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Journal Highlights

NEW FINDINGS FROM *OPHTHALMOLOGY, AJO,* AND *JAMA OPHTHALMOLOGY*

Ophthalmology

Assessing Retinal and Systemic Toxicity of Intravitreal Melphalan

September *Ophthalmology*

Although intravitreal melphalan has gained acceptance as a treatment for refractory vitreous seeds in retinoblastoma, limited data are available on its retinal and systemic toxicity. **Francis et al.** assessed toxicity issues in a two-part investigation and found evidence of retinal toxicity but not of systemic toxicity.

The researchers conducted two studies: a clinical study of 16 retinoblastoma patients and a preclinical study of 12 rabbits. In the human study, 16 eyes received a total of 107 weekly injections of 30 µg of melphalan; the median number of injections per eye was 6.5 (range, 5-8). In the animal study, the rabbits were given three weekly injections of 15 µg of intravitreal melphalan or vehicle in the right eye.

Complete blood counts were obtained in both studies, and no adverse systemic effects were noted in either study. Electroretinogram (ERG) responses were also recorded. In the humans, ERG testing was performed at baseline, before each injection, and at each follow-up visit. In the rabbits, ERG responses were obtained before and after melphalan injections. Histopathology was also evaluated in the rabbits' eyes. Using linear regression analysis, the researchers found that for every weekly 30-µg injection of melphalan in humans, the ERG response decreased by about 6 µV. However, once treatment ended, ERG responses remained stable. From these findings, the researchers concluded that 1) the drug appears to have an abrupt impact on retinal function in the initial phase of treatment, 2) the effect is apparently permanent, and 3) the effect does not appear to progress once the treatment course is complete. These results were validated in the rabbit study.

Three Years of Dexamethasone Implant for Diabetic Macular Edema

Ophthalmology

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Boyer et al. evaluated the dexamethasone (DEX) intravitreal implant in patients with diabetic macular edema (DME). They found that up to one-third of patients who received the DEX implant achieved 20/40 vision or better after their first implant—and that the benefit persisted over the long term when cataracts were removed as needed.

The researchers conducted two randomized masked, sham-controlled trials with identical study protocols; results were pooled for this analysis. A total of 1,048 patients with DME were enrolled; at baseline the patients had best-corrected visual acuity (BCVA) of 20/50 to 20/200 and a central retinal thickness of 300 µm or greater.

The patients were randomized into three treatment groups: 0.7-mg DEX implant (n = 351), 0.35-mg DEX implant (n = 347), and sham (n = 350). Outcome measures included BCVA, adverse events, and intraocular pressure (IOP).

At three years, 607 patients had completed the study (0.7 DEX = 225; 0.35 DEX = 230; sham = 152). With regard to visual outcomes, 22.2 percent of the 0.7-mg DEX group gained 15 letters or more compared with 18.4 percent of the 0.35-mg DEX group and 12 percent of the sham group. Rates of cataract-related adverse events in phakic eyes were 67.9 percent, 64.1 percent, and 20.4 percent in the 0.7-mg DEX group, the 0.35-mg DEX group, and the sham group, respectively. Increases in IOP were generally well controlled, though two patients who received DEX implants required glaucoma surgery. Patients who received either of the DEX implants had a greater reduction in central retinal thickness than those in the sham group.

Finally, the DEX patients received

an average of four to five implants during the study. This represents a significant decrease in treatment burden for patients when compared with anti-VEGF injections for DME, the researchers noted.

Characteristics of Bilateral Lacrimal Gland Disease

Ophthalmology
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In the largest study of bilateral lacrimal gland (LG) disease to date, **Tang et al.** characterized the diagnoses, clinical features, and outcomes in a series of patients with the condition. They found that the cause was most often inflammatory, followed by structural and lymphoproliferative etiologies. In addition, they found that despite local control with corticosteroids or radiotherapy, the underlying disease persisted in 71 percent of patients and led to death in 3 percent.

For this retrospective case series, the authors evaluated 97 patients who were drawn from the practices of oculoplastic specialists and ocular oncologists at 18 institutions in the United States and Australia. The patients ranged in age from 8 to 84 years, and most (77 percent) were female; 49 percent of the patients were black, 38 percent were white, and 12 percent were Hispanic.

