Visual outcome of idiopathic epimacular membrane surgery

Uspešnost kirurškega zdravljenja idiopatske epimakularne membrane

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Abstract

Background: Vitrectomy and removal of idiopathic epimacular membrane (IEM) is one of the most effective procedure in vitreoretinal surgery. The aim of our study was to evaluate the visual outcome after vitrectomy in eyes with IEM. Because of potential dose-dependent toxicity of indocyanin green (ICG) the authors compared the visual outcome after different concentration of ICG assisted vitrectomy.

Methods: A retrospective analysis of visual outcome in 104 consecutively operated patients (65 female, 39 male) with IEM. The comparison in pre-operative and post-operative visual acuity, as visual gain was undertaken. Furthermore, the comparison in visual outcome between 1.25 mg/ml ICG (patients) and 0.5 mg/ml ICG (patients) assisted vitrectomy was performed.

Results: Main pre-operative best corrected visual acuity (BCVA) was 0.3 ± 0.2; 0.01 – 0.8 (mean ± SD; min.-max.). Main post-operative BCVA 3 and 8 months after the procedure was 0.5 ± 0.3; 0.1 – 1.00 and 0.6 ± 0.3; 0.01 – 1.00 (mean ± SD; min.-max.), respectively. After 8 months the mean visual gain was 0.29 ± 0.27; -0.40 – 0.9 (mean ±SD; min.-max.). In comparing 1.25 mg/ml ICG and 0.5 mg/ml ICG assisted vitrectomy there was no significant difference in pre-operative visual acuity (p = 0.65), post-operative visual acuity after 3, 8 months (p = 0.2, p = 0.83) and visual gain after 8 months (p = 0.7).

Conclusions: Vitrectomy with peeling of epiretinal membrane and ILM leads to significant improvement in visual acuity. The potential dose-dependent toxicity and damage to the retina should always be kept in mind whenever using the ICG assisted vitrectomy, although we did not found any difference in visual gain comparing the 1.25 mg/ml ICG and the 0.5 mg/ml ICG assisted vitrectomy.

Izvleček

Izhodišča: Vitrektomija pri epimakularnih membranah je ena od prognostično najbolj uspešnih vitreoretinalnih operacij. Analizirali smo pooperativno izboljšanje vida pri bolnikih z idiopatsko epimakularno membrano (IEM). Zaradi opisanega, s koncentracijo pogojenega toksičnega učinka zelenega indocianina (ICG), smo primerjali pooperativni izid po uporabi različnih koncentracij ICG za barvanje membrane limitans interne (MLI) med vitrektomijo.

Metode: Retrospektivna študija. Analizirali smo pooperativno izboljšanje vida pri 104 zaporedno operiranih bolnikih (65 žensk, 39 moških) z IEM. Ugotavljali smo vidno ostrino pred operacijo in po njej ter izboljšanje vida 3 in 8 mesecev po operaciji. Primerjali smo pooperativno vidno ostrino in izboljšanje vida med skupinama, pri katerih smo uporabili 1,25 mg/ml ICG (n=41) ali 0,5 mg/ml ICG (n=63).

Rezultati: Predoperativna najboljša korigirana vidna ostrina (VO) je bila 0,3 ± 0,2; 0,01 – 0,8 (srednja vrednost ± SD; min.-maks.). 3 in 8 mesecev po operaciji je bila VO 0,5 ± 0,3; 0,1–1,00 in 0,6 ± 0,3; 0,01 – 1,00 (srednja vrednost ± SD; min.-maks.). Pridobljeno izboljšanja vida 8 mesecev po operaciji je bilo 0,29 ± 0,27; -0,40 – 0,9 (srednja vrednost ± SD; min.-maks.). Pri primerjavi skupin, pri katerih smo uporabili 1,25 mg/ml ICG ali 0,5 mg/ml ICG ob vitrektomiji, ni bilo pomembne razlike v predoperativni VO (p = 0.65), VO 3 in 8 mesecev po operaciji (p = 0,2, p = 0,83) in v pridobljenem izboljšanju vida 8 mesecev po operaciji (p =0 ,7).

Zaključek: Vitrektomija z odstranitvijo epiretinalne membrane in MLI omogoča pomembno izboljšanje vidne ostrine. V študiji nismo ugotovili razlik v pooperativni vidni ostrini in izboljšanju vida med skupinama, kjer smo uporabljali različni koncentraciji ICG.

