ORIGINAL ARTICLE

Topical insulin for healing of diabetic epithelial defects?: A retrospective review of corneal debridement during vitreoretinal surgery in Malaysian patients

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SUMMARY

Purpose: To investigate whether topical insulin improves healing rate of corneal epithelial erosions induced during vitreoretinal surgery in diabetics.

Methods: We retrospectively reviewed case notes and serial post-operative photographs of 15 eyes of 14 patients who had corneal epithelial debridement performed during various vitreoretinal surgeries to improve one surgeon's view over a 10 month period in 2010.

Results: Three groups were identified: DTI, comprising diabetics who received topical insulin 1 unit qds post-operatively (n=5); DCT comprising diabetics treated with conventional post-operative medications only (n=5) and NDCT comprising non diabetic patients on conventional post operative therapy (n=5). Only eyes in which the corneal epithelial defect had been serially photographed at time, t= 0, 12, 24, 36, 48, 60, 72 and 120 hours following commencement of topical medications were included. The size of the defect was calculated using local software. DTI eyes had a significantly smaller defect size at t= 24 (p=0.009), 36 (p=0.009), 48 (p=0.015) and 60 hours (p=0.005) compared to DCT eyes and had no statistical difference from NDCT eyes at all times in the Mann Whitney U analysis (p>0.05). In the diabetic operated bilaterally, the insulin treated eye re-epithelialised by 48 hours whereas fellow eye treated conventionally re-epithelialised in 72 hours.

Conclusions: Topical insulin or insulin eye drops 1 unit qds may be applied to the corneal surface to normalize the rate of healing of epithelial defects in diabetic patients undergoing epithelial debridement to improve the surgeon's view.

INTRODUCTION

Diabetic corneal epithelial erosions are hard to treat as the healing is impaired. Insulin is normally present in human tear film, and insulin receptors have been detected in the human ocular surface and cornea. The functions of insulin receptors within structures of the eye have not been fully investigated [1]. Corneal epithelial erosions in diabetic animal studies seem to respond to topical insulin [2].

Here we show that topical insulin or insulin eye drops may be safely and effectively applied to the corneal surface to normalize the rate of healing of epithelial defects in patients who have undergone epithelial debridement. Epithelial debridement during vitreoretinal surgery is routinely performed to improve the surgeon's view intraoperatively.

MATERIALS AND METHODS

The vitreoretinal surgical record from January 2010 to October 2010 at the Department of Ophthalmology, University Kebangsaan Malaysia Medical Centre (UKMMC), a tertiary referral center in the capital city of Kuala Lumpur, Malaysia, was traced. The operative record was extracted noting all patients who had received intraoperative corneal debridement to improve surgical view. Only patients who had been serially photographed post-operatively were included in the retrospective analysis.

Epithelial defects had been stained with sodium fluorescein using a digital camera (NIKON digital camera D3000 with magnification factor 1.5) in all eyes included in the study. Serial photographs had been taken at regular intervals of 0, 12, 24, 36, 48, 60, 72 and 120 hours after the postoperative eye drops were commenced until the defect closed whichever was earlier.

The photographs were downloaded into a computer. The surface area measurements of the epithelial defects were made using QISM (Quick Image System Measurement) software, invented by Mohammed Hanif bin Mohammed Saad from the Smart Engineering System Research Group, University Kebangsaan Malaysia. The software was able to calculate the size of the epithelial defect. This allowed the rate of healing or percentage of the original defect size to be quantitatively measured. Figure 1 shows the entrance of reference points into the QIMS software which enables plotting of the wound margin and automatic calculation of the wound surface area in mm^2. Statistical analysis was performed using IBM SPSS Statistics version 19 of the mean residual wound defined as a percentage of the size at time x hours and the mean wound size change in mm^2. Various statistical analyses including Mann-Whitney, multivariate analysis and post hoc analysis were performed.

