A comparison of outcomes after indocyanine green and trypan blue assisted internal limiting membrane peeling during macular hole surgery

K L Lee, S Dean, S Guest

Aims: To compare the anatomical and visual outcomes of macular hole repair surgery using indocyanine green (ICG) or trypan blue (TB) staining of the internal limiting membrane (ILM).

Method: Retrospective analysis of 37 eyes from 37 consecutive patients with stage 2, 3, and 4 idiopathic macular holes who underwent macular hole repair by one surgeon using the same technique but utilising different dyes for ILM peeling. In 19 patients ICG was used while 18 patients had TB. The anatomical and visual results in these two groups were compared.

Results: There were no significant differences in the demographic and macular hole characteristics of the ICG and TB groups. Macular hole closure was achieved in 91.9% of all patients of which the ICG group had an 89.5% hole closure rate and the TB group had a 94.4% closure rate. After excluding cases with failed hole closure and other vision affecting complications, there was no significant difference between the preoperative visual acuities in the TB and ICG groups but the postoperative visual acuities were better in the TB than the ICG group (p = 0.036). The TB group also had more Snellen lines of improvement than the ICG group (2.94 ± 1.79 lines; p = 0.046).

Conclusion: TB appears to be less toxic than ICG when used in dye assisted peeling of ILM during macular hole repair as reflected by the better visual results in the TB group of patients.

Materials and Methods

Thirty seven eyes of 37 consecutive patients with stage 2, 3, and 4 idiopathic macular holes underwent macular hole repair by one surgeon (SG) using the same technique on all patients, but using different dyes (ICG or TB) for ILM peel (Table 1). ICG was used in 19 cases and TB in 18 cases. There was no selection bias in the choice of dye used. ICG was used in the initial cases but as TB became available, it became the dye of choice.

The surgical technique involved lens extraction by phacoemulsification and posterior chamber intraocular lens insertion (except for one patient who was already pseudophakic), followed by three port pars plana vitrectomy. Posterior vitreous detachment was induced where necessary and any visible epiretinal membrane was removed with forceps. This was followed by dye assisted ILM peeling in a continuous curvilinear fashion leaving a circular ILM defect with a radius of 2 disc diameters centred on the macular hole. A standard Accurus illumination probe (Alcon Laboratories, Fort Worth, TX, USA) was used for illumination (HI2 setting). All patients had gas tamponade and were advised to position prone for 1 week (in 36 cases 15% C3F8 was used and in one case 20% SF6 was used).

In the ICG group, 0.5% solutions were used in the initial patients but using different dyes (ICG or TB) for ILM peel (Table 1). ICG was used in 19 cases and TB in 18 cases. There was no selection bias in the choice of dye used. ICG was used in the initial cases but as TB became available, it became the dye of choice.

The advent of trypan blue (TB) as a second generation vital stain in vitreoretinal surgery may address some of these issues. Less have been reported to exert minimal toxic effects at the neurosensory retina following a contact time of 1 month in an animal model. Short exposure of TB with concentrations of up to 0.3% were not found to have a toxic effect on cultured RPE cells. The purpose of this study is to compare the anatomical and visual outcomes of macular hole surgery using ICG or TB.

Abbreviations: BSS, balanced salt solution; ERM, epiretinal membrane; ICG, indocyanine green; ILM, internal limiting membrane; RPE, retinal pigment epithelium; TB, trypan blue
vials of ICG (IC-Green, Akorn, Buffalo Grove, IL, USA) were reconstituted with 1 ml of supplied diluent (Aquous Solvent) and 4 ml of balanced salt solution (BSS, Alcon Laboratories, Fort Worth, TX, USA) to obtain a 0.5% ICG solution. A volume of 1 ml of this solution was mixed with Solvent) and 4 ml of balanced salt solution (BSS, Alcon laboratories, Zuidland, Netherlands). In the initial cases, available 0.15% TB solution (MembraneBlue, DORC International bv, Zuidland, Netherlands). In the initial cases, following vitrectomy, fluid-air exchange was performed before injection of TB and the dye was aspirated under air. More recently, the technique was modified to direct application of the dye over the macula in a fluid filled posterior segment with immediate aspiration. ILM peeling was performed using the technique described above.

