Interatrial Shunt-Associated Migraine: Serendipity, Empiricism, Hope, or Hype?

To the Editor:

Anzola et al found a dramatic reduction in incidence of migraine with aura after closure of patent foramen ovale (PFO) as well as overall improvement in migraine in a case-control study. For a disease that runs its course over several decades, a 12-month period of observation after PFO-closure is rather short. The suggestion that migraine may be causally linked to an unpredictable or intermittent right-to-left shunt (RLS) of PFO is seriously challenged by almost immediate aggravation or de novo appearance of migraine with aura after closure of atrial septal defect (ASD) that is, in turn, always associated with a left-to-right shunt. Closure of ASD interrupts any putative transfer of emboli (platelet-thrombi complexes) or serotonin or other chemicals from the pulmonary to the systemic circulation. Furthermore, access to the left heart at the level of the atria in PFO by air-bubbles during Valsalva maneuver is a laboratory artifact that does not reflect a common real-life situation; in paradoxical embolism, it is a platelet-thrombin plug that embolizes—such an embolus has physical properties markedly different from air bubbles. The larger-sized PFO may permit air bubbles to easily crossover to the left heart because of rheological factors that fundamentally differ from those that affect platelet-thrombin complexes. Methodologically, whereas pre-PFO closure assessment of migraine scores was based on 6-month recall, the post-PFO closure was well-documented, introducing an avoidable confounding factor. Also, the test group was given aspirin 300 mg whereas the control group was not; this dose of aspirin is analgesic and anti-inflammatory. Next, absence of difference in amount of RLS between study groups cannot be reconciled with the results of the study. Finally, persistent recurrence of migraine aura post-PFO closure in 7 patients indicates that the link between aura of migraine and PFO-related physiology is tenuous. The logic for closing PFO for otherwise unexplained symptoms is premature and ignores fundamental tenets of relevant basic and clinical sciences. Also, randomized controlled trials do not supplant the need for conceptual biological groundwork.

The investigators further speculate about a type of migraine with aura specifically associated with atrial shunts. Migraine aura is incompletely understood. Instantaneous resolution of migraine aura by drugs that do not readily cross the blood-brain barrier as well as hemianopic (not homonymous) distribution of the migrainous scintillating scotoma clearly indicate the need to distinguish between the origins of negative and positive visual phenomena in migraine.

Three patients in the stroke asymptomatic group experienced increased frequency of scintillating scotoma in the last month pre-PFO closure; the composite analysis of aura masks the effect of PFO-closure on occurrence of migrainous scintillating scotoma.

The suggestion that a RLS may be the “most potent trigger” of migraine attacks as well as the “major” determinant of migrainous aura is premature and ignores fundamental tenets of relevant basic and clinical sciences. Also, randomized controlled trials do not supplant the need for conceptual biological groundwork. In the absence of pathophysiological clarity, it is better to avoid experimental interventional therapies.

Disclosures

None.

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Stroke. 2006;37:2212; originally published online August 10, 2006; doi: 10.1161/01.STR.0000237167.80526.13
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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