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# RETINA DIGEST®

SUMMER 2015

## Anti-VEGF and Quality of Life in Neovascular Age-related Macular Degeneration

Neovascular age-related macular degeneration (nAMD) is treated with regular intravitreal injections of vascular endothelial growth factor (VEGF) inhibitor to stabilize vision. From a patient's perspective, the most important outcome is vision-related quality of life (VRQoL). Variations in clinical trial results using the 25-item National Eye Institute Visual Functioning Questionnaire to assess VRQoL following anti-VEGF treatment have proven the test psychometrically invalid.

Finger et al from the University of Melbourne, Australia, performed a prospective case series using the Impact of Vision Impairment (IVI) profile, a VRQoL instrument containing 28 items utilizing 3 to 4 active response options using Likert scaling, and its 3 subscales (Reading and Accessing Information, Mobility and Independence, and Emotional Well-being). The IVI has proven to be a reliable tool, validated using modern psychometric methods.

Each of the 169 patients (56% female; mean age, 70 years) newly diagnosed with nAMD received 3 monthly intravitreal injections of 0.5 mg ranibizumab, with injections then on an extended protocol or continuing at intervals of 4 weeks, depending on disease activity. VRQoL was assessed at baseline, 6 months and 12 months. At the 6-month follow-up, 138 patients were available; at 12 months, 120 patients were available.

From baseline to 6 months, mean visual acuity (VA) in the treated eye improved by 7 letters; mean retinal thickness on optical coherence

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tomography decreased by 96 µm. At 12 months, an average of 6.5 injections produced a mean VA improvement of 8 letters and a decrease in mean retinal thickness of 87 µm compared with baseline. Patients who lost visual acuity reported significantly worse VRQoL at 12 months for the Accessing Information and Mobility subscales. No VRQoL change was seen in patients who had unchanged visual acuity, while patients with considerable gain (>2 lines) reported significantly improved VRQoL on the Accessing Information and Emotional Well-being subscales.

Anti-VEGF treatment for nAMD improved VRQoL in those who gained vision and maintained it in those with no vision change. A positive change in visual acuity at 12 months was associated with an uptick for the IVI's Accessing Information and Emotional Well-being subscales.

*Finger RP, Guymer RH, Gillies MC, Keeffe JE. The impact of anti-vascular endothelial growth factor treatment on quality of life in neovascular age-related macular degeneration.* Ophthalmology *2014;121:1246-1251.*

## Myopic Choroidal Neovascularization

Myopic choroidal neovascularization (mCNV) was once thought to occur only in eyes with pathological myopia, but is now known to occur at any degree of myopia and in eyes without the typical myopic degenerative fundus changes. The prevalence of mCNV is unclear, because previous studies lacked uniform definitions of myopia, pathological myopia and mCNV.

The standard tests for mCNV are fundus biomicroscopy, fluorescein angiography and optical coherence tomography. On slit-lamp biomicroscopy, mCNV appears as a small, flat, grayish membrane that may have a hyperpigmented border (Figure 1). The differential diagnoses and pathologies of mCNV are summarized in Table 1.

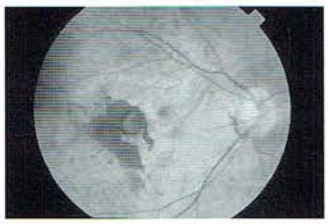

**Figure 1.** Fundus optic disc photograph showing mCNV along with hemorrhage. (*Image courtesy of Dr. Daniel Berinstein.*)

Laser photocoagulation and verteporfin photodynamic therapy (vPDT) were originally used to treat mCNV. Laser treatment has not been proven effective, can cause retinal tissue damage and does not maintain visual acuity (VA) in the long term. vPDT stabilizes VA but can cause long-term chorioretinal atrophy, leading to further vision loss. Anti-vascular endothelial growth factor (VEGF) therapy has been used recently to treat mCNV. Clinical trials of ranibizumab show sustained VA gains, better disease activity outcomes than vPDT and no retinal detachments. Other anti-VEGF therapies have limited safety and efficacy profiles or are still under investigation.

