Recovery of visual field and acuity after removal of epiretinal and inner limiting membranes

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ABSTRACT

Background: Visual acuity serves as only a rough gauge of macular function. The aim therefore was to ascertain whether central an assessment of the central visual field afforded a closer insight into visual function after removal of epiretinal membranes and Infracyanine-Green- or Trypan-Blue-assisted peeling of the inner limiting membrane.

Patients and methods: Fourty-three patients undergoing pars-plana vitrectomy for the removal of epimacular membranes and dye-assisted peeling of the inner limiting membrane using either Infracyanine Green (n = 29; group 1) or Trypan Blue (n = 14; group 2) were monitored prospectively for 12 months. Preoperatively, and 1, 6 and 12 months postoperatively, distance and reading visual acuities were evaluated; the central visual field was assessed by automated static perimetry.

Results: Twelve months after surgery, distance and reading visual acuities had improved in both groups, but to a significant degree only in Trypan-Blue-treated eyes. The difference between the two groups was not significant. Likewise at this juncture, the mean size of the visual-field defect remained unchanged in Trypan-Blue-treated eyes (preoperative: 4.3 (SD 2.1) dB; 12 months: 4.0 (2.1) dB ($p = 0.15$)), but had increased in Infracyanine-Green-treated ones (from 5.3 (3.7) dB to 8.0 (5.2) dB ($p = 0.027$)).

Conclusion: Unlike visual acuity, the central visual field had deteriorated in Infracyanine-Green-treated eyes but not in Trypan-Blue-treated eyes 12 months after surgery. Hence, as a predictor of functional outcome, testing of the central visual field may be a more sensitive gauge than visual acuity. Furthermore, Infracyanine Green may have a chronic and potentially clinically relevant effect on the macula which is not reflected in the visual acuity.

The clinical picture of idiopathic and postoperative epiretinal membranes has been well recognised for 40 years,[1 2] and the routine of surgical removal of these structures has been conducted since the late 1970s.[3] Epiretinal membranes increase in prevalence with age. They have been estimated to occur in 6% of the population above 50 years of age and to be manifested bilaterally in every fifth case.[4] Consequently, as the life expectancy of the population continues to increase, a further increase in the incidence of epiretinal membrane is expected. Efforts to optimise surgical strategies and outcomes, as well as to identify predictors of postoperative results, are thus justified. In most centres, macular surgery is advocated if the best-corrected decimal visual acuity (BCVA) falls below 0.6 (20/30).[5 6] Clearly, patients desire surgery if they are significantly disturbed by metamorphopsies or by impaired binocular function.[7] Nowadays, the surgical removal of epiretinal membranes is not a highly challenging undertaking, and it yields results of reproducible quality. At least in experienced hands, the procedure is not associated with significant early postoperative problems, although the persistence of metamorphopsies and a retarded visual recovery may compromise the functional outcome. Nevertheless, most patients are satisfied with at least a partial recovery of their binocular function.[7]

Whether the inner limiting membrane should or should not be removed together with the epiretinal membrane is a moot question.[8–10] The role of the inner limiting membrane in the physiological functioning and integrity of the retina argues against its removal.[11] On the other hand, a removal of the inner limiting membrane between the retina and the vitreous is crucial for the morphological and functional success of macular hole surgery,[8 10 12–14] and reduces the risk of recurrences without compromising visual function.[14–17]

Nowadays, dyes such as Infracyanine Green and Trypan Blue are routinely used to facilitate peeling of the inner limiting membrane after the successful removal of epiretinal membranes. Moreover, they permit the surgeon to control the completeness of the procedure.[18] On the basis of in vitro data, a long-term toxicity of intraoperatively applied dyes has to be expected.[19–21] However, using visual acuity as the sole measurement, the clinical significance of these data has not yet been established.[22–26] Pre- and intraoperative structural damage to the retina, including the duration of macular oedema, residual mechanical distortion of photoreceptors after membrane removal, and a mechanical damage due to the peeling down of epiretinal and internal limiting membranes cannot be excluded.[27]

In this situation, a determination of Snellen's distant single optotype visual acuity may not appropriately describe preoperative macular function, the impact on life quality or the outcome of macular surgery.[7 28] Unsurprisingly, a discrepancy is not infrequently observed between clinically assessed visual acuity and the patient's own estimation of visual function.[29]

The aim of the present study was to compare best-corrected distance and reading visual acuities with macular visual-field indices before and after the removal of epiretinal membranes and dye-assisted peeling of the inner limiting membrane using either Infracyanine Green or Trypan Blue.

