Editors’ Note: In response to “Evolving use of seizure medications after intracerebral hemorrhage: A multicenter study,” Srinivasan et al. suggest that newer antiseizure drugs (ASD) (e.g., levetiracetam) are safer, influencing drug prescription behavior. They also report their own experience that initiation of ASD in patients with intracerebral hemorrhage has not changed in 2 cohorts 10 years apart; ASDs were more frequently discontinued prior to discharge in the recent cohort. Naidech et al., authors of the study, agree that the use of levetiracetam is rational, but they note that the use of levetiracetam may be futile. Clinical trials are needed to determine whether prophylactic seizure medications alter patient outcomes and the occurrence of seizures in high-risk patients. Commenting on “Neurologists and the economics of MS treatment: Lighting candles, not cursing the darkness,” Dr. Otulana, Chief Medical Officer for Mallinckrodt Pharmaceuticals, which produces Acthar Gel, argues that considering Acthar Gel for multiple sclerosis (MS) relapse as a treatment option is in the best interest of patients. He explains that steroids are the first-line treatment of MS relapse but some patients cannot tolerate or do not respond to steroids and Acthar has a different side effect profile including hypertension and edema. Dr. Otulana also stresses the importance of considering the total cost related to the management and treatment of MS, citing a study that suggested that Acthar is a cost-effective treatment option for MS relapse. Dr. Bourdette disagrees and stands by the editorial, pointing out that the study cited by Dr. Otulana supporting cost-effectiveness was paid for by Mallinckrodt and is not a cost-effectiveness analysis. Furthermore, this study compares costs of health care services delivered to patients who received Acthar compared with a group that received either plasmapheresis or IV immunoglobulins (IVIg) for MS relapse. Patients receiving Acthar had much higher medication costs over 12 months vs the plasmapheresis/IVIg group (mean of $87,200 vs $12,300). Acthar costs $34,000–$102,000/treatment course. Dr. Bourdette concludes that neurologists should not use repository corticotropin to treat MS relapses.

—Chafic Karam, MD, and Robert C. Griggs, MD

LETTER RE: EVOLVING USE OF SEIZURE MEDICATIONS AFTER INTRACEREBRAL HEMORRHAGE: A MULTICENTER STUDY
Shraddha Srinivasan, New York; Hae Won Shin, Chapel Hill, NC; Jong Woo Lee, Boston: Naidech et al.1 concluded that increased prophylactic antiseizure drug (ASD) use in intracranial hemorrhage (ICH) between 2007 and 2012 was due to clinicians’ hesitation to abandon a longstanding practice despite an established guideline.2 We offer an additional interpretation.

It can be challenging to determine if the patient had a seizure at presentation using reported history when altered mental status is a factor. In addition, with more frequent continuous intensive care unit EEG monitoring, EEG patterns arise that lie on the ictal-interictal continuum. Starting an ASD is, therefore, a risk–reward calculation. As levetiracetam is safer than phenytoin across multiple conditions,3,4 the risk–reward balance inevitably changes, resulting in greater ASD use.

Clinicians do appreciate the futility of using prophylactic ASD. In a retrospective study,5 we examined ASD use in patients with ICH in 2 cohorts 10 years apart (1999–2000 and 2009–2010). Initiating ASDs at presentation had not changed. However, ASDs were more frequently discontinued prior to discharge in the recent cohort (50% vs 20%).5 This was likely due to the awareness of the potentially deleterious effects of ASDs, particularly of phenytoin, even prior to the guideline.5

The authors’ reported observation may be the result of completely rational behavior.

AUTHOR RESPONSE: EVOLVING USE OF SEIZURE MEDICATIONS AFTER INTRACEREBRAL HEMORRHAGE: A MULTICENTER STUDY
Andrew M. Naidech, Babak Jahromi, Shyam Prabhakaran, Jane L. Holl, Chicago: We thank Srinivasan et al. for the interest in our article.1 We agree that the use of levetiracetam is rational and stated so in the last paragraph of the article.2 Separately, Srinivasan et al. state that clinicians “appreciate the futility of using prophylactic” seizure medications. It is not clear how best to reconcile the rational and common use of levetiracetam with the potential futility of this approach. Definitive clinical trials are needed to determine whether prophylactic seizure medications alter patient outcomes and the occurrence of seizures in high-risk patients.


