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CLINICAL INVESTIGATION

Effects of Internal Limiting Membrane Peeling in Vitrectomy on Diabetic Cystoid Macular Edema Patients

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Abstract

Purpose: We evaluated the effects of the peeling of the internal limiting membrane (ILM) during vitrectomy in diabetic cystoid macular edema (CME) patients.

Methods: Visual outcome and intraoperative and postoperative complications were evaluated retrospectively in 84 CME patients (100 eyes), all of whom had been followed for at least 1 year postoperatively. Before January 2001, we did not perform ILM peeling at our hospitals; 57 patients (66 eyes) treated before 2001 were included in this retrospective study as the non-peeling group. After January 2001, ILM peeling was performed in 27 (34 eyes) CME patients, who were included in this study as the peeling group. In the peeling group, indocyanine green (ICG) staining was performed at the time of ILM peeling.

Results: Visual acuity improved significantly after vitrectomy regardless of ILM peeling. Visual acuity improved gradually from 6 months to 1 year after the operation, and improved further at the final observation point in both groups. Visual acuity did not differ significantly between the two groups at any time point. There was no difference in the incidence of intraoperative and postoperative complications between the two groups. There were no adverse events associated with ICG-assisted ILM peeling.

Conclusions: Visual acuity improved with vitrectomy for diabetic cystoid macular edema in both groups. ILM peeling was not found to improve visual acuity postoperatively. **Jpn J Ophthalmol** 2005;49:297–300 © Japanese Ophthalmological Society 2005

Key Words: diabetic cystoid macular edema, diabetic retinopathy, indocyanine green, internal limiting membrane, vitrectomy

Introduction

Many studies have demonstrated the efficacy of vitrectomy for diabetic macular edema (CME).[1–4] The role and mechanism of vitrectomy in reducing macular edema have been a topic of interest. Lewis et al.[1] suggested that the pathogenesis of diabetic macular edema is traction of the posterior vitreous membrane. They suggested that vitreous membrane traction damages both internal and external blood-retinal barriers, resulting in shallow foveal retinal detachment similar to that observed in impending macular holes. On the other hand, Tachi[5] speculated that vitreous membrane traction reduces extravascular hydrostatic pressure in the retina, inducing marked extravascular leakage, and that surgical removal of the posterior vitreous membrane causes a hydrostatic pressure gradient and relieves extravascular leakage and edema. Yamamoto et al.[3] suggested that vitrectomy in eyes with posterior vitreous detachment has two main mechanisms in reducing macular edema. First, vitrectomy enhances the intraocular circulation of oxygen, increasing intraocular oxygen pressure as oxygen enters the fluid in the vitreous cavity from arterial blood in the ciliary processes. Second, vitrectomy removes substances in the vitreous gel that enhance vascular permeability to such substances as cytokines.

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In addition to these mechanisms, internal limiting membrane (ILM) peeling has been considered to relieve macular traction by the vitreous owing to the complete removal of the residual posterior vitreous cortex, and furthermore, it prevents the development of secondary epimacular membrane and eliminates the scaffold for astrocyte reproliferation.[6] Since the ILM in diabetic retinopathy develops pathological thickening,[7] peeling of this pathologically thickened ILM has been suggested to improve retinal plasticity and facilitate diffusion of water retained in the retina.[8] However, there is no agreement on the effectiveness of ILM peeling on this disorder.[6,9–11] In this study, we evaluated the effect of ILM peeling during vitrectomy on diabetic cystoid macular edema patients.

Materials and Methods

The subjects were 84 consecutive patients (100 eyes) who underwent vitrectomy for diabetic CME at the Surugadai Hospital of Nihon University or the Nihon University Itabashi Hospital between June 1994 and April 2002. We obtained informed consent from the patients regarding the surgery. All patients were followed up for at least 1 year after the vitrectomy. Between June 1994 and December 2000, ILM peeling was not performed in these hospitals. Sixty-six eyes of 57 patients who underwent vitrectomy in this period were classified as the non-ILM peeling group (nonpeeling group) in this study. From January 2001 to April 2002, 34 eyes of 27 patients who underwent ILM peeling during vitrectomy were classified as the ILM peeling group in this study (peeling group). Patients who underwent ILM peeling during a reoperation between June 1994 and December 2000 were excluded from the study.