PATIENTS AND METHODS

In this prospective, comparative, non-randomised study, we monitored a consecutive series of

patients who had undergone vitrectomy, the removal of epimacular membranes and dye-assisted peeling of the inner limiting membrane using either 0.5% Infracyanine Green [(in 5% glucose) group 1: n = 29] or 0.15% Trypan Blue ((Membrane Blue®, Dorc, Antwerp, Netherlands) group 2: n = 14)). The operations were performed by one of two surgeons at the Department of Ophthalmology, University of Bern during a 48-month period.

Preoperatively, and 1, 6 and 12 months postoperatively, best-corrected visual acuity and reading vision were assessed, and static computerised testing of the central visual field was performed (Octopus Perimeter 101 (M2-program), Interzeag, Haag-Streit Company, Koeniz, Switzerland). The condition of the macula was evaluated clinically and documented photographically using a fundus camera at a viewing angle of 30° (TRC 501 A, Topcon America, Paramus, NJ).

In all cases, a standard three-port pars plana vitrectomy was performed (as complete as possible), and the visible epiretinal membrane was removed. After fluid–air exchange, one of the two dyes was applied at the surgeon's discretion to the retinal surface for 30 s. It was rinsed away by air–fluid exchange. The inner limiting membrane was then removed from the entire macular region. The peripheral retina was thoroughly examined for the presence of iatrogenic breaks. If these were identified, air or SF-6 gas was applied at the end of the operation. The procedure was combined with cataract surgery in five of the 29 patients in group 1 and in 10 of the 14 individuals in group 2. In all except three of the remaining cases, cataract surgery was performed within 6 months of vitrectomy. Patients in whom surgery was not dye-assisted were excluded from the study.

Descriptive and comparative statistics were performed using SPSS for Windows (V13.0). For statistical purposes, visual acuity was converted into a logMAR equivalent (logarithm of the minimal angle of resolution (logMAR) = –logarithm of the best-corrected decimal visual acuity). On this scale, hand motions and the counting of fingers at a distance of 60 cm correspond approximately, to visual acuities of 0.001 and 0.01, respectively. For the analysis of descriptive data, median values (for graphic representation), means (for the statistical evaluation), the standard deviation, and minimal and maximal values were determined. Differences between sets of quantitative data were evaluated using the Student t test. For all comparisons, the level of significance was set at $p = 0.05$.

RESULTS

In terms of age, duration of symptoms, best-corrected visual acuity, reading vision, retinometer vision and the presence of functionally disturbing metamorphopsies, no differences were observed between the patients of each group at the time of surgery (table 1).

During the 12-month postsurgical follow-up period, vitrectomy had to be repeated in two patients, due to the recurrence of an epimacular membrane in one instance (group 1) and to retinal detachment in the other (group 2). Data that were gleaned from these two patients after the second operation were excluded from the analysis.