After reviewing available evidence, Wong et al from the National University of Singapore proposed a clinical algorithm to diagnose and treat mCNV. Patients presenting with myopia and reduced vision, central scotoma, and/or metamorphopsia should be referred to a retinal special-

**Table 1.** Coexisting pathologies and differential diagnoses for mCNV

| Other coexisting degenerative changes associated with myopia | Differential diagnosis for CNV |
|---|---|
| Myopic traction maculopathy (foveoschisis) | Neovascular AMD |
| Macular hole | Myopic macular hemorrhage due to lacquer cracks |
| Retinal tear/detachment | Punctate inner choroidopathy (usually coexists with myopia) |
| Dome-shaped macula | Multifocal choroiditis |
| Staphyloma | Idiopathic CNV[a] |
| Atrophic changes (patchy atrophy, tesselated changes and diffuse atrophy) | |

*AMD, age-related macular degeneration; CNV, choroidal neovascularization.*
*[a]Idiopathic CNV in a person with myopia is myopic CNV.*

ist immediately. Previously diagnosed patients should be treated promptly with a single intravitreal injection of anti-VEGF. Patients treated with vPDT can be switched to anti-VEGF therapy.

After the initial injection, all patients should be monitored monthly for the first 2 months for disease activity; if present, a second injection should be given. If 2 successive visits following the initial injection show no disease activity, 3-month follow-ups may be considered, with monitoring frequency determined by the treating specialist. Patients should be instructed to return at any time if they experience any vision loss or metamorphopsia recurrence.

*Wong TY, Ohno-Matsui K, Leveziel N, et al. Myopic choroidal neovascularisation: current concepts and update on clinical management.* Br J Ophthalmol *2015;99:289-296.*

**Table 2.** Clinical features of endophthalmitis caused by *Streptococcus* species

| Clinical scenario | No. of patients (%) | No. of *Streptococcus* organisms (% of clinical scenario) | | |
|---|---|---|---|---|
| | | β-Hemolytic | *Streptococcus pneumoniae* | *Streptococcus viridans* |
| Bleb associated | 17 (27) | 2 (12) | 4 (23) | 11 (65) |
| After intravitreal injection | 16 (25) | 0 (0) | 1 (6) | 15 (94) |
| After cataract surgery | 13 (21) | 1 (8) | 4 (31) | 8 (61) |
| After PKP/K-Pro surgery[a] | 8 (13) | 2 (25) | 1 (12) | 5 (63) |
| Ruptured globe | 4 (6) | 0 (0) | 0 (0) | 4 (100) |
| Miscellaneous[b] | 3 (5) | 0 (0) | 3 (100) | 0 (0) |
| Endogenous | 2 (3) | 0 (0) | 0 (0) | 2 (100) |
| **Total** | **63 (100)** | **5 (8)** | **13 (21)** | **45 (71)** |

*K-Pro, keratoprosthesis; PKP, penetrating keratoplasty. [a]Includes 6 PKP and 2 K-Pro patients. [b]Includes 2 postoperative glaucoma drainage device patients and 1 perforated corneal ulcer patient.*

## Endophthalmitis and Streptococcal Species

An ocular infection, endophthalmitis is caused by various microbes. Streptococcal infection often results in poorer visual outcomes than coagulase-negative *Staphylococcus* infection, the most common cause of postoperative endophthalmitis. A study performed from 1977 through 1990 reported clinical settings, antibiotic susceptibilities and treatment outcomes for endophthalmitis caused by streptococci. Since then, the use of intravitreal injections and the antibiotic nonsusceptibility of streptococci have increased. Kuriyan et al from the University of Miami, Florida, performed a retrospective, observational case series of 63 patients with *Streptococcus*-caused endophthalmitis between January 1, 2000, and December 31, 2011.

