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ABSTRACT & COMMENTARY

Which Is Better for Nonconvulsive Seizures: Lacosamide or Fosphenytoin?

By David Chuang, MD

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Dr. Chuang reports he receives research funding from UCB and Eisai.

SYNOPSIS: Intravenous lacosamide was found to be noninferior to fosphenytoin in the treatment of nonconvulsive seizures in a prospective, multicenter, randomized clinical trial.

SOURCE: Husain AM, Lee JW, Kolls BJ, et al; for the Critical Care EEG Monitoring Research Consortium. Randomized trial of lacosamide vs fosphenytoin for nonconvulsive seizures. *Ann Neurol* 2018;83:1174-1185. doi: 10.1002/ana.25249.

Nonconvulsive seizures (NCS) are seizures that can be identified only with electroencephalography (EEG) because of an absence of obvious clinical correlation. Up to 21% of patients monitored with continuous EEG in the intensive care unit have been found to have NCS.[1] The presence of NCS is associated with worse overall outcome, and experts recommend treating NCS with multiple trials of nonsedating anti-seizure drugs (ASD) before moving on to anesthetic agents. Fosphenytoin (fPHT), the prodrug of phenytoin, is an ASD that long has been used in treatment of NCS, whereas lacosamide (LCM) is a newer ASD with recent data suggesting its role in treating NCS. Husain et al compared an intravenous (IV) formulation of LCM and fPHT to determine if IV LCM is noninferior to IV fPHT.

The authors performed a prospective, multicenter (12 centers), randomized clinical trial in which they recruited patients monitored with continuous EEG (cEEG) who had a nongeneralized convulsive seizure. Patients were randomized to receive either IV LCM or IV fPHT. The study also included a crossover phase in which the other study ASD was added if seizures persisted on the first study ASD. Patients were excluded if they already were taking the study ASD or phenytoin, had anoxic encephalopathy, were undergoing hypothermia protocol, or did not have at least 16 hours of cEEG following ASD administration. The cEEGs were read on site by one blinded reader, and NCS was determined using previously established criteria.[2] The direct caregivers were not blinded to which ASD the patients received.

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The cEEG later was transferred to a central site where it was reviewed by two blinded readers for seizure burden.

Sixty-two patients completed the study, of which there were 30 in the LCM arm and 32 in the fPHT arm. The demographics of both arms were similar, and there was no statistical difference in baseline seizure burden prior to treatment. The authors found that 63.3% of the LCM arm and 50% of the fPHT arm became seizure-free after the study ASD was administered, which was statistically significant for noninferiority of LCM compared to fPHT ($P = 0.02$) but not superiority of LCM over fPHT ($P = 0.29$). Baseline seizure burden also was found to be reduced by 98% in the LCM arm vs. 76% in the fPHT arm, but it did not reach statistical significance ($P = 0.129$). No significant differences were seen during the crossover phase and incidence of adverse events between LCM and fPHT.

The authors found that IV LCM was noninferior to IV fPHT in the treatment of NCS and that there was no significant difference in adverse events. A limitation to the study included the potential bias to recruit subjects during working hours when study coordinators are more likely to be available. In addition, this was not a true blinded study since only the EEG reader was blinded. Finally, there was no placebo arm; it is possible some of the NCS would have self-resolved, but given that treatment of NCS is standard of care, it is not possible to have a placebo arm. Authors also noted the study specifically excluded NCS lasting more than 30 minutes; thus, the question of IV LCM vs. IV fPHT was not assessed in that group.

■ COMMENTARY

Currently, both IV LCM and IV fPHT are used for treatment of NCS, but no one has performed a head-to-head comparison until now. The authors showed that LCM is just as good an option as fPHT. In fact, LCM had a higher seizure cessation rate, and perhaps a larger sample size would have shown statistical superiority. Of interest, adverse events were similar between the two groups despite prior studies suggesting LCM may have a superior adverse event profile. In light of these results, the decision about which ASD to use needs to be determined based on the clinical situation. The advantage of LCM is that it has a favorable drug interaction profile compared to fPHT. The benefit of fPHT is that patients can be discharged on oral phenytoin, which is more affordable and thus patients are more likely to be compliant.

