Drug Monitor

Treatment May be Effective for Mild Stroke

While it has been shown that treatment with intravenous (IV) tissue plasminogen activator (t-PA) within 3 hours of symptom onset of an acute ischemic stroke can improve a patient's clinical outcomes, many neurologists are reluctant to use the same treatment for patients with milder stroke. Results of previously published reports suggest that patients with milder stroke may improve spontaneously and may not benefit from IV thrombolysis. However, researchers from University of Medicine and Dentistry of New Jersey (UMDNJ), Newark, and University of Minnesota, Minneapolis, now are saying that using IV t-PA treatment for patients with mild stroke can lead to better clinical outcomes in that group as well.

The researchers conducted a retrospective review to identify all patients who presented to UMDNJ with acute ischemic stroke and received IV t-PA between January 1, 2005, and July 31, 2005. Of 52 patients identified, 31 had a score of 10 or less on the National Institutes of Health Stroke Scale (NIHSS). An NIHSS score of lower than 4 indicates minimal disability, while a score higher than 20 indicates severe disability. Their data were compared with those of 98 patients in a placebo group.

The researchers used the modified Rankin scale (mRS) to assess clinical outcomes at 7 to 10 days poststroke or discharge. They defined good outcomes as an mRS score of 0 or 1, while complications were defined as symptomatic hemorrhages with an increase in the NIHSS score of 4 or greater.

The mRS score at discharge for the treatment group reflected a better clinical outcome than the placebo group that was statistically significant ($P < .009$). In the treatment group, 7 patients had an mRS score of 0 and 16 patients had an mRS score of 1; 74% had a good outcome. One patient had a symptomatic hemorrhage, but there were no asymptomatic hemorrhages in this group. In the placebo group, 16 patients had an mRS score of 0 and 17 had an mRS score of 1; 34% had a good outcome. In this group, 3 patients had symptomatic hemorrhages and 1 patient had an asymptomatic hemorrhage.

The researchers say their study indicates that administering IV t-PA to patients with mild stroke can lead to improved clinical outcomes. Given the small sample size and the lack of long-term follow-up, they say their study should be considered "hypothesis generating." They suggest prospective studies be conducted to ascertain whether increasing the scope of therapeutic IV t-PA treatment is beneficial and safe in cases of mild stroke.

Source: *J Stroke Cerebrovasc Dis.* 2010;19(2):116–120. doi:10.1016/j.strokecerebrovadis.2009.03.019.

Opinions About Medications Change Over Time

Although results from previous studies have shown that negative beliefs (such as self-reported low necessity for medications and high concerns about taking medications) are significantly associated with nonadherence to medications, researchers conducting these studies have performed only single assessments of beliefs—thus failing to test whether beliefs change over time. As such, in a recent study, researchers from Duke University, Durham, North Carolina, sought to determine how patients' beliefs change over a designated period. They believe that such an understanding may be useful in improving long-term adherence to medications.

All of the patients included in the study had chronic ischemic heart disease and all previously had participated in the Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes with Early Implementation of the American College of Cardiology/American Heart Association Guidelines (CRUSADE) trial. From January 2006, through September 2007, the participants (patients at 41 hospitals) were consented for participation in a longitudinal follow-up survey study called Medication Applied and Sustained Over Time (MAINTAIN).

In the MAINTAIN study, patients completed 2 follow-up surveys (via telephone) at 3 and 12 months postdischarge, during which patients were asked questions about their current medication regimen, out-of-pocket medication expenses, rehospitalizations, angina symptoms, communication with health care providers regarding medications, and beliefs in heart medications.

The researchers used the Beliefs about Medicines Questionnaire-Specific (BMQ-Specific), a validated test instrument that assesses personal beliefs about necessity and concerns related to disease-specific medications (in this case, related to heart medications). There are 2 scales within the questionnaire, 1 that assesses necessity of prescribed medications for the specified disease and 1 that assesses concerns about potential adverse consequences of taking the medications for the specified disease. Both of the

scales consist of 5 statements, and participants were asked to provide their level of agreement with each statement using a 5-point Likert scale (where 1 = strongly disagree and 5 = strongly agree). Any scores that are above the scale midpoint indicate strong beliefs, either in the necessity or concerns concept. By subtracting the concerns score from the necessity score, the researchers were able to asses the relative importance of necessity and concerns for a patient. In order to assess how the patients' beliefs changed over time, the differences in BMQ-Specific scores at 3 months vs 12 months were explored.

