Long-term Follow-up of Iatrogenic Phototoxicity

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Objective: To evaluate the outcomes of a group of patients who suffered iatrogenic phototoxic injury.

Methods: The medical records of 24 patients (24 eyes) with iatrogenic phototoxicity from 3 medical centers were reviewed. We report the findings from long-term follow-up of these patients with particular attention to visual outcome, type and duration of procedure, and location of the phototoxic lesion.

Results: Phototoxic injury occurred after anterior segment surgery in 20 eyes and after vitrectomy in 4 eyes. The mean duration of surgery was 109 minutes; there was no statistically significant difference in duration between the anterior segment procedures and the vitrectomies. Mean final visual acuity was 20/40 for all cases (range, 20/15 to counting fingers) and 20/25 for all anterior segment cases. In vitrectomized eyes, the mean final visual acuity was 20/900. Phototoxic lesions tended to spare the fovea after anterior segment surgery and involve the foveal center after vitrectomy.

Conclusions: In general, patients who suffer phototoxicity do well, and the prognosis is good for extrafoveal lesions. Foveal injury, which often occurs with vitrectomy, usually leads to a worse visual outcome. The development of choroidal neovascularization may have an effect on the ultimate visual outcome as well.


MICROSCOPE-induced retinal phototoxicity in humans was first reported by McDonald and Irvine in patients who underwent extracapsular cataract extraction with posterior chamber intraocular lens implantation (ECCE). Subsequent studies found that phototoxicity occurs in 7% to 28% of eyes undergoing cataract extraction. Khwarg et al found that the best correlate with photic injury was the duration of the surgery. Phototoxicity has been reported with other anterior segment procedures as well as with vitrectomy.

Most previous clinical studies of iatrogenic phototoxicity have been relatively small in size and the prognosis for patients with this condition is still largely undefined. We therefore reviewed 24 cases of iatrogenic phototoxicity to determine the long-term outcome.

RESULTS

Twenty-four eyes of 24 patients developed lesions after surgery that were consistent with previous descriptions of iatrogenic phototoxicity. The average patient age was 67 years (range, 53-86 years). Eleven patients were female, 13 male; 4 African American, 18 white, and 1 did not have his race recorded. The injury occurred in the left eye in 11 patients and in the right eye in 13. Six patients underwent phacoemulsification with posterior chamber lens implantation, 13 had extracapsular cataract extraction with posterior chamber lens implantation, 13 had extracapsular cataract extraction with posterior chamber lens implantation (ECCE), 1 had a combined phacoemulsification with posterior chamber lens implantation and trabeculectomy with 5-fluorouracil, and 4 had pars plana vitrectomy (vitrectomy) and membrane stripping alone or combined with autologous serum or fluid-gas exchange for macular hole or epiretinal membrane. One of these patients underwent simultaneous penetrating keratoplasty. Most of the anterior segment surgery was performed by residents with a faculty member present.

Surgery time ranged from 50 to 220 minutes, with a mean of 109 minutes. The number of procedures performed and mean time for each type of procedure was as follows: 6 phacoemulsifications, 78 minutes; 13 extracapsular cataract extractions, 109 minutes; and 5 combined procedures, 115 minutes.
PATIENTS AND METHODS

We retrospectively identified and reviewed the medical records of 24 patients with iatrogenic phototoxicity at 3 medical centers. We report the findings of the long-term follow-up of these patients with particular attention to visual outcome, type and duration of procedure, and location and size of the phototoxic lesion.

All patients received complete preoperative and postoperative examinations, including slitlamp biomicroscopy and indirect ophthalmoscopy. Twenty-three of 24 patients had postoperative photographs taken within 2 weeks of surgery. Fluorescein angiography was performed simultaneously. Fundus photographs were taken of 10 patients late in their course of recovery and used for lesion analysis.

To determine if lesions changed in size over time, fluorescein angiograms or serial photographs were analyzed. In the 10 patients described, the photographs or angiograms allowed such comparisons. The images were digitized with a ccd camera (Kodak megaplus, Eastman Kodak, Rochester, NY) and reproduced under constant magnification. Commercially available software (ImageNet 2-12, Saratoga, Calif) was used for area and perimeter measurements. The lesions’ perimeters were traced and areas measured in a masked fashion by 3 investigators (E.A.P., J.S.P., and W.F.M.). For any given patient, these areas could be compared and changes in the lesion size determined.

