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Neurology [ALERT®]

Evidence-based summaries of the latest clinical neurology research

ABSTRACT & COMMENTARY

Migraine Prophylaxis in Children

By Devorah Segal, MD, PhD

Assistant Professor of Clinical Pediatrics, Division of Child Neurology, Weill Cornell Medical College

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

SYNOPSIS: In a randomized, double-blind, placebo-controlled trial of migraine prophylaxis in children ages 8-17 years, treatment with neither amitriptyline nor topiramate showed significant differences in headache frequency or headache-related disability compared to placebo.

SOURCE: Powers SW, Coffey CS, Chamberlin LA, et al. Trial of amitriptyline, topiramate, and placebo for pediatric migraine. *N Engl J Med* 2016; Oct 27 [Epub ahead of print] DOI: 10.1056/NEJMoa1610384.

Migraines are a common health problem in children, with a prevalence of about 3% in pre-school-aged children and rising to up to 23% in adolescents. Six million children in the United States suffer from migraines, with about 1% of children meeting criteria for chronic migraines. Despite these high numbers, there are currently no medications approved by the Food and Drug Administration (FDA) for prevention of migraines in children younger than 12 years of age, and there have been few high-quality studies available to guide treatment decisions. Therefore, pediatric neurologists must rely on data from trials in adults and on general consensus when treating these children.

The Childhood and Adolescent Migraine Prevention (CHAMP) trial was designed to test amitriptyline and topiramate against each other and against placebo to assess the effect of each in the preventive treatment of migraine in children. Amitriptyline and topiramate were selected based on a survey of pediatric headache specialists showing that these were the two most commonly prescribed medications used to prevent migraines in children. This was a Phase III, multicenter trial with patients enrolled at 31 sites across the United States. Subjects were assigned to one of three arms in a 2:2:1 ratio of amitriptyline, topiramate, and placebo, respectively. The study was funded by the NIH with no industry contribution. The primary endpoint was at least a 50% reduction in headache frequency in a

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28-day period. Secondary endpoints were decreased disability as measured by a Pediatric Migraine Disability Assessment (PedMIDAS) score, absolute number of headache days in a 28-day period, number of trial completers, and adverse events. Interim analyses were scheduled to assess for futility.

Patients eligible for the study were 8-17 years old and carried a diagnosis of migraine with or without aura. To qualify, patients completed a baseline 28-day headache diary that showed at least four migraines during that period. They also completed a baseline PedMIDAS survey and had a score of 11-139, indicating mild to severe disability due to migraines. There were no significant differences among groups with respect to age, sex, race, baseline PedMIDAS score, or number of headache days during the baseline 28-day period. As expected, more girls than boys were recruited across all treatment arms.

Initially, medications were escalated over eight weeks to target doses of 1 mg/kg/day of amitriptyline and 2 mg/kg/day of topiramate, followed by a 16-week maintenance phase and then a two-week weaning phase. Subjects then completed a 28-day follow-up period in which they again maintained a headache diary and completed a PedMIDAS survey. During the treatment phase, adherence was measured by testing blood levels of the active medications. At the time of the interim assessment, 361 patients had been randomized, with 144 assigned to amitriptyline, 145 to topiramate, and 72 to placebo, and the majority of patients had endpoint data available. Statistical analysis at that time showed no difference among the three groups regarding the primary endpoint, with nearly two-thirds of patients in each group experiencing a 50% decrease in headache days. Secondary endpoints of headache disability (PedMIDAS score), number of headache days, and completion of trial also were not significantly different among the three groups. Adverse events were generally manageable in all three groups, with fatigue more common in the amitriptyline group and paresthesias in the topiramate group. A small number of serious adverse events (syncope and altered mood) were reported in the amitriptyline and topiramate groups. Notably, each group had patients who became headache free during the study, and most patients in each arm achieved headache disability in the mild range. All patients are being followed for 36 months, and the authors reported at the recent Child Neurology Society Annual Meeting that most patients continue to exhibit a sustained response.