Of the 1,195 patients who were enrolled in MAINTAIN, 812 completed both of the follow-up surveys. One-third of the patients reported a negative change in their beliefs about heart medications. At both 3 and 12 months, 74% of patients had a score higher than the midpoint for perceived necessity of heart medications. From 3 to 12 months, only 9.2% of patients shifted from a high to low necessity score, whereas 20.7% of patients shifted from a low to high concern score. There were certain factors found to be statistically significant and independently associated with increased concern, such as the perception that the provider did not listen carefully to the patient, depression at 12 months, hospital discharge with 7 or more medications, and not receiving a medication list/instructions at hospital discharge. The factors that were associated with decreased necessity included not having a cardiologist and nonpersistance at 12 months with lipid-lowering medication.

The researchers say that, although some changes were observed in perceived necessity, 1 of every 5 patients displayed negative changes in concerns. They say that because patients' beliefs about medications can largely influence their adherence, understanding and addressing changes in perception may help them adhere to their regimens and can help improve clinical outcomes.

Source: *Am Heart J.* 2010;159(4):561–569. doi:10.1016/j.ahj.2009.12.025.

Liver Injury Warning for Orlistat

The weight-loss medication orlistat (marketed as Xenical [Genentech, South San Francisco, California] and Alli [GlaxoSmithKline, Brentford, Middlesex, United Kingdom]) has a risk of severe liver damage, according to the FDA. While rare—so far, 13 cases have been identified, among an estimated 40 million people taking the drugs—the risk has led the FDA to revise the label. Twelve of the cases were reported outside the United States.

At this time, the FDA says, a cause-and-effect relationship of severe liver injury with orlistat has not been established. However, those taking the drug should be made aware of the signs and symptoms of liver injury, including itching, yellow eyes or skin, dark urine, loss of appetite, or light-colored stools.

Source: FDA news release. May 26, 2010.

Fracture Risk with Proton Pump Inhibitors

High doses or long-term use of proton pump inhibitors, used for treatment of frequent heartburn, may raise the risk of fractures of the hip, wrist, and spine, according to results from several epidemiologic studies.

Proton pump inhibitors are available both by prescription and over the counter. They include esomeprazole, dexlansoprazole, omeprazole, and lansoprazole. A warning issued by the FDA includes a decision to require changes to both over-the-counter and prescription labeling describing the potential increased risk.

The FDA advises health care professionals to "consider whether a lower dose or shorter duration of therapy would adequately treat the patient's condition."

Source: FDA news release. May 25, 2010.

Medication Reconciliation: Still Some Gaps to Fill

In 2005, the Joint Commission mandated hospitals to put a process in place for comparing patients' current medications with those newly ordered to pass to the next health care provider. Many health care organizations have had difficulties meeting the requirements, however. Results from a real-world study of implementation of medication reconciliation reveal some areas to help improve patient safety. In the retrospective study—conducted by researchers from Duke University Medical Center and Durham VA Medical Center, both in Durham, North Carolina; University of North Carolina at Chapel Hill; and Monroe Carell Jr. Children's Hospital at Vanderbilt, Nashville, Tennessee—one-fourth of participants had at least 1 discrepancy between at-home medications and those prescribed in the hospital.

The study cohort was a random sample, identified from all patients admitted to the general medicine, cardiology, or general surgery services of Duke University Medical Center between July 1, 2006, and August 31, 2006.

Of the 205 patients in the study, 27 had no medications recorded on admission. Among the remaining 178 patients, 41 (23%) had 1 or more discrepancy identified by the reconciliation process on admission, and 19% of those medications were considered

to be potentially high risk for adverse drug events (ADEs), according to the Institute for Safe Medication Practices high alert list or the North Carolina Narrow Therapeutic Index list. At discharge, 196 patients had 1 or more medication change from their home regimen, with 1,102 differences for all 205 patients. But fewer than half (44%) were alerted explicitly at discharge to their new medications or dose changes. Only 12% were given written instructions to stop taking discontinued home medications. (The researchers acknowledge that health care providers often give oral instructions that may not be recorded consistently in the patients' charts.)

