Spotlight on headache

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The current issue of *Neurology® Clinical Practice* reflects many of the exciting changes in headache medicine that are transforming the field and setting the stage for a new chapter in the diagnosis and treatment of the broad range of conditions that cause headache. This editorial will address 3 major themes that cut across the articles in this issue: secondary headaches, emerging treatments for primary headaches, and improving outcomes in neurologic practice for people with migraine.

Secondary headaches

Secondary headaches are attributable to an underlying cause. The current issue highlights remote poststroke headache in children,¹ ophthalmoplegias,² and mild traumatic brain injury including posttraumatic headache.³ Establishing the causal link between a headache syndrome and a putative underlying cause is often difficult for an individual patient. If the underlying disorder is associated with headache, if it begins before the headaches start, and if treating the underlying disorder relieves the headache, attribution is straight forward. But for many individual patients, these conditions are not fully met.

Chelse et al.¹ conducted a single-center observational study on remote (>30 days) poststroke headache in children. In their sample of 115 children, more than one-third developed poststroke headache at a median of 6 months after the initial stroke. Poststroke headaches were more likely with increasing age, in children with a family history of headache, and in children with arteriopathy. Poststroke headache was associated with more than a 2-fold increased risk of stroke recurrence. This important study suggests that poststroke headache in children is of both mechanistic and prognostic importance. Because poststroke headache is associated with a positive family history, in some cases, stroke may unmask a predisposition to migraine, a primary headache disorder. In other cases, an underlying arteriopathy may give rise to a secondary poststroke headache.

Lai and Caplan² address a still controversial question about the mechanisms of headache associated with ophthalmoplegias. The term ophthalmoplegic migraine (OM) has long been used to describe patients who developed involvement of the cranial nerves III, IV, or VI in association with migraine headaches. The term implies that OM has a migraine mechanism. In the third edition of the International Classification of Headache Disorders, the term OM was replaced with recurrent painful ophthalmoplegic neuropathy (RPON). The new name RPON implies that ophthalmoplegia arises, not from a migraine-based mechanism, but because of a postviral or demyelinating cranial neuropathy. The change was motivated by the observation that a proportion of patients with headache and ophthalmoplegia have enhancement of their cranial nerves on gadolinium-enhanced MRI (GdMRI) during ophthalmoparesis. Based on their own observations and literature review, Lai and Caplan note that in some patients, the evidence favors a non-migraine-related pathogenesis based on cranial nerve enhancement, prolonged headache, and the temporal disconnection of headache and ophthalmoplegia. In other patients, ophthalmoplegia occurs in the setting of typical migraine, with a strong temporal correlation between ophthalmoplegia and headache, sometimes in the absence of a positive GdMRI. Lai and Caplan wisely recommend replacing

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the tyranny of either or, with the possibility that OM and RPON may be distinct disorders with overlapping clinical presentations, which can often, but not always, be differentiated.

Primary headaches and their treatment

Primary headache disorders and their treatment were covered in a study by Robblee and Kelly⁴ and in another study by Goadsby.⁵ Goadsby summarizes clinically important advances in the treatment of primary headache disorders including pharmacotherapies and neuromodulatory treatments. Two new classes of acute treatments, developed based on insights into migraine pathophysiology, were designed to be free of the vasoconstrictive effects of triptans and ergot alkaloids. Gepants, as exemplified by rimegepant and ubrogepant, are small molecule calcitonin gene related peptide (CGRP) receptor antagonists. Ditans, represented by lasmitidan, are 5HT_{1F} (serotonin) 1F receptor antagonists. These new classes of medications have completed their Phase III programs and will address genuine unmet acute treatment needs. They will provide alternatives for patients who do not respond to triptans, do not tolerate triptans, or have cardiovascular contraindications to triptans.

Goadsby also highlights the emergence of CGRP-targeted monoclonal antibodies for migraine prevention. These designer drugs for migraine, were developed based on insights from Edvinsson and Goadsby, among others, on the role of CGRP in migraine.^{6,7} One of the approved drugs targets the CGRP receptor (erenumab), whereas 2 target the CGRP ligand (fremanezumab and galcanezumab). All of these drugs are given by subcutaneous injection monthly although one of them can be given quarterly (fremanezumab). These agents have found expanding use in migraine therapy because of their efficacy and tolerability.

Neuromodulatory approaches have also become available. Three noninvasive approaches approved as acute treatments include single-pulse transcranial magnetic stimulation, external trigeminal nerve stimulation, and noninvasive vagal nerve stimulation. The first 2 approaches are also approved as preventive treatments. These approaches are important for people who do not want or cannot take medication, including pregnant women, and provide a useful adjunct to pharmacologic for and behavioral treatments. These treatments are under-utilized because of a lack of awareness and poor reimbursement.

Quality improvement in headache management

The expanding therapeutic armamentarium will deliver on its promise only if treatments are delivered to the right patients. Turner et al.⁸ implemented and assessed a quality improvement (QI) program for pediatric headaches in a large academic pediatric neurology practice. Based on the American Academy of Neurology's set of 10 Headache Quality Measures, they identified 3 areas for performance improvement targeting

disability assessment, provision of written action plans and acute treatment based on nurse triage, and infusion centers for acute attacks. They selected specific interventions for each area and used the Plan-Do-Study-Act model to implement and refine their QI program. For disability, they implemented the use of the Pediatric Migraine Disability Scale (PedMIDAS) and saw its use increase from 15% to 55%. The provision of written headache action plans increased by 50%, from 10% to 15%; although levels of utilization were low, the increase was significant. They also saw a 32% decrease in the use of the emergency department (ED), perhaps attributable to the nurse triage program and the infusion order set. They also estimated that reduced ED use generated substantial cost savings.

The authors provide a number of insightful take-home points and note that although their program resulted in an increased use of PedMIDAS, it did not result in measurable reductions in disability. Nonetheless, this program is an important demonstration of the benefits of QI for headache. Although measuring disability is a key step toward managing it, stratified care-based treatment guidelines, which match the severity of disability to the intensity of therapeutic interventions, may be needed to close the loop between process measures and functional outcomes.

By improving the recognition of secondary headaches, by developing novel acute and preventive treatment approaches using drugs and devices, and by assessing and implementing QI programs, we should be able to improve the lives of our patients with headache disorders.

Author contributions

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CORRECTIONS

Message from the Editors to our Reviewers

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In the article “Message from the Editors to our Reviewers” by Corboy et al.,¹ first published online April 8, 2019, the penultimate sentence in Dr. John Corboy's disclosures should have read ‘He is a consultant to Novartis, participating on a steering committee, and Mylan, on a legal issue.’ The author regrets the error.

Reference

1. Corboy JR, Powers LB, Anderson DC, and Barbano RL. Message from the Editors to our Reviewers. *Neurol Clin Pract* 2019;9:90-92.

Lymphopenia and DMTs for relapsing forms of MS: Considerations for the treating neurologist

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In the infographic for the article “Lymphopenia and DMTs for relapsing forms of MS: Considerations for the treating neurologist” by Fox et al.,¹ first published online January 8, 2019, a red “X” should have appeared on the arrow pointing to “egress into bloodstream.” This was corrected online on February 11, 2019. The authors regret the error.

Reference

1. Fox EJ, Buckle GJ, Singer B, Singh V, and Boster A. Lymphopenia and DMTs for relapsing forms of MS: Considerations for the treating neurologist. *Neurol Clin Pract* 2019;9:53-63.