# Letters to the Editor

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## **Response to Letter by Gupta**

#### Response:

Dr Gupta's letter highlights the need to avoid prejudicially mislead conclusions inasmuch as his quotation of postclosure aggravation of migraine is misplaced as long as patent foramen ovale (PFO) is mistaken for an atrial septum defect. However, his observations offer the opportunity to try to disentangle the apparent paradox of migraine associated with PFO on one side and the reported aggravation or the novo appearance of headache after the fixing of atrial septal defects (ASD) on the other. This superficially apparent contradiction is likely to result from the attitude, among many noncardiologists, to assimilate PFO to ASD, whereas the 2 conditions are totally different in terms of both hemodynamics and outlook. Indeed, PFO is a paraphysiological benign condition in which an exclusively right-to-left shunt occurs as a rule during Valsalva strain but may also manifest on normal breathing probably for selective streaming of blood from inferior vena cava toward the atrial wall.1 On the contrary, ASD brings about a predominantly left-to-right shunt which by definition is present throughout the entire cardiac cycle and which, if left untreated, almost invariably leads to right atrium dilatation and in many cases also to pulmonary hypertension. The presence of a PFO is of no consequence to heart hemodynamics and the only effect of PFO closure is to prevent a small fraction of the cardiac output to bypass the lung, whereas ASD profoundly disrupts the physiology of blood circulation in atrial chambers and ASD repair brings about an abrupt remodeling of atrial sizes and pressures. Therefore, it is no surprise that (1) migraine is associated with PFO but not with ASD, and (2) ASD but not PFO closure has been reported to aggravate migraine or give birth to de novo headache.2 The occurrence of scintillating scotoma that we have reported after PFO closure is a different phenomenon probably unrelated to migraine.3

Whatever the speculations on naturally occurring shuntassociated migraine or the interpretations for the novel appearance of headache after ASD closure, these are clearly 2 different conditions probably stemming from different mechanisms. Forcing them together with the aim of disproving the so-called shunt theory of migraine is akin to comparing pears with apples.

The hypothesis of right-to-left shunt as a trigger for migraine attacks is not only plausible but also strengthened by the recent demonstration that migraine patients have larger shunts than controls, and in migraine with aura the shunts tend to be larger than in migraine without aura.<sup>4,5</sup>

This by no means is meant to support the idea that PFO causes migraine, as Gupta seems to blame on us, but just that it may enhance the attacks with or without aura to a different extent according to different degrees of susceptibility, which may also change with time, and in interplay with other biochemical, hormonal, psychological and environmental triggers.

Finally, the fact that aura seems to be particularly responsive to PFO closure, as well as the simultaneous presence of migraine with aura and PFO in first degree relatives in different kinships, suggests that genetically determined factors may underlie the co-occurrence of migraine and PFO. Whether the association with PFO confer to migraine a special clinical profile is currently being investigated in an ongoing multicenter study in Italy.<sup>6</sup>

### **Disclosures**

None.

#### Gian Paolo Anzola, MD

Service of Neurology S. Orsola Hospital FBF Associazione Fatebenefratelli per la Ricerca (AfaR) Brescia, Italy

#### Eustaquio Onorato, MD, FSCAI Francesco Casilli, MD

Division of Cardiology I Humanitas Gavazzeni Hospital Bergamo, Italy

#### Eva Morandi, MD

Neurology Clinic University of Brescia Brescia, Italy

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# Response to Letter by Gupta

Gian Paolo Anzola, Eustaquio Onorato, Francesco Casilli and Eva Morandi

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