Twelve months after surgery, visual acuity had improved in both groups from preoperative values of 0.40 (SD 0.18) (group 1) and 0.35 (0.16) (group 2) to 0.49 (0.29) and 0.52 (0.25), respectively (fig 1A). The recovery of visual acuity tended to be more rapid in patients who had been treated with Trypan Blue than in those who had been treated with Infracyanine Green. Reading vision also improved in both groups, from preoperative values of 0.32 (0.21) (group 1) and 0.30 (0.14) (group 2) to 0.44 (0.27) and 0.47 (0.24), respectively. The recovery of reading vision likewise tended to be more rapid in the Trypan-Blue-treated group of patients than in the Infracyanine-Green-treated group, but the difference was not statistically significant at any time during the 12-month follow-up course (fig 1B). Retinometer vision remained unchanged in Infracyanine-Green-treated patients but improved in Trypan-Blue-treated patients (table 1). According to the Amsler grid test, distortion of the vision was reported in 88% of group 1 patients and in 91% of group 2 individuals at the time of surgery. Twelve months after surgery, the frequencies had dropped to 55% and 71%, respectively ($p = 0.113$; table 1). At this latter juncture, the visual distortion was reported to be less or not disturbing in nearly all instances. Twelve months after surgery, the mean size of the central visual-field defect (measured in decibels) remained unchanged in Trypan-Blue-treated patients (4.3 (2.1) (preoperative), through 4.0 (1.8) (6 months) to 4.0 (2.1) (12 months)), but had increased in Infracyanine-Green-treated individuals (from 5.3 (3.7) (preoperative), through 7.9 (4.2) (6 months) to 8.0 (5.2) (12 months)) (fig 2A). Changes in the mean sensitivity of the central visual field mirrored those in the mean size of the defect (reciprocal relationship between the two parameters (fig 2B)).

DISCUSSION

In this prospective study, testing of the central visual field by automated static perimetry was applied to gauge macular function 12 months after vitrectomy, the removal of epiretinal membranes and dye-assisted peeling of the inner limiting membrane using either Infracyanine Green (group 1) or Trypan Blue (group 2). An evaluation of the central visual field revealed differences between the two groups of patients which were not detected by monitoring of either visual acuity or reading vision. Hence, testing of the central visual field appears to be a more sensitive gauge of macular function. However, the clinical relevance of this finding remains to be established.

In several retrospective studies relating to the functional outcome of macular surgery, testing of the central visual field has been correlated with morphological parameters, but it has not been directly compared with visual acuity.[26 30 31] In the study conducted by Yamashita *et al*,[26] areas in which the thickness of the nerve-fibre layer was reduced were reported to correspond well with visual field defects. Husson-Danan *et al*[30] also reported an association between damage to the nerve-fibre layer and functional defects in the visual field. In the non-comparative study conducted by Tari *et al*,[31] a reduction in the sensitivity of the visual field and in the focal ERG was observed to correlate with residual macular thickening 3 months after surgery. Using ERG, epiretinal membranes have been revealed to cause the damage and dysfunctioning of neurons within the inner retinal layers. The resulting visual impairment was similar to that induced by cystoid macular oedema.[32 33] The observed changes were partially and gradually reversed after peeling away the epimacular membranes. For epimacular membranes that arise idiopathically, decreases in the electrophysiological response of the retina partially coincide with the morphologically affected area.[32] Since the extent of the damage would be expected to increase with time, it is hardly surprising that the duration of the symptoms and the presence of cystoid macular oedema are important predictors of the functional outcome.[15] These studies afford evidence that circumscription of the macular visual field is the functional correlate of damage to the macular nerve fibres or receptors. Our own data indicate that the central visual field may be a more sensitive gauge of

Table 1 Perioperative data relating to the two groups of patients

	Infracyanine Green (n = 29)	Trypan Blue (n = 14)
Age (years)	70.1 (5.2)	70.3 (7.5)
Duration of symptoms (weeks)	57.5 (35.2)	47.3 (36.8)
Best-corrected visual acuity (decimal values)		
Preoperative	0.40 (0.18)	0.35 (0.16)
12 months	0.49 (0.29)	0.52 (0.25)*
Reading vision (decimal values)		
Preoperative	0.32 (0.21)	0.30 (0.14)
12 months	0.44 (0.27)	0.47 (0.24)*
Central visual-field indices		
Mean size of defect (dB)		
Preoperative	5.3 (3.7)	4.3 (2.1)
12 months	8.0 (5.2)*	4.0 (2.1)
Mean sensitivity (dB)		
Preoperative	24.4 (3.9)	25.2 (2.1)
12 months	21.3 (5.1)*	25.5 (2.2)
Retinometer vision		
Preoperative	0.49 (0.29)	0.45 (0.29)
12 months	0.42 (0.23)	0.83 (0.10)*
Distorted vision according to the Amsler grid test		
Preoperative	87.5%	90.9%
12 months	54.5%	71.4%
Pseudophakia		
Preoperative	20.7%	28.6%
12 months	82.8%	100%

Data are represented either as mean values (SD) or as a percentage.
*t test (preoperative vs 12 months): $p<0.05$; in all other instances $p>0.05$.

surgical trauma or of the toxicity of intraoperatively applied dyes (such as Infracyanine Green or Trypan Blue) than visual acuity.

