
News in Review

COMMENTARY AND PERSPECTIVES

Regular Aspirin Use Linked to Wet AMD

Researchers mining data from the Beaver Dam Eye Study have found a small but statistically significant association between regular aspirin use and the increased incidence of late and

neovascular age-related macular degeneration (AMD).¹ The finding was based on patient reports of regular aspirin use 10 years prior to retinal examination compared with those who did not regularly use aspirin during that time.

The researchers noted that aspirin use is common in the United States for pain relief and cardioprotective effects, and its use will become more widespread as the population ages. They undertook the study to address the concerns of ophthalmologists who either are planning to perform ocular surgery or who are treating

patients with AMD.

The Beaver Dam Eye Study is a longitudinal study of age-related eye diseases that assessed thousands of adults, aged 43 to 86 at baseline, every five years over a 20-year period. Participants were asked about their aspirin use. Those who used aspirin at least twice a week for more than three months were categorized as regular users.

The current study found that regular aspirin use 10 years prior to retinal examination was associated with increased incidence of late AMD, with an estimated incidence of 1.76 percent in



ASSOCIATION. A population-based study found a small but statistically significant association between neovascular AMD and regular use of aspirin 10 years earlier.

regular aspirin users, versus 1.03 percent in nonusers. A further breakdown by late AMD subtype found that neovascular AMD was significantly associated with aspirin use, whereas this was not the case with pure geographic atrophy.

No increase in AMD was observed among patients who reported regular aspirin use five years prior to exam. And, interestingly, the study did not find an association between incidence of AMD and use of warfarin or oral nonsteroidal anti-inflammatory medication.

The authors said that future studies will have to

confirm their observations and that such confirmation could lead to a better understanding of causal mechanisms and help in developing treatments that prevent or retard neovascular AMD in regular aspirin users.

Andreas K. Lauer, MD, said, "This well-designed study adds substantial interest to the question of whether a causal relationship exists between aspirin and AMD progression." But Dr. Lauer, associate professor of ophthalmology and chief, vitreoretinal division, Casey Eye Institute, Portland, Ore., said it is not a game changer in terms of

clinical practice. “The study is reporting a difference in incidences between these groups and is not suggesting that there is causality.”

Therefore, the findings should not influence ophthalmologists’ decisions regarding aspirin use prior to surgery, he said. And they shouldn’t alter the advice that ophthalmologists cur-

rently give to patients with AMD as to whether or not to continue aspirin therapy. In fact, this study doesn’t address whether stopping aspirin in long-term regular aspirin users would reduce the incidence of AMD to that seen in nonusers.

Dr. Lauer added that future studies will help determine whether aspirin

offers a clear advantage to the overall well-being of the patient, one that may or may not outweigh the AMD-related concerns.

For now, he said, “Additional information from other population-based studies may help us better understand whether a causal relationship exists between aspirin and AMD progres-

sion.”^{2,3} —Miriam Karmel

1 Klein BE et al. *JAMA*. 2012; 308(23):2469-2478.

2 Liew G et al. *JAMA Intern Med*. 2013 Jan 21. [Epub ahead of print.]

3 Kaul S, Diamond GA. *JAMA Intern Med*. 2013 Jan 21. [Epub ahead of print.]

Dr. Lauer reports no related financial interests.

Retina Report

Beta-Blockers May Reduce Need for AMD Injections

A highly variable response to antiangiogenic treatment has created a bit of a quandary for vitreoretinal specialists, who’ve sometimes chalked it up to idiosyncratic factors such as tachyphylaxis or genetic differences. Not so fast, say Spanish researchers. There may be more to this phenomenon than first meets the eye.

In a retrospective, non-randomized case series study, researchers from Valladolid, Spain, evaluated responses to intravitreal bevacizumab injections in 46 patients with choroidal neovascularization secondary to age-related macular degeneration (AMD) who were on concomitant systemic therapy.¹

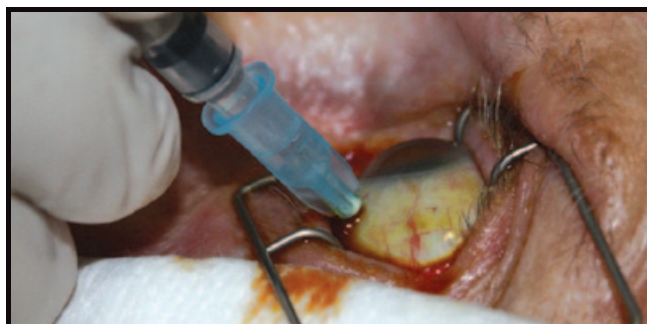
The patients received three consecutive monthly injections of 1.25 mg bevacizumab, followed by a monthly evaluation. Subsequent injections were given only if intraretinal or subretinal fluid or blood was

observed with optical coherence tomography (OCT) or funduscopy.

During the study, the researchers mainly analyzed changes in ETDRS best-corrected visual acuity, central foveal thickness, severe adverse effects, and the number of bevacizumab injections required to achieve inactivation of choroidal neovascularization.

Of the nine types of concomitant systemic medications used by various patients, beta-adrenergic blocking agents emerged as an interesting outlier. Patients on this type of medication required significantly fewer (2.9) intravitreal injections than those not using it.

“The different response patterns intrigued us,” said coauthor Javier A. Montero, MD, PhD, associate professor of ophthalmology and head of the vitreoretinal unit at the Pio del Rio Horta University Hospital. “We were surprised by



LESS AVASTIN. In a small study conducted by Spanish researchers, patients on systemic beta-blockers needed 2.9 fewer intravitreal injections of bevacizumab to achieve inactivation of choroidal neovascularization secondary to AMD than did their counterparts who were taking other systemic medications.

the leading role of the various beta-blocking agents.”