In addition to the limitations raised by the author, this study likely overestimated the efficacy of LCM and fPHT because patients were monitored on cEEG for only 24 hours after the study ASD was administered. A previous study showed that 12% of NCS occurs after the first 24 hours.[3]

[Further prospective studies comparing the efficacy of anti-seizure drugs in nonconvulsive seizures are needed in this field. Theoretically, administering the most effective anti-seizure drugs would give the highest chance of nonconvulsive seizure cessation in the shortest time possible.]

Further prospective studies comparing the efficacy of ASD in NCS are needed in this field, as administering the most effective ASD theoretically would give the highest chance of NCS cessation in the shortest time possible, which hopefully will translate to better outcomes. ■

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ABSTRACT & COMMENTARY

Initial Management of Patients With Medication-overuse Headache

By Louise M. Klebanoff, MD

Assistant Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Klebanoff reports no financial relationships relevant to this field of study.

SYNOPSIS: As part of a randomized treatment trial for medication-overuse headache, a simple protocol that provided early advice on stopping excessive medications was effective in one-third of patients, even before any prophylactic medications were started.

SOURCE: Corbelli I, Sarchielli P, Eusebi P, et al; SAMOHA Study Group. Early management of patients with medication-overuse headache: Results from a multicenter clinical study. *Eur J Neurol* 2018;25:1027-1033.

Medication-overuse headache (MOH) is a chronic headache disorder resulting from frequent intake of pain medication, including analgesics, nonsteroidal anti-inflammatory drugs, triptans, opioids, and ergotamine. The estimated prevalence of MOH in the Western world is 1-2%, with a peak incidence of 5% in women 40-50 years of age. Patients with MOH have lower scores on quality-of-life assessment scales when compared to patients with chronic headaches without MOH, episodic headache, and healthy controls. Despite the frequency of the condition and the high burden of disability it causes, there is no established consensus on the standard of care. Withdrawal of the abused medication is advised, but recommendations regarding the methods of detoxification and administration of prophylactic medications are inconsistent. In addition, the prognosis remains poor, with approximately 30% of patients relapsing within one year of withdrawal of medication.

Patients with MOH can be divided into two subtypes, simple (Type I) and complex (Type II). Type II patients have significantly more comorbidities, including psychopathology (mood, anxiety, or substance addiction disorders), a long duration of MOH (> 1 year), a history of relapse following withdrawal, and daily use of multiple doses of symptomatic medication.

Corbelli et al reported on patients enrolled in the multicenter, placebo-controlled Sodium vAlproate in the Treatment of Medication Overuse HeadAche (SAMOHA) study. At the initial visit, patients were given simple advice regarding MOH; they were advised to stop the abused medication. After initial assessment, each patient completed a four-week observation period followed by a six-day inpatient detoxification phase during which the abused drugs were discontinued and then a 12-week, double-blind treatment period in which they were treated with valproate 800 mg/day or placebo. After the four-week observational period, patients were reassessed to see if they still met International Headache Society revised criteria for MOH, at which point they were randomized to the treatment arm of the study. The researchers screened 130 patients at the nine participating centers. Most patients (80%) were women; the mean age was 42 years; and the headaches were chronic for an average of 4.6 years, with an average of 24 days of headache per month. The most commonly abused medications were acetaminophen, acetylsalicylic acid, or other nonsteroidal anti-inflammatory drugs.

After the initial observation period, 88 (67.7%) patients still met inclusion criteria and continued the study; 34 patients no longer met inclusion criteria. The patients whose headaches improved so that they no longer met inclusion criteria were significantly younger and had a significantly shorter history of chronicity when compared to those who continued to meet inclusion criteria. Since a significant proportion of patients with MOH improved after receiving simple advice, it is important to counsel patients regarding MOH early in their clinical care. In addition, when conducting studies regarding the management of MOH, it is important to have a period of observation following simple advice to ensure that the patients studied have persistent MOH.