Introduction

Epimacular membrane has been called by a variety of names, including epiretinal membrane, cellophane maculopathy, preretinal macular gliosis, preretinal macular fibrosis and macular pucker. Epimacular membrane is avascular fibrocellular membrane that proliferates on the surface of the retina. Because of membrane's contractile properties it can lead to visual acuity deterioration and metamorphopsia.[1]

The source of the cells producing the membrane in idiopathic epimacular membrane (IEM) is still debatable. The reports proposed glial cells (primarily fibrous atrocities) from the inner layers of the neurosensory retina.[2] Etiologically posterior vitreous detachment (PVD) can lead to small breaks in the ILM, allowing retinal atrocites to access to the vitreous cavity, where they may subsequently proliferate.[2]

Iwanoff first described this ocular pathology in 1865 and it has been shown to be a relatively common entity, occurring in about 7 % of the population, bilaterally in 31 % of cases.[3] The prevalence of epimacular membrane formation is 2 % under the age of 60 years and 12 % beyond the age of 70 years.[4] Progressive visual loss was registered in 10–20 %.[4]

The first report on successful removal of epiretinal tissue was published by Machemer in 1978.[5] Since then a number of reports on success rates and indications for the removal of epimacular membranes have been published.[6-13] Mostly, macular surgery is advocated if the best corrected visual acuity (BCVA) falls below 0.6.[14,15] However, the indication is present even with better visual acuity, if the patient complains of metamorphoses or impaired binocular function.[16]

Despite one report of possible adverse effect of ILM peeling during epimacular membrane surgery,[17] the surgical removal of the ILM has become a standard procedure.[18-21]

Indocyanine green (ICG) has been introduced to stain and visualise ILM to facilitate the surgical manoeuvre for its removal.[22-24] Despite widespread routine use, there have been some unfavourable clinical and experimental reports of ICG related retinal damage.[25-30] Among other possible toxic effect, the toxicity of ICG staining was proposed to be dose-dependent.[31]

The study was designed to evaluate visual gain after pars plana vitrectomy in eyes with IEM and to compare visual outcome in patients using different concentration of ICG; 1.25 mg/ml ICG and 0.5 mg/ml ICG for ILM staining during vitrectomy.

Methods

The present study was designed as a retrospective analysis of visual outcome in consecutively operated eyes with IEM, from 2004 to 2007, at the Eye Hospital, University Medical Centre Ljubljana. All surgeries were performed by the same surgeon (MGP). Patients with other diseases possibly limiting visual acuity such as cataract, glaucoma, diabetic retinopathy or age-related macular degeneration, were excluded. A total of 104 patients with IEM (65 female, 39 male), aged 40 to 81 years, mean 65 years, were retrospectively recruited.

Surgical technique

74 patients underwent 20-gauge three-port pars plana vitrectomy, while 25 patients in the last year of the study underwent sutureless 25-gauge and 5 patients sutureless 23-gage three port pars plana vitrectomy. Posterior vitreous detachment was performed by suction with the vitrectomy probe around the optic disc if necessary. The removal of epimacular membrane was performed without the use of any dye with end-gripping forceps. Peeling of ILM was performed with the assistance of 0.1 ml ICG staining; the concentration used was 1.25 mg/ml ICG in the first group (41 patients) and 0.5 mg/ml ICG in the second group (63 patients). To avoid hypo-osmolar toxic effect, the ICG was always diluted in 5 % dextrose. ICG was washed out immediately by irrigation. In all patients the same Hallogen light source was used. The light exposure (with endoillumination probe) of the retina after ICG staining and removing was not measured. It usually tooks around few minutes. The light exposure time could be