Patients on these agents also had slightly improved visual acuity. They gained an average of 1.8 letters at 24 months versus 0.1 letters lost in the other patients, but these changes were not statistically significant.

Still, the study may help guide future practice.

Once an adequate amount of retinal “dryness” has been achieved (in this case, when no fluid was observed on OCT or funduscopy), said Dr. Montero, additional treatment may not be necessary. “That’s because it’s not clear that complete inhibition of VEGF leads to better visual outcomes,” he said, “whether the patient is using

bevacizumab, ranibizumab, and/or aflibercept.”

Following further study on the impact of drugs such as systemic beta-blockers, it may become possible to decrease the number of intravitreal injections in AMD patients. This could reduce the need for repeated exams and treatment, thereby lowering costs and risks, such as endophthalmitis and retinal detachment, as well as atrophic retinal pigment epithelium changes that are linked specifically with the use of ranibizumab, said Dr. Montero. —Annie Stuart

1 Montero J et al. *Retina*. 2012 Oct 24. [Epub ahead of print.]

Dr. Montero reports no related financial interests.

Pediatrics Update

Better Dx of Abuse

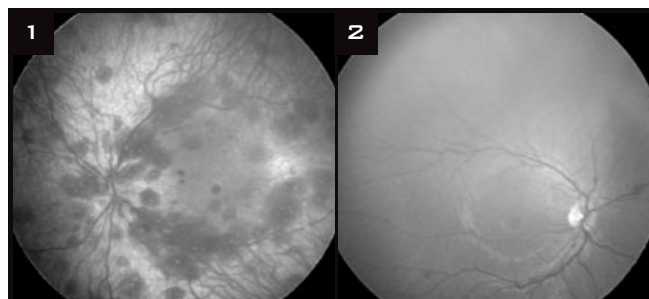
Inflicted traumatic brain injury (ITBI), including shaken baby syndrome, has been a challenging diagnosis to prove. A prospective study that differentiates characteristics of retinal hemorrhages resulting from all types of brain injury, including auto accidents and falls, may help diagnose abuse with more certainty.¹

The study clarifies criteria for ITBI diagnosis, using wide-field retinal imaging (RetCam) of children admitted to the PICU with traumatic and nontraumatic encephalopathies over six years.

The lead author, Robert Minns, FRCP(Edin),

FRCPC, PhD, emeritus professor of pediatric neurology at the University of Edinburgh, Scotland, said that significant differences were identified. “A diagnosis of ITBI can be distinguished from other causes by the presence of more than 25 dot-blot [intraretinal layer] hemorrhages. Retinal hemorrhages in ITBI children were significantly found in deeper layers of the retina and significantly toward the retinal periphery. Retinal hemorrhages in accidental TBI were, by comparison, near the optic disc and more in the superficial retinal layers.”

Average numbers of



EXAMPLES OF TWO INJURIES. (1) An inflicted traumatic brain injury case showing extensive hemorrhagic retinopathy in all retinal zones. (2) An accidental injury case showing five small- and moderate-sized intraretinal hemorrhages near the optic disc.

hemorrhages in the different retinal layers and zones are described for inflicted and accidental injuries, and medical conditions, he said.

“Doing a prospective study with objective measuring and analysis and including all possible causes [e.g., accidents, meningitis, inflicted injuries] allows us to be much more statistically certain of results,” he

said. “We were pleased at the degree of positive predictive value we found: 93 percent. That should be of considerable use legally and in child protective conferences.” —*Laura B. Kaufman*

1 Minns RA et al. *Pediatrics*. 2012;130(5):e1227-e1234.

Dr. Minns reports no related financial interests.

Eye on Ethnicity

Topiramate & Glaucoma

Taiwanese patients who use topiramate are seven times more likely to develop glaucoma in the month after they begin taking the drug than those who do not take it, a recent study has concluded.¹

In a retrospective review of records from the Taiwan national health system, the researchers found that 0.36 percent of new topiramate users (n = 1,956) developed glaucoma during the first month of taking the drug, compared with 0.04 percent of the 15,648 controls. In the subsequent 11 months, there were no statistically

significant differences in the incidence of glaucoma diagnoses between the two groups, the researchers at Taipei Medical University Hospital, in Taipei, Taiwan, reported.

“Furthermore, we found the relative risks of developing glaucoma among the topiramate users of Taiwan to be much higher than those obtained from a Canadian population,” they wrote. In that Canadian study,² in which white subjects predominated, the risk ratio for new users of topiramate was 1.54, compared with subjects who did not

take the drug. The Taiwanese researchers calculated new users’ adjusted hazard ratio at 7.41. The authors also noted that several Asian ethnic groups, including Chinese, are more prone to having narrow angles than non-Asians.

The association between topiramate and acute secondary, bilateral angle-closure glaucoma has been recognized for more than a decade, said Rick W. Fraunfelder, MD, MBA, professor of ophthalmology at the Casey Eye Institute, at Oregon Health & Science University in Portland, and director of the National Registry of Drug-Induced Ocular Side Effects.

In affected eyes with narrow angles, topiramate causes fluid to accumulate

in the choroid, pushing the lens-iris diaphragm forward and shallowing the anterior chamber, Dr. Fraunfelder said. This occludes the angle and causes acute glaucoma. The patient should stop taking the drug immediately upon diagnosis, he added. “This is angle-closure glaucoma, but it’s not the angle closure that we’re accustomed to. It does not involve pupillary block, so a peripheral iridotomy won’t help. Instead, you should do peripheral iridoplasty.”

—*Linda Roach*

1 Ho JD et al. *Am J Ophthalmol*. 2013;155(2):336-341.

2 Etminan M et al. *Am J Ophthalmol*. 2012;153(5):827-830.

Dr. Fraunfelder reports no related financial interests.