Graefe's Arch Clin Exp Ophthalmol
(2004) 242:273–278

CLINICAL INVESTIGATION

DOI 10.1007/s00417-003-0731-8

Sven Radetzky
Peter Walter
Sascha Fauser
Kan Koizumi
Bernd Kirchhof
Antonia M. Joussen

Visual outcome of patients with macular edema after pars plana vitrectomy and indocyanine green-assisted peeling of the internal limiting membrane

Received: 18 December 2002
Revised: 7 May 2003
Accepted: 5 June 2003
Published online: 23 March 2004

This study was presented in part at the 100th meeting of the German Ophthalmological Society in Berlin, September 2002

S. Radetzky · P. Walter · S. Fauser · K. Koizumi · B. Kirchhof · A. M. Joussen (✉)
Department of Vitreoretinal Surgery, Center for Ophthalmology, Joseph Stelzmann-Strasse 9, 50931 Cologne, Germany
e-mail: JoussenA@aol.com

Abstract *Purpose:* To evaluate the efficacy of inner limiting membrane (ILM) peeling in persistent macular edema. *Methods:* This retrospective review analyzed a series of 23 eyes from 23 patients with persistent macular edema treated by pars plana vitrectomy (PPV) with indocyanine green (ICG)-assisted peeling of the ILM. Thirteen female and 10 male patients with a mean age of 57.2±15.6 (24–77) years underwent operation between May 2000 and October 2001. The main diagnoses were uveitis (anterior, intermediate, posterior and panuveitis) (*n*=9), central retinal vein occlusion (CRVO) (n=4), diabetic retinopathy (DR) (*n*=5), vitreoretinal traction syndrome (*n*=2), and Irvine–Gass syndrome (*n*=3). Nine eyes had undergone phacoemulsification (PE) previously and two eyes had been subjected to combined PE and ILM peeling. The eyes were tamponaded with gas (3), silicone oil (5) or air (11). In four cases no endotamponade was used. Improvement in visual acuity of 2 lines or more was regarded as significant. *Results:* Visual acuity improved after 3 months in 9 of the 23 patients. After 6 months and at the follow-up, a significant improvement was found in 6/21 and 7/21 patients. This improvement was predominantly seen in patients with uveitis (5/9), or diabetic maculopathy (3/5); One patient with Irvine–Gass syndrome showed a significant reduction, one with vitreoretinal traction an improvement in visual acuity. The group of patients with CRVO showed no significant change during the follow-up. The choice of endotamponade did not alter the visual acuity outcome. *Conclusions:* Different patient groups respond differently to ILM peeling. Although overall significant visual acuity improvement was observed in only one third of all cases 12 months after ILM peeling for persistent macular edema, patients with uveitis and nonproliferative diabetic maculopathy demonstrated a benefit. The lack of long-term improvement in the majority of cases is in accordance with the hypothesis that ILM peeling may reduce the intraretinal edema, but does not affect the underlying mechanism causing macular edema. So far, only diabetics have shown improvement (still unproven) from ILM peeling, and this study provides no justification for extending the treatment to macular edema of other causes. Large-scale investigations are needed to evaluate the efficacy in certain diagnosis groups.

Introduction

Macular edema is a major cause of visual loss in a number of ocular disorders, including diabetes, retinal vein occlusion, postoperative edema (Irvine–Gass), uveitis, vitreomacular traction syndrome, and retinitis pigmentosa. The reasons discussed for the development of persistent macular edema are diverse. Breakdown of the blood–retinal barrier (BRB) and vitreoretinal traction are probably the most relevant factors [25, 30].

Treatment of persistent macular edema remains a major challenge. Best analyzed is the clinical course of the macular edema in diabetes. The ETDRS study demonstrated that early photocoagulation of a clinically significant macular edema in diabetic patients reduces the visual loss by half in a subgroup of eyes with mild to moderate nonproliferative diabetic retinopathy [8]. Nevertheless, in about 50% of the patients laser photocoagulation fails to improve the functional and anatomical outcome. Due to the limited success rate and associated complications such as visual field defects, laser treatment, especially macular grid laser photocoagulation, is currently controversial. Whereas nonischemic diabetic macular edema, which has emerged only recently, still may prove to benefit from laser photocoagulation, there is no such treatment option for persistent macular edema, in which laser treatment has demonstrably failed to improve the pathology [19].

