VITRECTOMY WITH PEELING OF THE INNER LIMITING MEMBRANE FOR TREATING DIABETIC MACULAR EDEMA

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ABSTRACT

Purpose: to evaluate the results of pars plana vitrectomy with peeling of the inner limiting membrane (ILM stained with infracyanine green (IfCG) in 26 patients with diabetic macular edema, and to identify which factors are associated with a better postoperative visual outcome.

Patients and methods: 26 patients with diabetic macular edema were included in the study. A pars plana vitrectomy with ILM peeling stained with IfCG was performed, in some cases combined with cataract surgery. In 22 patients the ILM was retained, examined with electron microscopy and compared with normal ILM's. Visual acuity and fundus examination were recorded several months after surgery. To determine which factors lead to the best postoperative results, patients were divided into different groups and compared.

Results: during surgery, a taut posterior hyaloid was found in 26 patients, which was successfully detached in all cases. ILM peeling within the vessel arcade succeeded in all patients. Postoperative examination showed improved visual acuity and decreased macular edema in 19 patients, unaltered visual acuity in 3 patients and decreased visual acuity in 4 patients. Comparison between different groups of patients revealed that young patients with recent vision loss and without previous macular laser treatment, had better postoperative results. Electron microscopical examination showed a more condensed ILM in diabetic patients, consisting of a layer of fine curled fibers.

Conclusion: pars plana vitrectomy with peeling of the ILM stained with IfCG leads to good postoperative results in young diabetic patients with recent vision loss due to macular edema and without previous macular laser treatment.

ABSTRACT

But: Evaluer les résultats de la vitrectomie avec pelage de la membrane limitante interne après coloration au vert d'infracyanine pour l'oedème maculaire diabétique et identifier les facteurs qui pourraient être associés à une bonne acuité visuelle postopératoire.

Méthodes: 26 patients diabétiques avec une baisse d'acuité visuelle suite à une oedème maculaire ont été inclus dans l'étude. On a effectué une vitrectomie pars planaire avec pelage de la membrane limitante interne après coloration au vert d'infracyanine. On a aussi opéré la cataracte en même temps chez quelques patients. Chez 22 patients on a conservé et comparé la membrane limitante interne avec des membranes normales.

Nous avons suivi l'acuité visuelle et le fond d'oeil pendant plusieurs mois après l'opération. On a divisé les patients en plusieurs groupes pour déterminer quels facteurs avaient un effet favorable sur l'acuité visuelle postopératoire.

Résultats: Chez tous les patients on a détaché l'hyaloide postérieure qui était attachée, et on a pelé la membrane limitante interne. L'examen postopératoire a montré une amélioration de l'acuité visuelle chez 19 patients, une baisse d'acuité visuelle chez

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4 patients et une acuité visuelle stable chez 3 patients. Les résultats suggèrent aussi qu'une intervention rapide chez des patients jeunes qui n'ont jamais eu de traitement maculaire au laser, est plus favorable pour une bonne acuité visuelle postopératoire. L'examen microscopique a montré une membrane limitante interne plus condensée et composée d'une couche de fibres fines et tortillées.
Conclusion: Une vitrectomie rapide, avec pelage de la membrane limitante interne après coloration au vert d'infracyanine, est favorable chez des jeunes patients diabétiques qui n'ont jamais eu de traitement au laser pour oedème maculaire.

KEY WORDS:

Diabetes, macular edema, vitrectomy, inner limiting membrane, infracyanine green

MOTS-CLÉS:

Diabète, oedème maculaire, vitrectomie, membrane limitante interne, vert d'infracyanine

INTRODUCTION

Macular edema is a major cause of visual loss in patients with diabetes. Different factors play a role in the pathogenesis of this disease, such as duration of the disease, associated arterial hypertension, insulin use and panretinal photocoagulation (8,10).