■ COMMENTARY

The study, part of the SAMOHA study, suggests that simple advice given at an early clinical assessment can be helpful in the management of MOH, especially in the younger patient population with fewer years of chronic headache. In addition, when conducting research on this patient population, an observation period is needed to exclude patients who rapidly improve following simple advice. The patients with persistent MOH who failed to improve following simple advice have more psychological comorbidities and a longer duration of chronic headache and remain more challenging to treat. The management of this patient population, including recommendations regarding type of detoxification and institution of prophylactic medications, needs further study. Perhaps the results of the completed SAMOHA study will provide additional treatment recommendations. ■

ABSTRACT & COMMENTARY

Unilateral Scapular Winging

By Michael Rubin, MD

Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Rubin reports no financial relationships relevant to this field of study.

SYNOPSIS: Scapular winging is an occasional finding on a neurological examination, rarely a chief complaint, and usually is caused by long thoracic nerve or spinal accessory nerve lesions.

SOURCE: Seror P, Lenglet T, Nguyen C, et al. Unilateral winged scapula: Clinical and electrodiagnostic experience with 128 cases, with special attention to long thoracic nerve. *Muscle Nerve* 2018;57:913-920.

Classically associated with long thoracic nerve (LTN) palsy, winged scapula may be static, due to a fixed deformity of the shoulder girdle, spine, or ribs, or dynamic, due to a neuromuscular disorder. Often asymptomatic, it can be missed on examination, but symptoms of pain, weakness, and cosmetic deformity may bring it to medical attention. What are the clinical and electrodiagnostic (EDX) patterns of scapular winging?

Among 128 patients referred for clinical and EDX examination over a 25-year period for unilateral winged scapula and pain at the Clinical Neurophysiology Department at Pitié-Salpêtrière Hospital in Paris, data on 109 patients were collected prospectively between 2001-2016, with 19 added retrospectively from 1992-2000.

[Neuralgic amyotrophy, characterized by pain, weakness, and sensory loss, is rare in children.]

Information gathered included age, gender, handedness, duration of symptoms, history of onset, and thorough neuromuscular examination. Scapular winging was defined as medial when it occurred near the spine, lateral when it occurred near the axilla, static when it was present at rest without changing during arm elevation, and dynamic when it was evident only during arm elevation. Nerve conduction studies were performed in the standard fashion, using both needle and surface methodology for the LTN, and encompassed bilateral LTN and spinal accessory nerve evaluation, median and ulnar nerve study, and other nerves as clinically indicated. Additional testing, as warranted, included magnetic resonance imaging (MRI) of the cervical and thoracic spine, MRI of the scapula, genetic testing for facioscapulohumeral dystrophy, and blood work for autoimmune diseases, myopathy, and Lyme disease. Patients with sensorimotor polyneuropathy were excluded from this study. Statistical analysis comprised the Student t-test or Wilcoxon-Mann-Whitney test, with $P < 0.05$ considered significant.

Winged scapula was caused by LTN palsy (n = 70) most often, usually due to neuralgic amyotrophy (n = 61), with four resulting from stretch injury, two from brachial plexus radiotherapy, and one each due to surgery for breast cancer, lung cancer, or thoracic outlet syndrome. Serratus anterior muscle digitation atrophy was apparent in 20 of 38 male LTN palsy patients, and 77% of all LTN palsy patients demonstrated a rope-like lower trapezius muscle. Spinal accessory nerve palsy was the cause in 39 patients, either due to neck surgery (n = 13) or of medical origin (n = 26), the latter most often due to neuralgic amyotrophy (n = 20). Severe lower trapezius atrophy was seen in all instances due to spinal accessory nerve palsy, and severe upper trapezius atrophy was seen in most. Other causes of winged scapula included combined LTN and spinal accessory nerve palsy (n = 5), facioscapulohumeral dystrophy (n = 5), and orthopedic issues (n = 11), consisting of scoliosis, acromion exostosis, clavicular trauma, and rotator cuff impingement. In six cases, winging was voluntary, with the patient able to produce the winging on request on the healthy side as well. In two instances no cause was found. Winged scapula is most often due to LTN palsy from neuralgic amyotrophy. Careful examination can distinguish LTN from spinal accessory nerve palsy. In young patients, in addition to neuralgic amyotrophy, facioscapulohumeral dystrophy and traumatic causes should be considered.

