European Journal of Ophthalmology / Vol. 15 no. 6, 2005 / pp. 795-799

Visual acuity after vitrectomy and epiretinal membrane peeling with or without premacular indocyanine green injection

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PURPOSE. *To compare postoperative visual acuity of eyes operated for an epiretinal membrane (ERM), with or without intraoperative intraocular indocyanine green (ICG) injection.*
METHODS. *Retrospective study of 75 pseudophakic eyes with epiretinal membrane operated by vitrectomy-peeling. In 20 cases operated in 2001 and 2002 (Group 1), ICG diluted in 5% glucose solution was injected intraoperatively into the vitreous. In another group of 55 cases operated between 1996 and 1999 (Group 2), ICG was not used.*
RESULTS. *The mean visual acuity was 0.32^{+1} and 0.32^{+2} preoperatively, 0.4^{+2} and 0.5 at 1 month, and 0.63 and 0.63^{+2} on the final examination in Groups 1 and 2, respectively. Visual acuities were not significantly different between the two groups.*
CONCLUSIONS. *Premacular injection of ICG during vitrectomy to facilitate epiretinal membrane peeling did not appear to compromise postoperative improvement of visual acuity. However, its use is questioned since it did not yield better postoperative results and because potential toxic adverse reactions could not be excluded by this study. (Eur J Ophthalmol 2005; 15: 795-99)*

KEY WORDS. *Epiretinal membrane, ICG, Indocyanine green, Vitrectomy*

Accepted: June 19, 2005

INTRODUCTION

Internal limiting membrane (ILM) ablation appears to improve the functional prognosis of epiretinal membrane (ERM) surgery (1). This delicate surgical procedure is facilitated by intraoperative premacular injection of indocyanine green (ICG) (2), as ICG selectively stains the ILM (3, 4), making it more clearly visible during peeling.

However, intraoperative intravitreous injection of ICG does not appear to be devoid of adverse effects. Several authors have observed poorer functional results after the use of ICG during macular hole surgery (5-7), while other authors have observed lesions of the neurosensory retina and retinal pigment epithelium during experimental studies (8-11).

The present study was designed to compare postoperative visual acuity of eyes operated for ERM with or without intraoperative intraocular ICG injection.

METHODS

We retrospectively studied patients operated at Jules Gonin Eye Hospital in Lausanne between 1996 and 2002 for ERM by vitrectomy-peeling, with or without intraoperative intraocular ICG injection.

 1120-6721/795-05$15.00/0

Eyes presenting idiopathic or secondary ERM and not previously operated were included in this study. To avoid bias due to secondary cataract occurring after vitrectomy, we only included pseudophakic eyes with transparent media on the final examination. These eyes were either pseudophakic before vitrectomy or were phakic with a transparent lens before vitrectomy, and were subsequently operated for cataract after vitrectomy.

We excluded eyes with a macular lesion due to a disease other than ERM, a lamellar or transfixing macular hole, and retinal tears or detachments occurring during or after vitrectomy.

Group 1 consisted of 20 cases operated in 2001 and 2002 with the use of ICG and the control group (Group 2) consisted of 55 cases operated from 1996 to 1999 without the use of ICG. This second group has been described elsewhere (1). From 1996 to 2002, the technique of vitrectomy for macular ERM did not change: the procedure, type of instruments, illumination, and viewing system all remained the same.

The following factors were studied in the two groups: age; sex; best-corrected visual acuity measured with an Early Treatment Diabetic Retinopathy Study chart, preoperatively, at 1 month and at the final examination; time interval between cataract surgery and vitrectomy; appearance of the posterior capsule on the final examination (capsule open or closed); intraoperative and postoperative complications; and follow-up between vitrectomy and final examination.

Vitrectomy was performed by the same surgeon (E.H.B.) according to a standard technique: three-port pars plana vitrectomy using a vitreous cutter equipped with a light source (Lausanne set, Oertli, Switzerland). The ocular fundus was visualized by a personal wide-angle system (12) or a planoconvex contact lens. When the vitreous was still adherent to the retina, the posterior hyaloid was detached using a silicone tipped aspiration needle.