Presently, diabetic macular edema is treated with laser photocoagulation on focal leaking microaneurysms or grid treatment on areas of diffuse macular edema, mainly to obtain stabilization of the visual acuity (4). Furthermore, several types of diabetic maculopathy may not be amenable for macular laser therapy such as ischemic maculopathy, cystoid macular edema, and dense foveal exudates. Because vitreomacular traction was described as an important causative factor in diabetic macular edema, vitreoretinal surgery has been proposed as a possible treatment (6,7,9,11,17,18). Removing the inner limiting membrane (ILM) was found to be crucial in macular hole surgery and led to the idea of performing the same in vitrectomy for diabetic macular edema (5). Another technique used in macular hole surgery, was staining the ILM with a green dye, such as indocyanine green (ICG) or infracyanine green (IfCG), for increased visualisation (4,16,20). The goal of this study is to evaluate whether vitrectomy with removal of the ILM after staining with IfCG has a beneficial effect to treat diabetic macular edema.

PATIENTS AND METHODS

The medical records of 26 patients who had persistent diabetic macular edema leading to significant vision loss were reviewed. Patients with decreased visual acuity caused by other ocular pathology such as vitreous haemorrhage, prominent fibrovascular proliferation or epiretinal membranes, retinal detachment and previous vitreous surgery were not included in this study. The following patient data were recorded: age, gender, type and duration of diabetes, presence of associated arterial hypertension, duration of visual loss, previous focal macular or panretinal laser photocoagulation, previous ocular surgery, optimal corrected Snellen visu-

al acuity, slit lamp examination, stereoscopic fundus ophthalmoscopy and fluorescein angiography. During surgery, thickening and firmly attachment of the posterior hyaloid was recorded if present. Postoperatively, at regular time intervals visual acuity, postoperative complications and clinical fundoscopic resolution or recurrence of the macular edema were monitored. In most patients, optical coherence tomography (OCT) was also performed.

Because of the high incidence of cataract formation after vitrectomy with a gas or oil tamponade, a phacoemulsification with implantation of a BL27 intraocular lens (Bausch & Lomb, St-Louis, USA) preceded the vitrectomy during the same procedure in several patients.

The surgical technique included a standard three-port pars plana vitrectomy using a variable port vitrectome (Bausch & Lomb, St-Louis, USA). First, a core vitrectomy was performed. If not already present, a detachment of the posterior hyaloid membrane was created by suction around the optic disc. With the vitrecteous cutter set to a slit opening and lower aspiration, the vitreous base was shaved 360°. After closing the infusion line, 0.3 ml of IfCG (Laboratoires S.E.R.B., Paris, France) was sprayed over the macular area. After 2 minutes, the infusion line was reopened and the excess green dye removed by passive aspiration using a blunt backflush-needle. Next, the ILM was removed with a two-teethed retinal forceps in a rhexis-like manner. If necessary, additional laser therapy was applied to the retinal periphery. At the end of the surgery, the eye was filled with a 15% SF_6 / air mixture.

The best-corrected Snellen visual acuity was evaluated 2 weeks, 4-8 weeks, 12-20 weeks, 24-40 weeks and one year after surgery. Additional check-ups at different time intervals were sometimes performed by the patient's own ophthalmologist. The macular edema was evaluated at each of these time intervals clinically with stereoscopic fundoscopy and occasionally with OCT. In some patients, a fluorescein angiography was also performed.

From 22 patients with diabetes and ILM peeling, the ILM was retained and fixed in glutaraldehyde and prepared for routine electron microscopy with embedding in epoxy resin.

The electron microscopy pictures of the diabetic patients were compared with normal ILM's of cornea-donor eyes and with the ILM's of patients with macular holes and macular pucker.

RESULTS

We included 29 eyes of 26 patients: 15 right eyes and 14 left eyes with significant diabetic macular edema. Three patients underwent a vitrectomy in both eyes. The group was composed of 12 women and 14 men. The patients had a mean age of 56 years, varying from 25 to 73 years. Diabetes mellitus type 1 was found in 34,5 % of the patients, type 2 in 65,4%. The average duration of vision loss was 14 months ranging from 1 month to 36 months. The mean visual acuity, measured with the Snellen Visual acuity chart, was 20/200 before surgery, varying from counting fingers to 20/40. All patients had persistent macular edema after treatment with panretinal photocoagulation. Previous focal or grid macular laser treatment was performed in 53,8% of the patients. Uncomplicated cataract extraction with implantation of an intraocular lens was performed previously in 19% of the patients.