For macular edema due to other underlying conditions, potential treatment approaches are even more limited. Central retinal vein occlusion (CRVO) leads to a poor visual outcome in most cases, especially in ischemic types or in eyes with persistent macular edema. The Central Vein Occlusion Study Group reported a visual acuity of 20/100 or less after 3 years in 58% of the patients and an improvement by 2 lines or more in only 20% of cases. Treatment with laser photocoagulation or isovolemic hemodilution has no significant impact on the visual outcome of eyes with CRVO and macular edema [28]. Similar limited success is reported for treatment of persistent macular edema in patients with uveitis. In 21–52% of patients with uveitis a clinically significant macular edema with decrease of the visual acuity is found [33]. Long-term examination demonstrates a persistent reduction in visual acuity in 74% of the patients despite antiinflammatory treatment with topical NSAIDs, steroids and systemic antiinflammatory and immunosuppressive agents. Similarly, topical and systemic treatment with CAI (carbonic anhydrase inhibitors) failed to reduce the macular edema [7].

Previous publications demonstrated favorable results after pars plana vitrectomy (PPV) in patients with macular edema secondary to diabetes and CRVO with respect to the visual outcome [1, 27]. Surgical detachment of the posterior vitreous combined with gas or air tamponade leads to morphologically reduced macular edema and improved visual acuity [24]. Previous studies also showed a significant role of vitreous surgery in the management of chronic uveitis; a regression of the macular edema was observed after vitrectomy [9, 14, 31]. In addition, the treatment with systemic steroids or cytotoxic agents for vision-impairing macular edema in uveitis could be tapered and drug-related side effects reduced.

In order to further improve fluid diffusion from the retinal tissue, a removal of the remaining barrier between the vitreous cavity and the retina might be a promising approach. The inner limiting membrane (ILM) is thought to be formed by the footplates of the Müller cells; however, there is controversy as to whether the ILM can be considered a real basement membrane [22]. Peeling of the ILM has been performed previously to reduce vitreoretinal traction and in combination with the removal of macular epiretinal membranes [23]. Following the description by Kadonosono et al. [18] of the use of ICG for staining of the ILM, the advantages of the dye visualization and the easier and more complete removal of the ILM has led to several studies of ILM peeling in macular disease [4, 5, 10]. However, to date there are no long-term reports about the efficacy of ILM removal for diabetic macular edema. ILM peeling for macular edema associated with uveitis or CRVO has not been reported at all.

In this retrospective case evaluation study we examined the effect of PPV with indocyanine green (ICG)-assisted peeling of the ILM on the visual outcome in macular edema in patients with uveitis, CRVO, diabetic retinopathy, vitreoretinal traction forces, vasculitis and Irvine–Gass syndrome.

Patients and methods

Patients

A series of 23 eyes from 23 patients (13 female and 10 male) with diffuse macular edema which had persisted longer than 6 months were treated in our department between May 2000 and October 2001. All therapeutic options, e.g., grid laser photocoagulation or pharmacological treatments had been tried but had failed to have an effect. The last treatment was performed at least 3 months prior to surgery. Patients with ischemic maculopathy were excluded from the study. The only indication for surgery was the macular edema.

The mean age (±SD) was 57.2±15.6 years, with a range of 24–77 years. The patients' diagnoses were uveitis (9 eyes), diabetic retinopathy (5 eyes), CRVO (4 eyes), vitreoretinal traction (2 eyes) and Irvine–Gass syndrome (3 eyes). Nine eyes had undergone phacoemulsification previously and 2 eyes, combined phacoemulsification and ILM peeling. The preoperatively collected data included age, sex, underlying disease, past medical history, medication, previous intraocular surgery, best-corrected visual acuity (ETDRS charts; Lighthouse, Long Island, USA), slit-lamp examination and stereoscopic biomicroscopy. Visual acuity was recorded in logMAR units, where a change of 1 line on the ETDRS chart is equivalent to 0.1 logMAR unit. A change in visual acuity of 2 lines or more was regarded as significant. Intraocular pressure was recorded pre- and postoperatively. Patients were followed up

for between 3 and 23 months (mean 9.4±7.1 months). The follow-up examination included best-corrected visual acuity, slit-lamp examination and stereoscopic biomicroscopy. Fluorescein angiography was performed in selected cases.