The most common diagnoses were idiopathic orbital inflammation (30 percent), sarcoidosis (20 percent), LG prolapse (15 percent), and lymphoma (11 percent). Inflammatory conditions were more likely in younger patients and in those with pain and mechanical blepharoptosis. Conversely, lymphoma was more likely in older patients who had no signs of active inflammation. Black patients were more likely to have sarcoidosis.

The authors recommended that history and physical examination take precedence in the initial workup, with serologic analysis and imaging providing supplementary information when warranted. LG biopsy remains the gold standard for histopathologic diagnosis, they said.

American Journal of Ophthalmology

Reduction in Mean Deviation Values in Automated Perimetry in Eyes With Multifocal IOLs

August *AJO*

Farid et al. used a prospective, age-matched comparative analysis to evaluate differences in mean deviation (MD) values on automated perimetry in healthy eyes with multifocal versus monofocal intraocular lens (IOL) implants. A significant reduction in MD was found with multifocal IOLs compared with monofocal IOLs.

A total of 37 healthy eyes in 37 patients with bilateral multifocal (n = 22) or monofocal (n = 15) IOLs were studied. Humphrey Visual Field 10-2 testing was performed on all patients. MD and pattern standard deviation (PSD) numerical values were evaluated and compared between groups. The average MD was –2.84 dB for the multifocal IOL group and –0.97 dB for the monofocal IOL group. There was no significant difference in PSD between the two groups. Eyes that had visual field testing six or more months after IOL placement showed no improvement in MD compared with eyes tested at less than six months.

The authors concluded that multifocal IOL implants cause significant nonspecific reduction in MD values that does not improve with time or neuroadaptation. They emphasized that clinicians should be cautious in considering multifocal IOLs for eyes that require regular visual field testing, such as those with glaucoma; and for eyes where central visual disease already exists, such as those with macular degeneration.

Progression of Presbyopia After Laser In Situ Keratomileusis

August *AJO*

Tsuneyoshi et al. assessed the effect of laser in situ keratomileusis (LASIK) on near visual function in presbyopic patients aged 45 years or older in a retrospective cohort study.

Fifty-three eyes of 40 patients 45 years of age and older who had undergone LASIK for high myopia were included. For each eye, the minimum add power needed to obtain the best-corrected near visual acuity was measured preoperatively and three months postoperatively; and the correlations with the powers corrected by LASIK, corneal higher-order aberrations (HOAs), ocular HOAs, and patient ages were evaluated using univariate and multivariate analysis.

The mean patient age was 50 ± 4.1 years; the power corrected by LASIK was –7.56 ± 1.06 D. The mean add power was 1.80 ± 0.60 D preoperatively, which increased significantly to 2.18 ± 0.69 D postoperatively. Significant correlations with the increased add powers were detected for age and for the power corrected by LASIK but not for corneal and ocular HOAs. After multivariate analysis, only age correlated significantly. The overall percentage of eyes that required an increase of 0.5 D add or more was 60.4 percent. However, when this result was analyzed by age, 70 percent of patients aged 45 to 49 experienced that increase, compared with 14.3 percent in the 50 to 59 age group.

The study confirmed the apparent progression of presbyopia after LASIK for high myopia and the importance of obtaining informed consent from patients, especially those with early presbyopia.

JAMA Ophthalmology

Atropine vs. Patching for Treatment of Moderate Amblyopia: Follow-up at 15 Years of Age

July *JAMA Ophthalmology*

Initial treatment of amblyopia with patching of, or atropine sulfate eyedrops in, the fellow eye has been shown to improve visual acuity (VA) in the short term. To investigate the durability of the effect, **Repka et al.** evaluated VA at 15 years of age among patients who were younger than 7 years when enrolled in the Pediatric Eye Disease Investigator Group

(PEDIG) treatment trial for moderate amblyopia. The PEDIG trial randomly assigned 419 children with amblyopia (VA, 20/40-20/100) to patching (minimum of six hours per day) or atropine sulfate eyedrops 1 percent (one drop daily) for six months, with treatment after six months at the discretion of the investigator.