We performed a vitrectomy combined with cataract surgery in 13 eyes. Intraoperatively, we found an attached hyaloid membrane in 26 patients. There was an epiretinal membrane in one patient. A successful circular or oval peeling of the ILM around the fovea extending between the temporal vascular arcade could be performed in all patients.

The visual acuity improved in 20 eyes because of resolved or diminished macular edema. In 4 eyes the visual acuity remained unaltered and in 5 eyes the visual acuity decreased. Postoperatively, one patient developed a peripheral retinal detachment for which extra surgery was required. Lens opacities developed in 4 patients and required cataract surgery after the vitrectomy.

Since the visual acuity varied between patients before the surgery, all postoperative measurements were normalized relative to the preoperative value. When all patient data were grouped and averaged, a progressive increase in visual acuity was observed (Figure 1). After statistical analysis with a two tailed t-test, visual acuity did not significantly increase after 2 weeks ($p=0.539$), but increased from week 4-8 on

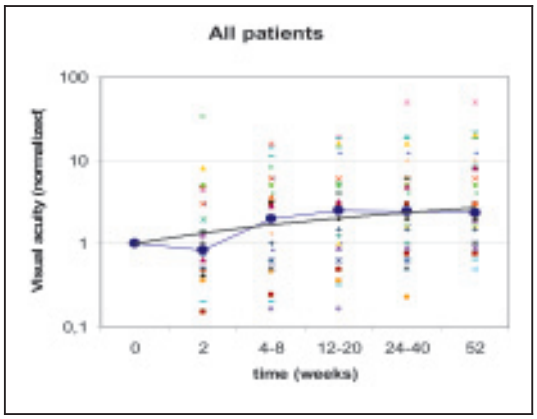


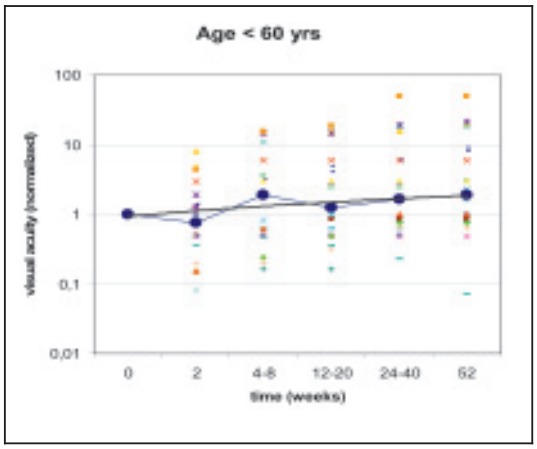
Fig 1. The normalized visual acuity (VA) of all patients at several time intervals. Each different symbol represents another patient. The line with the closed circles connects the median values. The straight line is the trendline.

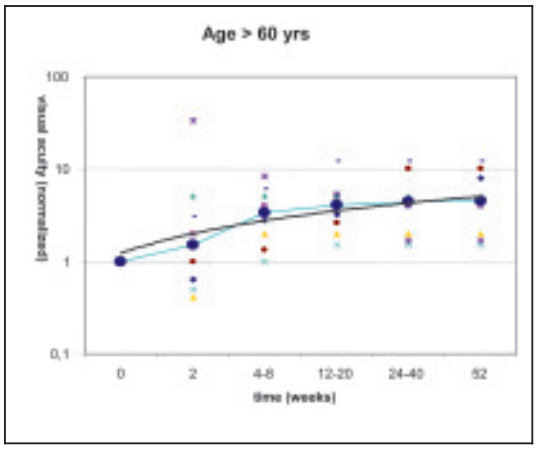
(p=0,002) up to 12 months (p<0.001). To determine which factors can be used to determine the outcome of the surgery, the patients were divided in different groups and compared. The investigated factors were: age, type of diabetes, initial visual acuity, duration of vision loss and previous focal macular laser treatment. (Table 1) We found that patients younger than 60 years old (p=0,002, n=18) improved better than the older patients (p=0,056, n=8) (Figure 2). Patients with vision loss during a period less than one year (p=0,006, n=12), improved more than patients with vision loss during a longer time (p=0,01, n=14) (Figure 3). Despite the fact that no statistically significant results were found, an initial visual acuity of 1/10 or better (p=0,14, n=10) resulted in a better visual outcome compared to the group