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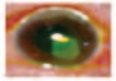
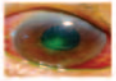
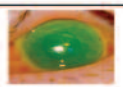
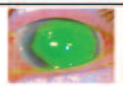
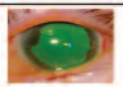
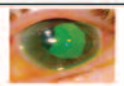
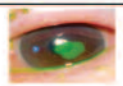
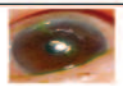
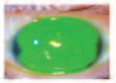
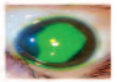
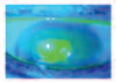
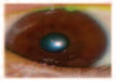
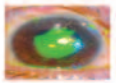
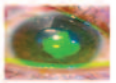
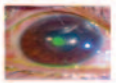
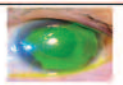
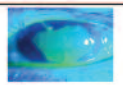
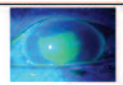
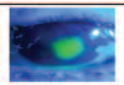
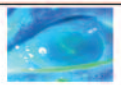
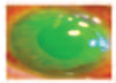
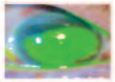
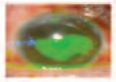
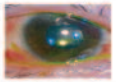
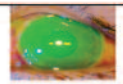
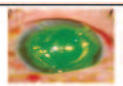
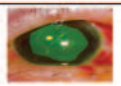
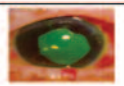
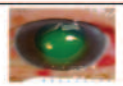
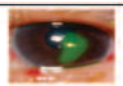
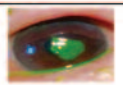
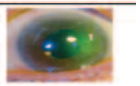
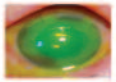
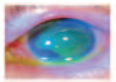
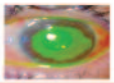
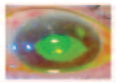
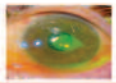
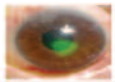
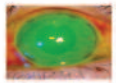
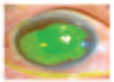
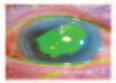
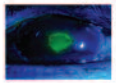
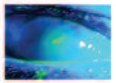
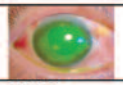
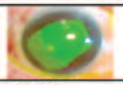
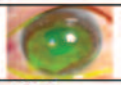
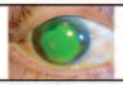
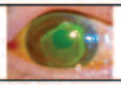
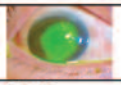
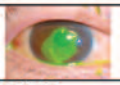
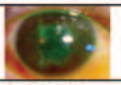
Table I: Demographical data of the subjects included in the study. The above table shows the 3 groups of subjects: DTI – group treated with topical insulin. DCT – group in which topical insulin was not given. NDCT – non diabetic group.

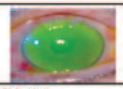
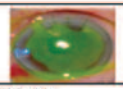
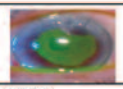
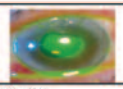
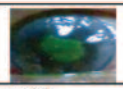
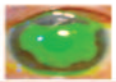
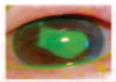
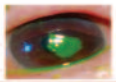
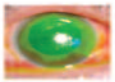
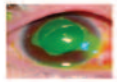
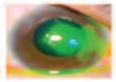
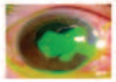
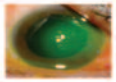
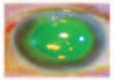
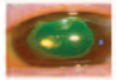
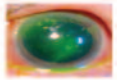
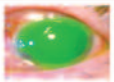
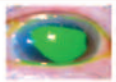
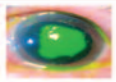
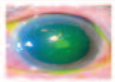
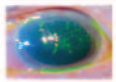
SUBJECTS	Eye no AND LATERALITY	AGE (YRS)	GENDER	Ethnicity	Duration of diabetes (years)	HbA1c (%)	Treatment for diabetes	OCULAR HISTORY	INDICATION FOR OP	DATE OF OP	PROCEDURE	POST OP MEDICATIONS and no of doses per 24 hours
Diabetic on topical insulin (DTI)												
A	1L	50	M	C	16	8.0	OHA	BE POAG DM NO DR	LE RRD	25.02.10	PPV/ HL/EL/CRYO/SIO	CLX 12 MXD 12
B	2L	63	F	C	25	8.8	INSULIN	BE PDR LASERED LE PSEUDOPHAKIA	LE VH	10.06.10	PPV / EL	CLX 12 MXD 12
C	3L	31	M	M	15	7.8	INSULIN	BE PDR LASERED	LE VH	24.06.10	PPV/ IVTA/ EL	CLX 12 MXD 12
D	4R	43	F	M	20	7.3	INSULIN	BE PDR LASERED	RE VH TRD	24.06.10	PPV/ PEA/ IOL	CLX 12 MXD 12
E	5L	58	M	C	15	7.0	OHA	BE PDR LASERED	LE COMBINED RRD & TRD	12.08.10	PPV/PEA/IOL/MP/EL/SIO	CLX 12 MXD 12 TML 2 APG 2
DM CONTROL (DCT)												
F	6R	53	F	C	10	8.2	INSULIN	RE PDR LASERED	TOTAL RD	25.02.10	PPV/ PEA/ HL/ SIO	CLX 12 MXD 12 TML 2 APG 2
G	7L	69	F	C	10	8.3	INSULIN	LE PDR LASERED	LE ERM	01.04.10	PPV/ PEA/ ILM PEELING/ EL/ IOL/ AIR	CLX 12 MXD 12
H	8R	63	M	M	20	6.9	OHA	POST PPV FOR RRD PSEUDOPHAKIA	SECONDARY GLAUCOMA	01.07.10	ECP VIA PARS PLANA	CLX 12 TML 12 APG 2
D	9L	43	F	M	20 (as above)	6.7	INSULIN	BE PDR LASERED RE POST PPV	LE VH TRD RRD	22.07.10	PPV/ PEA/ MP/ EL/ HL/ SIO/ IOL GA	CLX 12 MXD 12
I	10L	54	M	M	15	7.8	INSULIN	BE PDR	LE VH	23.09.10	PPV/ PEA/ EL/ IOL/ AIR / IOL LA	CLX 12 MXD 12
NON-DM CONTROL (NDCT)												
J	10L	60	M	C	NA	NA	NA	-	RRD	29.04.10	PPV / PEA / HL / C3F8 16%	CLX 12 MXD 12 TML 2 APG 2 OCMC 1

