Retinal toxicity of intravitreal drugs

Essay
Submitted for partial fulfillment
of master degree of ophthalmology

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List of abreviations

AIDS	Acquired immunodeficiency syndrome
AMB	Amphotericin B
AMBLC	Amphotericin B lipid complex
AMD	Age related macular degeneration
BAB	Blood-aqueous barrier
BRB	Blood retinal barrier
BRVO	Branch retinal vein occlusion
BSS	Balanced salt solution
CME	Cystoid macular edema
CMV	Cytomegalovirus
CMVR	Cytomegalovirus retinitis
CRVO	Central retinal vein occlusion
DHFR	Dihydrofolate reductase
DME	Diabetic macular edema
DNA	Deoxy ribonucliec acid
DR	Diabetic retinopathy Exudative age related macular
EAMD	degeneration
EC	Endothelial cell
EDTA	Ethylene diamine tetraacetic acid
ERG	Electroretinogram
ETDRS	Early Treatment Diabetic Retinopathy Study
ETROP	Early Treatment for Retinopathy of Prematurity
EVS	Endophthalmitis Vitrectomy Study
FA	Fluerescein Angiography
FDA	Food and Drug Administration
FEVR	Familial exudative vitreoretinopathy
F6H8	Perfluorohexy loctane
FLCZ	Fluconazole

5-FU	5-Fluorouracil
GCV	Ganciclovir
HIV	Human immunodeficiency virus
IC	Inhibitory concentration
ICG	Indocyanine green
ID50	Median infective dose
ILM	Internal limiting membrane
IOP	Intra ocular pressure
IVTA	Intravitreal Triamcinolone acetonide
L-AMB	Liposomal amphotericin B
LMWH	Low-molecular-weight heparins
MGC	Multinucleated giant cells.
MIC	Minimum inhibitory concentration
MMC	Mitomycin C
MMC-TA	Mitomycin C Triamcinolone conjugate
NADPH	Nicotinamide adenine dinucleotide phosphate
NEI	National Eye Institute
NVD	Neovascularization at the disc
NVE	Neovascularization elsewhere
OCT	Optical coherence tomography
PCL	Polycaprolactone
PDR	Proliferative diabetic retinopathy
PDT	Photodynamic therapy
PED	Pigment epithelial detachment
PEDF	Pigment epithelium derived factor
PFC	Perfluorocarbon liquids
PFD	Perfluorodecalin
PKC	Protein kinase C
PLA	Poly lactic acid
PLGA	Poly (lactide-co-glycolide acid)
PRP	Panretinal photocoagulation

PVR	Proliferative vitreoretinopathy
RA	Retinoic acid
RPE	Retinal pigment epithelium
RNA	Ribonucleic acid
SAILOR	Safety Assessment of Intravitreal Lucentis for AMD
SiO	Silicone oil
Sub-RPE	Subretinal pigment epithelium
TAAC	Triamcinolone acetonide
Tfr-rRA	Transferrin-ricin A chain toxin
TPA	Tissue plasminogen activator
VA	Visual acuity
VEGF	Vascular endothelial growth factor
VISION	VEGF Inhibition Study in Ocular Neovascularization

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Protocol

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Introduction

Avariety of systemic medications can generate retinal toxicity but fortunately, in the majority of cases the loss of visual function is minimal or reversible following discontinuation of the offending drug .However, in some cases, permenant or progressive visual loss may occur. Ocular toxicity may result from either over dose, chronicity of use, host susceptibility, or illegall abuse of medications. **(Blair JR, and Mierler WF,1995.)**

The concentration of various drugs in the vitreous after systemic administration as apercentage of concurrent serum concentrations is poor unless the eye is inflamed. The vitreous humour drug concentration can reach as high as 10% of the serum drug concentration. **(Ogden TE,1994.)**

Drug levels after sytemic administration are the result of a dynamic process in which many factors play a role, these include, the serum concentration, drug protein binding, the lipid solubility of the drug, the active transport of the drug across the blood ocular barrier which is formed by two main barriers ; the blood retinal barrier (BRB) and the blood aquous barrier(BAB) and also the presence or absence of inflammation or any condition which may alter the blood ocular barrier . **(Lesar TS, and Fiscilla RG,1985.)**

Intraocular drug penetration may be enhanced by increasing the systemically adminsterated dose.However,

increased systemic doses are often associated with significant side effects. **(Geroski DH, and Edelhauser HF,2001.)**

Because of the long delay in the drug delivery to the vitreoretinal compartement from systemic or subconjuctival injection, direct injection into the vitreal cavity (Intravitreal injections) is required, it provides the most direct approach for delivering drugs to the tissues of the posterior segment, and therapeutic tissue drug levels can be achieved. Intravitreal injections, however, have the inherent potential side effects of retinal detatchement, haemorrhage, endophthalmitis, and cataract. Repeated injections are frequentaly required,and they are notalways well tolerated by the patient. Since multiple intravitreal injections are traumatic to the patient , it is clear that means must be developed to sustain drug concentration in the vitreous cavity while minimizing its toxicity and enhancing its efficacy,These novel systems are called sustained release intravitreal implants. **(Velez G and Whitcup SM, 1999.)**

The possible danger of intravitreal injection has limited its use to conditions at which the eye is at high risk for considerable visual loss. These may include endophthalmitis, proliferative viteroretinopathy, tumors, and sever inflammation. The danger of injection may be somewhat overstated; it is probably safe when administerated carefully. **(Peyman GA, et al., 1992.)**