Table 1: *distribution of preoperative and 1 year postoperative VA in all patients.*

	EYE	AGE (years)	DIABETES TYPE	LASER FM PREOP	DURATION VISION LOSS (months)	VA PREOP (decimal)	VA 1 YEAR POSTOP (decimal)
Preop VA < 0,1					**average: 15,3**	**average: 0,03**	**average: 0,24**
Patient 1	RE	69	2	-	20	0,003	0,005
Patient 2	LE	59	2	-	11	0,016	0,8
Patient 3	LE	72	2	+	22	0,016	0,08
Patient 4	LE	57	2	-	2	0,016	0,016
Patient 5	LE	70	2	-	28	0,025	0,25
Patient 6	RE	62	2	+	6	0,025	0,2
Patient 7	LE	57	1	+	22	0,033	0,1
Patient 8	RE	58	2	-	6	0,033	0,3
Patient 9	LE	57	1	+	45	0,033	0,016
Patient 10	RE	73	2	+	11	0,033	0,4
Patient 11	RE	56	2	+	4	0,033	0,1
Patient 12	RE	58	2	+	17	0,033	0,025
Patient 13	RE	46	1	-	14	0,05	0,4
Patient 14	LE	26	1	-	15	0,055	1
Patient 15	RE	58	2	-	16	0,07	0,005
Patient 16	LE	66	2	-	6	0,08	0,16
Preop VA > 0,1					**average: 14,2**	**average: 0,24**	**average: 0,39**
Patient 17	RE	55	1	-	8	0,1	0,16
Patient 18	RE	60	2	-	30	0,1	0,6
Patient 19	RE	63	2	+	23	0,1	0,4
Patient 20	RE	25	1	-	14	0,16000	0,3
Patient 21	RE	60	1	+	5	0,16	0,16
Patient 22	LE	49	1	+	2	0,16	0,16
Patient 23	LE	45	1	+	19	0,2	0,16
Patient 24	LE	57	2	-	10	0,3	0,7
Patient 25	RE	67	2	-	8	0,4	0,6
Patient 26	RE	32	1	-	23	0,8	0,7

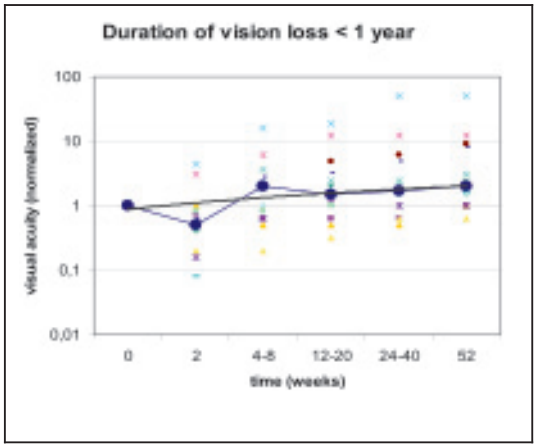
VA=visual acuity, RE=right eye, LE=left eye, FM laser= focal macular laser.