K	11R	68	M	C	NA	NA	NA	-	RRD	20.05.10	PPV / PEA / SF6 20%	CLX 12 MXD 12 TML 2 APG 2
L	12R	53	F	C	NA	NA	NA	MYOPIA ? AMBYLOPIA	RRD VH SUBLUXATED LENS	25.05.10	PPV / LENSECTOMY / HL / SIO	CLX 12 MXD 12 TML 2 APG 2
M	13R	57	F	C	NA	NA	NA	-	FTMH	17.06.10	PPV/ PEA/ ILM PEELING/ C3F8/ IOL	CLX 12 MXD 12
N	14L	59	M	C	NA	NA	NA	-	POST DISLOCATED LENS AND GRT	05.08.10	PPV / LENSECTOMY / HL/ SIO	CLX 12 MXD 12
Chi square Kruskal Wallis (p values)		0.367	0.799		0.775	0.334						

Legend:
Eye no and laterality: R- right eye; L- left eye
Gender: F- female; M-male
Ethnicity: C-Chinese; M-Malay
Duration of diabetes mellitus, HbA1c & treatment for diabetes: NA- not applicable
Ocular history: BE – both eyes; POAG – primary open angle glaucoma; DM- diabetes mellitus; DR – diabetic retinopathy; PDR- proliferative diabetic retinopathy; RRD- rhegmatogenous retinal detachment; PPV- pars planar vitrectomy
Indications for operation: VH – vitreous haemorrhage; RD- retinal detachment; TRD – tractional retinal detachment; ERM – epiretinal membrane; FTMH – full thickness macula hole; GRT – giant retinal tear (retinal tear > 3 clock hours of the retina)
Procedure: PPV – pars planar vitrectomy; PEA- phacoemulsification (small incision cataract surgery); HL- heavy liquid; SiO –silicone oil; EL- endolaser; ILM – internal limiting membrane; IOL – intraocular lens; ECP – endoscopic cyclophotocoagulation
Post-operative medications: CLX – ciprofloxacin HCl 0.3% (Ciloxan TM, Alcon); MXD – dexamethasone 0.1% (MaxidexTM, Alcon); TML – timolol maleate 0.5% (TimoptolTM, MSD); ALP – brimonidine tartrate 0.1% (Alphagan PTM, Allergan); OCMC – chloramphenicol eye ointment BP 1% w/w