The total of 84 subjects comprised 51 male (60 eyes) and 33 female (40 eyes) patients, and their ages at the time of surgery ranged from 25 to 77 years, average 58.6 ± 9.8 years (mean ± SD).

There were no differences in surgical techniques between the groups except for ILM peeling. After removal of the vitreous gel, the presence or absence of posterior vitreous detachment (PVD) was determined using a Glizzard's needle. If there was no posterior vitreous detachment (PVD), PVD was intentionally created. In the peeling group, indocyanine green (ICG) staining was performed at the time of ILM peeling by the method of Kadonosono et al.[12] in which ICG (Diagnogreen, Daiichi Pharmaceutical, Tokyo, Japan) was mixed with a low-molecular-weight viscoelastic substance (Opegan, Santen Pharmaceutical, Osaka, Japan) to obtain a concentration of 0.06% and introduced to the surface of the retina for 30 s. If the patients were more than 50 years old and had phakic eyes, lens extraction with intraocular lens implantation was also performed.

Retrospectively, we evaluated the preoperative factors in the two groups. The main outcome in this study was the visual acuity at 6 months and at 1 year after the operation, and at the final examination time. Adverse events due to ILM peeling assisted by ICG staining were also documented. Statistical analysis was performed using a *t* test, χ^2 test, and Fisher's direct probability calculation method. $P < 0.05$ was regarded as significant.

Results

Preoperative Factors

Table 1 shows the results of preoperative clinical findings between the two groups. There were no significant differences in patient age at the time of surgery, duration of diabetes mellitus, hemoglobin A_{1c} (HbA_{1c}) level, incidence of nephropathy, preoperative visual acuity by the logarithm of the minimal angle of resolution (logMAR), incidence of posterior vitreous detachment, or mean postoperative follow-up period between the two groups. Nephropathy was defined as the presence of proteinuria.

Based on these results, the preoperative conditions were considered to be similar in the two groups, making it possible to evaluate the postoperative visual acuity between the two groups without adjusting for other variables.

Postoperative Visual Acuity

Table 2 summarizes the logMAR change of visual acuity between the two groups. Significant improvement was

Table 1. Preoperative factors in each group

Characteristics	Non-peeling group	Peeling group	*P* value
Age (years)[a]	58.9 ± 10.3	57.7 ± 9.2	0.60
Duration of diabetes mellitus (years)[a]	10.8 ± 7.9	8.3 ± 5.4	0.09
Hemoglobin A_{1c} (%)[a]	7.0 ± 1.2	6.9 ± 1.5	0.75
Presence of nephropathy (%)	43.9	40.7	0.97
Preoperative logMAR visual acuity[a]	0.76 ± 0.31	0.73 ± 0.31	0.67
Presence of PVD (%)	40.9	47.1	0.79
Mean follow-up period (months)[a]	25.3 ± 13.2	21.0 ± 6.6	0.06

LogMAR, logarithm of the minimum angle of resolution; PVD, posterior vitreous detachment.
[a] Values are means ± SD.

Table 2. Comparison of logMAR visual acuity between the two groups at each time point

	LogMAR VA mean ± SD		
Time of VA Measurement	Non-peeling group	Peeling group	*P* value
Preoperative	0.76 ± 0.31	0.72 ± 0.30	0.67
Six months after surgery	0.63 ± 0.32	0.60 ± 0.31	0.67
One year after surgery	0.56 ± 0.34	0.48 ± 0.34	0.26
Final	0.49 ± 0.34	0.43 ± 0.32	0.41

VA, visual acuity.

Table 3. Intraoperative/postoperative complications

	No. of eyes (%)		
	Non-peeling group	Peeling group	
Complication	(*n* = 66)	(*n* = 34)	*P* value
Intraoperative			
Iatrogenic retinal tears	9 (14)	3 (9)	0.48
Postoperative			
Transient IOP elevation	4 (6)	1 (3)	0.50
Neovascular glaucoma	3 (5)	0 (0)	0.21
Vitreous hemorrhage	2 (3)	0 (0)	0.31

IOP, Intraocular pressure.

observed, as compared with the preoperative value, in both groups at each postoperative time point.

At each postoperative measurement, visual acuity was slightly better in the peeling group than in the non-peeling group, but the differences did not show statistical significance.

In both groups, visual acuity showed a significant improvement with postoperative time: 6 months versus 1 year, $P < 0.002$; and 1 year versus final examination time, $P < 0.002$ for the non-peeling group, $P < 0.01$ for the peeling group.