Endpoint criteria

The endpoint criteria for this retrospective evaluation included the distance logMAR value and the anatomical result (e.g., assessment by fluorescein angiography, or at least clinical observation, of whether the macular edema resolved completely, partially or not at all).

Surgical procedure

Surgery was performed solely to resolve macular edema. PPV was performed under general anesthesia in a conventional three-port approach. Removal of vitreous was performed as completely as possible after surgical posterior vitreous detachment (PVD). ILM peeling was performed after fluid–air exchange following visualization of the ILM with ICG. Briefly, 3–5 drops of ICG (<0.2 ml, 25 mg/100 ml solvent) were applied to the macular area after fluid–air exchange and were removed after a few seconds. After removal of the ICG, ILM peeling was performed either after scraping with the diamond-dusted scraper according to Tano or directly with a fine end-gripping forceps according to the individual preferences of the surgeon. ICG did not have direct contact to the pigment epithelium in either case. Persisting autofluorescence of the macular area or the optic nerve was observed 3 months after surgery.

The ILM peeling included the macular area with all adjacent zones of retinal swelling. Usually it extended to the vascular arcade in a round shape with a radius minimally smaller than the distance from the macula to the vascular arcades.

The eyes were filled with gas (n=3; 2×C_3F_8, 1×SF_6), silicone oil (n=5), or no endotamponade was used. Pre- and postoperative intraocular hypertension was seen in one patient. No intraoperative complications were observed in any of the patients.

Results

Postoperative visual acuity (3 months, 6 months and at the follow-up visits) was compared to preoperative data. Overall, the visual acuity improved by 2 lines or more in 7 of the 23 patients. A reduction in visual acuity compared with the preoperative value was found in 3 cases, with no significant change in the remaining 11 patients.

Three months after surgery, improvement in visual acuity was seen in 8 of 23 patients, reduction in visual acuity in 6 cases, and no significant change in 9 patients. The eight cases of visual improvement were seen in five uveitic eyes, two diabetic eyes, and one eye with vitreoretinal traction. Six months after surgery we observed an improvement in 6, a reduction in 5 eyes and no change in 10 of 23 eyes.

At the last observation point three of five patients in the diabetic group showed an improvement after ILM peeling. These three patients were classified as having nonproliferative diabetic retinopathy and had received panretinal laser photocoagulation prior to surgery if necessary according to the ETDRS criteria. In contrast, a reduction or no change of visual acuity respectively was found in the two remaining diabetic patients, who both demonstrated a proliferative diabetic retinopathy. In these two patients panretinal laser coagulation had been insufficient to stabilize the retinopathy and surgery was performed to treat the macular edema. On this occasion photocoagulation was simultaneously completed by endolaser treatment.

In both the uveitis group and the diabetes group no significant vitreous opacities from previous inflammation or vitreous hemorrhages were observed preoperatively.

In the uveitis group, three of the nine patients improved overall, three showed no change, and in one case a reduction of the visual acuity was seen at the last observation point.

No significant change of visual acuity was found in the patients with CRVO. One patient with Irvine–Gass syndrome showed significant reduction in visual acuity and one patient with vitreoretinal traction showed improvement. The detailed data are shown in Table 1.

Endotamponade was used in complicated cases, employing either gas (mostly if peripheral holes became apparent during surgery) or oil (in cases with high risk of progressing proliferative retinopathy or PVR). The 15 eyes without tamponade showed improvement in 7 cases, reduction in two cases, and with no change in 6 cases. Gas tamponade led in one case each to an improvement, a reduction, and no significant change in visual acuity. In the five cases in which silicone oil was used as an endotamponade, no significant change in visual acuity over the observation period was noted in four patients, while one patient demonstrated an improvement. Overall the endotamponade did not influence visual outcome.

During the follow-up period no epiretinal membrane was observed in any of the patients. There was no correlation between the preoperative lens status and improvement or deterioration of the visual acuity after ILM peeling. Two patients underwent phacoemulsification with intraocular lens implantation during the follow-up period, which did not result in a significant change of visual acuity in the observation period.