■ COMMENTARY

This study is remarkable because of the rarity of large, double-blind, placebo-controlled studies of neurological disorders in children, particularly of headaches. Previous studies have suggested a large placebo effect in migraine treatment, and this study was designed taking that into account. The results of this trial, with no differences among the three arms, again highlights an enormous placebo effect in treating migraines in children. However, it also indirectly highlights the importance of non-pharmaceutical approaches to treating headaches. Notably, all study participants received guidance on healthy lifestyle choices (such as sleep hygiene, appropriate diet, and hydration) that have been associated with better headache control. Another study from the same group[1] demonstrated that treating frequent migraines with amitriptyline together with cognitive behavioral therapy (CBT) had better results than amitriptyline plus "placebo" headache education therapy. Putting those earlier findings in the context of the current study suggests that CBT and related behavioral treatment strategies are more effective than medication in preventing migraines and their associated disability.

Rather than being disheartened by the apparent lack of efficacy of our most commonly used preventive medications, this study provides an opportunity for pediatric neurologists to emphasize to children and their parents that taking a daily pill is not sufficient or perhaps even necessary to achieve long-lasting headache control. Rather, a multi-modal and multidisciplinary approach is needed, one that helps children take control of their migraines by modifying lifestyle risk factors and learning to modulate their own responses to pain. ■

REFERENCE

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ABSTRACT & COMMENTARY

Cognition in Older Migraine Sufferers: The Data Are Not Clear!

By Dara Jamieson, MD

Associate Professor of Clinical Neurology, Weill Cornell Medical College

Dr. Jamieson reports she is a consultant for Bayer and Boehringer-Ingelheim.

SYNOPSIS: Older migraineurs, particularly migraineurs with aura, tend to score higher in tests of executive functioning and fine motor skills than do non-migraineurs. However, the lack of a detailed analysis of an unrepresentative headache population may confound the conclusions.

SOURCE: Wen K, Nguyen NT, Hofman A, et al. Migraine is associated with better cognition in the middle-aged and elderly: The Rotterdam Study. *Eur J Neurol* 2016;23:1510-1516.

Data from the Rotterdam Study were analyzed to determine the general and domain-specific cognitive function of middle-aged and elderly migraineurs compared with non-migraineurs. The Rotterdam Study is a prospective, population-based cohort study of middle-aged and elderly inhabitants of the district Ommoord in the Netherlands. Participants were given a questionnaire at a home interview, and 6,708 participants were included who had information for both migraine history and cognitive state, excluding those with obvious dementia. Cognition was assessed by the Mini Mental State Examination (MMSE) and a dedicated cognitive test battery, performed between migraine attacks. A general cognitive factor (g-factor) was calculated from the cognitive data, with a higher g-factor indicating better performance. Based on modifications of the International Classification of Headache Disorders (second edition) criteria, 6,708 participants were classified as non-migraineurs (n = 5,399; average age 66 years), migraineurs (n = 1,021; average age 64 years), or probable migraineurs (n = 288; average age 64 years). Multivariable linear regression was used to evaluate the association between migraine and cognition, adjusting for age, sex, and cardiovascular risk factors. The analysis was stratified by sex and by migraine subtype. Migraineurs were younger with lower diastolic blood pressure, and were more likely to be female and non-smokers with less alcohol intake than were non-migraineurs. Depression scores were higher in migraine participants. Migraineurs had higher mean MMSE scores and higher global cognition than non-migraineurs, with a most marked difference for migraineurs with aura. Migraineurs performed better on tests of executive function and fine motor skills among specific cognitive domains. The difference in MMSE between migraineurs and non-migraineurs was greater in women than in men, whereas the difference in global cognition was similar in men and women. The investigators stated that migraineurs with non-active migraine (> 1 year since last migraine attack) had higher cognitive scores (MMSE, g-factor) compared with non-migraineurs, and that migraineurs with active migraine (< 1 year since last migraine attack) did not differ significantly in general cognition outcomes compared with non-migraineurs. The authors concluded that migraineurs, particularly migraineurs with aura, tend to score higher in cognition tests, especially using executive functioning and fine motor skills, than non-migraineurs.

■ COMMENTARY

The variable effect of migraine of different subtypes and frequency on both immediate and long-term cognitive outcome has been debated, without consensus. This study, which purports to show generally better cognition in an older migraine cohort, adds to the already published conflicting data that concluded there is either no difference or a decrement in cognitive processing associated with migraines, both during and between attacks. However, the lack of detail in this analysis of an unrepresentative headache population may affect the strength of the study results. Extraction of limited data from a population of older individuals with migraine headaches continuing past the usual age of headache resolution hampers the ability to reach robust conclusions.

