Letters to the Editor

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ASD closure for migraine: is there a scientific basis?

Mortelmans et al. studied the closure of atrial septal defect (ASD) for preventing migraine. These investigators speculate about small right-to-left shunt (RLS) in ASD during Valsalva or exercise, blurring the characteristic haemodynamic difference between patent foramen ovale (PFO)–RLS and ASD–left-to-right shunt (LRS). Additionally, in contrast to PFO with unpredictable RLS, a predictable LRS is maintained in ASD. Migraine, however, particularly the menstrual variant, is frequently predictable. Second, there are no significant differences in the basal haemodynamic values (Table 1) that might predict the occurrence of intermittent RLS in this cohort. A higher basal right atrial (RA) pressure might permit intermittent RLS; however, after ASD closure, the lowest RA pressures (Table 3) were seen in patients whose migraines persisted or developed de novo. Thirdly, the implication of atrial natriuretic peptide (ANP) in migraine pathogenesis post-ASD correction is controversial. Falling RA pressure in uncomplicated ASD after correction would correspond with decline in plasma ANP values; in any case, ANP is known to lower central neuronal hyperexcitability. Next, larger defects in ASD are likely to be accompanied by larger LRS, a feature that makes intermittent RLS even less likely. Larger ASD sizes, however, as suggested by the size of the Amplatzer device used, prevailed in younger patients whose migraines persisted or developed a new post-ASD closure. Also, as with PFO, completeness of closure of ASD does not seem to be associated with migraine relief; this feature invites yet another pathophysiological assumption involving unpredictable thromboembolism from the left-sided disk of the occluder. Finally, atenolol—a first-line migraine prophylactic—does not readily cross the intact blood–brain barrier or significantly influence either brain neuronal function or circulation. This pharmacologic absolute does not support a pathogenetic role for embolic brain ischaemia in migraine. Lateralization of headache is a characteristic feature of migraine. The concept of paradoxical embolization of gas, thrombi, or vaso-active neuromodulators escaping pulmonary filtration/degradation assumes that these potential precipitants of migraine are being streamed regularly over decades to the same brain parenchymal site or circulatory segment in order to produce consistently lateralizing headache. After crossing over at the atrial level, however, paradoxical emboli are generally distributed randomly. Furthermore, cluster headache (CH), a strictly lateralized primary headache, is also associated with a strikingly similar incidence of RLS. Embolic brain ischaemia has not been invoked in the pathogenesis of CH. Besides, implicating congenital defects such as PFO/ASD in migraine mandates a plausible explanation for the characteristic and predictable late appearance (in the teens or twenties) and spontaneous disappearance (second and third trimesters of pregnancy and the later decades of life), in general, of migraine. The mean age of the subgroup in which migraine disappeared after ASD closure was 52 ± 13. Migraine generally remits spontaneously in the fifth and sixth decades, a feature which critically confounds remission of migraine post-ASD closure. Conversely, younger patients developed migraine after ASD closure.

Optimal size and design of future trials will not obviate the need for such conceptual groundwork.

References


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We greatly appreciate the comments made by Gupta on our paper entitled 'The influence of percutaneous atrial septal defect closure on the occurrence of migraine'. However, we have to warn the reader for over-interpreting our findings. With this study, we did not want to prove migraine prevention, but we were interested in the effect of percutaneous atrial septal defect (ASD) closure on migraine. Indeed, the reason for this study was our experience that migraine occurred in some patients and disappeared in others, almost immediately after the percutaneous procedure. We do agree with Gupta that the haemodynamics of a patent foramen ovale and ASD differ substantially. However, right-to-left shunting in ASD patients is considerably underestimated. A right-to-left shunt can easily be documented by an intravenous contrast injection during a transoesophageal echocardiogram, even without a Valsalva manoeuvre. Contrast passage is more pronounced in larger (less restrictive) ASDs, which implicates lower pressure differences between left and right atria. In contrast, in smaller (restrictive) ASDs, the pressure differences between the atria are higher, which implicates less or even absent contrast passage. The smaller ASDs were not included in the study because they were not indicated to be closed. Therefore, we are not convinced that the right-heart haemodynamics of our study population might identify the degree of the potential right-to-left shunt. The explanation for the latter is probably much more complex. Finally, paradoxical embolism through an ASD leading to a cryptogenic stroke seems not to be so uncommon, which highlights the clinical relevance of a right-to-left shunt in these patients.

The implication of atrial natriuretic peptide (ANP) in the pathogenesis of migraine remains controversial. Today, no clear relationship is documented between ANP and migraine. However, transient changes in ANP levels after ASD closure are reported. Future research will be necessary to determine its relationship with the occurrence of migraine.

On the basis of the data available in the literature and with regard to our study results, we do believe that micro-thrombi play an important role in the occurrence of migraine. The latter might explain the relationship between stroke and migraine.