Progression of diabetic retinopathy, or a recurrent inflammation in patients with uveitis, was not observed after surgery with the exception of one patient who demonstrated a mild uveitic episode without deterioration of visual acuity, which was successfully treated with topical steroids. Three patients required a surgical revision due to peripheral retinal detachment in the follow-up period. In all these three cases the underlying disease was CRVO with proliferative retinopathy. At the final examination these patients had at least the same visual acuity as preoperatively. One of these CRVO patients demonstrated an exudative swelling of the choroid at the last examination (17 months postoperatively), which was not causally linked to the ILM peeling.

Table 1 Patient data

No.	Age	Sex	Disease	Lens-status[a]	Tampo-nade[b]	Visual acuity (logMAR)[c]				Preoperative treatment[d]
						V/Ap	V/A3	V/A6	V/Afu	
1	67	M	CRVO	PS	No	1.3	1.3	1.5	1.0	–
2	57	F	CRVO	PH	No	1.3	1.3	2.0	1.3	–
3	24	F	CRVO	PH	SO	1.5	1.3	1.3	1.3	SY[e]
4	30	F	CRVO	PH	SO	1.7	2.0	2.0	2.0	–
5	72	M	Irvine–Gass	PS	Gas^1	1.0	1.0	1.3	1.3	SY
6	72	F	Irvine–Gass	PS	Gas^1	0.4	1.7	0.7	1.0	NSAID
7	51	F	Irvine–Gass	PS	No	1.0	1.3	1.0	1.0	SY
8	45	M	NPDR	ICS	Gas^2	1.0	0.5	0.4	0.1	[e]
9	67	M	NPDR	PH	No	2.0	1.5	1.5	1.5	[e]
10	69	F	NPDR	PH	No	0.7	1.0	1.0	0.5	[e]
11	74	M	PDR	PS	No	1.3	1.0	1.0	1.0	[e]
12	77	F	PDR	PS	No	1.3	2.0	2.0	2.0	[e]
13	69	M	Traction	PH	No	0.7	1.0	0.7	0.7	NSAID
14	62	M	Traction	PH	No	0.7	0.3	0.3	0.3	[e]
15	39	F	Uveitis (MS)	PS	No	0.4	0.2	0.2	0.1	SY
16	44	F	Uveitis post. (idiopathic)	PH	No	0.8	0.5	0.5	0.5	–
17	50	F	Uveitis interm. (Behçet)	PH	No	1.0	0.7			IS
18	62	F	Uveitis interm. (arthrosis)	PS	No	1.7	1.3			SY, NSAID
19	64	M	Panuveitis (HLA-B27)	AP	SO	2.0	1.0	1.0	1.0	SY
20	64	M	Uveitis interm. (*Yersinia enterocolica*)	PH	No	0.3	1.0	0.3	0.3	–
21	63	F	Uveitis ant. (idiopathic)	PS	SO	0.6	0.5	0.5	0.5	–
22	27	F	Uveitis interm. (idiopathic)	PH	No	0.5	0.9	0.9	0.9	SY, IS
23	66	M	Uveitis (vascular occlusion)	ICS	SO	1.7	1.7	1.7	1.7	SY

[a] *AP* Aphacic, *PH* phacic, *PS* pseudophacic, *ICS* intraoperative cataract surgery
[b] *SO* Silicone oil, Gas^1 C_3F_8 16%, Gas^2 SF_6 20%
[c] *V/Ap* Preoperative visual acuity, *V/A3* visual acuity 3 months postoperatively, *V/A6* visual acuity 6 months postoperatively, *V/Afu* visual acuity at last follow-up ($\geq$6 months)
[d] *SY* Systemic steroids, *NSAID* nonsteroidal antiinflammatory drugs, *IS* immunosuppressive therapy
[e] All diabetic patients received panretinal and central laser coagulation >3 months prior to surgery; focal or panretinal laser coagulation was usedfor patients without diabetes

Discussion

In this study 23 eyes of 23 patients with persistent (>6 months) diffuse macular edema were treated by PPV combined with ILM peeling. We observed an overall significant visual acuity improvement in 8 of 23 eyes at the end of the follow-up period. A benefit from ILM peeling with respect to visual acuity was found in five of the nine patients with uveitis and in three of the five with diabetic maculopathy.