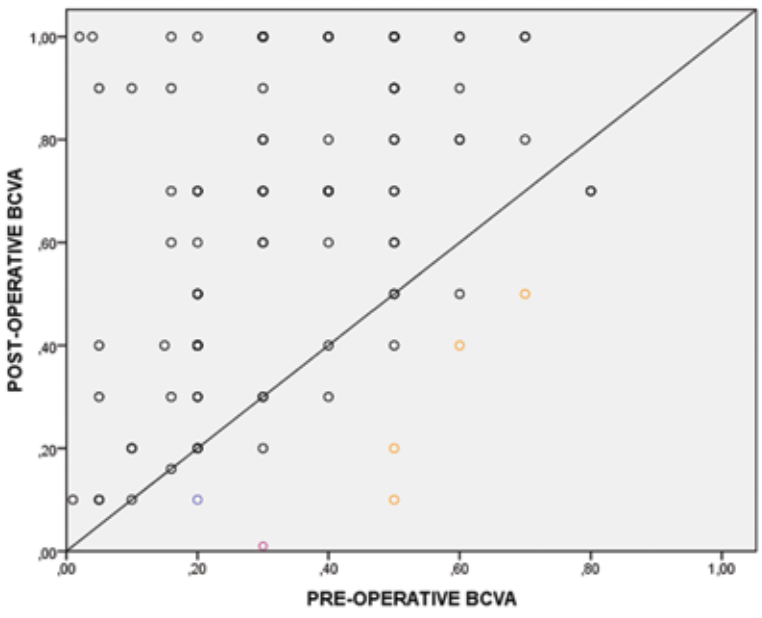

Figure 1: Pre-operative and post-operative (8 months after vitrectomy) BCVA in patients operated for idiopathic epimacular membrane. O – *patients with significant cataract,* O – *patient with post-operative macula off retinal detachment managed with re-operation,* O – *patient with atrophic changes in photoreceptor layer, BCVA–best corrected visual acuity*

prolonged for approx. 10 minutes in intra-operative complications, as in our 3 patients with intraoperative retinal breaks.

Combined vitrectomy with standard phacoemulsification intraocular lens surgery was performed in 78 patients. 6 phakic eyes underwent cataract surgery up to 8 months after vitrectomy. 11 pre-operatively pseudophakic eyes patients had undergone cataract surgery 10 to 115 months before vitrectomy.

Pre-operative and post-operative (3 and 8 months after vitrectomy) complete clinical examination was performed including best corrected visual acuity (BCVA) by Snellen visual acuity chart, pneumotonometry, slit-lamp examination and stereoscopic biomicroscopy with a 90-diopter lens (Volk Optical, Mentor, Ohio, USA).

The study was designed to evaluate visual gain (pre-operative and post-operative visual acuity, as visual gain 3 and 8 months) after pars plana vitrectomy in eyes with IEM.

Furthermore, the comparison in pre-operative and post-operative visual acuity and visual gain between 1.25 mg/ml ICG and 0.5 mg/ml ICG assisted vitrectomy, was undertaken. The results were statistically compared (Mann Whitney U test, chi-square test and t-test)) using SPSS 14.0 software (SPSS Inc. Chicago, IL, USA).

Results

In the whole group of patients with IEM (n=104) mean pre-operative BCVA was 0.31 ± 0.23; 0.01 – 0.8 (mean ± SD; min.-max.). Mean post-operative BCVA after 3 months was 0.53 ± 0.32; 0.1 – 1.00 (mean ± SD; min.–max.) and after 8 months was 0.61 ± 0.33; 0.01 – 1.00 (mean ± SD; min.-max.). Mean visual gain after 8 months was 0.29 ± 0.27; -0.40 – 0.9 (mean ±SD; min.-max.). Post-operative BCVA was better in 87 patients (84 %), equal in 6 patients (6 %) and worse in 11 patients (11 %). Worsening for 2 or more Snellen lines was presented in 5 patients (5 %). 22 patients (21 %) had BCVA 1.00 (Figure 1).

Intra-operative complications: retinal break at the periphery in 2 patients and retinal detachment at the periphery in one patient were successfully managed intra-operatively with laser photocoagulation and gas tamponade in retinal detachment case.

Post-operatively, after 7 months, rhegmatogenous retinal detachment with giant retinal tear was present in one patient. This complication was managed with re-operation and silicone oil injection.

Among 11 patients with worse post-operative BCVA, one patient had retinal detachment and was reoperated with silicone oil tamponade, one patient had changes in photoreceptor level demonstrated by post-operative OCT (Figure 2), and 4 patients had significant cataract. In the other 5 patients with BCVA deterioration for one Snellen line we could not find any clinical or OCT explanation for visual acuity deterioration.