The ERM was peeled with forceps. For the patients in Group 1, ICG was prepared according to our technique described elsewhere (13) and was diluted in 5% glucose solution (at a concentration of 0.1%). ICG was slowly injected over the macula so that the dye spread over the retina as far as the superior and inferior temporal vascular arcades. The dye was flushed out within 30 seconds of injection. The ERM was then peeled in the macular area. In four cases of Group 1, ICG was reinjected to confirm complete peeling of the ERM, also including the ILM. In cases in Group 2, all resected membranes were examined by light microscopy and electron microscopy and the presence of ILM on the fragments analyzed was confirmed in 55 cases.

Nonparametric Kruskal-Wallis and Wilcoxon tests were used to compare continuous variables between the two groups. A chi-square test was used to compare categorical variables.

RESULTS

Tables I through III describe the main results. The mean visual acuity, measured preoperatively, 1 month after the operation, and on the final examination, was not significantly different between the two groups ($p>0.05$).

All eyes in Group 1 (20 cases) were pseudophakic at the time of vitrectomy. The mean interval between cataract surgery and vitrectomy was 23.4 months. In Group 2 (55 cases), 20 eyes were pseudophakic at the time of vitrectomy. The mean interval between cataract surgery and vitrectomy was 16.9 months. The other 35 eyes were operated for cataract after vitrectomy after a mean interval of 16.7 months. In the control group, the visual acuity measured before vitrectomy and at the final examination did not differ between eyes that were pseudophakic and those that were phakic before vitrectomy.

DISCUSSION

Ablation of the ILM of the retina during ERM surgery remains controversial. A recent study (1) showed that ILM peeling was associated with a better functional prognosis. ILM peeling is a delicate and sometimes difficult procedure and has been facilitated by the use of intraocular ICG injection (2), which selectively stains the ILM (3, 4). However, several authors have suggested a possible toxicity of ICG to the retina and pigment epithelium, as they observed poorer functional recovery after injection of ICG in idiopathic macular hole surgery (6, 7). Atrophy of the macular pigment epithelium has been described clinically (5). Alterations of the plane of separation between the ILM and the underlying neurosensory retina have also been observed on electron microscopy (14-16). In vitro and in vivo experimental studies demonstrated direct toxicity of ICG on the pigment epithelium and neurosensory retina (11, 17-19). These adverse effects were correlated with the sodium concentration in the ICG solvent (20, 21),

osmolarity (10, 22), ICG exposure time (17), and the concentration of the solution (8-10, 23-26). Some of these investigators proposed the use of 5% glucose rather than balanced salt solution (BSS) to dilute ICG and preferred infracyanine green (noniodinated ICG) to ICG.

It is noteworthy that the complications due to ICG described in the literature mainly concern macular hole surgery. The supposed toxicity of ICG could therefore be less marked during ERM peeling, as ICG is not in direct contact with the pigment epithelium during this procedure. In some cases of thick ERM, the dense center is frequently less intensely stained than the thinner peripheral part. This is most likely due to the fact that ICG selectively stains the acellular ILM, but not the cellular ERM (3, 4, 27). We could therefore assume that the cellular ERM acts as a protective film between ICG and the macular retina.

TABLE I - CLINICAL DATA OF GROUPS I AND II

	Group 1 (with ICG)		**Group 2** (without ICG)		**Difference between groups**
Number of eyes	20		55		
Age (yrs), min–max	6-81		17-85		
					ns
Mean age (yrs)	72.1		69.7		
M/F	11/9		24/31		ns
Mean visual acuity	LogMAR	Decimal	LogMAR	Decimal	
Preoperatively	0.48	0.32^{+1}	0.46	0.32^{+2}	ns
One month postoperatively	0.35	0.4^{+2}	0.31	0.5	ns
Final	0.21	0.63	0.15	0.63^{+2}	ns
Mean follow-up, mo	20.7 months		19.2 months		ns