Intraoperative and Postoperative Complications

The only significant intraoperative complication was iatrogenic retinal tears, which occurred in 14% of the non-peeling group and 9% of the peeling group. However, no patients developed postoperative retinal detachment.

In terms of postoperative complications, a transient raised intraocular pressure was observed in 6% of the non-peeling and in 3% of the peeling group, and neovascular glaucoma in 5% of the non-peeling, but 0% of the peeling, group. In addition, vitreous hemorrhages requiring wash out by an additional surgery occurred in 3% of the non-peeling group but 0% of the peeling group. There was no significant difference in the incidence of any complication between the two groups (Table 3).

Postoperative Adverse Events due to ICG Assisted ILM Staining

None of the 34 eyes in the peeling group showed ophthalmoscopic abnormalities compatible with retinal nerve fiber layer defects. Kinetic quantitative perimetry was performed in 18 of the 34 eyes in the peeling group. However, no visual field defect, such as has been reported in patients undergoing macular hole surgery,[13] was observed.

Discussion

As to the effectiveness of ILM peeling in vitreous surgery for diabetic macular edema, Gandorfer et al.[6] reported rapid improvement in visual acuity soon after surgery with ILM peeling and early absorption of edema. Kumagai et al.[9] found no improvement in visual acuity, but ILM peeling promoted absorption of edema in patients with hard macular exudates. Tamura et al.[10] evaluated visual outcomes between ILM peeling and non-peeling groups, based on the state of the posterior vitreous membrane, and reported a significantly higher visual improvement rate in the ILM peeling group with the absence of thickening of the posterior vitreous membrane. Gotoh et al.[11] reported no difference in the degree of improvement in visual acuity between ILM peeling and non-peeling groups, but the rate in the reduction of foveal retinal thickness was significantly higher in the ILM peeling group.

In this study, visual acuity improved significantly after vitreous surgery regardless of ILM peeling. Visual acuity had gradually improved from 6 months to 1 year after the operation, and improved further toward the final observation point. However, visual acuity did not differ significantly between the two groups at any time point, indicating that ILM peeling does not improve visual outcome. The present visual outcome results are similar to those reported by Gotoh et al.[11] Using optical coherence tomography (OCT), they reported that the foveal retinal thickness decreased more rapidly in the ILM-peeling group than in the non-ILM peeling group, in a total of 22 eyes. However, the number of eyes in our study was about five times greater, and the cases were consecutive. The follow-up period in our study was longer than 1 year after the vitrectomy.

ILM peeling was performed using the ICG staining method in this study. Therefore, there is a possibility of complications due to ILM peeling alone or in conjunction with the toxicity of ICG staining. Complications due to ILM peeling alone in vitreous surgery for macular hole and epimacular membrane have been reported, but none have been reported in patients with diabetic macular edema. This may be attributed to the difficulty of identifying complications when there are abnormalities in the retina other than in the macular area or an influence from panretinal photocoagulation in diabetic macular edema.

Complications due to the ILM peeling itself include inadequate improvement in central retinal sensitivity following vitrectomy for idiopathic epimacular membrane,[14] delay of b-wave recovery in focal macular electroretinogram after macular hole surgery,[15] and a high incidence of retinal nerve fiber layer defects after macular hole and epimacular membrane surgery.[16] As to the complications due to toxicity of ICG staining, Haritoglou et al.[13] found marked semilateral visual field defects on the nasal side in 7 of 20 eyes undergoing vitrectomy for macular hole combined with ICG-assisted ILM peeling. In this study, we found no visual field abnormalities. Ashikari et al.[17] showed residual fluorescence detected by scanning laser ophthalmoscopy even 6 months postoperatively in patients with diabetic macular edema. Although ICG staining has enabled us to carry out accurate ILM peeling, we must always take into account the possible adverse effect of ICG on retinal tissue.

The efficacy of vitrectomy for diabetic macular edema is widely accepted. However, in this study, we could not find any beneficial effects of ILM peeling as a supplemental technique in enhancing postoperative visual acuity. The indications for ILM peeling should be carefully determined because the main purpose of surgery is an improvement of pathologic conditions and visual acuity, without impairing the physiological retinal structure.