For the purpose of comparing visual acuity outcome between the 1.25 mg/ml ICG and the 0.5 mg/ml ICG assisted vitrectomy, the patients in whom the post-operative visual acuity might be affected by a non-dye related factor such as clinical significant cataract (4 patients) or macula involving retinal detachment (one patient), were excluded. Comparing the 1.25 mg/ml ICG (59 eyes) and the 0.5 mg/ml (40 eyes) assisted vitrectomy groups there was no statistically significant difference in age (p = 0.7) and gender (p = 0.3), pre-operative visual acuity (p = 0.65), post-operative visual acuity

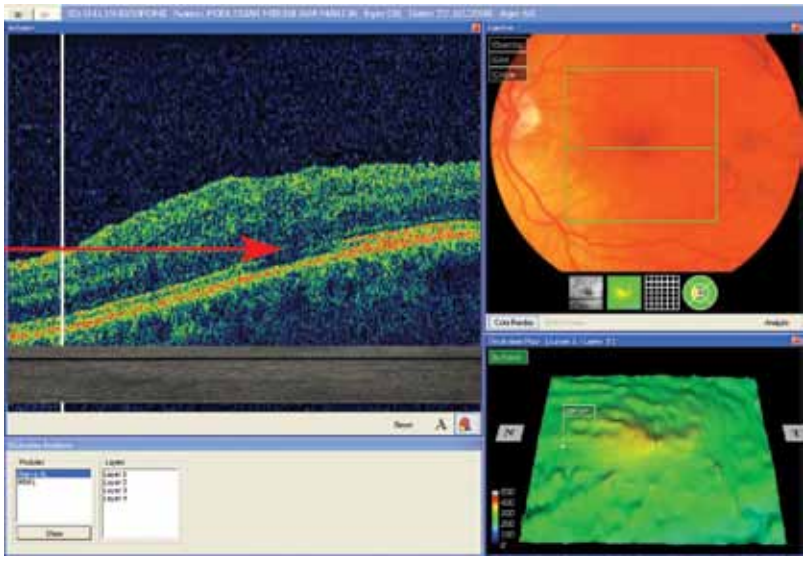

Figure 2: Post-operative OCT in patient with visual acuity deterioration after vitrectomy for idiopathic epimacular membrane. *Patient presented with atrophy of the photoreceptor level, as potential reason for visual loss, 8 months after the operating procedure.*
OCT- Optic coherent tomography

after 3 months (p = 0.2) and after 8 months (p = 0.83) and visual gain after 8 months (p = 0.7) (Table 1, Figure 3).

Discussion

Our study demonstrated the expected visual gain after vitrectomy for IEM. There was no statistically significant difference in visual outcome comparing the 1.25 mg/ml ICG and the 0.5 mg/ml ICG assisted vitrectomy.

A number of reports on success rates and indications for the removal of epimacular membranes have been published.[6-13] Our findings in post-operative visual acuity are in accordance with other authors demonstrating positive functional outcome after ICG assisted vitrectomy.[32-35]

In 11 patients visual acuity deterioration was present after the vitrectomy (Figure 1). Among those 4 patients had significant cataract and visual acuity is expected to improve after cataract operation. In one patient with post-operative retinal detachment the re-operation was performed successfully, but BCVA deteriorated due to long standing macula detachment. In 5 patients with visual acuity deterioration for one Snellen line we did not found any clinical or OCT explanation for this. However, a deterioration of one Snellen line could not be objective; and in many studies visual acuity change is determined as a minimum of 2 Snellen lines change.

In one patient the atrophy at the photoreceptor level was demonstrated by post-operative OCT (Figure 2). The pre-operative visual acuity was 0.2 and post-operative was 0.1 after 8 months. The patient was operated by 1.25 mg/ml ICG for ILM staining. We do not have the pre-operative OCT to evaluate potential changes at the photoreceptor level pre-operatively. However changes in the photoreceptor level could be provoked by ICG toxicity.[36]

Kwok demonstrated that intravitreal application of 2.5 mg/ml ICG with endoillumination in experimental rabbits resulted in morphological changes with loss of photoreceptor outer segments. The concentration of ICG in this experimental study is much higher than the standard concentrations used for surgery. However the article provides evidence of ICG toxicity affecting photoreceptors, as it could happen in our patient.