The middle-aged to elderly population of the Rotterdam Study is not representative of the population with migraine, a disorder prevalent in teens and younger adults. Migraine is relatively rare in postmenopausal women and older men, the population examined in this study. Clinicians experienced in interviewing patients about their headaches know that it can be difficult to extract an accurate history of remote headache in older individuals who have outgrown their migraines. Very likely a percentage of the "non-migraineurs" actually did have migraines in their youth, with the expected resolution of headaches with maturity. These non-migraineurs could be considered migraineurs with non-active (remote) migraine. Thus, the statement that migraineurs with non-active (remote) migraine had higher cognitive testing results, but migraineurs with active (recent) migraine did

not differ in cognitive outcomes, as compared with non-migraineurs, appears to confuse the authors' conclusion that migraineurs had better general cognition than non-migraineurs. This subgroup analysis of the relationship between migraine frequency and cognition, with recent migraineurs having no difference in cognition compared to non-migraineurs, would suggest that recent migraine is associated with worse cognition than remote migraine. Analysis of a population of migraine patients requires attention to details about the headaches, beyond the presence or absence of aura. The frequency and severity of headaches and the degree of headache-related disability are important variables that affect the analysis of migraineurs. Medications used in the prevention of migraines can have an effect on cognition and need to be accounted for in data analysis.

The authors cite data on the association between migraine and stroke and brain lesions, without differentiating between the vascular risk associated with different migraine types and frequencies, to point out the cerebrovascular risk of migraine. Since migraine with aura is most associated with increased risk of vascular disease, then why would these older migraine individuals with aura have the greatest preservation of cognitive functioning compared to non-migraineurs? The authors speculated on "compensatory neurovascular benefits later protecting cognition" as a putative explanation. A more cogent argument offered by the authors is that encouragement of a healthy lifestyle as a way of managing headaches may have eventual cognitive benefit. However, this analysis of an unrepresentative, inadequately described population of migraine individuals has some seemingly paradoxical results and only serves to illustrate the complexity of studying the relationship, or lack thereof, between migraine and intellectual functioning. ■

ABSTRACT & COMMENTARY

Prognosticating Ulnar Neuropathy at the Elbow

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: In a large retrospective review of treatment outcome for ulnar neuropathy at the elbow, no difference was found in outcomes between any of the various conservative or surgical therapies, but prognosis was determined by the severity of the lesion at time of diagnosis.

SOURCE: Beekman R, Zijlstra W, Visser LH. A novel points system to predict the prognosis of ulnar neuropathy at the elbow. *Muscle Nerve* doi: 10.1002/mus.25406.

With an incidence of 24.7/100,000, ulnar neuropathy at the elbow (UNE) is the second most common compression neuropathy, following carpal tunnel syndrome. Choosing between conservative measures and surgery is the major management decision in UNE, and is confounded by its many diverse causes, and an uncertainty as to which, if any, improve spontaneously. Accurate prognostication of UNE would be helpful to address this question.

Baseline information, including clinical, electrodiagnostic, and ultrasound data, was collected on two cohorts of UNE patients, diagnosed between 1998-2002 and 2006-2008, at Atrium Medical Centre, Heerlen, and St. Elisabeth Hospital, Tilburg, The Netherlands, and compared to outcome on follow-up, at least four or six months following surgery or conservative management, respectively.

Diagnosis of UNE was based on the presence of at least one symptom or sign of UNE, comprising tingling or numbness in the ulnar territory, or weakness or atrophy of ulnar innervated muscles, including first dorsal interosseous (FDI) and abductor digiti minimi (ADM), in association with supportive electrodiagnostic or ultrasonographic evidence. Electrodiagnostic evidence comprised motor conduction block across the elbow of at least 16%; motor nerve conduction velocity slowing across the elbow to < 46 m/s or > 15 m/s slower than in forearm segment; low motor- or sensory ulnar-evoked response amplitudes; and needle EMG showing abnormal spontaneous activity, enlarged or long duration motor unit potentials, or increased (> 15%) polyphasicity. Ultrasound evidence of UNE required enlargement of the ulnar nerve diameter at the level of the medial epicondyle, or 2 cm above or below, to > 2.4 mm, > 2.5 mm, or > 2.6 mm, respectively. Exclusionary criteria encompassed prior UNE surgery or severe traumatic origin of UNE, evidence of polyneuropathy, or genetically proven liability to pressure palsies. Conservative treatment included minimizing elbow flexion, avoidance of repetitive elbow flexion, and avoidance of crossing arms when seated, while surgery encompassed simple decompression or transposition, as determined by the