ICG = Indocyanine green

TABLE II - FINAL VISUAL ACUITIES IN GROUPS I AND II

Visual acuity (decimal)	**Group 1** 20 eyes (N%)	**Group 2** 55 eyes (N%)	**Total** 75 eyes (N%)
>0.4	16 (80)	51 (92.7)	67 (89.3)
>0.5	14 (70)	45 (81.8)	59 (74.7)
>0.63	12 (60)	39 (70.9)	51 (68.0)
>0.8	5 (25)	14 (25.5)	19 (25.3)

ICG = Indocyanine green
N= Number

TABLE III - CONCOMITANT OCULAR DISEASES

	Group 1 (with ICG)	**Group 2** (without ICG)
Glaucoma filtration surgery	1	
Episcleral surgery for retinal detachment		2
Ocular contusion		1
Implantable contact lens	1	
Uveitis		1

ICG = Indocyanine green

Our study was designed to determine the influence of intraoperative ICG injection on the postoperative visual acuity. We therefore compared two groups of operated ERM: one group (20 cases) with intraoperative ICG injection and another group (55 cases) without intraoperative ICG injection.

In our study, the mean visual acuity was identical in the two groups preoperatively, 1 month after vitrectomy, and at the final examination, performed an average of 20 months after vitrectomy. The intraoperative use of ICG according to our technique therefore did not appear to have a negative impact on the final functional results.

In contrast to our observations, unsatisfactory functional results from ERM peeling with the intraoperative use of ICG have been published by other authors. Haritoglou et al (28) reported decreased visual recovery and a higher rate of postoperative visual field defects. Histologic examination of the excised membranes also showed a greater proportion of retinal cells, suggesting increased surgical trauma to the retina.

How can we explain the marked discrepancy of the results between that study and our own? First, our encouraging results could possibly be related to our operative technique or our technique of dilution and application of ICG. In most published studies, ICG was diluted in BSS; in our series, ICG was diluted in 5% glucose, which appears to be less toxic according to some authors (22, 24). ICG was injected slowly over the macula so that it covered only the posterior pole and the dye was then rapidly flushed out within 30 seconds after injection. Secondly, in order to avoid bias related to postoperative cataract, we only included in our study pseudophakic eyes with transparent media on the final examination. In the series reported by Haritoglou et al, a greater number of pseudophakic eyes on the final examination was observed in the group operated without ICG than in the group operated with ICG (13/20 [65%] and 7/20 [35%], respectively).

Furthermore, the final examination was performed, on average, about 20 months after vitrectomy for the two groups in our study, while the mean follow-up in Haritoglou et al's study was 5.4 months and 8.5 months for groups without ICG and with ICG, respectively. It is possible that, even if ICG is toxic to the retina, the longer follow-up in our series allowed a certain degree of recovery, which would explain the good results obtained in the group operated with ICG.

We eliminated from our series all cases complicated by another disease likely to modify the final functional result. The series reported by Haritoglou et al comprised a not insignificant incidence of postoperative retinal detachment (4/20 after the use of ICG, and 2/28 in the control group).

Our study shows that final visual acuity was not significantly different between the group with and the group without ICG. However, not all of the functional tests necessary to exclude a retinal lesion due to ICG toxicity were performed, such as near visual acuity, contrast sensitivity, and electrophysiologic tests. Also, we did not perform visual field examinations looking for defects such as those reported by certain investigators (28, 29). This study therefore cannot formally exclude a possible toxicity of ICG to the retina.

In conclusion, the use of ICG for staining of epimacular membranes remains controversial. Some authors have stated worse final visual results after using ICG during macular surgery and they conclude that ICG is toxic for the retina and that it should not be used. Others have not seen different results using or not using ICG; they conclude that ICG is probably nontoxic.

The message of our study is different and does not relate to a possible retinal toxicity of ICG. Our study shows that the intraoperative use of ICG did not improve the final visual acuity.

This fact gives a partial answer to the following question: Is ICG useful in macular epiretinal membrane surgery, and does it improve the final visual acuity? By staining selectively the ILM, ICG certainly facilitates the peeling of epimacular membrane and the removal of ILM. However, since this has no effect on the final visual acuity, we cannot endorse the use of ICG for this type of surgery.

The authors have no proprietary interest in any aspect of the article.

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