How ILM peeling reduces diabetic macular edema is unclear; however, it is likely that the peeling can only increase diffusion of fluid from the retinal tissue by eliminating the barrier function of the ILM, a pseudomembrane formed by the endplates of Müller-cells, which is thought to act as a diffusion barrier between the retina and the vitreous. The blood–retinal barrier as evidenced by fluorescein angiography, in contrast, seems to be unaffected.

Blood–retinal barrier breakdown as seen in persistent macular edema is the result of several pathophysiological alterations which have been investigated clinically and experimentally, including increased passive permeability, structural defects of junction molecules, and increased expression of permeability factors [3, 6, 25, 29, 30]. Our results demonstrate an initial positive response but a less beneficial effect in the long term. This indicates that the ILM peeling does not influence the pathophysiological changes such as growth factor expression or altered fluid dynamics. It is much more likely that ILM peeling merely reduces the diffusion barrier towards the vitreous and thus is more efficient in patients with preexisting interface alterations. Of the two patients with vitreomacular traction syndrome, one demonstrated an improvement in visual acuity at the end of the follow-up, while the other remained unchanged. The importance of the posterior hyaloid on the development of diabetic macular edema is underlined by the observation of Nasrallah and coworkers that eyes with diabetic macular edema had a significantly higher incidence of an attached posterior vitreous than eyes without macular edema [21]. Several authors have reported favorable anatomic and functional results in patients with diabetic macular edema undergoing vitrectomy combined with removal of the posterior hyaloid and premacular hyaloid-associated traction forces [13, 23, 26]. Gandorfer et al. [10] reported favorable results with additional peeling of the ILM; visual improvement was obtained in 11 of 12 patients. These

results are explained by complete release of traction forces at the vitreoretinal interface and a decrease in the risk of subsequent epiretinal membrane formation by elimination of the scaffold for proliferating astrocytes. After ILM peeling none of our patients demonstrated postoperative epiretinal membrane formation.

In addition, the removal of the vitreous might have a beneficial effect due to a potential accumulation of growth factors and inflammatory cytokines in the vitreous gel. Previous studies showed a significant role of vitreous surgery in the management of chronic uveitis [7, 9, 14, 31], demonstrating a potential antiinflammatory effect by removal of the vitreous leading to a decrease in the frequency and severity of relapses [31]. In this study we demonstrated an improvement in more than half of the eyes with macular edema secondary to uveitis. The improvement in these patients, however, may have been due to removal of media opacity and not associated with clinical improvement of macular edema. This is consistent with our data, as we observed no reduction of the macular edema on fluorescein angiography in these patients. The loss of the vitreous opacity, rather than the ILM peeling, may have made the main contribution to the visual improvement. Inflammatory reactions, however, may be relevant to the formation of macular edema not only in uveitis, but also in other conditions such as diabetic maculopathy. Recently, leukostasis-mediated endothelial cell damage and apoptosis in experimental diabetes have been demonstrated to increase the vascular permeability [16, 17]. With respect to the inflammation-mediated fluid accumulation, intravitreal application of triamcinolone in combination with ILM peeling could be a promising approach. Triamcinolone treatment alone has recently been reported to have a beneficial effect on diabetic macular edema that fails to respond to conventional treatment [15, 20]. Similarly, preliminary studies were performed in patients with uveitis, central vein occlusion, and cystoid macular edema after cataract surgery [2, 12, 32]. Details of the mechanism by which crystalline cortisone reduces the retinal swelling and fluid accumulation are unknown. A reduction in the inflammatory response most likely plays a role. However, there is currently no broad-based clinical investigation analyzing the long-term effect of these treatment approaches on persistent macular edema and its interaction with ILM peeling.

Despite the limited number of patients, the current study indicates that only selected patients may benefit from ILM peeling. Not only the state of the disease, but also the underlying condition may influence the surgical outcome. In the current study patients with CRVO failed to improve after ILM peeling and seemed to have a poor visual prognosis similar to that described for patients without treatment by the Central Vein Occlusion Study Group [28]. Furthermore, our findings show an improvement in visual acuity as well as a reduction in the edema on fluorescence angiography only in patients with nonproliferative diabetic retinopathy. Patients who suffered from proliferative diabetic retinopathy failed to change or worsened. Thus, our data are not as favorable as those of previous reports, which could be attributed to the unselected diabetic group in the present study [10].