surgeon. Statistical analysis comprised Student t-test, Mann-Whitney U test, chi-square test, and multiple logistic regression analysis, with $P < 0.05$ considered to be significant.

Among 220 patients with UNE at baseline, 84 and 136 in each cohort, 178 were available for re-evaluation (69 and 109, respectively), with 42 patients lost to follow-up, including three deaths, 18 refusing to participate, and 21 not responding. Among 178 responders, 94 men and 84 women, mean age was 52.8 years, and 161 had unilateral UNE. Complete recovery was reported in 23% (n = 40) and improvement in 37% (n = 66), with 40% (n = 72) noting either no change (28%, n = 49) or worsening (12%, n = 23). Overall, patients with left-sided UNE had a better outcome ($P < 0.001$), but there was no prognostic correlation found with respect to age, gender, symptom duration, presence of weakness, or type of treatment. Electrodiagnostically, conduction block to the ADM, but not the FDI, was associated with a good outcome, whereas low motor or sensory amplitudes presaged a poor outcome. Smaller ultrasound nerve diameter (mean 3 mm) predicted a good outcome, compared to a poor outcome where mean diameter was a mean of 3.3 mm. Right-sided UNE, more severe ADM weakness, and more pronounced ulnar thickening are poor prognostic indicators in UNE, whereas conduction block across the elbow of > 15% is a good prognostic sign, allowing outcome of UNE to be predicted by scoring these four parameters.

■ COMMENTARY

Can careful clinical examination of UNE distinguish demyelinating injury (Class I, neuropraxia) from axonal (Class II, axonotmesis) pathophysiology? In a prospective study of consecutively recruited subjects, four blinded examiners performed neurological examinations, electrodiagnostic studies, and ultrasound evaluations on patients with suspected UNE, and compared examination findings with pathophysiologic results. Although pronounced weakness and atrophy predicted axonal UNE, whereas normal muscle bulk and moderate weakness predicted neuropractic injury, in the majority of examinations the prediction was not reliable. Electrodiagnostic studies remain the single most reliable test to determine pathophysiology of UNE, more so than examination or ultrasound evaluation. ■

ABSTRACT & COMMENTARY

Disability in Patients with Multiple Sclerosis: A Long-Term Study

By Jai S. Perumal, MD

Assistant Professor of Neurology, Weill Cornell Medical College

Dr. Perumal reports she receives grant/research support from Genzyme Corp., and is on the speakers bureau for Biogen Idec, Genzyme Corp., Acorda Therapeutics, and Teva Pharmaceuticals.

SYNOPSIS: In a long-term study, the rate of disability progression in treated relapsing and progressive, multiple sclerosis patients was lower than that reported in earlier natural history studies.

SOURCE: Cree BA, Gourraud PA, Oksenberg JR, et al, for the University of California, San Francisco, MS-EPIC Team. Long-term evolution of multiple sclerosis disability in the treatment era. *Ann Neurol* 2016;80:499-510.

Five hundred and seventeen patients, including 366 relapsing-remitting (RMS), 48 secondary progressive (SPMS), 21 primary progressive (PPMS), and 82 clinically isolated syndrome (CIS) patients participated in a prospective, longitudinal study of disability in multiple sclerosis (MS) patients. The study was conducted at the MS center at the University of California, San Francisco. Patients were enrolled between July 2004 and September 2005. Ninety-one percent of patients were followed for the entire duration of the study. Median follow-up for the group was 9.8 years. The mean disease duration at enrollment was seven years, mean age was 42.7 ± 9.9 years, and mean Expanded Disability Status Scale (EDSS) at enrollment was 1.5.