A recent study showed that residual vitreous cortex in the macular area can be visualized with triamcinolone acetonide after surgical creation of a posterior vitreous detachment during vitreous surgery for diabetic retinopathy, suggesting that residual cortex impairs visual recovery.[18] Complete removal of residual vitreous cortex by means of visualization using triamcinolone acetonide might improve surgical outcomes in macular hole surgery. We have also initiated a technique without ILM peeling in which residual vitreous cortex is removed completely by means of visualization using triamcinolone acetonide. We intend to compare the results of this technique with those obtained in the present investigation.

References

1. Lewis H, Abrams GW, Blumenkranz MS, Campo RV. Vitrectomy for diabetic macular traction and edema associated with posterior hyaloidal traction. Ophthalmology 1992;99:753–759.
2. Tachi N, Ogino N. Vitrectomy for diffuse macular edema associated with diabetic retinopathy. Atarashii Ganka (J Eye) 1994;11: 1077–1081.
3. Yamamoto T, Yamamoto S, Takeuchi S. Pars plana vitrectomy for diabetic macular edema with posterior vitreous detachment. Atarashii Ganka (J Eye) 2000;17:133–138.
4. Sato Y, Lee Z, Shimada H. Vitrectomy for diabetic cystoid macular edema. Jpn J Ophthalmol 2002;46:315–322.
5. Tachi N. Vitrectomy for macular edema. Ganka Shujutsu (J Jpn Ophthalmic Surg) 1994;7:407–414.
6. Gandorfer A, Messmer EM, Ulbig MW, Kampik A. Resolution of diabetic macular edema after surgical removal of the posterior hyaloid and the inner limiting membrane. Retina 2000;20:126–133.
7. Ljubimov AV, Burgeson RE, Butkowski RJ, et al. Basement membrane abnormalities in human eyes with diabetic retinopathy. J Histochem Cytochem 1996;44:1469–1479.
8. Yamamoto T. Vitrectomy for diabetic macular edema—new horizon in vitrectomy. Atarashii Ganka (J Eye) 2003;20:903–907.
9. Kumagai K, Ogino N, Furukawa M, et al. Internal limiting membrane peeling in vitreous surgery for diabetic macular edema. Nippon Ganka Gakkai Zasshi (J Jpn Ophthalmol Soc) 2002;106: 590–594.
10. Tamura T, Hirakata A, Oda H, et al. Outcome of vitreous surgery with internal limiting membrane peeling for diabetic macular edema. Ganka Rinsho Iho (Jpn Rev Clin Ophthalmol) 2003;97: 979–982.
11. Gotoh T, Imai M, Iijima H. Effect of peeling the internal limiting membrane for diabetic macular edema. Nihon Ganka Kiyo (Folia Ophthalmol Jpn) 2003;54:109–112.
12. Kadonosono K, Itoh N, Uchio E, et al. Staining of internal limiting membrane in macular hole surgery. Arch Ophthalmol 2000;118: 1116–1118.
13. Haritoglou C, Gandorfer A, Gass CA, et al. Indocyanine green-assisted peeling of the internal limiting membrane in macular hole surgery affects visual outcome: a clinicopathologic correlation. Am J Ophthalmol 2002;134:836–841.
14. Kumagai K, Ogino N, Demizu S, et al. Foveal thickness and retinal sensitivity following surgery for idiopathic epiretinal membrane. Rinsho Ganka (Jpn J Clin Ophthalmol) 2000;54:59–62.
15. Terasaki H, Miyake Y, Nomura R, et al. Focal macular ERGs in eyes after removal of macular ILM during macular hole surgery. Invest Ophthalmol Vis Sci 2001;42:229–234.
16. Ishikawa F, Ogino N, Okita K, et al. Retinal nerve fiber layer defect after vitrectomy and internal limiting membrane peeling for idiopathic macular hole and epiretinal membrane. Rinsho Ganka (Jpn J Clin Ophthalmol) 2001;55:1539–1544.
17. Ashikari M, Nozaki M, Kojima M, Ogura Y. Outcome of removal of internal limiting membrane with adjunct use of indocyanine green. Rinsho Ganka (Jpn J Clin Ophthalmol) 2001;55:863–866.
18. Sonoda K, Sakamoto T, Enaida H, et al. Residual vitreous cortex after surgical posterior vitreous separation visualized by intravitreous triamcinolone acetonide. Ophthalmology 2004;111: 226–230.