EXPERIMENTAL INDUCTION OF POSTERIOR VITREOUS DETACHMENT BY INTRAVITREAL INJECTION OF HYALURONIDASE AND PLASMIN

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"وَقُل رَّبِّ زِدْنِي عِلماً"

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ABSTRACT

***Title*:** Experimental induction of posterior vitreous detachment by intravitreal injection of hyaluronidase and plasmin.

***Aim*:** To study and compare the effect of both hyaluronidase and plasmin in induction of posterior vitreous detachment (PVD) and vitreous liquefaction in rabbits.

***Subjets and Methods* :** The study was performed on 40 white New Zealand rabbits .Twenty rabbits had one eye injected with hyaluronidase (20 IU/ 0.1 ml) .The other 20 rabbits had one eye injected with plasmin (1 IU /0.1 ml). The fellow eye of all rabbits was injected with lactated Ringer's solution as a control . The specimens were examined after 2 and 4 weeks of injection using light microscopy and scanning electron microscopy .

***Results*:** The control eye of all rabbits revealed no histopathological changes. Group A (2 weeks after hyaluronidase injection) revealed no histopathological changes resembling the control group. Group B (4 weeks after hyaluronidase injection) revealed partial PVD in 70% of cases and no effect on the rest of cases with disorganization of photoreceptors in 30% of cases. Group C (2 weeks after plasmin injection) revealed partial PVD in 80% of cases and no effect in the rest of cases with no disorganization of photoreceptors . Group D (4 weeks after plasmin injection) revealed total PVD in 80% of cases and partial PVD in the rest 20% of cases with no photoreceptors disorganization. No retinal hemorrhage or oedema were detected in any group.

***Conclusion*:** The safety of intravitreal hyaluronidase and plasmin in induction of PVD has given encouraging results .The duration factor

plays an important role in their effect with more effect in having longer duration of action . Plasmin ,however, is more effective than hyaluronidase in PVD induction inspite of having lower concentration in the same duration of action .

KEY WORDS

Hyaluronidase, plasmin,intravitreal injection, posterior vitreous detachment, vitreous liquefaction, retinal toxicity, light microscopy, scanning electron microscopy

CONTENTS

List of Abbreviations

α_2-antiplasmin	:	Alpha 2-antiplasmin
AION	:	Anterior ischemic optic neuropathy.
APE	:	Autologous plasmin enzyme
APVD	:	Anomalous posterior vitreous detachment.
ATF	:	Amino terminal fragment
A II t	:	Annexin II tetramer
BSS	:	Balanced salt solution
Ca	:	Calcuim
cm	:	Centimeter
cc	:	Cubic centimeter
°C	:	Degree centigrade
D	:	Diopter
DLS	:	Dynamic light scattering
ECM	:	Extracellular matrix
EGF	:	Epidermal growth factor
ERG	:	Electroretinogram
G	:	Gauge
HS	:	Highly significant
H&E	:	Hematoxylin and eosin
ICG	:	Indocyanine green
ILM	:	Internal limiting membrane
IU	:	International unit
KDa	:	Kilodalton
LM	:	Light microscopy
mg/ kg	:	Milligram / kilogram
µ l	:	Microliter
ml	:	Milliliter

mm	:	Millimeter
µ m	:	Micrometer
MMPs	:	Matrix metalloproteinases .
Nd : YAG	:	Neodymium : yttrium – Aluminium – Garnet
nm	:	Nanometer
no.	:	Number
nPA	:	Lanoteplase plasminogen activator.
NS	:	Non significant
OCT	:	Optical coherence tomography
PAI- 1	:	Plasminogen activator inhibitor-1
PBS	:	Phosphate buffered saline
PHM	:	Posterior hyaloid membrane.
Pro-CB	:	Pro-cathepsin B
PRP	:	Panretinal photocoagulation
PVD	:	Posterior vitreous detachment
PVR	:	Proliferative vitreoretinopathy .
RAPD	:	Relative afferent pupillary defect.
RD	:	Retinal detachment
rPA	:	Reteplase plasminogen activators
SEM	:	Scanning electron microscopy
SPSS	:	Statistical package for the social science
TCF	:	Time correlation function
TNC	:	Tenascin C
TNK-tPA	:	Tenecteplaset - tissue plasminogen activator.
tPA	:	Tissue plasminogen activator.
UHR OCT	:	Ultraligh resolution optical coherence tomography
U-PA	:	Urokinase type –plasminogen activator

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INTRODUCTION

AND AIM OF THE WORK

Vitreous surgical procedures have been performed to relieve vitreoretinal tractions or adhesions to facilitate reattachment of a detached retina and to reduce retinal oedema . The level of difficulty of vitreous surgery depends on the presence or absence of PVD and the degree of adhesion between the vitreous body and the retina . **(Sebag , 1989).**

The techniques and instruments for vitreous surgery have greatly improved in recent years . However , the surgical removal of the vitreous cortex is still difficult in some patients and carries the risk for complications such as retinal breaks , retinal detachment , and retinal nerve fiber damage **(Han et al , 1998).**

Certain chemicals have been used to induce PVD and vitreolysis to facilitate vitreous surgery for better outcome or even to avoid vitrectomy **(Harooni et al , 1998).**

The enzymes used for Pharmacologic vitreolysis include : hyaluronidase **(Harroni et al., 1998),** plasmin **(Verstraeten et al., 1993),** dispase**(Tezel et al., 1998)**, chondroinase **(Bishop et al, 1999),** microplasmin **(Sebag,2005)**, collagenase**(Sebag,2005)**, nattokinase **(Takano et al ,2006)** tissue plasminogen activator**(Trese et al 2002)** and urokinase-type plasminogen activator**(Trese et al 2002).**

The goal of such pharmachological vitreolysis is to manipulate the vitreous collagen both centrally achieving liquefaction , as well as along the vitreoretinal surface to be able to achieve a cleavage plane cleaner than can be mechanically achieved currently , and to get a better anatomic results **(Trese, 2002) .**