For the analysis, CIS and RMS patients were grouped together as RMS, and SPMS and PPMS patients were grouped together as PMS, respectively. In terms of treatments, the patients were divided into two tiers. The first tier included patients on glatiramer acetate, one of the interferons, monthly pulsed steroids, azathioprine, and mycophenolate mofetil. The second tier were patients on natalizumab, rituximab, mitoxantrone, and cyclophosphamide. Clinical evaluations and MRIs were obtained at least annually for the duration of the study. Disability progression was assessed based on EDSS, timed 25-foot walk, nine-hole peg test, and paced serial auditory addition test. In the first two years of follow-up, patients were deemed to have met NEDA (No Evidence of Disease Activity) if they had no relapses, no clinically significant increase in EDSS, no new or enlarging T2 lesions, or gadolinium-enhancing lesions on MRI. Vitamin

D levels also were measured annually in the first two years of follow-up.

Over the 10 years of follow-up, 225/471 (55.3%) patients experienced a clinically significant increase in EDSS. EDSS progression was defined as a ≥ 1.5 increase for patients with a baseline score of 0, a 1-point increase for scores between 1-5, and a 0.5-point increase for those with scores > 5 at baseline. In the RMS group, 4.7% of patients reached an EDSS of ≥ 6 at 10 years after disease onset and 16.2% after 20 years since disease onset.

Forty-six out of 407 (10.1%) RMS patients at baseline transitioned to SPMS in the 10 years. Female sex was modestly associated with a lower risk of SPMS, and a later age at onset was associated with an increased risk of SPMS. The risk of transition to SPMS was 6.4% at 10 years and 24.2% at 20 years from disease onset.

Seventy-three (17.9%) RMS patients met the criteria for NEDA in the first two years of the study. NEDA during this period did not show a statistically significant association with disability progression at year 10. When radiologic disease over the initial two-year period was examined, the development of new T2 lesions during this period was not associated with disability progression at year 10. Similarly, serum levels of vitamin D in the first two years did not show an association with disability at year 10.

■ COMMENTARY

The rates of transition to SPMS and disability worsening in this study are lower than the rates reported in prior natural history studies.[1,2] The authors noted that after 16.8 years from disease onset, 10.7% of their patients reached an EDSS of 6, while in some natural history studies, rates as high as 50% were reported. This might point to a long-term, therapeutic benefit from disease-modifying treatment. However, one needs to keep in mind that there may be inaccuracies in the data from older natural history studies and changing inherent characteristics of the disease itself as possible explanations. The authors reported no correlation between the clinical and MRI activity during the initial two years of enrollment to disability progression at 10 years. This highlights the limitations of predicting long-term prognosis by examining a brief two-year window of the disease. Since most therapeutic clinical trials are of two-year duration, this finding exposes the drawbacks of judging long-term efficacy of therapies based on results from such short-term studies. However, the mean disease duration at baseline of patients in this study was seven years; thus, this was not a study of patients who were very early in their disease course. Hence, the lack of prognostic utility by examining a two-year window in this study does not necessarily refute studies that have tried to delineate clinical and radiologic prognostic factors early in the disease course. Lastly, 59% of the patients in this study showed clinically significant disability progression. This shows the shortcomings of our current treatment strategies in managing patients with MS. ■

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Stroke Alert

By Matthew E. Fink, MD

Time to Treatment with Endovascular Thrombectomy Remains a Critical Variable

SOURCE: Saver JL, Goyal M, van der Lugt A, et al., for the HERMES Collaborators. Time to treatment with endovascular thrombectomy and outcomes from ischemic stroke: A meta-analysis. *JAMA* 2016;316:1279-1288.

In 2015 and 2016, five prospective trials of endovascular thrombectomy for large vessel occlusions with second-generation devices were published and showed dramatic efficacy in terms of reperfusion and functional outcomes (*N Engl J Med* 2015;372:11; *N Engl J Med* 2015;372:1009; *N Engl J Med* 2015;372:1019; *N Engl J Med* 2015;372:2296; *N Engl J Med* 2015;372:2285; *Lancet* 2016;387:1723). In an attempt to obtain more information about the effect of time delays on outcomes, all of the investigators agreed to pool the data and analyze them as a larger group, with a specific goal of assessing the effects of "time to treatment" on the outcomes, and to what extent treatment delay was related to functional outcomes, mortality, and symptomatic hemorrhage. Clinical information, brain imaging data, as well as functional and imaging outcomes were pooled and analyzed from a group of 1,287 treated patients. The primary outcome was degree of disability, as measured by the modified Rankin scale (mRS) at three months, with common odds ratios calculated for various time intervals to show a distribution of outcomes related to time delays.