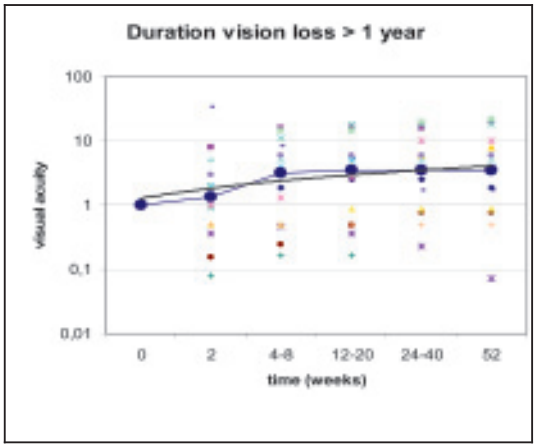




(a) *(b)*

Fig 2. The normalized VA at several time intervals comparing younger (a) and older (b) patients.





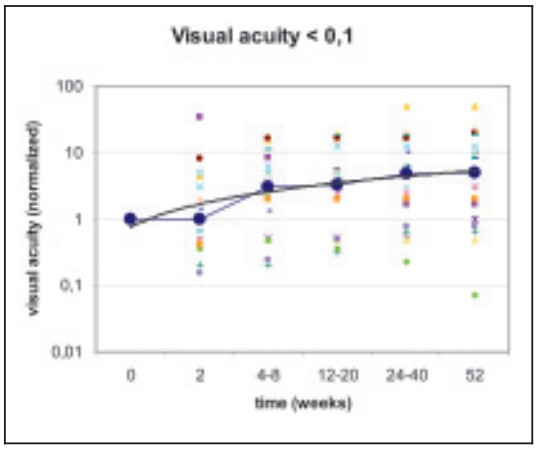
(a) *(b)*

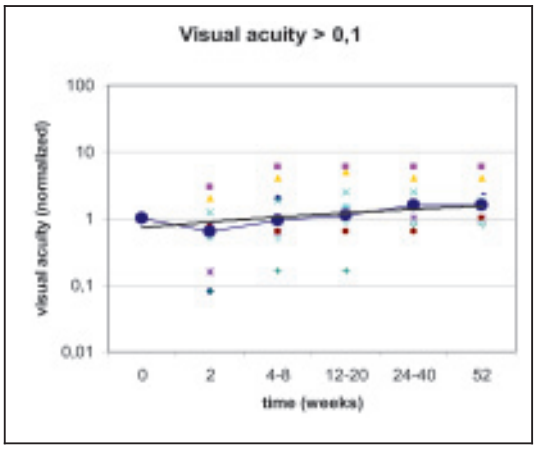
Fig 3. The normalized VA at several time intervals comparing patients with short-term (a) and long-term (b) visual loss.

with a worse initial visual acuity (p< 0,001, n=16) (Figure 4). Patients with previous macular laser treatment (p=0,005, n=14) progressed less than patients without previous macular laser treatment (p=0,01, n=12) (Figure 5). We found nearly no difference in progression between type 1 (p=0,13, n=10) and 2 (p=0,27, n=16) diabetes.(Figure 6)
Electron microscopy of the ILM's of the diabetes patients showed in the specimens only a long curled or plicated layer of very fine fibers without any other intracellular component, corresponding to basement membrane material. In all pictures of the diabetes patients the ILM was more condensed when compared to the ILM obtained from surgery in patients with macular holes or puckers (Figure 7). This was also true when correcting for the age difference.

DISCUSSION

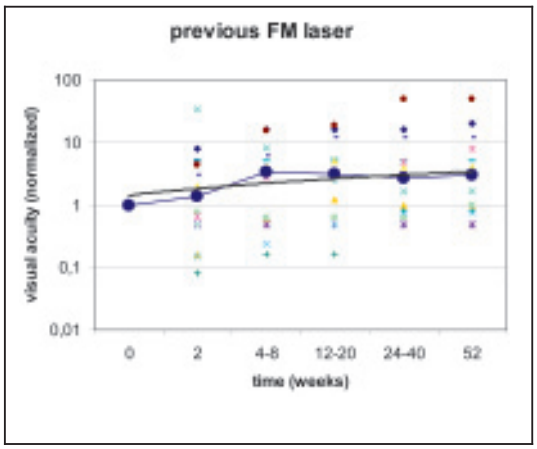
Macular edema is the most common cause of decreased visual acuity among diabetics. Several factors play a role in the pathophysiology of diabetic macular edema: increased vascular permeability from micro-aneurysms or by vascular permeability factors, such as vascular endothelial growth factor and traction of the posterior vitreous on the macula (17). This vitreomacular traction has led to vitrectomy as treat-