Cardiovascular drugs were the most frequent class involved at both admission and discharge in medication discrepancies or differences (27%). The next most common were central nervous system, gastrointestinal, antimicrobial, and hematologic/oncologic medications. Potentially high-risk medications represented 18% of the discharge differences.

Age (odds ratio [OR] per 5-year increase = 3.31; 95% confidence interval [CI], 1.4–7.87), presence of medications known to be high risk for ADEs at admission (OR = 76.68; 95% CI, 9.13–634.76), and general surgery service (OR = 3.31; 95% CI, 1.4–7.87) were associated with a higher proportion of patients with medication discrepancies. Number of preadmission medications was not associated with discrepancies on admission, however—a surprising finding, say the researchers. Therefore, preadmission medication class may be the most important factor in predicting medication discrepancies. They also suggest that other models of medication reconciliation need to be tested, such as use of electronic personal records, to achieve standards for communicating information clearly to the next health care provider and to ensure patient safety and regulatory compliance.

Source: *Am J Geriatr Pharmacother.* 2010;8(2):115–126. doi:10.1016/j.amjopharm.2010.04.002

Capsaicin Patch Effective and Safe Over the Long Term?

Postherpetic neuralgia (PHN) and HIV-associated distal sensory polyneuropathy (HIV-DSP) are painful peripheral neuropathic pain syndromes that have long resisted easy treatment—most patients end up taking a combination of medications, with the consequent complications of drug interactions without necessarily achieving relief.

Patients with these conditions may have a much simpler option for managing their pain: a high-concentration (8%) capsaicin patch (NGX-4010, NeurogesX, Inc., San Mateo, California). In phase 2 and phase 3 studies, the NGX-4010 patch was shown to reduce pain after single and repeated applications in patients with PHN or HIV-DSP. The relief was observed irrespective of concomitant use of neuropathic pain medication, such as opioids.

But how long would the relief last? To find out, researchers from the NGX-4010 C118 Study Group assessed repeated applications of NGX-4010 over 1 year in 54 patients with moderate to severe PHN and 52 patients with HIV-DSP. All of the patients were participants in a prior NGX-4010 trial who had severe enough pain to warrant further treatment. Twenty-seven patients withdrew prematurely (1 due to an adverse event related to NGX-4010), leaving 43 patients with PHN and 36 with HIV-DSN who completed the study.

Almost half of the patients with PHN were in the control groups in previous studies and had received no NGX-4010 treatments. More than half of the patients with HIV-DSP had received 3 or 4 treatments. More patients with HIV-DSP than patients with PHN were receiving concomitant neuropathic pain treatment. Patients received pretreatment with a topical local anesthetic for 60 minutes followed by either a 60-minute (PHN and HIV-DSP patients) or a 90-minute (HIV-DSP patients) treatment. Patients could receive up to 3 additional treatments at intervals of 12 or more weeks.

Although this was primarily a safety trial, the researchers assessed pain relief at weeks 12 and 48. Patients with PHN had a mean decrease in Numeric Pain Rating Scale score during week 12 of 19.4% from baseline and week 48 of 35.6%. Patients with HIV-DSP had a mean percent decrease of 0.3% at week 12 and 12.4% at week 48.

At week 12, 65% of patients with PHN and 74% of patients with HIV-DSP reported pain improvement; 33% of both groups described their pain as very improved. At week 48, 44% of patients with PHN and 54% of patients with HIV-DSP reported very improved pain.

Up to 4 treatments with NGX-4010 were well tolerated, with more than 98% of all patients completing at least 90% of treatment. Pain associated with the patch was common but self-limited and adequately controlled by cooling measures or rescue pain medications. Treatment-emergent adverse events were similar in both groups; the most common were application site erythema and pain.

Source: *J Pain Symptom Manage.* 2010;39(6):1053–1064. doi:10.1016/j.jpainsymman.2009.11.316.