Among all 1,287 enrolled and randomized patients, 634 underwent endovascular intervention with a median time from symptom onset to randomization of 196 minutes (142 to 267). Median symptom onset to arterial puncture was 238

minutes (180 to 302) and time to reperfusion was 286 minutes (215 to 363). At 90 days, the mean mRS score was 2.9 (95% confidence interval [CI], 2.7-3.1) in the endovascular group and 3.6 (95% CI, 3.5-3.8) in the medical therapy group. The odds of reduced disability at 90 days in the endovascular group declined with longer time from symptom onset to arterial puncture: Odds ratio at 3 hours = 2.79, at 6 hours = 1.98, and at 8 hours = 1.57, retaining a statistical significance up to 7 hours and 18 minutes. Among the 390 patients who achieved substantial reperfusion with thrombectomy, each one-hour delay to reperfusion was associated with more disability and less functional independence. However, there was no difference in mortality due to delay. Overall, this meta-analysis of thrombectomy in patients with large vessel ischemic stroke demonstrated that earlier treatment compared with medical therapy alone was associated with lower degrees of disability at three months. Each hour delay resulted in worse outcome. ■

Pulmonary Embolism Common Cause for Syncope in Hospitalized Patients

SOURCE: Prandoni P, Lensing AW, Prins MH, et al. Prevalence of pulmonary embolism among patients hospitalized for syncope. *N Engl J Med* 2016;375:1524-1531.

Syncope is a chief complaint for which neurologists often are consulted. In most cases, the neurological concern is possible stroke or an epileptic seizure. However, a variety of cardiopulmonary problems are most often the underlying cause of syncope, including cardiac arrhythmias and pulmonary embolism. The investigators of this study reviewed the clinical records of 560 patients (mean age of 76 years) who were admitted to the hospital with syncope. Diagnosis of pulmonary embolism was ruled out in 330 of the 560 patients on the basis of a negative D-dimer assay and low pretest clinical probability. Of the remaining 230 patients, pulmonary embolism was identified in 97 (42.2%). In the entire cohort, prevalence of pulmonary embolism was 17.3% and there was evidence of an embolus in a main pulmonary or lobar artery larger than 25% of the total area of both lungs in 61 patients.

Based on this careful and detailed review of clinical features of patients with syncope, it appears that pulmonary embolism may be one of the most common causes, and should be considered by all physicians who are evaluating such patients, including neurologists. ■

Intensive Blood-pressure Lowering in Acute Intracerebral Hemorrhage

SOURCE: Qureshi AI, Palesch YY, Barsan WG, et al, for the ATCH-2 Trial Investigators and the Neurological Emergency Treatment Trials Network. Intensive blood-pressure lowering in patients with acute cerebral hemorrhage. *N Engl J Med* 2016;375:1033-1043.

Acute intracerebral hemorrhage comprises about 10% of all strokes in the United States, and continues to carry a high morbidity and mortality related to hematoma expansion. Acute lowering of high blood pressure has been a primary treatment for these patients, but the actual range of optimal blood pressure control has yet to be determined. This study was designed to randomize eligible patients with intracerebral hemorrhage, volume < 60 cc, and Glasgow Coma Scale score of 5 or more into two treatment groups, one with a target systolic blood pressure of 110-139 mmHg (intensive treatment group) and the other to a target systolic blood pressure of 140-179 mmHg (standard treatment group), to test the superiority of intensive reduction of blood pressure compared to standard. Intravenous nicardipine was used to lower blood pressure and was administered within 4.5 hours after symptom onset. The primary outcome was death or disability, using modified Rankin scale, at three months after randomization.

