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Factors Contributing to Corneal Complications After Vitrectomy in Diabetic Patients

Miina Hiraoka,* Shiro Amano,†
Tetsuro Oshika,† Satoshi Kato* and Sadao Hori*

*Department of Ophthalmology,
Diabetes Center, Tokyo Women's Medical College, Tokyo, Japan;
†Department of Ophthalmology, University of Tokyo, Tokyo, Japan

Purpose: To elucidate factors contributing to corneal complications after vitrectomy in diabetic patients.

Methods: The records of a series of 129 diabetic patients (202 eyes) who underwent pars plana vitrectomy performed by a single surgeon between March 1997 and February 1999 were analyzed retrospectively. Logistic regression analysis was performed to determine possible factors contributing to corneal complications.

Results: Of the 202 eyes, 102 (50.5%) developed corneal complications after surgery; 90 (44.6%) had epithelial disturbance; and 48 (23.8%) had corneal edema. The degree of surgical invasion during vitrectomy was significantly correlated with the occurrence of epithelial disturbance and corneal edema.

Conclusion: Surgical invasion is a risk factor for corneal complications after vitrectomy in diabetic patients. **Jpn J Ophthalmol 2001;45:492–495**

Key Words: Corneal edema, corneal epithelial disturbance, diabetes mellitus, vitrectomy.

Introduction

In diabetic patients, a high incidence of corneal complications after vitrectomy including epithelial defect and stromal edema have been reported.[1–6] These complications are often resistant to ordinary therapy and require long-term treatment. Local factors, such as intraoperative lensectomy and a history of previous vitreous surgery, have been reported to increase the incidence of corneal complications after surgery.[3–6] However, the influence of systemic conditions, such as the level of hemoglobin A_{1c} (HbA_{1c}) and the presence of diabetic neuropathy and nephropathy, on the occurrence of corneal complications after vitrectomy remains unknown. In this study, we employed logistic regression analysis to define factors that contribute to the development of corneal complications after pars plana vitrectomy in diabetic patients.

Materials and Methods

We retrospectively reviewed the records of 129 diabetic patients (202 eyes) who underwent pars plana vitrectomy by a single surgeon at the Diabetes Center in Tokyo Women's Medical College between March 1997 and February 1999. When 2 eyes of the same patient were treated independently, the data on the systemic condition of these patients were used twice in the analysis.

Pars plana vitrectomy was performed by the standard three port incisions. During vitrectomy, floating contact lens (Seed Contact Lens, Tokyo) was used. The surgical indications for vitrectomy were: (1) macular edema in 16 eyes; (2) vitreous, subhyaloid, or premacular hemorrhage in 13 eyes; (3) progressive fibrovascular proliferation without retinal detachment in 85 eyes; and (4) tractional retinal detachment in 88 eyes. In eyes with diabetic macular edema, vitrectomy with separa-

Received: September 25, 2000
Correspondence and reprint requests to: Shiro AMANO, Department of Ophthalmology, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan

Published by Elsevier Science Inc.
0021-5155/01/$–see front matter
PII S0021-5155(01)00376-8

tion of the posterior hyaloid was performed to resolve the macular traction associated with a thickened and taut premacular posterior hyaloid.[7] In eyes with proliferative diabetic retinopathy, vitrectomy was performed to remove media opacities or to relieve tractional elements in the retinal surface. In cases requiring extensive surgery, membrane peeling, endophotocoagulation, lensectomy, fluid–gas exchange, scleral buckling, or cryotherapy were applied as needed. At the end of surgery, sulfur hexafluoride (SF_6) gas or silicone oil was injected as an intraocular tamponade as needed. Combined lensectomy was performed by pars plana approach in 110 (54.4%) eyes and a subsequent posterior chamber intraocular lens was implanted by limbal approach in 75 (37.1%) eyes. The central corneal epithelium was removed intraoperatively in 2 (1.0%) eyes. After surgery, patients received topical 0.1% betamethasone sodium phosphate, 0.3% ofloxacin, and 0.1% diclofenac sodium four times daily, and topical 1% atropine sulphate once daily.

Postoperative slit-lamp biomicroscopy was performed during hospitalization to detect any corneal changes. An epithelial disturbance was defined as superficial punctate keratopathy, persistent epithelial defect, or recurrent corneal erosion that lasted 7 days or longer after the surgery. Corneal edema was defined as the presence of any corneal stromal haze or thickening, or wrinkling of Descemet's membrane that lasted at least 7 days or longer. Nine eyes that had corneal epithelial edema due to elevation of intraocular pressure over 30 mm Hg that lasted 7 days or longer were excluded from the study.

Of the 105 patients (129 eyes) who had primary pars plana vitrectomy, specular microscopic examination of the corneal endothelium was performed on 85 patients (104 eyes) preoperatively to determine whether the condition of the endothelium would have an influence on postoperative corneal complications.