■ COMMENTARY

Neuralgic amyotrophy, characterized by pain, weakness, and sensory loss, is rare in children. Between 2003 and 2017, 22 children 18 years of age or younger (14 boys and eight girls) were diagnosed with neuralgic amyotrophy at Boston Children's Hospital. Pain was the presenting symptom in all, with periscapular weakness in 16 and scapular winging in 13. Persistent pain and weakness remained in more than 50% when seen in follow-up. Clinically, neuralgic amyotrophy in children is very similar to that seen in adults.[1] ■

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ABSTRACT & COMMENTARY

Hypercapnic Acidosis and Clinical Outcomes in Patients With Acute Brain Injury

By Alexander E. Merkler, MD

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Dr. Merkler reports no financial relationships relevant to this field of study.

SYNOPSIS: In this multicenter retrospective study, hypercapnic acidosis was associated with worse clinical outcomes in mechanically ventilated patients with acute brain injury.

SOURCE: Tiruvoipati R, Pilcher D, Botha J, et al. Association of hypercapnia and hypercapnic acidosis with clinical outcomes in mechanically ventilated patients with cerebral injury. *JAMA Neurol* 2018;75:818-826.

Acute brain injury is becoming increasingly common worldwide. Methods to reduce secondary brain injury following acute cerebral injury remain elusive. Prior studies regarding the association between hypercapnia and clinical outcomes in patients with acute brain injury have revealed conflicting results.[1,2] Establishing the role of hypercapnia in patients with acute brain injury may provide a useful laboratory measure for prognostication; in addition, it may provide a novel target to reduce secondary brain injury and improve clinical outcomes.

In this multicenter retrospective study, investigators evaluated the association between hypercapnia and mortality among mechanically ventilated patients with acute brain injury. The study included all patients with acute brain injury, including stroke, traumatic brain injury, and cardiac arrest, who were mechanically ventilated. Patients were classified into three categories based on arterial pH and arterial carbon dioxide (pCO_2): 1) normocapnia and normal pH; 2) compensated hypercapnia; and 3) hypercapnic acidosis. Patients were classified into these groups based on their worst pH/pCO_2 in the first 24 hours of ICU admission. Patients with other acid-base abnormalities were excluded (including metabolic acidosis). The primary outcome was in-hospital mortality. Multivariate logistic regression and Cox proportional hazard regression models were used to adjust for demographics, illness severity, Glasgow Coma Scale (GCS) score, and type of acute brain injury.

A total of 30,742 patients were included in the study: 11,785 had cardiac arrest, 9,507 had traumatic brain injury, and 9,477 had stroke. Out of the 30,742 patients, 13,052 had normocapnia and normal pH, 1,338 had compensated hypercapnia, and 16,352 had hypercapnic acidosis. Compared to patients with normocapnia and normal pH, patients with hypercapnic acidosis were older and had more medical comorbidities, had higher severity illness scores (based on APACHE III scores), and had lower GCS scores. In multivariable analyses, patients with hypercapnic acidosis had an increased risk of in-hospital death compared to patients with normocapnia and normal pH levels. Although the association was present in all three diagnosis categories (stroke, traumatic brain injury, cardiac arrest), the association was more robust in patients with cardiac arrest (odds ratio [OR], 1.51; 95% confidence interval [CI], 1.34-1.71) than stroke (OR, 1.43; 95% CI, 1.27-1.6) and traumatic brain injury (OR, 1.22; 95% CI, 1.06-1.42). Among patients with hypercapnic acidosis, the adjusted odds of in-hospital mortality appeared to rise with increasing levels of pCO_2, but this trend was not present among patients with compensated hypercapnia.

■ COMMENTARY

This multicenter retrospective study demonstrates that hypercapnic acidosis is associated with an increased risk of in-hospital mortality among mechanically ventilated patients with acute brain injury. Although the authors performed multiple sensitivity analyses to try to account for illness severity in their models, it certainly is plausible that other risk factors for mortality existed, for which the models remained unaccounted. As the primary outcome was in-hospital mortality, the effect of acute hypercapnia on long-term mortality and functional status is uncertain.