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LETTER RE: NEUROLOGISTS AND THE ECONOMICS OF MS TREATMENT: LIGHTING CANDLES, NOT CURSING THE DARKNESS
Tunde Otulana, Hampton, NJ: In their editorial, Drs. Bourdette and Whitham1 mentioned “avoiding use of repository corticotropin (Acthar gel) to treat MS relapses.” Objectively considering H.P. Acthar Gel, the only Food and Drug Administration–approved noncorticosteroid therapy option for multiple sclerosis (MS) relapse, as a treatment option is in the best interest of patients.

Steroids are the first-line treatment of MS relapse; however, North American Research Committee on Multiple Sclerosis data indicate that 30% of patients with MS relapse had no response to steroids.2 In addition, some patients cannot tolerate steroids. Nearly 20% of patients consider avoiding relapse therapy due to steroid adverse effects (AEs).3 The AE profile for steroids trended toward gastrointestinal and CNS side effects.4 Acthar is different, trending toward hypertension and edema. When considering putative mechanism-of-action differences between the 2 treatment options, these AE findings are not surprising.3 Organizations like the American Academy of Neurology and the National Multiple Sclerosis Society have stated the need for alternative therapies for patients who cannot or will not take methylprednisolone for treatment of MS relapse.

It is important to consider the total cost related to the management and treatment of MS relapse, which includes inpatient, outpatient, and pharmacy costs. By this measure, Acthar is a cost-effective treatment option for MS relapse.6 H.P. Acthar Gel, with its qualitatively different side effect profile and different putative mechanism of action, provides an alternative treatment option for appropriate patients.

Note: Tunde Otulana, MD, is Chief Medical Officer, Mallinckrodt Pharmaceuticals, Hampton, NJ.


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AUTHOR RESPONSE: NEUROLOGISTS AND THE ECONOMICS OF MS TREATMENT: LIGHTING CANDLES, NOT CURSING THE DARKNESS
Dennis N. Bourdette, Portland, OR: Dr. Otulana, Chief Medical Officer for Mallinckrodt Pharmaceuticals, which produces H.P. Acthar Gel, claims that Acthar is cost-effective in a response to our editorial.1 To support this statement, Dr. Otulana references a study paid for by Mallinckrodt that is not a cost-effectiveness analysis.2 The cited study compares costs of health care services delivered to patients who received Acthar compared with a group that received either plasmapheresis or IV immunoglobulins (IVlg) for multiple sclerosis (MS) relapse.3 While there was a modest difference in total cost of care over 12 and 24 months after treatment between the 2 groups, the article by Gold et al.2 revealed that those receiving Acthar had much higher medication costs over 12 months compared with the plasmapheresis/IVlg group (mean cost of $87,200 vs $12,300). The high medication costs may reflect the expense of Acthar. The current average acquisition price of a 5-mL vial of Acthar containing
80 IU/mL of repository corticotropin is $34,000.¹ Patients receive 80 IU of Acthar once a day for 5–15 days,² costing a stunning and unjustified $34,000–$102,000. I stand by our editorial, in which we state that neurologists “should not be using repository corticotropin to treat MS relapses given its high cost.”³


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CORRECTIONS

Transplantation of spinal cord-derived neural stem cells for ALS: Analysis of phase 1 and phase 2 trials

In the article “Transplantation of spinal cord-derived neural stem cells for ALS: Analysis of phase 1 and phase 2 trials” by J.D. Glass et al.,¹ there is an error in Dr. Boulis’s disclosure, which should have included “Dr. Boulis served as an employee and received compensation (December 2014–November 2015) from Above and Beyond, LLC.” The author regrets the omission.

REFERENCE


Carotid artery web and ischemic stroke: A case-control study

In the article “Carotid artery web and ischemic stroke: A case-control study” by J.M. Coutinho et al.,¹ there is an error in the Discussion. The last sentence in the fifth paragraph should have cited reference 8 rather than reference 6 as originally published. The authors regret the error.

REFERENCE


Physical activity, but not body mass index, predicts less disability before and after stroke

In the article “Physical activity, but not body mass index, predicts less disability before and after stroke” by P.M. Rist et al.,¹ there is an error in the first sentence of the Results section of the abstract, which should have read “risk difference = −0.09 and −0.09 for ADLs and IADLs, respectively.” The authors regret the error.

REFERENCE


Author disclosures are available upon request (journal@neurology.org).
Transplantation of spinal cord-derived neural stem cells for ALS: Analysis of phase 1 and phase 2 trials

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