Logistic regression analysis (step-wise method) was performed to evaluate several variables as possible contributing factors to the occurrence of epithelial disturbance and corneal edema. Preoperative factors for this analysis included age, sex, duration of diabetes mellitus, presence of diabetic neuropathy and nephropathy, level of HbA_{1c}, severity of diabetic retinopathy, presence of iris neovascularization, history of cataract surgery, simultaneous lensectomy, surgery time, and performance of intraocular tamponade. Severity of diabetic retinopathy was graded as follows; macular edema = 1, vitreous or subhyaloid hemorrhage = 2, fibrovascular proliferation = 3, and tractional retinal detachment = 4.

Intraoperative factors (simultaneous lensectomy, duration of surgery, and intraocular tamponade) were highly correlated with each other (Spearman rank correlation). Thus, these factors were used to evaluate the degree of intraoperative invasion, which is the total sum of the following scores: (1) lensectomy (No = 0, Yes = 1); (2) surgery time (<60 minutes = 0, 60–120 minutes=1, >120 minutes = 2); (3)intraocular tamponade (No = 0, SF_6 = 1, silicone oil = 2).

First of all, the association among the independent variables was evaluated by Spearman rank correlation. Age, presence of diabetic neuropathy, severity of diabetic retinopathy, and presence of iris neovascularization were significantly correlated with other factors. Accordingly, these factors were excluded from multiple regression analysis.

First logistic regression analysis was performed in 104 eyes that had primary vitrectomy and specular microscopic examination. In this first analysis, the dependent variable was the occurrence of corneal edema, and the data of endothelial cell density, coefficient of variation and percentage of hexagonal cells were included as possible explanatory variables.

Second logistic regression analysis was done using the data from all 202 eyes, and the dependent variables were the occurrence of corneal edema and corneal epithelial disturbance. In the second analysis, the specular microscopic data were not used.

Results

The patients' clinical profile is presented in Table 1. Superficial punctate keratopathy was observed in

Table 1. Clinical Profile of Patients*

No. of eyes	202
Sex (Male/Female)	139/63
Average age (years)	52.5 ± 13.6
Average duration of diabetes (years)	14.6 ± 8.1
No. with neuropathy	187 (92.6)
No. with nephropathy	149 (73.8)
Average hemoglobin A_{1c}	7.1 ± 1.5
Status of diabetic retinopathy	
Score 1: macular edema, no.	16 (7.9)
Score 2: vitreous hemorrhage, no.	13 (6.4)
Score 3: fibrovascular proliferation, no.	85 (42.1)
Score 4: tractional retinal detachment, no.	88 (43.6)
No. with iris neovascularization	44 (21.8)
No. with preoperative aphakia	33 (16.3)
No. with previous vitrectomy	55 (27.2)
No. with preoperative superficial punctate keratopathy	14 (6.9)

*Values in parentheses are percentages.

Jpn J Ophthalmol
Vol 45: 492–495, 2001

Table 2. Vitrectomy Data*

Simultaneous lensectomy	110 (54.5)
Simultaneous intraocular lens implantation	75 (37.1)
Sulfur hexafluoride (SF_6) gas tamponade	40 (19.8)
Silicone oil tamponade	39 (19.3)
Average surgery time (min)	72.0 ± 30.4
No. epithelial debridement	2 (1.0)
Total score of operative invasion†	
0	33 (16.3)
1	55 (27.7)
2	63 (31.2)
3	34 (16.8)
4	10 (5.0)
5	7 (3.5)

*Values in parentheses are percentages.
†(1) 0 = no lensectomy, 1 = lensectomy, (2) duration of surgery (<60 minutes = 0, 60–120 minutes = 1, >120 minutes = 2, (3) intraocular tamponade (no = 1, SF_6 gas = 1, silicone oil = 2).

Table 3. Results of Multiple Logistic Analysis

Results	Dependent Variable	Factors	*P* value	*R*
1*	Corneal edema	Score of operative invasion	<.0001	.358
		Sex	.99	
		Surgery time	.057	
		Nephropathy	.12	
		Hemoglobin A_{1C}	.43	
		Previous cataract surgery	.13	
		Endothelial cell density	.54	
		Coefficient of variation	.47	
		Percentage of hexagonal cells	.81	
2†	Epithelial disorder	Score of operative invasion	<.0001	.397
		Sex	.69	
		Surgery time	.41	
		Nephropathy	.49	
		Hemoglobin A_{1C}	.43	
		Previous cataract surgery	.25	
	Corneal edema	Score of operative invasion	<.0001	.314
		Sex	.67	
		Surgery time	.65	
		Nephropathy	.78	
		Hemoglobin A_{1C}	.51	
		Previous cataract surgery	.15	

*n = 104 eyes.
†n = 202 eyes.

