Does the presence of aura inform us regarding migraine severity and response to treatment?

In 1944, Leão described cortical spreading depression, the phenomenon now widely believed to underlie what some persons with headache perceive as “aura.” Aura is a somewhat misleading term because it can occur before a migraine, during or after a migraine, or occur without any associated headache. It can also occur with many other types of headache, but in clinical practice it is usually in association with migraine that we consider it. Less than 30% of migraineurs will experience an aura, and some patients will have some attacks with and other attacks without an associated aura. The symptoms due to aura are well known to clinicians and are usually visual, but may be somatosensory (“chiro-oral aura”), motor/speech (hemiparesis/aphasia), or appear to emanate from the brainstem. Aura is suspected of being a trigger for the cascade of events that occur during a migraine attack by activating the “trigeminovascular system.” It is hard to use that as a complete explanation because many migraineurs do not experience aura with their attacks and the aura when it does occur may not begin until the clinical attack has begun or even may occur after the headache. One wonders whether cortical spreading depression might occur in “silent” areas of the brain and still function as a trigger for headache attacks. It is unknown whether the headache pain during attacks of migraine with aura is more severe overall than that of attacks of migraine without aura.

In this issue of Neurology, Hansen et al. studied whether the presence or absence of migraine aura influenced the outcome of acute headache treatment. They utilized a large pooled database from multiple clinical trials to look at the efficacy of oral sumatriptan and data from one large randomized clinical trial to evaluate inhaled dihydroergotamine (a formulation that as of this writing is not approved for clinical use in the United States). In short, they showed that migraineurs taking 100 mg of oral sumatriptan were substantially less likely to achieve pain freedom (i.e., be headache-free) at 2 hours if they treated an attack of migraine with aura than if the attack was migraine without aura. No such difference was found for inhaled dihydroergotamine.

That there should be a different outcome found for the 2 agents should not be surprising because they have very different pharmacokinetics and pharmacodynamics. As a clinician, I would expect inhaled dihydroergotamine, which bypasses the gastrointestinal tract, to be more reliable, consistent, and efficacious in a migraineur with nausea or vomiting. Also, the sources of the outcome data are quite different and make comparisons suspect. What is more interesting and relevant is the difference the authors found between the 2 groups for oral sumatriptan. Does this suggest that attacks of migraine with aura are more severe and therefore harder to treat effectively? Does it mean, as the authors wonder, that attacks of migraine with aura have a markedly different pathophysiology than attacks without aura and therefore respond to (some) treatments differently?

There are a number of concerns regarding the content of this study. Comparing a large pooled set of different sumatriptan studies and data from a single large randomized clinical trial is problematic, just as is comparing treatment results from 2 very different agents (oral sumatriptan and inhaled dihydroergotamine). Patients themselves sometimes determined the presence of aura and the possibility is real of confusing “prodrome” or other symptoms (such as “blurry vision”) with aura, or of over- or underreporting aura. Also, other antimigraine treatments such as nonsteroidal anti-inflammatory drugs or calcitonin gene-related peptide antagonists were not evaluated but certainly could be looked at in future studies.

This study raises a number of interesting questions and reminds us that the study of migraine is complex and requires attention to what is understood of the underlying pathophysiology and how that relates to the myriad different clinical manifestations among individual patients but also to differences in individual attacks in a given individual. The authors should be commended for attempting to use a common clinical symptom as a prognostic guide and for opening up a

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new line of inquiry as to how the presence or absence of aura affects treatment of migraineurs.

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REFERENCES