Drug Monitor

Investigational Vaccine Protects Against Shingles and PHN

Elderly patients not only are at increased risk for developing herpes zoster (commonly known as shingles) but also are far more likely to experience the debilitating chronic pain of postherpetic neuralgia (PHN). As such, the availability of a vaccine to prevent or reduce the severity of this disease in adults would represent a significant medical advance. This goal may be just within reach, based on results from a multicenter, randomized, placebo-controlled study, involving 38,546 adults aged 60 or older, conducted by the Shingles Prevention Study Group.

In VA Cooperative Study 403, a live, attenuated varicella-zoster virus (VZV) vaccine decreased the incidence of herpes zoster by 51%, reduced pain and discomfort by 61%, and cut the incidence of PHN by 66%. While the vaccine's reduction of herpes zoster incidence was not as great among patients aged 70 and older compared with those aged 60 to 69, the researchers say the older group saw a larger benefit in terms of illness severity, thus balancing the vaccine's overall protective effect.

The vaccine used in this study was derived from the same varicella strain (Oka/Merck) as the vaccine currently licensed to prevent chicken pox in children (Varivax, Merck & Co., Inc., Whitehouse Station, NJ), but its minimum potency in this study was at least 14 times greater. According to the investigators, preliminary research suggested that this level of potency is required to elicit a significant increase in cell-mediated immunity to VZV in older adults.

Source: *N Engl J Med*. 2005;352:2271–2284.

Thrombosis in Drug-Eluting Stents

The first 30 days after percutaneous coronary interventions (PCIs) traditionally are regarded as the window for stent thrombosis. The use of drug-eluting stents has reduced the risk, but outside of clinical trials, little is known about the long-term risk of stent thrombosis after 30 days, say researchers from Klinikum Siegburg Rhein-Sieg GmbH in Siegburg, Germany and Centro Cuore Columbus, San Raffaele Hospital, Mediolanum Cardio Research, and University of Milan, Milan, Italy.

To learn more, they prospectively studied 2,229 patients who underwent successful implantation with sirolimus- or paclitaxel-eluting stents. At nine months postprocedure, the cumulative incidence of stent thrombosis was 1.3%. Specifically, thrombosis occurred in nine (0.8%) of the 1,062 patients who received sirolimus-eluting stents and 20 (1.7%) of the 1,167 patients who received paclitaxel-eluting stents. Thirteen patients died.

The researchers further analyzed the thrombotic events according to whether they occurred within 30 days of the procedure (subacute) or after 30 days (late). There were 14 subacute events (four in the sirolimus group and 10 in the paclitaxel group), 10 (71%) of which occurred within one week of the procedure. Of the 15 cases of late thrombosis (five in the sirolimus group and 10 in the paclitaxel group), eight (53%) occurred within three months of the procedure.

While a 1.3% incidence may seem low, the researchers point out that it's substantially higher than the rates reported in clinical trials (0.4% at one year for sirolimus-eluting stents and 0.6% at nine months for paclitaxel-eluting stents). They also note that the widespread availability of drug-eluting stents has expanded "the scope of percutaneous coronary intervention…to more complex lesions and patients." In their study, 27% of the patients had diabetes and 79% of the lesions were complex. The clinical consequences, the researchers say, were severe, with a case-fatality rate of 45%.

Premature discontinuation of antiplatelet therapy was the most important predictor of stent thrombosis. Other key factors were renal failure, bifurcation lesions, diabetes, low ejection fraction, and, for subacute thrombosis, stent length. Although they did not find stent type to be an

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independent predictor of thrombosis, the researchers were concerned about the almost double incidence of thrombosis associated with paclitaxel-compared with sirolimus-eluting stents.

Source: *JAMA*. 2005;293: 2126–2130.

Behavioral vs. Pharmacologic Interventions for Nocturia

Exercises and other behavioral strategies reduce nocturia better than drug treatment, say researchers from the Birmingham/Atlanta Geriatric Research, Education, and Clinical Center at the VA medical centers in Birmingham, AL and Decatur, GA; Emory University, Atlanta, GA; and the University of Alabama at Birmingham. They performed a secondary analysis of data from 197 women aged 55 to 92 with incontinence and urodynamic evidence of bladder dysfunction.

At baseline, 131 women had nocturia. All participants visited the clinic every two weeks for eight weeks and completed a daily bladder diary.

At the clinic visits, women in the behavioral therapy group (47 patients) were taught pelvic floor muscle contractions, which they were to practice at home daily. If they awakened at night with an urge to void, they were instructed to use the exercises to suppress the urge, inhibit detrusor contractions, and prevent urine loss. Women who did not experience at least a 50% improvement with this strategy by the third visit received combined bladder-pelvic floor muscle biofeedback.

The other 84 patients were randomly assigned, in a double-blind fashion, to receive immediate-release oxybutynin 2.5 mg/day or placebo. Based on symptoms and adverse effects, dosages were titrated at clinic visits up to 5 mg three times daily.

Both behavioral therapy and oxybutynin treatment performed significantly better than placebo, but behavioral therapy showed a clear advantage. Nearly one quarter of the women in this group reduced their nocturia by at least half, compared with only 8.7% of the oxybutynin group and 2.6% of the placebo group.

The researchers say this is among the first reports to show benefits from behavioral therapy for older women with urge-predominant incontinence. They admit to being a bit surprised that interventions largely designed for daytime urge-predominant incontinence would show such good results for nocturia.

Source: *J Am Geriatr Soc*. 2005;53:846–850.