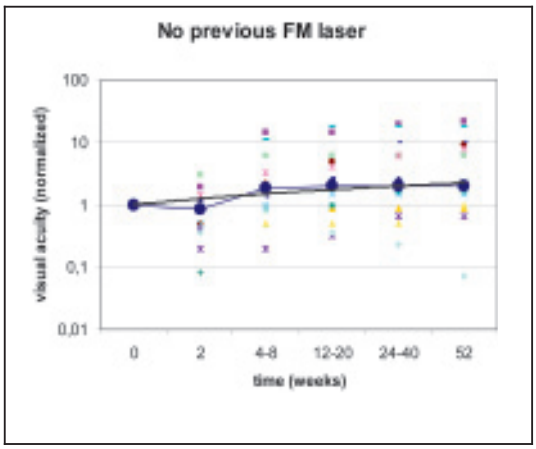




(a) *(b)*

Fig 4. The normalized VA at several time intervals comparing patients with a worse (a) or better (b) preoperative VA.

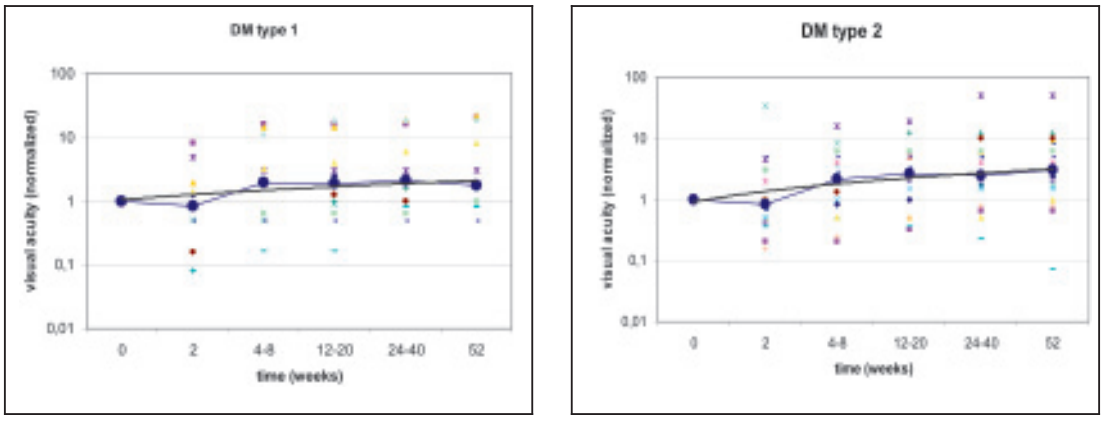




(a) *(b)*

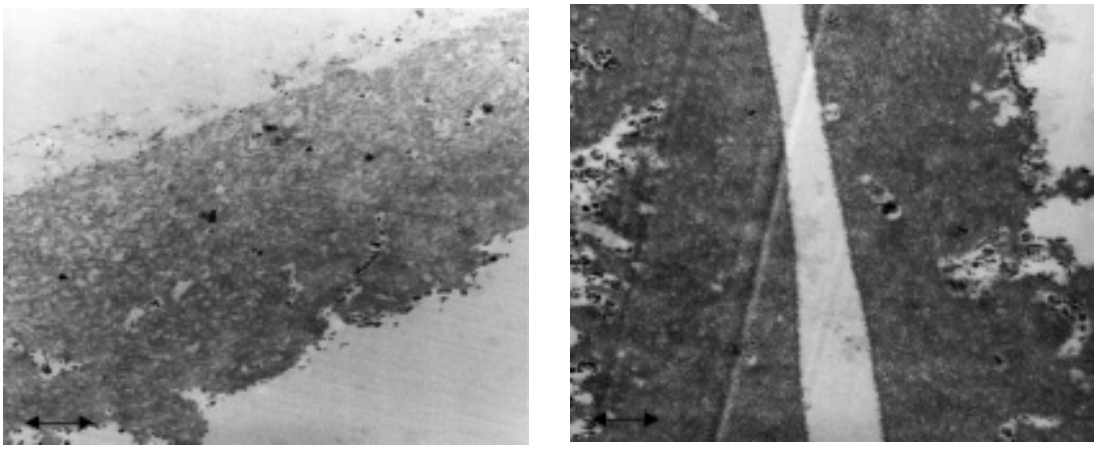
Fig 5. The normalized VA at several time intervals comparing patients with (a) and without (b) previous focal maular laser treatment.

