
News in Review

COMMENTARY AND PERSPECTIVES

Statin-AMD Finding Is Unexpected

A study that set out to find evidence that statins may help prevent age-related macular degeneration (AMD) yielded a surprise finding. One subset of patients—those with consistently

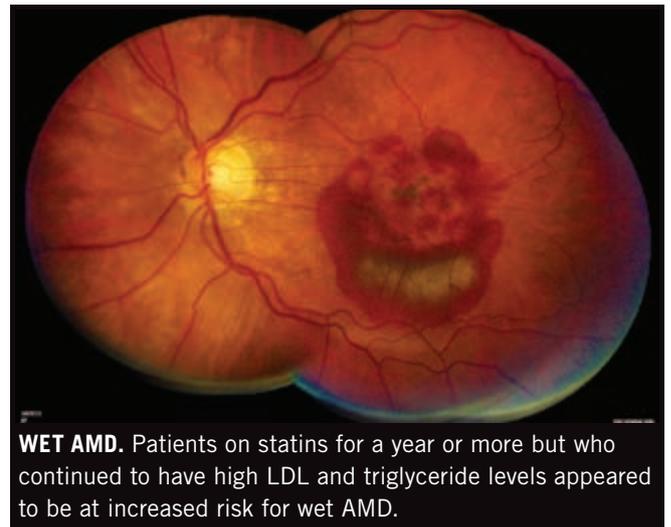
high serum low-density lipoprotein (LDL) or serum triglyceride (TG) levels despite a year or more of statin use—had an increased risk of developing wet AMD.¹

Statins, the most commonly prescribed drugs in the United States, are used to treat underlying pathologic processes that lead to heart disease. Those same processes are thought to play a role in the development of AMD, so a team of researchers, led by Brian L. VanderBeek, MD, MPH, theorized that statins might confer a protective effect in the eye. He is assistant professor of ophthalmology,

retina and vitreous service, Scheie Eye Institute, University of Pennsylvania.

The researchers asked two main questions. First: Is statin use associated with the development of nonexudative AMD? They found that it is not.

And second: Is statin use associated with the development of exudative AMD? The answer to that is more nuanced. “There is potentially a subset of individuals who, despite taking statins regularly, continue to have elevated cholesterol levels; and these individuals may have an elevated hazard for developing exudative AMD,”



WET AMD. Patients on statins for a year or more but who continued to have high LDL and triglyceride levels appeared to be at increased risk for wet AMD.

said Dr. VanderBeek.

The study reviewed records of more than 100,000 beneficiaries from a national insurance claims database for the years 2001 through 2007. About half of the patients used statins. All were age 60 and older, had been enrolled in the database for two or more years, and had visited an eye care provider at least once in two years. Only those who had baseline laboratory values for LDL, HDL, and TG were included because statins alter levels of those serum lipids.

The researchers created

three models from the pool of beneficiaries. Statins and lipid values were treated as independent variables in all models. In the first model, “development of nonexudative AMD,” individuals had no diagnosis of any AMD in the first two years in the plan (n = 107,007). In the second model, “development of exudative AMD,” individuals had no previous diagnosis of wet AMD in the first two years of the plan (n = 113,111). In the third, “progression from nonexudative AMD to exudative AMD,” individuals had no

previous diagnosis of exudative AMD and at least one diagnosis of nonexudative AMD in the first two years of the plan (n = 10,753).

Sixteen previous publications have reported either positive, negative, or no association between statin use and AMD. This study is distinguished by the size of its population for each type of AMD studied, Dr.

VanderBeek said. Also, the researchers were able to control for lab values of all of the individuals, which was something not previously done on such a scale.

Despite the elevated hazards for wet AMD in the one subset of patients, people taking statins should stay on them, Dr. VanderBeek said. “Statins have proved to have great cardiovascular bene-

fits; and until the biological mechanism of statins and its effects on the progression of AMD are better understood, I feel there is not ample evidence to stop the medication.”