Overall, this study indicates that hypercapnic acidosis is associated with in-hospital mortality. However, it remains uncertain whether avoidance of hypercapnic acidosis will reduce secondary brain injury and improve long-term outcomes or whether the presence of hypercapnic acidosis is merely a marker of overall brain injury. ■

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ABSTRACT & COMMENTARY

Recanalization Treatment in Pediatric Arterial Ischemic Stroke

By Renatta Knox, MD, PhD, and Barry Kosofsky, MD, PhD

Dr. Knox is Pediatric Neurology Resident, Department of Pediatrics, Division of Child Neurology, Weill Cornell Medicine/New York Presbyterian Hospital. Dr. Kosofsky is Professor of Pediatrics and Neurology, Weill Cornell Medical College.

Dr. Knox reports no financial relationships relevant to this field of study. Dr. Kosofsky reports he is a major stockholder in b2d2, a biotechnology company.

SYNOPSIS: In a population-based study from Switzerland, the authors found that recanalization treatment (intravenous thrombolysis or endovascular treatment) overall was safe without significant side effects or increased mortality compared to standard care.

SOURCE: Bigi S, Dulcey A, Gralla J, et al. Feasibility, safety, and outcome of recanalization treatment in childhood stroke. *Ann Neurol* 2018;83:1125-1132.

The incidence of pediatric arterial ischemic stroke (AIS) is about two per 100,000. Up to half of pediatric stroke patients subsequently have neurologic deficits or epilepsy. The American Heart Association guidelines on infant and pediatric stroke give recommendations based on etiology. Treatment options include intravenous thrombolysis (IVT), intra-arterial thrombolysis (IAT), and mechanical thrombectomy. However, use of these interventions varies by center, and, often, the appropriate diagnosis is made late and outside the window for intervention. Several groups have published small series about pediatric stroke patients detailing their experience with IVT, IAT, and mechanical thrombectomy. Using the International Pediatric Stroke Study (IPSS), Amlie-Lefond et al found that 15 patients receiving alteplase over a four-year period tolerated the treatments.[1] However, most patients (12/13) had neurologic deficits at the time of discharge. Tabone et al created a stroke protocol for two regional centers in France, and published their experience with 13 children receiving recanalization therapy. They also found these procedures were tolerated without significant side effects, and 11/12 survivors had modified Rankin Scale of 0-2.[2] Tatum et al published results on four pediatric stroke cases who underwent mechanical embolectomy using FDA-approved devices over a six-year period.[3] Three out of four of these cases had improved pediatric modified Rankin scale scores, which were ≤ 2. These studies demonstrate that recanalization procedures are tolerated, but not frequently used, in diverse pediatric stroke populations.

Bigi et al published the first population-based cohort to assess the safety of recanalization in pediatric AIS. The cohort was drawn from a nationwide registry in Switzerland of all pediatric stroke cases, and they reported on data from 2000 to 2015. There were 150 AIS cases with a pediatric NIH Stroke Scale (NIHSS) ≥ 4. Sixteen of these cases underwent recanalization, which was defined as IVT, IAT, or mechanical recanalization. Mean age was 7 years. Etiology was unknown in 40% of cases, 18% were cardioembolic, and 17% were focal cerebral arteriopathy. Four patients died secondary to stroke. Only two complications were noted: asymptomatic intracerebral hemorrhage and mucosal bleeding. Five patients developed malignant middle cerebral artery infarctions. Complete recanalization was achieved in 25% of cases, and partial recanalization in 38%, with 25% having no recanalization. Of note, they found that patients receiving recanalization therapy had higher PedNIHSS scores, were older, and had a shorter time interval from symptom onset to diagnosis. A multiple regression analysis showed that higher baseline PedNIHSS was associated with higher morbidity six months after treatment. Overall, these investigators concluded that recanalization is well tolerated, but stressed the importance of needing larger studies.

■ COMMENTARY

The research by Bigi et al adds to the rich emerging literature regarding improvements in the diagnosis and treatment of pediatric stroke, which in part has resulted from, as well as contributed to, the establishment of regional centers of excellence. Although randomized, controlled trials and larger studies are needed, this study adds further evidence that recanalization should be considered and performed more frequently. In their cohort, at most, four children per year underwent recanalization treatment. They also noted that more strokes were recognized between 2011 and 2015 than previous time periods, highlighting the importance of education and awareness of strokes in the pediatric population. Without recognition of stroke and appropriate imaging early in the course, children are not candidates for these potentially life-saving interventions. More research into this important area is necessary to continue to make therapeutic advances and determine potential differences in the best practices for pediatric and adult patients following stroke, as is greater participation in multisite clinical trials

and registries, such as those that have been conducted by the International Pediatric Stroke Society. ■