Two years after initial enrollment, an unselected subgroup of 188 children was enrolled into long-term follow-up. Of these, 147 were examined at 15 years of age. Mean VA in the amblyopic eye measured at that age was approximately 20/25; 60 percent had a VA of 20/25 or better, including 33 percent with 20/20 or better. Mean interocular acuity difference (IOD) was 0.21 logMAR (2.1 lines); 48 percent had an IOD of two or more lines, and 71 percent had one or more lines.

Better VA was achieved in children who were younger than 5 years at enrollment into the initial trial (mean logMAR, 0.09) compared with those aged 5 to 6 years (mean logMAR, 0.18; $p < .001$). No significant VA differences were seen between the atropine and patching groups in either the amblyopic eye ($p = .44$) or the fellow eye ($p = .43$).

The authors concluded that, at age 15, most children treated for moderate amblyopia when younger than 7 years have good VA, though mild residual amblyopia is common, and outcomes are similar whether the initial treatment was with atropine or patching. Further, the treatment benefit persists until at least 15 years of age.

Efficacy and Safety of Antifungal Additives in Optisol-GS Corneal Storage Medium

July *JAMA Ophthalmology*

Optisol-GS, the most common corneal storage medium in the United States, contains antibacterial but no antifungal supplementation. However, most cases of postkeratoplasty endophthalmitis and keratitis are now caused by fungi, most commonly *Candida* species. **Layer et al.** performed in vitro studies to assess the efficacy and safety of voriconazole and amphotericin B in reducing *Candida* contamination of Optisol-GS under normal storage conditions.

For the efficacy study, the researchers used two sets of 10 vials of Optisol-GS containing different concentrations of voriconazole or amphotericin B, with two unaltered vials of Optisol-GS as controls. Known concentrations of *Candida albicans* were added to one set of vials, and *Candida glabrata* to the other set. Growth of *C. albicans* and *C. glabrata* was observed in all voriconazole-supplemented vials. In contrast, there was no growth of either organism in amphotericin B–supplemented vials, except at the lowest concentrations on day 2, when viable counts of *C. glabrata* were reduced by 99 percent and 96 percent, respectively.

For the safety study, researchers used 15 pairs of research-grade donor corneas, separated them, and randomly placed them into each of the different concentrations of the supplemented or control Optisol-GS. Compared with controls, corneas in supplemented Optisol-GS showed no apparent differences in endothelial cell density reduction, percentage of intact epithelium, or percentage of nonviable endothelial cells, except for those in the solution containing the highest concentration of amphotericin B (10 times minimum inhibitory concentration).

The authors concluded that the addition of amphotericin B to Optisol-GS may significantly improve activity against contamination with *Candida* species.

Ophthalmologic Examinations in Areas of Miyagi Prefecture Affected by the Great East Japan Earthquake

July *JAMA Ophthalmology*

One month after a severe earthquake in Japan in 2011, **Doi et al.** were granted free use of Bascom Palmer Eye Institute's Mission Vision Van, a customized bus that was airlifted to Japan. The authors describe their use of this mobile eye clinic to provide ophthalmologic care in the disaster zone in Miyagi Prefecture.

They evaluated 731 patients who received treatment in the eye care van between April 15 and May 29, 2011. Of the 914 diagnoses made, 358 were refractive disorders (39.2 percent), which were the most common ocular conditions observed; other diagnoses included 155 cataracts (17 percent), 106 dry eye (11.6 percent), and 73 infectious diseases (8 percent) such as conjunctivitis. Overall, emergency prescriptions included 871 bottles of eyedrops, among which were 222 prescriptions for dry eye (25.5 percent), 189 for cataracts (21.7 percent), and 107 for glaucoma (12.3 percent).

The authors had initially expected that ocular infectious diseases might be aggravated by conditions in the disaster area, but they found this to be a relatively minor concern. Instead, a substantial number of patients needed replacements for eyeglasses, contact lenses, and eyedrops lost in the earthquake; and the authors concluded that the mobile clinic appears to be a useful way to provide ophthalmologic examinations and support after a disaster.

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