...13 ECCEs, 104 minutes; and 4 vitrectomies, 138 minutes. The single combined procedure lasted 150 minutes. The difference in duration between the anterior segment cases (mean, 103 minutes) and vitrectomies (mean, 150 minutes) was not statistically significant (t test, P=.15).

Mean follow-up was 34 months (range, 1-65 months). The mean presurgical visual acuity for all cases, as well as anterior segment surgery, was 20/90 (range, 20/25 to hand motions). The mean presurgical visual acuity for the groups undergoing phacoemulsification, ECCE, or vitrectomy was 20/50, 20/120, and 20/90, respectively. The mean visual acuity for all cases immediately after surgery was 20/60 (range, 20/15 to hand motions). The mean final visual acuity for all cases was 20/40 (range, 20/15 to counting fingers), and for anterior segment cases it was 20/25. The mean final visual acuity for the groups undergoing phacoemulsification, ECCE, or vitrectomy was 20/30, 20/20, and 20/900, respectively. No statistically significant difference in final visual acuity was noted between eyes that underwent phacoemulsification and those that underwent ECCE (P=.15). There was, however, a highly significant difference in final visual outcome between eyes that underwent anterior segment surgery and those that underwent vitrectomy (P<.001). Eyes that underwent anterior segment surgery improved from a mean visual acuity of 20/90 to 20/25, while eyes undergoing vitrectomy actually experienced a decrease in mean visual acuity from 20/90 to 20/900 (Table).

The phototoxic lesion was located inferior to the fovea in 9 patients, superior in 5, temporal in 3, and subfoveal (Figure 1) in 5. One lesion was located nasal to the fovea, and 1 lesion could not be precisely located. The location of the phototoxic lesion played a role in visual outcome. Final visual acuity for lesions located inferiorly, superiorly, or temporally to the fovea ranged from 20/20 to 20/25. This difference was not statistically significant (P=.2). However, the mean final visual acuity in the 5 patients in whom the phototoxic lesion involved the entire fovea was worse than 20/400. The difference between the subfoveal group and the group in which the lesion was in other locations was statistically significant (P=.03, Kruskal-Wallis test). One patient who underwent ECCE, however, suffered a subfoveal lesion but maintained excellent visual acuity.

In 10 patients in whom serial photographs or, preferably, angiograms could be used to compare lesion sizes, digitized images were reviewed by 3 examiners who were masked to patient identity. A change in the size of the lesion was noted during follow-up (Figure 2). The lesion decreased in size an average of 21% (range, 59% decrease to 17% increase). Choroidal neovascularization developed in the eye in which the lesion increased in size by 17%. Laser ablation of the membrane was performed in this patient during follow-up.

We found that immediate postoperative vision was positively correlated with final vision (Pearson product moment correlation=0.81, P<.001). The difference in surgery was not closely correlated with final visual acuity (Pearson correlation=0.41, P=.07). No correlation was found between age of the patient and visual outcome, change in lesion size and visual outcome, presurgical and final visual outcome, and presurgical and postsurgical vision.

Eight (33%) of the 24 patients were symptomatic or had Amsler grid changes noted immediately postoperatively. Complaints included decreased vision, metamorphopsia, and scotomata. At the last follow-up, 7 of the 8 patients remained symptomatic or had persistent changes on Amsler grid testing. Two patients developed choroidal neovascularization presumably associated with the phototoxic lesion (J.S.P., unpublished data, 1996), 1 after phacoemulsification and 1 after vitrectomy. One patient developed cystoid macular edema that resolved after treatment with topical ketorolac tromethamine (Acular, Allergan, Irvine, Calif). One patient who underwent ECCE had nonproliferative diabetic retinopathy. His preoperative and postoperative visual acuity were both 20/60.