One thousand eligible participants had a mean systolic blood pressure of 200.6 ± 27.0 mmHg at baseline, and 500 were assigned to the intensive treatment group. The mean age of the patients was 61.9 years, and 56.2% were Asian. Enrollment was stopped before the planned endpoint because of futility determined after a pre-specified interim analysis. Death and disability was observed in 38.7% of the participants (186 of 481) in the intensive treatment group and 37.7% (181 of 480) in the standard treatment group, with no difference in relative risk, even after adjustment for age, initial Glasgow Coma Score, and presence of intraventricular hemorrhage. Serious adverse events occurred in the same proportions in both groups, but the rate of renal adverse events within seven days after randomization was significantly higher in the intensive treatment group then in the standard treatment group. In conclusion, treatment of patients with an intensive blood pressure-lowering regimen did not result in a lower rate of death or disability than standard reduction to a target systolic blood pressure of 140-179 mmHg. ■

Basilar Artery Thrombectomy Can Be Accomplished with Acceptable Outcomes

SOURCE: van Houwelingen RC, Luijckx GJ, Mazuri A, et al. Safety and outcome of intra-arterial treatment for basilar artery occlusion. *JAMA Neurol* 2016;73:1225-1230.

Mechanical thrombectomy for large vessel occlusion and ischemic stroke has been widely used based on recent successful randomized trials. However, treatment of basilar artery occlusion has been questioned because of the small number of cases, lack of randomized data, and a history of poor results. These investigators reported results of intra-arterial treatment in patients with basilar artery occlusion, from a single-center retrospective case series of 38 consecutive patients who underwent intra-arterial treatment between 2006 and 2015 at a stroke referral center in the Netherlands. Primary outcome included documentation of adequate recanalization, and favorable outcome was defined as a modified Rankin scale score of 0-3.

In 38 patients with basilar artery occlusion, mean age was 58 years, and 55% were male. Twenty-seven patients (71%) were treated with intravenous thrombolysis before undergoing mechanical thrombectomy, which was applied to 30 patients. Seven patients were treated with intra-arterial thrombolysis. The median NIH stroke scale score was 21 (range 15-32) and median time to intra-arterial treatment was 288 minutes (216-380). Adequate recanalization was achieved in 34 of 38 cases (89%), and functional outcome was favorable in 19 (50%)

patients. Symptomatic intracranial hemorrhage occurred in two patients. Overall, these results indicate that mechanical thrombectomy for basilar artery occlusion can be accomplished with a similar success rate as that which has been published in the large multicenter, randomized trials of thrombectomy. ■

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CME QUESTIONS

1. **Which of the following treatments results in improved control of chronic migraines compared to placebo?**
   a. Amitriptyline
   b. Topiramate
   c. Both of the above
   d. None of the above

2. **In the analysis of the Rotterdam study, which of the following groups had the highest scores in cognitive testing compared to non-migraineurs?**
   a. Women with migraine
   b. Men with migraine
   c. Migraineurs with aura
   d. Migraineurs without aura
   e. Migraineurs with an attack more than a year prior.

3. **Which of the following is associated with a poorer prognosis in ulnar neuropathy at the elbow?**
   a. Left-sided ulnar neuropathy at the elbow, compared to right-sided ulnar neuropathy
   b. More severe first dorsal interosseous weakness, as compared to abductor digiti minimi weakness
   c. Ulnar thinning on ultrasound evaluation of the ulnar nerve at the elbow, as compared to ulnar thickening
   d. None of the above

4. **In a long-term follow-up study of treated patients with MS, which of the following is NOT true?**
   a. Overall disability was less frequent than in earlier natural history studies.
   b. Rates of transition from RMS to SPMS were lower compared to natural history studies.
   c. Development of new T-2 lesions on MRI in the first two years predicted later disability.
   d. Overall, 59% of patients showed some progression of disability during the course of the study.

5. **Endovascular thrombectomy is effective in treating large vessel occlusions up to 8 hours after onset of symptoms.**
   a. True
   b. False

6. **After acute intracerebral hemorrhage, intensive lowering of systolic blood pressure to 120 mmHg results in better neurological outcomes**
   a. True
   b. False

7. **Endovascular thrombectomy for basilar artery occlusion can be performed with good results and acceptable morbidity.**
   a. True
   b. False

8. **Pulmonary embolism appears to be one of the most common causes of syncope.**
   a. True
   b. False

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