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2. Tabone L, Mediamolle N, Bellesme C, et al. Regional pediatric acute stroke protocol: Initial experience during 3 years and 13 recanalization treatments in children. *Stroke* 2017;48: 2278-2281.
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Neurology [ALERT™]

Stroke Alert

By Matthew E. Fink, MD

Atrial Flutter, Atrial Fibrillation, and Ischemic Stroke

SOURCE: Lin YS, Chen YL, Chen TS, et al. Comparison of clinical outcomes among patients with atrial fibrillation or atrial flutter stratified by CHA_2DS_2-VASc score. *JAMA Network Open* 2018;1:e180941. doi:10.1001/jamanetworkopen.2018.0941.

Atrial flutter (AFL) and atrial fibrillation (AF) often are grouped together in terms of risk stratification for ischemic stroke. Risk and decisions regarding institution of antithrombotic therapy have relied heavily on the use of a scoring system known as CHADS. The CHA_2DS_2-VASc scoring system was developed in 2010 and calculates according to a point system (possible score range, 0-9) in which two points are assigned for history of stroke/transient ischemic attack and age > 75 years; one point is assigned for age 65-74 years, a history of congestive heart failure, hypertension, diabetes, vascular disease, and female sex. A high score indicates an increased risk of ischemic stroke and often results in treatment with antithrombotic therapy. However, it is uncertain if risks in patients with AFL are similar to the risks in patients with AF. Lin et al conducted this study to analyze the incidence of ischemic stroke, hospitalization for heart failure, and all-cause mortality as it relates to the calculation of the CHADS score comparing patients with AF and AFL.

Data were analyzed from a nationwide database of the Taiwan National Health Insurance Research Database with information collected from 1997 through 2012, encompassing 23 million Taiwan residents. Patients with AF and AFL were paired with age- and sex-matched controls. There were 188,811 patients in the AF cohort and 6,121 patients in the AFL cohort, with 24,484 patients in the matched-control cohort. The patients with AF tended to be older, were more predominantly female, and had higher CHA_2DS_2-VASc scores than the patients with AFL and control participants. After stratification by CHA_2DS_2-VASc score, the incidence of ischemic stroke, heart failure hospitalization, and all-cause mortality were significantly higher in the AF cohort than in the matched-control cohort. In comparing the AFL cohort to matched controls, the incidences of heart failure and all-cause mortality were significantly higher, but ischemic stroke was higher only in patients who had a CHA_2DS_2-VASc score of 5 to 9. In the AF cohort, the incidence of ischemic stroke was significantly higher at a CHA_2DS_2-VASc score of 1 or higher. The authors of this well-designed study found significantly different clinical outcomes between patients with AFL and AF, and the significance of the CHA_2DS_2-VASc score in predicting stroke may be different when applied to AFL patients vs. AF patients. ■

Dual Antiplatelet Therapy for Acute Ischemic Stroke and TIA

SOURCE: Johnston SC, Easton JD, Farrant M, et al; Clinical Research Collaboration, Neurological Emergencies Treatment Trials Network and the POINT Investigators. Clopidogrel and aspirin in acute ischemic stroke and high-risk TIA. *N Engl J Med* 2018;379:215-225.

In a recent study of a Chinese population, early treatment with dual antiplatelet medications demonstrated a reduction in the risk of recurrent stroke. The POINT trial included an international population to test the hypothesis that early treatment of minor ischemic stroke or high-risk transient ischemic attack (TIA) with a combination of clopidogrel and aspirin would be better than aspirin alone in reducing the incidence of recurrent ischemic stroke at 90 days. POINT was a randomized trial that enrolled 4,881 patients at 269 sites. The trial was halted early after 84% of the anticipated number of patients were enrolled, because an interim analysis showed that the combination of clopidogrel and aspirin was associated with a lower risk of major ischemic events but a higher risk of major hemorrhage than aspirin alone at 90 days.