GROUP &SUBJECTS	Eye no	Duration after first eye drop with corresponding size of epithelial defect in mm^2 and (as a percentage of original size (%))							
DTI	Time (Hours)	0	12	24	36	48	60	72	120
A	1								
		77.28 (100.0)	70.10 (90.7)	30.14 (39.0)	15.73 (20.4)	7.37 (9.53)	0.00 (0)		
B	2								
		67.19 (100.0)	45.58 (67.8)	33.35 (49.6)	19.40 (20.8)	11.4 (17.0)	0.00 (0)		
C	3								
		76.44 (100.0)	43.94 (57.5)	30.01 (39.3)	14.7 (19.2)	0.00 (0)			
D	4								
		45.68 (100.0)	25.40 (55.6)	8.11 (17.8)	2.21 (4.8)	0.00 (0)			
E	5								
		53.01 (100.0)	32.65 (61.6)	14.79 (27.9)	10.00 (18.9)	0.00 (0)			

SUBJECTS		0	12	24	36	48	60	72	120
DCT									
F	6								
		71.65 (100.0)	69.10 (96.4)	62.84 (87.7)	29.25 (40.8)	19.70 (27.5)	2.56 (3.75)	0.00 (0)	
G	7								
		62.20 (100.0)	52.04 (83.7)	37.97 (61.0)	26.90 (43.2)	16.00 (25.7)	9.84 (15.8)	6.73 (10.8)	0.00 (PEE only) (0)
H	8								
		59.48 (100.0)	44.37 (74.6)	33.55 (56.4)	19.57 (32.9)	8.40 (14.1)	5.75 (9.7)	0.00 (0)	
D	9								
		86.65 (100.0)	73.62 (85.0)	58.33 (73.9)	28.45 (32.8)	16.05 (18.5)	6.65 (7.7)	0.00 (0)	
I	10								
		55.70 (100.0)	49.35 (88.6)	45.89 (82.4)	39.45 (70.8)	32.86 (59.0)	28.02 (50.3)	26.92 (48.3)	0.00 (0)

SUBJECTS		0	12	24	36	48	60	72	120
NDCT									
J	11								
		78.24 (100.0)	75.90 (97.0)	46.26 (59.1)	14.24 (18.2)	11.55 (14.8)	0.00 (0)		
K	12								
		75.42 (100.0)	53.88 (71.4)	39.48 (52.4)	17.17 (22.8)	6.75 (8.90)	0.00 (0)		
L	13								
		52.00 (100.0)	35.11 (67.5)	14.68 (28.2)	12.29 (23.6)	0.00 (PEE only) (0)			
M	14								
		51.82 (100.0)	30.65 (59.1)	20.62 (39.8)	6.75 (13.0)	0.00 (PEE only) (0)			
N	15								
		69.87 (100.0)	39.83 (57.0)	24.48 (35.0)	2.03 (2.9)	0.00 (PEE only) (0)			

Legend: PEE – punctuate epithelial erosions

Table III: shows the comparison of mean wound size at each time interval with Mann Whitney test and overall significance with multivariate analysis

TIME AFTER EYE DROPS COMMENCED (HOURS)		0	12	24	36	48	60	72	120
				Group DTI					
MEAN WOUND SIZE IN mm2 ± SD		63.92 ± 12.63	43.53 ± 15.21	23.28 ± 9.96	12.41 ± 5.92	3.75 ± 4.77	0	-	-
				DCT					
MEAN WOUND SIZE IN mm2 ± SD		63.14 ± 12.40	57.00 ± 12.87	47.72 ± 12.65	28.72 ± 7.12	18.60 ± 8.97	10.56 ± 10.10	6.73 ± 11.66	0
				NDCT					
MEAN WOUND SIZE IN mm2 ± SD		65.47 ± 11.39	47.07 ± 16.39	29.10 ± 11.86	10.50 ± 5.43	3.66 ± 4.73	0	-	-
Mann-Whitney asymp sig (2 tailed)	DTI vs NDCT	0.917	0.754	0.602	0.465	1.000	1.000	1.000	Significant
p values	DTI vs DCT	0.754	0.117	0.009	0.009	0.015	0.005	0.136	if p < 0.05
	DCT vs NDCT	0.754	0.347	0.117	0.009	0.015	0.005	0.136	
Wilks' lambda p value	0.013								
Multivariate analysis (LSD)	DCT vs DTI / NDCT	0.13/ 0.21							
p values	DTI vs DCT/ NDCT	0.13/ 0.783							
	NDCT vs DCT/ DTI	0.21/0.783							