Some information was not available. This included equipment specifications, patient skin temperature, blood oxygenation levels, and actual duration of light exposure. Statistical analysis was performed using statistical software (Stata Statistical Software, Stata Corp, College Station, Tex).

COMMENT

Retinal phototoxicity after cataract surgery was first reported by McDonald and Irvine in 1983,1 and many case reports and reports of small series have fol-
lowed.\textsuperscript{2,3,6,8,10-16} Since then, iatrogenic phototoxicity has been reported after glaucoma surgery,\textsuperscript{4} refractive surgery,\textsuperscript{5} penetrating keratoplasty,\textsuperscript{6,17} and vitrectomy.\textsuperscript{7-9} Phototoxic injury during cataract surgery has been reported in up to 7\%\textsuperscript{2} to 28\%\textsuperscript{3} of patients, although in another consecutive series\textsuperscript{12} of 37 patients, no phototoxic injury was noted. It may also occur in 2\%\textsuperscript{9} to 10\%\textsuperscript{18} of vitrectomies.

The clinical appearance of retinal phototoxic lesions from anterior segment surgery and vitrectomy has been described elsewhere,\textsuperscript{2,9,19,20} as have the histopathological findings associated with such injuries.\textsuperscript{21-25} The occurrence of phototoxic injuries has been linked to certain wavelengths of light, particularly blue light,\textsuperscript{19,26,27} and most strongly to the duration of surgery.\textsuperscript{1,2,14} Khwarg et al\textsuperscript{2} reported that the incidence of retinal phototoxicity during cataract extraction was 0.9\% in procedures lasting less than 100 minutes, but 39\% in longer procedures. Other factors that may play a role in potentiating or limiting phototoxic injury include fundus pigmentation,\textsuperscript{3,28-30} emmetropia, retinal vascular disease,\textsuperscript{3} diabetes, the use of hydrochlorothiazide,\textsuperscript{3} core temperature,\textsuperscript{19,31,32} tissue oxygen levels,\textsuperscript{33-35} ascorbic acid,\textsuperscript{36-38} vitamin A,\textsuperscript{39} total delivered power,\textsuperscript{11,16} focus of the light,\textsuperscript{11,16} and possibly use of the endoilluminator.

Generally, the visual outcome in cases of retinal phototoxicity has been quite good, although reported series have been limited in size and length of follow-up. Factors that influence visual outcome include location,\textsuperscript{9,19} size,\textsuperscript{9} and perhaps severity of the lesion. Also, the development of choroidal neovascularization may play a role in determining final visual acuity. Most patients are asymptomatic,\textsuperscript{2,14,19} and lesions are typically located inferior to the fovea\textsuperscript{39} after cataract surgery. Visual recovery and shrinkage of scotomata caused by phototoxic lesions have been reported in isolated cases and in small series,\textsuperscript{10,14,16} and numerous studies support the speculation that this recovery might occur.\textsuperscript{21,24,40-43}

All patients in our series were free of lesions resembling photic injuries preoperatively, and all had postoperative lesions similar to those described in previous reports of phototoxicity. Our results indicate that patients who suffer phototoxic injury during anterior segment surgery generally do very well. The mean final visual acuity for these patients was 20/25, an improvement of greater than 6 lines compared with their mean preoperative visual acuity. One such patient developed an extrafoveal choroidal neovascular membrane, which was successfully treated. A similar case has been noted in 1 previous report.\textsuperscript{44} Despite the development of neovascularization, that patient had a final visual acuity of 20/20. Another patient developed a choroidal neovascular membrane with photic injury from vitrectomy, but he refused further treatment. His visual acuity decreased from 20/400 postoperatively to counting fingers.

There was no difference in the outcome of patients who underwent phacoemulsification vs ECCE in our series. However, most of these surgical procedures were performed by residents early in their surgical careers, hence this may not be an accurate comparison of the 2 techniques. There was a marked and significant difference in

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*E indicates extracapsular extraction; EF, extrafoveal; P, phacoemulsification; ellipses, data not available; V, vitrectomy (membrane peeling); HM, hand motions; SF, subfoveal; C, combined phacoemulsification and trabeculectomy; PK, penetrating keratoplasty; and CF, counting fingers.