Despite evidence of potential toxic effect, ICG continues to be the most widely used intraocular dye in membrane peeling. After epimacular membrane removal, in most cases the retinal surface still showed visible striae caused by residual traction of the ILM, which may contribute to the persistence of metamorphopsia and macular oedema. This is the reason why the removal of ILM has become a standard procedure in epimacular membrane surgery.[18-21] To facilitate complete removal of very thin and transparent 1 micron thick ILM, ICG selective staining allows better visibility of ILM than any other dye.[37]

But there is concern about ICG related retinal toxicity. There are experimental studies showing ICG toxicity in RPE,[23] Müller cells,[9,13] photoreceptors[36] and retinal ganglion cells.[38] Several authors have reported good functional outcome of ICG assisted vitrectomy,[33,39-41] whereas some authors have reported less favourable results in visual acuity.[22,25,42] Clinical studies have shown visual field defects,[41] loss of VA,[15] and RPE atrophy.[39]

The sources of the published discrepancy in clinical studies are small sample size, different follow-up, and missing control group. The variability exists in concentration used, in exposure time or retinal contact time and endoillumination distance and power. The

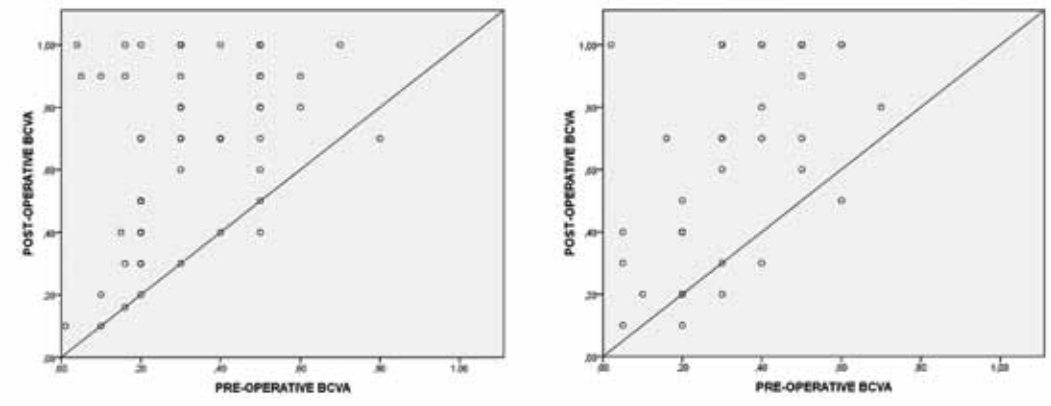

Figure 3: Pre-operative and post-operative (8 months after vitrectomy) BCVA in patients operated for idiopathic epimacular membrane with 0.5 mg/ml ICG (left) and 1.25 mg/ml ICG assisted vitrectomy. (right).

only randomised trial of ICG vital staining showed a small but significant reduction in VA in a group with dye, albeit using a hypo-osmolar preparation.[42]

ICG toxic effect has been shown dose-dependent, exposition-dependent, light-dependent.[31] Surgeons may consider using lower concentration, shorter exposure time, lower light levels, iso-osmolar solution, shorter light exposure, as well as using different wavelengths of light in order to avoid potential clinical toxicity.[43-47]

There is experimental evidence of direct dose-dependent cytotoxic effect.[26] However in our study we did not find any difference in post-operative visual acuity or visual gain between the 1.25 mg/ml ICG and the 0.5 mg/ml ICG assisted vitrectomy (Table 1, Figure 3). In our study all other safety parameters to avoid ICG toxicity were undertaken; ICG was diluted in 5 % glucose to avoid hypo-osmolarity and it was washed out immediately.

Just recently Yuen found ICG safe, without any toxicity at different surgically used concentration in retinal cell cultures.[48] However, at prolonged exposure time the toxicity became apparent.

Conclusions

Epimacular membrane peeling improves visual acuity in the majority of patients. The potential toxicity and damage to the retina should always be kept in mind whenever using ICG assisted vitrectomy, although we did not found any difference in visual gain comparing the 1.25 mg/ml ICG and the 0.5 mg/ml ICG assisted vitrectomy.

Table 1: The comparison between 1.25 mg/ml ICG and 0.5 mg/ml ICG assisted vitrectomy.

Variable	Group		
	1.25 mg/ml ICG (59 eyes)	0.5 mg/ml ICG (40 eyes)	P value
Gender- female (n)	41	23	0.28
Age (mean±SD)	67.84 ± 7.5	63.66 ± 8.1	0.7
Pre-operative BCVA (mean±SD)	0.31 ± 0.19	0.32 ± 0.18	0.65
Post-operative BCVA (3 M) (mean±SD)	0.46 ± 0.26	0.51 ± 0.26	0.2
Post-operative BCVA (8M) (mean±SD)	0.61 ± 0.32	0.63 ± 0.29	0.83
Visual gain (8M) (mean ±SD)	0.28 ± 0.26	0.31 ± 0.27	0.7

BCVA=best corrected visual acuity, SD=standard deviation, M=month

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