Data is normally distributed by Shapiro-Wilk test – not significant (p> 0.05)
Wound size calculated using QIMS software (University Kebangsaan Malaysia)

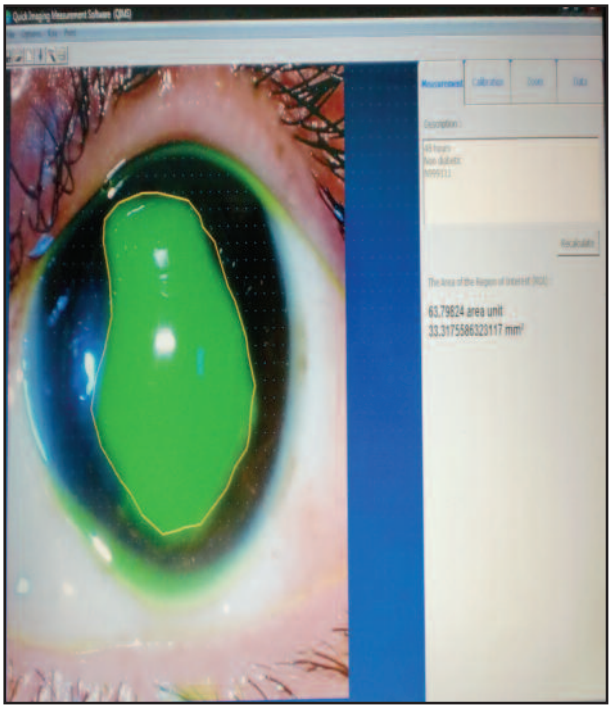


Fig. 1: Photograph of the computer screen showing the QIMS software from University Kebangsaan Malaysia which allows corneal epithelial defect sizes to be calculated.

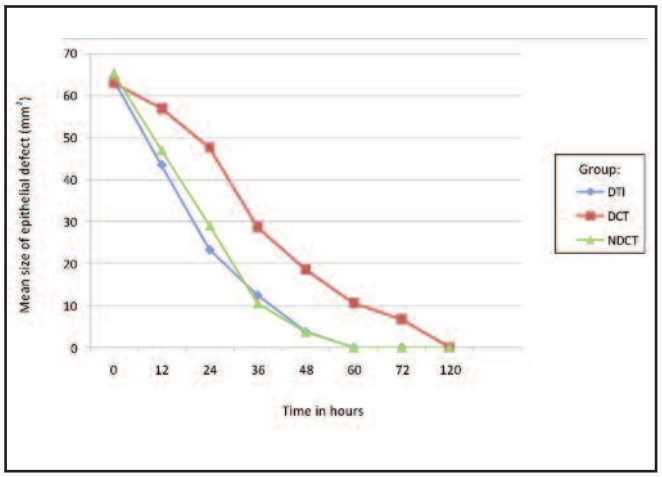


Fig. 2: shows the change in mean size of epithelial defect over time of the 3 groups.

Topical insulin 1 unit was prepared using aseptic technique with 2.5 mls of insulin (actrapid HM 1000 U, Novonordisk) containing 250 U insulin added to 2.5 ml normal saline in a commercial applicator bottle to give 50 U/ml of insulin. Given that commercial eye drop bottles of 5 ml size result in 20 uL per drop, then insulin at 50U/ ml from a conventional bottle delivers approximately 1U per drop. The drops were discarded and a new preparation made every 3 days.

Following vitreoretinal surgery, all patients routinely received post-operative topical therapy. These included topical dexamethasone 0.1% (Maxidex™, Alcon) and ciprofloxacin HCl 0.3% (Ciloxan™, Alcon) two hourly in the first week and is prescribed routinely for all patients undergoing vitrectomy regardless of whether there was an epithelial defect or not.