But the findings, he said, suggest that future studies of statins and AMD should consider assessing lipid values in their analyses. “Even if future studies confirm the

current findings, we’ll need to better understand the mechanism of the disease and the role statins play in the progression of AMD to be sure there is a causal link.” —Miriam Karmel

1 VanderBeek BL et al. *Retina*. 2013;33(2):414-422.

Dr. VanderBeek reports no related financial interests.

Pediatric Update

Algorithm May Predict Severe ROP

Screening for retinopathy of prematurity (ROP) presents a challenge for neonatal experts. On one hand, the disease can be blinding when severe and undetected, making screening crucial. On the other hand, ROP is mild or moderate and spontaneously regresses in 90 percent of those screened, making screening superfluous for these babies. A retrospective observational study at two tertiary neonatal units in the United Kingdom recently took steps toward refining an algorithm that can identify in advance those at greatest risk.¹

The genesis of the study came from local ophthalmologists’ anecdotal reports, supported by published data, said lead author Shahid M. Husain, MD, neonatal unit, Homerton University Hospital, London. That is, babies born to parents of black ethnic origin—from the Caribbean

or Africa—appeared to develop less severe ROP compared with other groups. Dr. Husain and colleagues tested whether ethnicity might factor into the ROP equation—along with variables previously identified and developed into a clinical tool in Sweden (WINROP).

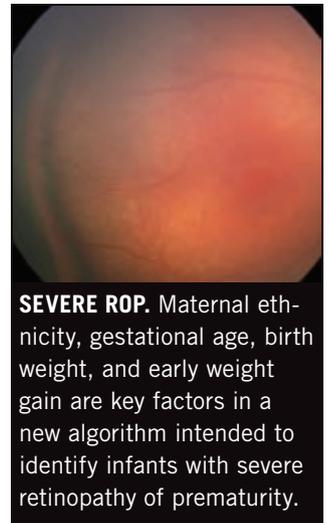
Using multiple logistic regression, the researchers analyzed data from 589 preterm infants from a multiethnic population. Of these, only 57 required laser treatment for ROP. Birth weight, early weight gain, gestational age, and maternal ethnicity all were significant predictors of ROP requiring treatment. Maternal ethnicity had greater predictive power than cumulative weight gain from birth to 6 weeks. Treatment was needed in 5.9 percent of babies born to black mothers, 9.4 percent of babies born to white mothers, and 12.8 percent of babies born to Asian mothers from the

Indian subcontinent.

Using the four variables, the researchers developed an algorithm with 100 percent sensitivity—identifying all babies at 6 weeks who would develop ROP requiring treatment—and 65.8 percent specificity.

“We tried to produce something very simple and straightforward that can be used in clinical practice without having to measure many variables,” said Dr. Husain. If it works prospectively, it has the potential to greatly reduce the number of ophthalmologic exams, he said, lessening burdens on both infants and health care systems. “Although cost-effective, screening requires physicians with the ophthalmic expertise to perform the exams, and it also requires coordination between ophthalmology and neonatal services,” he said. The exam’s side effects can also be troubling; Dr. Husain’s colleagues have published data on the physiological impacts on infants.²

Having a more precise predictive tool may prove particularly helpful in developing countries, said Dr. Husain. As neonatal services improve, more babies will survive, but other services



SEVERE ROP. Maternal ethnicity, gestational age, birth weight, and early weight gain are key factors in a new algorithm intended to identify infants with severe retinopathy of prematurity.

may lag behind, increasing the burden of ROP on the system. In addition, more mature babies develop ROP in developing countries. The reasons aren’t fully understood, he said, but, in resource-poor settings, poorly monitored factors, such as hyperoxia, may be partly to blame.

Before applying the algorithm prospectively, Dr. Husain hopes to further apply it to retrospective data.

—Annie Stuart

1 Husain SM et al. *J Pediatr*. Published online Jan. 25, 2013.
2 Mehta M et al. *Early Hum Dev*. 2005;81(4):355-360.

Dr. Husain reports no related financial interests.

Refractive Cataract Update

A Functional Cost for Multifocal IOL Users?

Pseudophakic patients who opt for a diffractive multifocal intraocular lens (IOL) may regret that choice, especially if they develop glaucoma later in life, Dutch researchers are warning.