† The outcome was diabetic macular edema.

‡ The outcome was choroidal neovascularization.
visual outcome for patients who underwent vitrectomy, whether or not it was combined with anterior segment surgery (ie, 1 vitrectomy patient underwent concomitant penetrating keratoplasty), compared with patients who had anterior segment surgery only. Those in the vitrectomized group fared much worse, with an average visual acuity from 20/90 preoperatively to a final visual acuity of 20/900. Presumably this difference is due to the use of the endoilluminator, particularly over the macular area, with subsequent severe foveal phototoxicity. In all 4 vitrectomized eyes, the phototoxic lesion involved the fovea. In patients with such foveal lesions, visual acuity was significantly worse (range, 20/300 to counting fingers vs 20/20 to 20/25, \(P = .03\)) than in patients in whom the fovea was spared.

During vitrectomy procedures for such indications, the endoilluminator is often held very close to the retina to provide maximum visualization. The proximity of the endoilluminator may play a role in the severity of the phototoxic damage, as has been suggested.9 Also, in these cases the media and pupil provide no protection from the light of the endoilluminator, whereas media opacities and pupillary constriction may provide some protection during anterior segment surgery. Although the vitrectomy procedures tended to last longer than the anterior segment surgical procedures, the difference was not statistically significant (\(P = .15\)), so the total duration of the surgery may not play a role in the different outcomes in these cases. The exact duration of exposure of the macula to the endoilluminator was not measured, however, nor was the distance from the endoilluminator tip to the retina. Both of these factors likely play a critical role in phototoxic injury in vitrectomies. The excellent outcome in 1 patient after foveal phototoxic injury from phacoemulsification would suggest that this injury was less severe than that caused by the endoilluminator during vitrectomy. Inspection of this patient’s photographs and fluorescein angiogram did not, however, provide an obvious reason for this difference.

In the 10 patients in whom image comparison was possible, the phototoxic lesions tended to decrease in size during the follow-up period. For each of the 10 patients in whom these measurements were made, we chose the best available images that would allow a consistent comparison (eg, we would not compare color photographs with fluorescein angiograms, or 30° with 60° images). This method of scrutiny showed that there may be remodeling of these lesions, which could be the result of retinal pigment epithelial migration21 and repair of the photoreceptor outer segments, perhaps in peripheral, less severely damaged areas of the lesion. Such remodeling did not have an appreciable effect on visual outcome in our series, however, because most of the measurable lesions were extrafoveal. In addition, the decrease in lesion size seemed to go unnoticed by the patients. Most patients were asymptomatic, and only 1 symptomatic patient noticed considerable improvement (decrease in the size of the scotoma) as the size of the lesion decreased in progressive photographs. He did complain of metamorphopsia at the latest visit, however.

Another correlation we noted was that between the visual acuity immediately after surgery (ie, on the first postoperative day) and the final visual acuity. A statistically significant positive correlation was found between the postoperative visual acuity and final visual acuity (Pearson correlation = 0.83, \(P < .001\)). This suggests that the possibility of phototoxic injury should be investigated when postoperative vision is worse than expected. It also suggests that if visual acuity is good immediately after surgery in patients with phototoxic injury, they will likely suffer few effects from the injury.

In summary, we have reported the long-term outcome of patients who have suffered photic injury during anterior segment surgery and during vitrectomy. In
general, patients who have undergone anterior segment surgery, whether ECCE or phacoemulsification, display a marked improvement in visual function, with no notable decrease directly attributable to the phototoxic lesion. However, patients who have undergone vitrectomy and suffered phototoxic injury seem to have a markedly worse prognosis, despite prophylactic visual function similar to that of patients who have undergone anterior segment surgery. This difference in outcome is owing to the location and severity of the injury. The damage involved the fovea in all vitrectomized eyes and in all eyes with a poor outcome. When the lesion spared the foveal center, good visual function was preserved.

Accepted for publication March 3, 1998.

This study was supported in part by an unrestricted grant from Research to Prevent Blindness Inc, New York, NY (Dr Pulido).

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REFERENCES