The hospital ethics committee approval for the study was sought and obtained for a retrospective study (No: FF-021-2012). Ethics committee approval for a prospective study could not be obtained because trials involving off-label usage of drugs was not covered in the hospital medical insurance at the time of the surgeries. The usage of off-label medications by the consultant who performed the surgeries was however, covered in the medical indemnity as is custom and widespread in medical practice.

The detailed photography performed in this study was however, conducted in a prospective manner and is not a routine procedure for our patients. The minimum sample size calculation for a prospective study was 5 treated diabetic

eyes, 5 untreated diabetic eyes and 5 non diabetic eyes. In all cases written, informed consent as well as blood sugar monitoring of all the diabetic subjects receiving topical insulin eyedrops was obtained during their admission. All patients were counselled as to the possible side effects of the treatment namely stinging and erythema following instillation of their post-operative eye drops and symptoms of hypoglycaemia. They were required to sign a written consent for therapy with topical insulin. The study was conducted according to the tenets of the Declaration of Helsinki.

RESULTS

Over the 10 month period, there were 15 eyes of 14 patients which had been debrided intraoperatively during vitreoretinal procedures. Table I shows the demographics of the subjects. Five eyes of diabetic patients were treated with topical insulin 1 unit qds until the epithelial defect healed (Group DTI) and five eyes were treated conventionally (Group DCT). One patient (D) had her right eye treated conventionally and her left eye treated with topical insulin. However, the debridement was performed during surgeries conducted at different time intervals and not concurrently. Five eyes were in non diabetic patients (Group NDCT).

Ointment chloramphenicol was prescribed to one patient from the NDCT group (Table I). Topical anti-glaucoma agents, timolol maleate 0.5% (TimoptolTM, MSD) and brimonidine tartrate 0.1% (Alphagan PTM, Allergan) were prescribed to 1 eye from the DTI group, 2 eyes from the DCT group and 3 eyes from the NDCT group (Table I). Vitrectomy surgery was combined with cataract surgery (phacoemulsification) in 2 DTI eyes, 4 DCT eyes and all NDCT eyes.

The topical insulin eye drops had then been instilled 4 times daily into Group DTI eyes only. The topical insulin eye drops were discontinued after the corneal epithelial defect completely closed. All the epithelial defects eventually closed, the longest being 120 hours from the DCT group.

Upon statistical analysis, the data was found to be normally distributed when analysed with the Shapiro-Wilk test for small sample sizes. The data was further analysed using the Mann Whitney test. All 3 groups were found to be comparable for age and gender (Table I). DTI and DCT groups were found to be comparable for HbA1c and duration of diabetes (Table I). DTI eyes had a significantly smaller defect size at t= 24 (p=0.009), 36 (p=0.009), 48 (p=0.015) and 60 hours (p=0.005) compared to DCT eyes and had no statistical difference from NDCT eyes at all times in the post hoc analysis (p>0.05).(Table II & III) DTI and NDCT eyes were statistically similar in their healing rates (Figure 1). DTI and NDCT eyes are significantly different in their healing rates from DCT eyes (Figure 1). The most marked difference between DTI and DCT was at 24, 36 and up to 60 hours. The mean time for complete epithelial closure was 60±15 hours in DTI, 78±30 hours in DCT and 65±31 hours in NDCT eyes. Sixty percent of NDCT and DTI eyes achieved complete wound resurfacing within 48 hours compared to 25% of DCT. Patient D, with bilateral operations at different settings, had the eye treated with topical insulin reepithelialise completely by 48 hours (Eye no 4, Table II) and show a more stable ocular surface while her left eye treated conventionally re-epithelialised later by 72 hours (Eye no 9, Table II). The different therapies in each eye was because the right eye was operated first during which the recruitment of topical insulin subjects. The left eye was operated subsequently during recruitment of consecutive diabetic controls. There were no systemic or local side effects recorded in the notes including absence of hypoglycaemic events. All diabetic patients routinely have qds dextrostix monitoring during their admissions and none had hypoglycaemia during their admissions.

DISCUSSION

The frequency of corneal debridement during diabetic vitrectomy averaged at 17.4% in a series by Friberg *et al*[3] with a range of 0-90%. Prompt resurfacing of injured corneal epithelium is needed to reestablish visual function through the restoration of its transparency and homeostasis. This will also restore its barrier function against ocular infection. Unfortunately, diabetic keratopathy can take the form of non-healing epithelial defects which can lead to infectious corneal ulcers, secondary scarring, and permanent loss of vision[4].

