUSION & RECOMMENDATION

Our study included both human and animal studies and was targeted to evaluate the role of PDGF in the healing of resistant infective and non-infective corneal ulcers.

The animal study was done to endorse our clinically based study through histopathological examination of the rabbits corneas.

The human study showed the following facts:

Although there was a statistically significant difference in ulcer size between the infective and non-infective groups at the beginning of the study, however, by the end of the study we found this difference did not influence the response of both groups to the PDGF.

Concerning both the infective and non-infective groups:

There was a highly statistically significant decrease in ulcer size during the first week of the study. The size reduction continued during the second week, however, during the period extending along the third and fourth weeks there was no statistical difference in size reduction in both the infective and non-infective groups. Also there was no regression in the healing of the corneal ulcer in the last two weeks of the study (i.e. a relatively stationary course in the last two weeks).

From this we can deduce that the maximal effect of PDGF occurs during the first week of therapy and it continues till the second week thereafter no change will occur denoting that the followup period for the improvement can be restricted to two weeks only.

The animal study showed the following facts:

There marked difference in the rate of epithelization in the first week being more rapid with the use of PDGF in both the infective and non-infective eyes.

By the end of the second week there complete epithelization of all eyes with or without PDGF.

From this we can deduce that the maximum effect of PDGF on epithelial healing occurs during the first week of therapy regardless of the nature of the ulcer.

Concerning vascularization, there is decreased vascularization in the eyes receiving PDGF in the first week with equal mild vascularization by the second week of the study. There is earlier disappearance of vascularization in the eyes Receiving PDGF.

Thus it is safe to say that PDGF decreases initial vascularization of the ulcer and also promote early regression of the vascularization.

There was not a statistically significant impact of PDGF on stromal infiltration.

As regards stromal fibrosis, there was a statistically significant difference in the degree of fibrosis being more in the eyes receiving PDGF. This endorses the possibility of presence of chemtactic properties of PDGF attracting fibroblasts to the ulcer site.

As regards stromal hyalinization, there was a statistically significant difference in the degree of hyalinization denoting that PDGF promotes stromal hyalinization.

INTRODUCTION

Throughout the 1980's, the focal point of wound healing knowledge was the role of tissue oxygenation. Today, however, the focal point of an expanding knowledge base are the identification, understanding, and now the means to use growth factors to enhance wound healing (**Andresen et al., 1997**).

The mechanism of corneal wound healing has not been clarified yet. However, evidence has accumulated that various kinds of growth factors such as epidermal growth factor (EGF), fibroblast growth factor (FGF), transforming growth factor (TGF) and platelet derived growth factor (PDGF) play a key role in corneal wound healing. For example, these factors are expressed in corneal epithelial cells, keratocytes and endothelial cells, and their receptors are expressed in the corneal cells. Thus these growth factors function in the regulation of corneal cell proliferation and in the maintenance of corneal transparency (**Imanishi et al., 2000**).

PDGF is a glycoprotein with a molecular mass of approximately 30 kd. Although it is the primary growth factor in platelets, it is also synthesized and secreted by other cells, such as macrophages and endothelial cells (**Tsubota et al., 1999**).

Platelets are concentrated in a small volume of plasma to form platelet rich plasma (PRP). If thrombin and calcium are added to the PRP, the platelets are activated to release their content, including PDGF. The thrombin and calcium also initiate clotting, including the conversion of fibrinogen to fibrin, resulting in a clinically useful platelet-rich gel (**Andresen and Ehlers, 1998**).