The reason: Patients implanted with this type of IOL have approximately 2 dB less retinal sensitivity than their phakic counterparts, the group found.¹ “Two decibels is equal to one-third of your retinal sensitivity. That’s a lot, especially if you consider, for example, that someone with normally progressing

glaucoma loses on average 0.12 dB a year,” said lead author Nancy Aychoua, MD, an ophthalmology resident at the University Medical Center Groningen in the Netherlands. This may put patients who develop glaucoma—whose disease can rob them of retinal sensitivity—at a particular disadvantage in terms of having sufficient visual acuity to see in challenging situations, like dim light.

The researchers compared the results of standard automated perimetry (SAP) in three age-matched groups. These were pseudo-

phakes with an aspheric diffractive multifocal IOL (16 eyes); those with a monofocal IOL (12 eyes); and a control group of healthy, phakic adults (18 eyes). The multifocal IOLs were the Tecnis ZM900 (Abbott Medical Optics, two eyes) and the AT LISA 809M (Carl Zeiss Meditec, 14 eyes).

The researchers found that the multifocal IOL patients had a mean deviation of -2.40 dB from the phakic controls ($p < 0.001$). In the monofocal IOL group, the mean deviation compared with controls was 0.32 dB, which was not statistically significant.

“To our knowledge, no previous study has evaluated the effect of diffractive multifocal IOLs on SAP compared with healthy controls. This mainly explains why findings of other studies were not always in line with

our results,” Dr. Aychoua noted.

A 2 dB loss is large enough to be clinically significant, and it would be in addition to normal age-related decline or loss from glaucoma, she said.

Dr. Aychoua has two clinical recommendations based on her group’s study results: 1) Preoperatively, inform patients who are considering multifocal IOLs that they might lose retinal sensitivity, and 2) when interpreting visual field tests, consider the possibility that a patient’s multifocal IOL has reduced his or her retinal sensitivity.

—Linda Roach

1 Aychoua N et al. *JAMA Ophthalmol*. Published online Feb. 21, 2013.

Dr. Aychoua reports no related financial interests.

Anti-VEGF Therapy

Injection-IOP Connection

Seeking to go beyond earlier findings regarding sustained intraocular pressure (IOP) elevation after intravitreal injection of anti-VEGF drugs, K. Bailey Freund, MD, and colleagues conducted a study to get at the causes of IOP elevation.¹ Dr. Freund is clinical associate professor of ophthalmology at New York University.

“One thing we learned is that the greatest risk factor for developing this complication was the total number of injections an eye has received,” said Dr. Freund. Of

the 443 study eyes, 32 had a pressure on two consecutive visits that met one of the study criteria for elevated IOP: an absolute IOP of more than 25 mmHg; an increase from baseline of more than 10 mmHg; or an absolute IOP of more than 21 mmHg with an increase of more than 5 mmHg. The 32 eyes had undergone a mean of 25.8 injections. This compares with a mean of 20.8 injections in those eyes without sustained IOP elevation.

“Looking at all of my patients who received injec-

tions for neovascular AMD, the 7 percent prevalence of sustained IOP elevation was unexpected,” Dr. Freund said.

Other investigations have suggested that protein aggregates and silicone microdroplets in compounded bevacizumab syringes might be responsible for these elevations. Dr. Freund said, “Our study argues against this hypothesis, as a majority of the injections were with commercial ranibizumab.”

Beyond the study’s findings, Dr. Freund is convinced that the repeated pressure spikes can cause reduced aqueous outflow, particularly when 32-gauge needles are used, as less reflux is seen when the needle

is withdrawn. Minor changes in protocol, including the use of 30-gauge needles and a small reduction in injection volume in at-risk eyes, have led to a virtual disappearance of sustained postinjection IOP elevation in his practice, he said.

The authors recommend routine monitoring of preinjection IOP in all patients receiving intravitreal anti-VEGF therapy. Dr. Freund suggested obtaining a baseline evaluation of the optic nerve prior to starting treatment. —Laura Kaufman

1 Hoang QV et al. *Retina*. 2013;33(1):179-187.

Dr. Freund consults for Regeneron and is on the scientific advisory board for Genentech.