14 eyes (6.9%) preoperatively. Information with regard to the vitrectomy is shown in Table 2. All data reported in this study are mean ± SD unless otherwise specified.

The overall rate of corneal complications after pars plana vitrectomy in all the 202 eyes was 55.4% (112 eyes). There were 90 eyes (44.6%) with epithelial disturbance and 48 eyes (23.8%) with corneal edema. As for the type of epithelial disturbance, 79 eyes had superficial punctate keratopathy, 7 eyes had persistent epithelial defect, and 4 eyes had recurrent corneal erosion. As for the type of corneal edema, there were 10 eyes with stromal haze or thickening, and 44 eyes with wrinkling of Descemet's membrane.

In the 104 eyes that had primary vitrectomy and a specular microscopic examination, endothelial cell density was 2688 ± 431 cells/mm_2, coefficient of variation was 0.33 ± 0.07 and the percentage of hexagonal cells was 60.5 ± 11.57%. In these 104 eyes, corneal edema occurred in 24 eyes (23.1%). Logistic regression analysis disclosed that the score of operative invasion was the only factor that was significantly related to the occurrence of corneal edema in these 104 cases ($P < .0001$). Because the endothelial cell density, coefficient of variation, and the percentage of hexagonal cells were not associated with the occurrence of corneal edema, the following analysis did not include the specular microscopic data.

In the 202 eyes, the factor significantly related to the development of epithelial disturbance was the score of intraoperative invasion ($P < .0001$). The occurrence of corneal edema was significantly correlated with the score of intraoperative invasion ($P < .0001$) (Table 3). Other factors concerning general condition, such as the duration of diabetes mellitus, the presence of diabetic nephropathy, and the level of HbA_{1c} were not significantly related to the corneal complications.

Discussion

The present study demonstrated that the overall rate of corneal complications was 55.4% in 129 diabetic patients (202 eyes) undergoing pars plana vitrectomy. This incidence is much higher than the 19.9% reported in the study by Chung et al.[6] However, in Chung's study, epithelial complication included only epithelial defect, and not punctate epitheliopathy. If Chung's criteria for assessing corneal complications were adopted in our study, overall incidence would be 15.8% (32 eyes), which would be similar to that in Chung's study. In the previous reports[4,5] over 20 years ago, severe corneal complications, including epithelial defect and corneal edema, occurred in over 50% of the diabetic patients after pars plana vitrectomy. Improvements in instrumentation and surgical techniques and reduction of surgical time might have decreased the incidence of severe corneal complications after vitrectomy.

In the multiple logistic analysis, it is unfavorable to include variables that are highly correlated with

each other. Thus, considering multicolinearity among variables related to the degree of surgical invasion, we created a new score using the data of several factors, ie, simultaneous lensectomy, intraocular tamponade, and duration of operative procedure. The results demonstrated that this score representing the degree of intraoperative invasion is significantly correlated with the occurrence of both epithelial disturbance and corneal edema. In the current study, we could not decide which specific surgical procedure contributed to the epithelial or endothelial disturbance. Considering a previous study[8] reporting that intraocular gas-treated patients had a significantly greater corneal endothelial cell loss than those where intraocular gas was not used, it seems reasonable to think that the performance of simultaneous lensectomy and intraocular tamponade are related to endothelial damage, and long surgical time is related to both epithelial and endothelial damage.

Severity of diabetic retinopathy was excluded from multiple regression analysis because Spearman rank correlation revealed that severity of diabetic retinopathy was highly correlated with age ($P = .017$, $R = -.168$) and the score of intraoperative invasion ($P < .001$, $R = .319$). Because the current results showed that the score of intraoperative invasion is significantly correlated with the occurrence of corneal complications, it may be reasonable to think that severe diabetic retinopathy made the vitrectomy complicated and caused corneal complications.

In the current study, a floating contact lens was used during vitrectomy. Some surgeons point out that a floating contact lens induces less corneal epithelial damage than an irrigating contact lens. However, as far as we know, there has been no study comparing the rate of corneal complications among different contact lenses for vitrectomy. Thus, we could not decide how the use of a floating contact lens influenced the rate of corneal complications in the current study.

Recently, we reported that the accumulation of advanced glycation end products in the corneal epithelial basement membrane might play a causative role in the corneal epithelial disorders of diabetic patients.[9] Thus, long-term hyperglycemia with concomitant accumulation of advanced glycation end products in the corneal epithelial basement membrane could have weakened the epithelial cell attachment to the Bowman's layer, making the corneal epithelium vulnerable to surgical stress.

In diabetic patients, corneal abnormalities have been demonstrated and have been termed diabetic keratopathy.[10] Histologic thickening of the corneal epithelial basement membrane[11–13] and morphologic changes of both corneal epithelium and endothelium[14–16] have been reported. The current results indicate that corneal complications after vitrectomy in diabetic patients take place due to intraoperative damage combined with pre-existing subclinical corneal abnormalities.

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