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LETTERS TO THE EDITOR

Intravenous Milrinone for Cerebral Vasospasm in Subarachnoid Hemorrhage

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To the Editor,

We read with great interest the article by Lakhal et al. [1] about the role of intravenous milrinone for cerebral vasospasm in patients with aneurysmal subarachnoid hemorrhage (aSAH). It is an appreciable work because it provides evidence for intravenous milrinone to reduce 6-month functional disability and vasospasm-related brain infarction in patients with aSAH. In 94 patients with aSAH who were studied, intravenous milrinone infusion was significantly associated with a lower likelihood of 6-month functional disability (modified Rankin Scale score ≥ 2), which occurred in 47 [50%] patients; adjusted odds ratio 0.28 [95% confidence interval 0.10–0.77]). Intravenous milrinone infusion was also independently associated with a lower likelihood of vasospasm-related brain infarction on imaging studies (which occurred in 22 [23%] patients; adjusted odds ratio 0.19 [95% confidence interval 0.04–0.94]). The authors conclude that intravenous milrinone may be regarded as a sufficiently safe option to conduct randomized controlled studies. We congratulate the authors on their tremendous work. However, the below-mentioned issues may need little consideration.

The sub-group analysis of patients with aSAH with anterior or posterior circulation aneurysms could have added to the information. The diagnosis of vasospasm by transcranial Doppler or transcranial color Doppler should include examination of both anterior and posterior circulation [2]. The transcranial color Doppler of middle cerebral artery (MCA) alone, as performed in this study might have missed inclusion of patients with only posterior circulation vasospasm.

In this study, the authors state that weaning from milrinone was left to the discretion of the attending intensivist. Thus, the end point of milrinone infusion was not clearly defined, whether, it was neurological improvement of the patient or resolution of vasospasm on imaging. Delayed cerebral ischemia and vasospasm are different entities that need to be separately assessed in such studies [3]. Because no follow-up imaging was performed for assessing the resolution of vasospasm after administration of milrinone, it cannot be reliably stated that it improved the caliber of vasospastic arteries. On the other hand, had milrinone improved the neurological status of the patients, then it possibly has a beneficial effect on delayed cerebral ischemia. Imaging performed post-milrinone infusion would add to the cost but at the same time provide essential information about its actual effect on vasospasm. Thus, information about the effect of milrinone on neurological symptoms and postoperative computed tomography angiography findings would have been more helpful. This may be included in future prospective trials.

We completely agree with the authors that it is difficult to assess whether cerebral infarction was secondary to vasospasm or due to other mechanisms, such as microthrombi, late embolic events, cortical spreading depolarization, or inflammation. This can somewhat reliably be said only on brain imaging, in which a cerebral infarction occurring in the area of the vasospastic artery indicates it as a vasospasm-related cerebral infarction.

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We appreciate the work and congratulate the authors again for their extensive work. It provides a reference for the framework of future randomized controlled trials.

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