Sample osmolarities of the 0.50% and 0.05% ICG dye solutions and the commercially available 0.15% TB solution were measured by our hospital biochemistry laboratory. The patient demographics and individual clinical features were recorded retrospectively. The anatomical outcome measured was the rate of macular hole closure postoperatively. All complications were noted for each group and visual outcomes were measured and compared for ICG and TB groups. The gradations on the Snellen visual acuity charts used were 6/6, 6/9, 6/12, 6/18, 6/24, 6/36, and 6/60, followed by counting fingers and hand movement.

Two tailed t tests were conducted for analyses of continuous variables between the two groups. The variables included preoperative and postoperative LogMAR BCVA, duration of symptoms, duration of follow up, size of macular hole and mean lines of BCVA improvement.

RESULTS
Thirty seven eyes of 37 patients from a consecutive series were included in the anatomical outcome analysis. Of these 37 patients, 19 underwent ILM peeling using ICG and 18 had TB.

Visual results for these groups were compared after exclusion of patients in whom the postoperative visual
The ICG group had 89.5% rate of macular hole closure postoperatively (17 of 19 eyes) compared to a 94.4% closure rate for the TB group (17 of 18 eyes). Three eyes had persistent macular holes postoperatively and these patients elected not to have further repair. One patient (case 4) had a postoperative macula involving rhegmatogenous retinal detachment associated with proliferative vitreoretinopathy and required silicone oil and a circumferential buckle. The retina remained attached but the final vision was poor. Two other patients had small macula on rhegmatogenous retinal detachments intraoperatively which were repaired at the time (cases 14 and 21) and did not affect the postoperative vision. One case with choroidal haemorrhages and another with epiretinal membrane development have already been mentioned.

Visual results (table 3)
The visual results of 14 ICG patients were compared with 16 patients on whom TB was used. There was no statistically significant difference between the preoperative logMAR visual acuities of the two groups, but there was a significant difference in the postoperative logMAR visual acuities, with the TB group having better postoperative visual acuities than the ICG patients (p = 0.036). As might be expected, both groups showed a statistically significant improvement in logMAR vision after surgery (p = 0.020 for ICG v 0.00005 for TB). The difference between preoperative and postoperative logMAR visual acuity was calculated for each patient and the difference between the two groups (p = 0.053). However, the average number of lines of improvement on the Snellen chart in the TB group was greater than that in the ICG group (2.94 lines v 1.79 lines) and this difference was statistically significant (p = 0.046). In the ICG group, there were only three patients who had the

Table 2  Patient demographics and macular hole characteristics

<table>
<thead>
<tr>
<th>Parameters (averages)</th>
<th>Total (n = 30)</th>
<th>ICG (n = 14)</th>
<th>TB (n = 16)</th>
<th>ICG v TB (t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (range)</td>
<td>69.6 (54–82)</td>
<td>70.7 (56–82)</td>
<td>68.6 (54–81)</td>
<td>p = 0.411</td>
</tr>
<tr>
<td>Number of female patients (%)</td>
<td>22 (73.3%)</td>
<td>10 (71.4%)</td>
<td>12 (75.0%)</td>
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</tr>
<tr>
<td>Duration between diagnosis and surgery (days) (range)</td>
<td>286.1 (10–1855)</td>
<td>317.3 (25–1855)</td>
<td>258.8 (10–1718)</td>
<td>p = 0.713</td>
</tr>
<tr>
<td>Follow up post (months) (range)</td>
<td>10.0 (1–30)</td>
<td>10.6 (1–30)</td>
<td>9.4 (1–27)</td>
<td>p = 0.729</td>
</tr>
<tr>
<td>Stage of holes (number; %):</td>
<td>9/30 (30.0%)</td>
<td>6/16 (42.9%)</td>
<td>3/10 (30.0%)</td>
<td></td>
</tr>
<tr>
<td>Stage 2</td>
<td>16/53.3%</td>
<td>6/42.9%</td>
<td>10/66.6%</td>
<td></td>
</tr>
<tr>
<td>Stage 3</td>
<td>5/16.7%</td>
<td>2/14.2%</td>
<td>3/18.8%</td>
<td></td>
</tr>
<tr>
<td>Average size of macular holes (µm) (range)</td>
<td>407.1 (200–700)</td>
<td>366.7* (200–700)</td>
<td>437.5 (200–800)</td>
<td>p = 0.270</td>
</tr>
</tbody>
</table>

* n = 12.