As predictors of functional outcome, visual acuity is insufficiently sensitive,[15 28] and retinometer vision is insufficiently accurate for use in a comparative setting.[34 35] Nevertheless, one would have expected a correlation to exist between preoperative measurements and the functional outcome of surgery, which was not the case. In the near future, and using a larger cohort of patients, we wish to compare the relative sensitivities of central visual-field testing and microperimetry in predicting the functional outcome of macular surgery.[36] To date, however, no generally accepted parameters for describing macular function by microperimetry have been established; the microperimetric measurement of fixation stability is too coarse an estimator.[36]

The search for outcome predictors of macular surgery is ongoing.[37] Since visual recovery improves with time after surgery, the choice of an appropriate follow-up period is important. Although a 6-month juncture is the most frequently chosen end-point for surgical studies, its appropriateness has not been experimentally established. The choice of a later date, namely, 12 months or more after surgery, may be advantageous in that by this time, cataracts will usually have been extracted (generally within 6 months of vitrectomy),[6 38] and recurrences of cystoid macular oedema will most probably have already occurred.

The recovery of visual acuity during the first 4 weeks of surgery was similar in all patients, irrespective of whether they had been treated with Infracyanine Green or Trypan Blue (figs 1A and B). This finding indicates that the acute toxicities of the dyes were comparable. However, the long-term recovery of the central visual field was significantly better in Trypan Blue-treated than in Infracyanine-Green-treated eyes (figs 2A and B). This finding indicates that the chronic toxicity of Infracyanine Green is more pronounced than that of Trypan Blue. That the recovery of visual acuity tended (albeit not significantly) to be more rapid in Trypan-Blue-treated than in Infracyanine-Green-treated eyes also supports this tenet. Despite thorough rinsing, intraoperatively applied dyes are known to be retained by the retina over a period of several months.[29] The quantitative difference in macular damage between Trypan-Blue-treated and Infracyanine-Green-treated eyes may reflect differences in the chronic toxicities of the two dyes,[5 39] and the finding may be of clinical relevance in that no such difference in visual acuity was observed between the two groups. In the study conducted by Hillenkamp *et al*,[40] no difference in macular damage was observed between Indocyanine-Green-treated and Trypan-Blue-treated eyes, the reason thereof being perhaps that the follow-up time was less than 6 months.

Since the primary aim of our prospective study was to assess the impact of visual-field testing in the two groups of patients, and not to compare the effects of each dye, the non-randomised design must not be a detraction. However, owing to the smallness of the patient cohort, the data must be interpreted with care. Although their potential clinical consequences cannot be weighed, our data support experimental findings relating to the expected toxicities of Infracyanine Green and Trypan Blue.[19–21] According to established indices, the retinal toxicities of these and other dyes have not hitherto been unambiguously revealed.[5 30 39–41] Our success in this respect may reflect the inclusion of central visual-field testing as a functional parameter.

In conclusion, unlike visual acuity, testing of the central visual field is a highly sensitive index of macular function which might be able to detect clinically relevant differences in the toxicity of intraoperatively applied dyes. Although visual field testing is a well-standardised and reproducible procedure, it is time-consuming and therefore not practicable in a routine