Charts from 63 patients (mean age, 66.9 years) were analyzed. Isolates were identified using standard microbiological procedures, and treatment strategies were determined by the treating physician. The clinical features of streptococcal endophthalmitis are summarized in Table 2. Initial treatment consisted of a vitreous tap and intravitreal antibiotics in 78% of patients and pars plana vitrectomy with intravitreal antibiotics in 22%. Endophthalmitis following either intravitreal injection and penetrating keratoplasty or keratoprosthesis was most likely to need additional therapeutic interventions. Vancomycin was used for intravitreal antibiotic treatment in all patients, with ceftazidime or amikacin also used in 97%. Intravitreal dexamethasone was part of the initial treatment for 56 patients, and all patients used topical antibiotic drops.

The most common *Streptococcus* organism isolated was *Streptococcus viridans*. The majority (92%) of patients were infected with a single *Streptococcus* species; 60 of the 63 streptococcal isolates were susceptible to vancomycin, 47 of 48 to ceftriaxone and 57 of 61 to levofloxacin. For vancomycin,

the minimum inhibitory concentration (MIC) for streptococcal isolates remained at 1 µg/mL throughout the entire 12 years, whereas the MICs increased for ceftriaxone from 0.5 µg/mL to 0.75 µg/mL and for levofloxacin from 1.5 µg/mL to 3.0 µg/mL during the second half of the study.

Bleb-associated and cataract patients had better visual acuity (VA) outcomes than the intravitreal injection patients, perhaps due to direct contamination of the vitreous cavity with bacteria. Patients receiving dexamethasone as part of their initial treatment had better VA outcomes than those who did not.

The antibiotic susceptibility data supports continued use of vancomycin in combination with a second antibiotic providing both gram-positive and gram-negative coverage. Increased MICs in the latter half of the study raise concerns about potential decreased clinical susceptibility to commonly used antibiotics.

*Kuriyan AE, Weiss KD, Flynn HW Jr, et al. Endophthalmitis caused by streptococcal species: clinical settings, microbiology, management, and outcomes.* Am J Ophthalmol *2014; 157:774-780.*

## Metamorphopsia and OCT After Rhegmatogenous Retinal Detachment Surgery

After corrective surgery for rhegmatogenous retinal detachment (RRD), many patients complain of unsatisfactory quality of vision despite successful reattachment and improvement of visual acuity (VA). Metamorphopsia is one of the most common complaints. Okamoto et al from the University of Tsukuba, Japan, performed a prospective, interventional, consecutive study to quantify the severity of metamorphopsia after successful RRD repair and investigate the relationship between metamorphopsia and morphologic changes as assessed with spectral-domain optical coherence tomography (OCT).

VA, metamorphopsia status and OCT images of 129 patients (mean age, 52.3 years) were obtained 6 to 12 months following successful surgery for unilateral RRD. Age, sex, surgical procedures, number and circumferential dimension of retinal tears, area of retinal detachment and macular status were recorded preoperatively. Severity of metamorphopsia was quantified by M-CHARTS. Logistic regression analysis determined the OCT parameters relevant to metamorphopsia presence.

The mean postoperative metamorphopsia score of all patients was 0.30 ± 0.46 (range, 0.0–2.0). The 50 patients with metamorphopsia had a larger area of retinal detachment than did those without; of these, 41 had macula-off RRD and 9 had macula-on RRD ($p < .001$). In the eyes with metamorphopsia, OCT showed 6 with epiretinal membrane, 5 with disrupted photoreceptor inner and outer segment junction, 3 with cystoid macular edema, 2 with macular holes, 2 with subretinal fluid and 32 with no morphologic change. The horizontal metamorphopsia score was significantly higher than the vertical score (0.86 vs 0.62, respectively; $p < .05$) in the 32 patients with no morphologic changes on OCT.

The authors concluded that retinal vertical displacement after surgery might induce horizontal metamorphopsia, whereas pre- and intraoperative macula-on retinal detachment did not. Results from the short-term follow-up in the present study may not predict long-term effects, given that previous studies with 1 to 5 years' follow-up reported improved VA, and potentially improved metamorphopsia. over time.

*Okamoto F, Sugiura Y, Okamoto Y, et al. Metamorphopsia and optical coherence tomography findings after rhegmatogenous retinal detachment surgery.* Am J Ophthalmol *2014;157:214-220.*

**AUTUMN 2015**

- Anti-VEGF therapy and glaucoma
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**In the Next Issue**