ment for diabetic macular edema. Several studies evaluated results and visual outcome after vitrectomy for macular edema, without approaching the ILM, and concluded that this surgery had a beneficial effect in patients with a thickened and taut posterior hyaloid membrane (6,9,18). Gandorfer evaluated the resolution of macular edema in diabetes after vitrectomy with removal of the ILM, with good results in 10 of 12 operated eyes (5). Because the ILM is known to be a thin and transparant layer, staining with green dyes such as ICG and IfCG to realize better visualization and more complete removal, was first evaluated in macular hole surgery (4,16,20). Staining of the ILM with ICG was applied in vitrectomy for diabetic macular edema, with a good postoperative visual outcome (2,12,14). Several publications reported a possible toxic effect of ICG on the retinal pigment epithelial cells or on the optic nerve, which is probably related to the solvent of the dye (1,15,16). ICG contains iodine to enhance its solubility and must be dissolved in pure H_2O. IfCG does not contain iodine, precipitates in H_2O and glucose 5% is rather used as a solvent. Since the IfCG dye is dissolved in 5 ml pure water for injection and then 1 ml of this solution is diluted in 4 ml BSS Plus, a hypo-osmotic solution is obtained.



(a) *(b)*

Fig 6. The normalized VA at several time intervals comparing patients with type 1 diabetes (a) and type 2 diabetes (b).



(a) *(b)*

Fig 7. ILM and nerve fiber layer of a normal control patient: bar of 1 cm is 0.4 μm (a). ILM of a diabetic patient of the same age: bar of 0.95 cm is 1 μm (b).

The results of this study suggest that vitrectomy with peeling of the ILM after staining with IfCG, may have a beneficial effect in patients with diabetic macular edema. Furthermore, this study indicates that age, duration of vision loss, initial visual acuity and previous macular laser treatment are the most important factors to determine the postoperative result. Younger patients (less than 60 years of age) with a relatively good initial visual acuity after a short-term vision loss (one year or less), but without previous macular laser treatment, seem to have the best visual outcome after this surgery. The patients in our study who had a postoperative decrease of visual acuity, all received focal macular laser treatment before surgery and had a preoperative loss of visual acuity for at least 16 months. After surgery, the decrease of visual acuity could be observed early (2-4 weeks) in the postoperative course.

Vitrectomy combined with phacoemulsification, made it initially difficult to differentiate whether the increased visual acuity was a result of the lens removal or of the vitreous surgery.

However, the progressively increasing postoperative visual acuity, even after several months, cannot be explained by the cataract surgery, and can therefore be interpreted as the result of the vitrectomy performed.

The electron microscopy study indicates that diabetes might have an influence on the basement membrane rendering it more condensed. This could possibly be secondary to a chemical reaction, such as glucosylation of basement membrane components.
In summary, this study indicates that vitrectomy with IfCG stained ILM-peeling may be beneficial in the treatment of diabetic macular edema. To determine whether laser treatment or vitrectomy is the best therapeutical choice in diabetic macular oedema, and to further refine the patient groups in which either treatment is preferred, a future randomized prospective study is necessary. A randomised controlled feasibility trial of vitrectomy versus laser for diabetic macular edema has already been performed. (19)

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