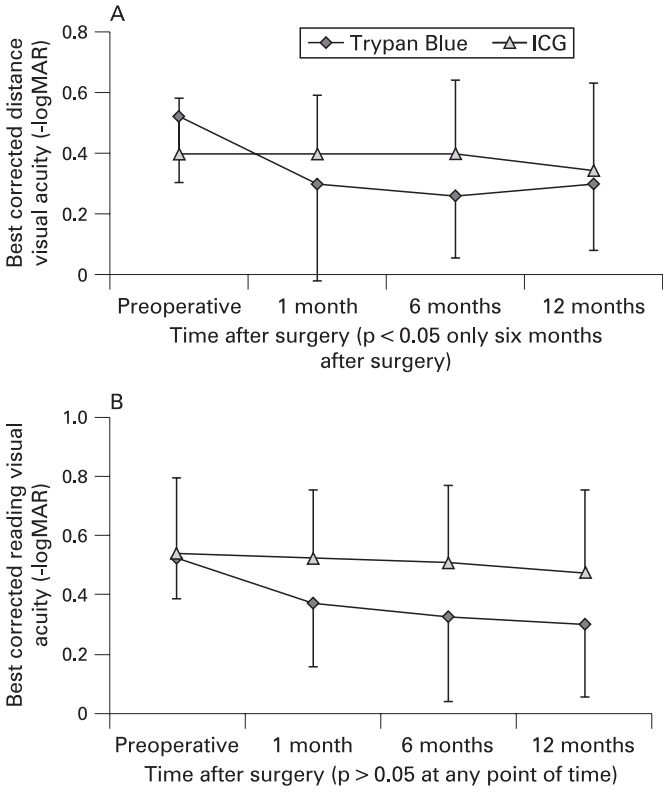

Figure 1 (A) Temporal evolution of best-corrected distance visual acuity for each group of patients during the first 12 postoperative months. Data (mean values and standard deviation) are represented as the negative logarithm of the maximal median angle of resolution (–logMAR). (B) Temporal evolution of best-corrected reading visual acuity (at a distance of 30 cm) for each group of patients during the first 12 postoperative months. Data (mean values and standard deviation) are represented as the negative logarithm of the maximal median angle of resolution (–logMAR).

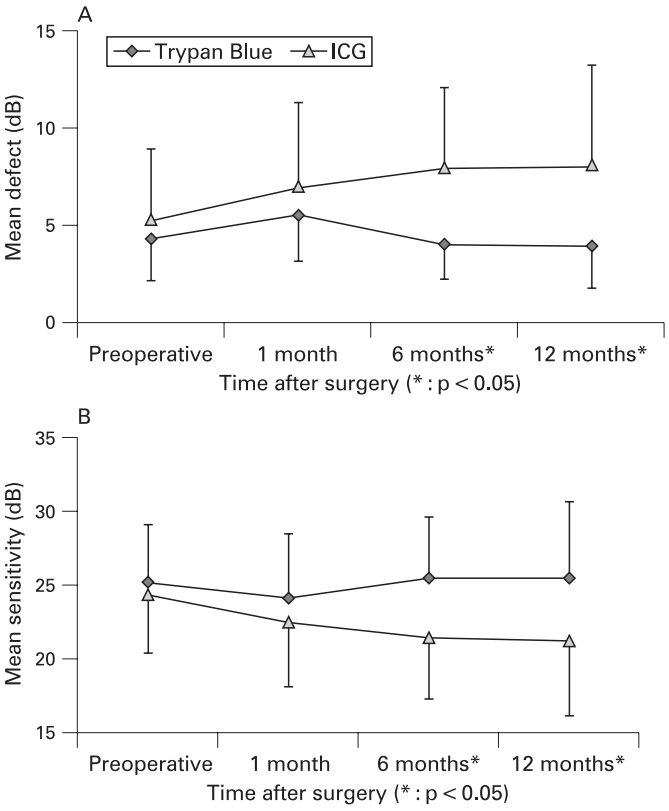

Figure 2 (A) Temporal evolution of the mean size of the defect within the central visual field (represented together with the standard deviation) for each group of patients during the first 12 postoperative months. (B) Temporal evolution of the mean sensitivity of the central visual field (represented together with the standard deviation) for each group of patients during the first 12 postoperative months.

setting. But for clinical studies that are designed to evaluate new surgical materials and methods, temporal monitoring of the macular visual field could yield potentially important clinical information respecting trauma and toxicity, which would not be disclosed by an assessment of visual acuity.

Competing interests: None.

Ethics approval: Dye-assisted surgery was conducted with the approval of the local institutional ethical committee.

Patient consent: Surgery was conducted with the informed consent of the patients.

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