In common with all previous reports, the current study is certainly limited by the small number of patients included. However, this is the first report of ILM peeling for macular edema associated with uveitis of CRVO. The data clearly demonstrate the limitations of the procedure: For CRVO, ILM peeling seems to be not effective. The improvement in diabetics and in patients with uveitis is just as likely to be attributable to the vitrectomy as to the ILM peeling. In uveitic patients, for example, we found a lack of anatomical improvement (continued FFA leakage) after ILM peeling. However, ILM peeling can be effective with respect to visual acuity in certain conditions, justifying further investigations. These future studies should include data on reading performance and retinal thickness to better correlate anatomical with clinically relevant alterations.

Acknowledgements We thank the Kämpgen Stiftung, Köln, and Köln Fortune for financial support.

References

1. Amirikia A, Scott IU, Murray TG, Flynn HW Jr, Smiddy WE, Feuer WJ (2001) Outcomes of vitreoretinal surgery for complications of branch retinal vein occlusion. Ophthalmology 108:372–376
2. Antcliff RJ, Spalton DJ, Stanford MR, Graham EM, Ffytche TJ, Marshall J (2001) Intravitreal triamcinolone for uveitic cystoid macular edema: an optical coherence tomography study. Ophthalmology 108:765–772
3. Barber AJ, Antonetti DA, Gardner TW (2000) Altered expression of retinal occludin and glial fibrillary acidic protein in experimental diabetes. Invest Ophthalmol Vis Sci 41:3561–3568
4. Brooks HL Jr (2000) Macular hole surgery with and without internal limiting membrane peeling. Ophthalmology 107(10):1939–1948
5. Da Mata AP, Burk SE, Riemann CD, Rosa RH Jr, Snyder ME, Petersen MR, Foster RE (2001) Indocyanine green-assisted peeling of the retinal internal limiting membrane during vitrectomy surgery for macular hole repair. Ophthalmology 108(7):1187–1192
6. De Vries C, Escobedo JA, Ueno H, Houck K, Ferrara N, Williams LT (1992) The fms-like tyrosine kinase, a receptor for vascular endothelial growth factor. Science 255(5047):989–991