Major ischemic events occurred in 5% of patients receiving clopidogrel plus aspirin and in 6.5% of patients receiving aspirin plus placebo (hazard ratio, 0.75; $P = 0.02$). Most of the recurrent ischemic events occurred during the first week following initial event. Major hemorrhages occurred in 0.9% of patients receiving dual antiplatelet therapy and 0.4% of patients receiving aspirin plus placebo. The most feared complication, symptomatic intracerebral hemorrhage, was rare in both groups, and there were only two cases in each group (0.1%). Most serious hemorrhages that occurred were related to gastrointestinal bleeding. Although dual antiplatelet therapy conferred modest benefit regarding recurrent ischemic events, the increased risk of serious hemorrhages must be taken into account when making

therapeutic decisions to use these medications in combination. ■

Treatment of Chronic Subdural Hematoma With Atorvastatin

SOURCE: Jiang R, Zhao S, Wang R, et al. Safety and efficacy of atorvastatin for chronic subdural hematoma in Chinese patients: A randomized clinical trial. *JAMA Neurol* 2018; Jul 30. doi: 10.1001/jamaneurology.2018.2030.

Chronic subdural hematoma is a common trauma-associated condition that often occurs in elderly people. Surgical evacuation is the treatment of choice, but often this is associated with recurring hemorrhages and poor outcomes. Nonsurgical treatments have not been proven to be effective. Researchers in China evaluated the effects of atorvastatin treatment on chronic subdural hematoma. In animal models, atorvastatin has been shown to have significant anti-inflammatory effects as well as the ability to mobilize endothelial progenitor cells for vascular repair. This was a double-blind, randomized, controlled trial performed in multiple centers in China. The authors enrolled 200 patients and randomly assigned them to receive either 20 mg of atorvastatin or placebo daily for eight weeks; patients were followed for 24 weeks. The primary outcome was changing hematoma volume by CT scan after eight weeks of treatment. Secondary outcomes were neurological function assessed at four weeks, eight weeks,12 weeks, and 24 weeks.

After eight weeks of treatment, hematoma volume in the treated group was reduced by more than 12.55 mL (mean) compared to those taking placebo ($P = 0.003$). Forty-six percent of patients who were taking atorvastatin had a significant improvement in neurological function compared to only 28% who were taking placebo. Eleven percent of patients taking atorvastatin and 23% of patients taking placebo eventually underwent surgery during the trial because of enlarging hematoma or deteriorating clinical condition. This study suggests that atorvastatin may be a safe and effective nonsurgical alternative for patients with chronic subdural hematoma. This study should be repeated in an international population to determine if the results can be reproduced and if the therapy will be effective in a broad and multiethnic population. ■

CME QUESTIONS

1. **Which of the following statements regarding nonconvulsive seizures is *false*?**
   a. Critically ill ICU patients have a significant risk of developing seizures.
   b. Nonconvulsive seizures can only be detected with continuous EEG monitoring.
   c. Nonconvulsive seizures are incidental and have no clinical significance.
   d. Nonconvulsive seizures should be treated with an effective anti-seizure medication.
2. **Patients with simple medication-overuse headaches should be:**
   a. given medications for headache prophylaxis.
   b. admitted for inpatient detoxification.
   c. continued on analgesics as needed.
   d. educated about medication-overuse headache and advised to stop the abused medication.
3. **Scapular winging may be caused by which of the following?**
   a. Long thoracic nerve palsy
   b. Spinal accessory nerve palsy
   c. Facioscapulohumeral dystrophy
   d. All of the above
4. **A 65-year-old man is admitted to the ICU with severe traumatic brain injury. Which of the following arterial blood gas patterns may be associated with increased in-hospital mortality?**
   a. pH = 7.42, pCO_2 = 48, PaO_2 = 94
   b. pH = 7.40, pCO_2 = 42, PaO_2 = 95
   c. pH = 7.34, pCO_2 = 48, PaO_2 = 96
   d. pH = 7.48, pCO_2 = 36, PaO_2 = 94
5. **Pediatric recanalization treatments are:**
   a. most effective in children older than 15 years of age.
   b. associated with worse outcomes than adults.
   c. widely used worldwide.
   d. rarely used.
6. **Dual antiplatelet therapy is effective and safe to reduce the risk of recurrent stroke in patients with minor stroke or TIA.**
   a. True
   b. False

[IN FUTURE ISSUES]

New Treatments for Multiple Sclerosis