Diabetes is believed to induce changes in epithelial morphology and fragility, cause abnormal basement membrane structure, poor epithelial adherence and healing rate, and ineffective epithelial barrier function. Other corneal changes resulting from diabetes include corneal neuropathy and alterations in the corneal stroma, Descemet membrane, and corneal endothelium. These epithelial abnormalities can result from surgical trauma including vitrectomy, and nonsurgical trauma[4].

The results of this study are interesting in that they confirm a delayed epithelial healing of diabetic eyes compared to normal eyes as represented by the control group NDCT (Table III). In animal studies by Zagon *et al.* it was found that topical insulin had no effect on corneal re-epithelialization of non-diabetic rats. However, the diabetic rats treated with topical insulin 1U 4 times daily had significantly enhanced corneal healing relative to diabetic rats without topical insulin[2]. This data demonstrates that topical application of insulin enhances corneal wound healing in a diabetic animal model. This study was also the basis for the concentration of insulin selected for our patients. Our results have extrapolated these findings to human subjects. The results of this study also indicate that topical insulin was successful in normalizing the rate of healing of epithelial defects. This effect is most noticeable on the end of the first and second post-operative days which is clinically relevant as patients are normally discharged or planned for discharge on these days. Topical insulin therapy is advantages in healing the defects rapidly so that patients are discharged faster, are more comfortable and less likely to develop complications.

In laboratory and clinical trials, agents known to influence epithelial migration, mitosis, apoptosis, adhesion, and differentiation have been studied as possible therapeutic agents to enhance corneal epithelial healing. These include growth factors, fibronectin[5], retinoids[6] and autologous serum[7].

We chose to look at insulin because insulin, a peptide closely related to insulin growth factor (IGF), is relatively cheap, widely available and easy to titrate in the laboratory. IGF is implicated in wound healing[8]. Insulin is a systemic drug whose safety and effectiveness has long been established and a naturally occurring compound. There are no studies of topical insulin usage in human diabetics published to date.

How does insulin work on the ocular surface? Insulin probably stimulates haptotactic migration of human epidermal keratinocytes [6]. Insulin administered as a topical ocular medication with a surfactant agent has been shown to be clinically effective in treating diabetes in animal models [2].

Human studies conducted by Bartlett *et al*[9,10] have shown that topical insulin is nontoxic to human corneal and conjunctival tissues. The results of one study [9] suggest that single-dose insulin in concentrations up to 100 U/ml formulated in saline has no detectable clinical toxicity to the anterior structures of the normal human eye. A similar study by Bartlett *et al.* 2009 [10] revealed that eye drops containing insulin were comfortable subjectively and appeared as innocuous as an instillation of sterile saline. The results of this study further confirmed the safety of insulin (100 U/ml) in saline even after multi-dose exposure.

In our study, 1 unit of insulin is instilled four times daily because Bartlett *et al* found that topical Humulin R eye drops up to 100U/ml twice daily or 2 units bds had no ocular side effect after long-term, multi-dose exposure on human study [10]. Meanwhile in an animal study done by Zagon *et al*, it was found that 1U of insulin eye drops 4 times daily had a significant faster the corneal wound healing in diabetic group compared to the control group [2].

This study is the first to analyse retrospectively the detailed photographic follow-up of human diabetic and non-diabetic patients who have undergone corneal epithelial debridement as part of ocular surgery. It demonstrates that topical insulin therapy normalizes the healing rate of corneal epithelium in human diabetics with no appreciable local or systemic side effects.

The criticisms of the study include its small sample size. This is due to the small number of patients that actually require epithelial debridement during VRS. A prospective randomized trial is preferred, however patient recruitment is slow and corneal debridement for the purpose of a study should never be deliberate. This study further selected patients in whom detailed photographic record was available.

The advantages of this study include its exciting and practical results, which have prompted us to write this up. Furthermore the meticulous recording of the rates of healing of the epithelial defects has given us reliable and useful data.

CONCLUSION

One unit of topical insulin administered qds should be prescribed for the treatment of epithelial debridement following vitreoretinal surgery in diabetics to restore the cornea's surface to a normal rate.

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