Table 3  Visual acuity outcomes

<table>
<thead>
<tr>
<th>Parameters (averages)</th>
<th>Total (n = 30)</th>
<th>ICG (n = 14)</th>
<th>TB (n = 16)</th>
<th>ICG v TB (t test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative VA LogMAR (range)</td>
<td>0.88 (0.3–1.5)</td>
<td>0.91 (0.6–1.5)</td>
<td>0.85 (0.3–1.2)</td>
<td>p = 0.550</td>
</tr>
<tr>
<td>Postoperative VA LogMAR (range)</td>
<td>0.46 (0–1.5)</td>
<td>0.60 (0.3–1.5)</td>
<td>0.36 (0–0.78)</td>
<td>p = 0.036</td>
</tr>
<tr>
<td>Change in VA (logMAR) (range)</td>
<td>0.42 (0–0.90)</td>
<td>0.30 (0–0.90)</td>
<td>0.50 (0–0.90)</td>
<td>p = 0.053</td>
</tr>
<tr>
<td>Snellen VA lines of improvement (range)</td>
<td>2.40 (0–5)</td>
<td>1.79 (0–5)</td>
<td>2.94 (0–5)</td>
<td>p = 0.046</td>
</tr>
<tr>
<td>VA 6/12 or better postoperatively (number; %)</td>
<td>17 (56.7%)</td>
<td>6 (42.9%)</td>
<td>11 (61.1%)</td>
<td></td>
</tr>
</tbody>
</table>
DISCUSSION
Some authors have reported no significant improvement in vision following ICG assisted ILM peeling in macular hole repair when compared with preoperative visual acuities or macular hole surgery without ILM peeling. Anda et al found no significant improvement in visual acuity in a group of patients having ICG assisted macular hole surgery, whereas they report of another group having ILM peeling without ICG dye that did improve postoperatively. In light of the possible toxic effects of ICG on the RPE and neural retina, TB is being used more frequently as an alternative dye in vitreomacular surgery. Whereas ICG selectively stains the acellular ILM, TB stains cellular structures such as epiretinal membrane, but also, to a lesser degree, the ILM. The application of TB onto the ILM or ERM results in good visualisation scores and ease of removal scores. In our experience, ICG stains the ILM better than TB although peeling of the ILM is still significantly facilitated by the use of TB. There have been a few preliminary reports of TB assisted ERM and ILM peeling in vitreoretinal surgery for proliferative vitreoretinopathy, idiopathic ERM, and macular hole with satisfactory anatomical and functional results. To our knowledge, there have been no other reports comparing the effectiveness of macular hole repair using TB and ICG.

In this study, macular hole closure was successful in 91.9% of all patients who underwent dye assisted ILM peeling. These rates are comparable to previous studies where macular hole repair was performed with ILM peeling without or without dye assistance. Patients who had undergone ILM peeling using TB achieved better postoperative visual acuities and greater lines of improvement on the Snellen visual acuity chart than patients in whom ICG had been used. The ICG group had slightly more longstanding holes in older patients, but the TB patients had larger holes of later stage and follow up was a little shorter. The better visual results of the TB patients may reflect the toxicity of ICG, but could simply be due to chance.

This is a retrospective study with several flaws. The patient numbers are low and the follow up period short in many cases. Acuities were not measured with ETDRS charts and varying concentrations of ICG and TB were used. In the study’s favour is the fact that all operations were performed by a single surgeon, eliminating individual variability, and all the patients were pseudophakic postoperatively thereby eliminating the effect of cataract progression on the postoperative visual acuity measures.

The awareness of possible ICG toxicity provided the impetus for us to start using TB for vitreomacular surgery in our institution. TB may have a better safety profile based on our current knowledge. The use of TB in ILM peeling for macular hole repair appears to give anatomical and visual results, that are at least as good as, if not better than those after ICG assisted surgery. TB has the potential to replace ICG as the first choice dye for vitreomacular surgery but more work needs to be done to establish the safety profile of both dyes.

REFERENCES


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