7. Dugel PU, Rao NA, Ozler S, Ligget PE, Smith RE (1992) Pars plana vitrectomy for intraocular inflammation-related cystoid macular edema unresponsive to corticosteroids. Ophthalmology 99:1535–1541
8. Early Treatment Diabetic Retinopathy Study (1985) Report number 1. Photocoagulation for diabetic macular edema. Arch Ophthalmol 103:1796–1806
9. Eckardt C, Bacskulin A (1992) Vitrectomy in intermediate uveitis. Dev Ophthalmol 23:232–238
10. Gandorfer A, Messmer EM, Ulbig MW, Kampik A (2000) Resolution of diabetic macular edema after surgical removal of the posterior hyaloid and the inner limiting membrane. Retina 20:126–133
11. Glacet-Bernard A, Zourdani A, Milhoub M, Maraqua N, Coscas G, Soubrane G (2001) Effect of isovolemic hemodilution in central retinal vein occlusion. Graefes Arch Clin Exp Ophthalmol 239:909–914
12. Greenberg PB, Martidis A, Rogers AH, Duker JS, Reichel E (2002) Intravitreal triamcinolone acetonide for macular oedema due to central retinal vein occlusion. Br J Ophthalmol 86(2):247–248
13. Harbour JW, Smiddy WE, Flynn HW, Rubsamen PE (1996) Vitrectomy for diabetic macular edema associated with a thickened and taut posterior hyaloid membrane. Am J Ophthalmol 121:405–413
14. Heimann K, Schmanke L, Brunner R, American B (1992) Pars plana vitrectomy in the treatment of chronic uveitis. Dev Ophthalmol 23:195–203
15. Jonas JB, Sofker A (2001) Intraocular injection of crystalline cortisone as adjunctive treatment of diabetic macular edema. Am J Ophthalmol 132:425–427
16. Joussen AM, Poulaki V, Pak J, Ju S-T, Rook SL, Mitsiadis N, Esser P, Kirchhof B, Adamis AP, Aiello LP (2002) Diabetic leukocytes mediate vascular endothelial cell apoptosis via Fas –Fas ligand mediated pathway. FASEB J:**XXX**
17. Joussen AM, Poulaki V, Qin W, Kirchhof B, Mitsiades N, Wiegand SJ, Rudge J, Yancopoulos GD, Adamis AP (2002) Retinal vascular endothelial growth factor induces intercellular adhesion molecule-1 and endothelial nitric oxide synthase expression and initiates early diabetic retinal leukocyte adhesion in vivo. Am J Pathol 160(2):501–509
18. Kadonosono K, Itoh N, Uchio E, Nakamura S, Ohno S (2000) Staining of internal limiting membrane in macular hole surgery. Arch Ophthalmol 118(8):1116–1118
19. Kremser BG, Kunze C, Troger J, Ulmer H, Kieselbach GK (1996) Grid pattern photocoagulation for diabetic macular edema: long term visual results. Ophthalmologica 210(3):160–162
20. Martidis A, Duker JS, Greenberg PB, Rogers AH, Puliafito CA, Reichel E, Baumal C (2002) Intravitreal triamcinolone for refractory diabetic macular edema. Ophthalmology 109(5):920–927
21. Nasrallah FP, Jalkh AE, Van Coppenolle F, Kado M, Trempe CL, McMeel JW, Schepens CL (1988) The role of the vitreous in diabetic macular edema. Ophthalmology 95:1335–1339
22. Nishihara H (1991) Studies on the ultrastructure of the inner limiting membrane of the retina-distribution of anionic sites in the inner limiting membrane of the retina. Acta Soc Ophthalmol Jpn 95:951–958
23. Pendergast SD, Hassan ST, Williams GA, Cox MS, Margherio RR, Ferrone PJ, Garretson BR, Trese MT (2000) Vitrectomy for diffuse diabetic macular edema associated with a taut premacular posterior hyaloid. Am J Ophthalmol 130:178–186
24. Saika S, Tanaka T, Miyamoto T, Ohnishi Y (2001) Surgical posterior vitreous detachment combined with gas/air tamponade for treating macular edema associated with branch retinal vein occlusion: retinal tomography and visual outcome. Graefes Arch Clin Exp Ophthalmol 239:729–732
25. Sander B, Larsen M, Engler C, Strom C, Moldow B, Larsen N, Lund-Andersen H (2002) Diabetic macular oedema: a comparison of vitreous fluorometry, angiography, and retinopathy. Br J Ophthalmol 86(3):316–320
26. Tachi N, Ogino N (1996) Vitrectomy for diffuse macular edema in cases of diabetic retinopathy. Am J Ophthalmol 122:258–260
27. Tachi N, Hashimoto Y, Ogino N (1999) Vitrectomy for macular edema combined with retinal vein occlusion. Doc Ophthalmol 97:465–469
28. The Central Vein Occlusion Study Group (1995) Evaluation of grid pattern photocoagulation for macular edema in central vein occlusion. Ophthalmology 102:1425–1433
29. Tolentino MJ, Miller JW, Gragoudas ES, Jakobiec FA, Flynn E, Chatzistefanou K, Ferrara N, Adamis AP (1996) Intravitreous injections of vascular endothelial growth factor produce retinal ischemia and microangiopathy in an adult primate. Ophthalmology 103(11):1820–1828
30. Vinores SA, Derevjanik NL, Mahlow J, Berkowitz BA, Wilson CA (1998) Electron microscopic evidence for the mechanism of blood-retinal barrier breakdown in diabetic rabbits: comparison with magnetic resonance imaging. Pathol Res Pract 194:497–505
31. Wiechens B, Nölle B, Reichelt JA (2001) Pars-plana vitrectomy in cystoid macular edema associated with intermediate uveitis. Graefes Arch Clin Exp Ophthalmol 239:474–481
32. Young S, Larkin G, Branley M, Lightman S (2001) Safety and efficacy of intravitreal triamcinolone for cystoid macular oedema in uveitis. Clin Exp Ophthalmol 29(1):2–6
33. Zimmerman PL (1999) Pars planitis and other intermediate uveitis. In: Yanoff M, Duker JS (eds) Ophthalmology. Mosby, St. Louis, pp 10.1–10.6