Drug Monitor

Managing Glucose Can Help With Diabetic Vision Problems

Patients with diabetes are at risk for diabetic macular edema (DME), a major cause of moderate vision loss. Current drug treatments are aimed at inhibiting vascular endothelial growth factor (VEGF), which plays a role in the pathogenesis of DME. The 3 therapies used for intravitreal injection (pegaptanib, bevacizumab, and ranibizumab) have had promising results in studies, but the benefits are variable, depending on, for instance, whether the patient has hypertension, how long the patient has had diabetes, and serum A1C level.

Researchers from Selcuk University, Konya, Turkey, say no published study, to their knowledge, had evaluated the relationship between glycemic control and the outcomes of intravitreal drug injection in DME. Ranibizumab seems to be the most promising of the 3 anti-VEGF-A drugs, but there are few studies on its effect on DME, so they conducted a study of 65 patients treated with intravitreal ranibizumab injection.

The main outcome measures of the study were the change in best corrected visual acuity (BCVA) and the central subfield macular thickness (CSMT) and its correlation with A1C values. At baseline, the mean A1C was 8.18% (range 5.7% to 12.7%). The median value of BCVA was 20/80 (52 letters), and the median CSMT was 468 µm. Thirty-three patients were in the preproliferative stage of diabetic retinopathy; 32 were in the proliferative stage.

Four to 6 weeks after 1 intravitreal injection, the researchers found "marked improvement" of visual acuity: The median value of BCVA increased to 20/50 (59.5 letters), and the median CSMT dropped to 310 µm—both significant changes. The change in BCVA was higher (6 letters) in patients who had received a previous treatment for DME, compared with those who received no previous treatment (1 letter). In this study, 29 patients had received previous treatment for DME at least 6 months previously, most being treated with intravitreal bevacizumab.

The duration of diabetes was not correlated with either the changes in macular thickness or visual acuity. However, the change in CSMT was inversely correlated with the serum A1C levels. The researchers cite other studies that have found glucose regulation reduces or delays the incidence and progression of diabetic retinopathy.

This preliminary study, the researchers say, suggests that patients with lower serum A1C levels might require fewer intravitreal anti-VEGF injections.

Source: *J Diabetes Complications.* 2011;25(5):298-302.

Anti-Alzheimer Disease Drugs in Real Life

Research-based information abounds on disease progression in patients with Alzheimer disease (AD), but not much is available outside the clinical-trial box, which is the reason researchers from the REseau sur la maladie d'ALzheimer FRançais (REAL.FR) study group conducted a 4-year "real-life" study.

The study followed 686 patients with mild-to-moderate Alzheimer disease who were enrolled in 16 memory clinics. The patients were evaluated twice a year via a protocol of cognitive and other tests. The researchers defined outcomes at 4 years according to 4 clinically significant endpoints: increase in functional incapacity, aggravation of behavioral and psychological symptoms, institutionalization, and death.

Although patients had been diagnosed with AD for a mean of 13 months (mean age at diagnosis, 77), many were still at a stage of mild cognitive impairment; 54% were completely independent for basic activities of daily living (ADL). About 88% had at least 1 behavior disturbance. Apathy was the most prevalent neuropsychiatric symptom, followed by anxiety, agitation, depression, and irritability. About one-third of the patients had 2 or more comorbidities.

More than 90% of the patients used AD-specific medication over the 4 years, usually cholinesterase inhibitors (ChEIs). Over the course of the study, the proportion of patients who used only ChEIs dropped from 89% to 70%, whereas the proportion of those using both ChEIs and memantine rose from 0% to 26%, and those who used only memantine rose from 0% to 4%. These patterns reflect current clinical practice guidelines.

At 4 years, 207 patients had completed the study; 104 had died and others had dropped out for reasons including medical problems and caregiver problems.

Whereas more than half of the patients had been independent in their ADL, by year 4, ADL scores had declined significantly with patients losing a mean of 2.7 points. The mean rate of functional decline was similar from one year to the next, equal to a loss of about 0.7 points per year. The most altered functions concerned bathing and dressing, affecting about 35% of patients. More than 20% developed incontinence.

Nonetheless, the researchers found the progression of cognitive changes is now slower than it was in the pre-ChEI era. They also found that even after 4 years, 11% of patients had no clinically meaningful decline in the Mini-Mental State Examination (MMSE) score. Further studies,

the researchers say, will help clarify whether the patients are good responders to cholinesterase therapy or whether they have a slow-progressing form of AD.

Another finding was the high occurrence of neuropsychiatric symptoms and functional incapacities from early disease stages and with increasing severity of cognitive syndromes. Apathy, the most common finding, is now recognized as a behavior marker of a more aggressive dementia, the researchers say, but seems to be helped with donepezil treatment.

In this study, 17% of the patients in the very mild stage of dementia at baseline did not experience a major life change (such as developing behavior issues or loss of functional capacity) over the study period. But the researchers observed a high level of variability of disease progression among AD patients, underscoring the need to assess patients and caregivers at least every 6 months.

Source: *Alzheimers Dement.* 2011;7(6):579-592.

Esomeprazole and Famotidine Work Well With Clopidogrel

Dual antiplatelet therapy with aspirin and clopidogrel increases the risk of gastrointestinal bleeding, leading to the addition of gastroprotective proton pump inhibitors (PPIs)—and concerns about the combination's risk of adverse cardiovascular outcomes. However, those concerns may be mitigated by the first head-to-head comparison of a PPI and a histamine 2-receptor antagonist (esomeprazole and famotidine) regarding their potential interference with clopidogrel. Neither drug reduced clopidogrel's platelet-inhibiting effect, say researchers from Ruttonjee Hospital, Hong Kong; University of Hong Kong; and The Chinese University of Hong Kong.

The study involved 88 patients with acute coronary syndrome or elective percutaneous coronary interventions treated with aspirin and clopidogrel. The patients were randomly assigned to receive esomeprazole 20 mg daily or famotidine 40 mg daily. Platelet reactivity units (PRUs) were measured at baseline and on day 28.

The researchers found no significant difference in PRUs from baseline to day 28 between the 2 groups. Half of the esomeprazole group and 43% of the famotidine group were classified as poor responders to clopidogrel on day 28. However, compared with baseline, this was a change of just 1 more patient per group. None in the esomeprazole group had upper gastrointestinal bleeding; 2 patients in the famotidine group did, with 1 due to duodenal ulcer and the other to gastric erosions.

Source: *Am Heart J.* 2011;162(5):870-874.

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