Letters to the Editor

Should Right-to-Left Shunts Be Detected Before Thrombolysis in Acute Ischemic Stroke Patients?

To the Editor:

We read with great interest the recent study by Kimura et al regarding the dramatic improvement with intravenously administered tissue plasminogen activator (IV-tPA) in patients with right-to-left shunts (RLS) detection by contrast-enhanced transcranial Doppler (TCD). The authors compared the rates of dramatic improvement (defined as a ≥10-point reduction in the total National Institutes of Health Stroke Scale [NIHSS] score or a total NIHSS score of 0 or 1 at 7 days after tPA infusion) between patients with and without RLS and found that patients with RLS more frequently had dramatic improvement (64.7% versus 32.3%; P = 0.030). Importantly, in a multivariate model presence of RLS (odds ratio, 5.9; 95% CI, 1.3 to 27.3; P = 0.022) was found to be the only independent factor associated with dramatic improvement. The results of this article are thought-provoking.

tPA has a short half-life and is rapidly metabolized by the liver. One possible reason for the better rates of dramatic clinical recovery is higher rates of recanalization in patients with RLS due to shunting of some ‘extra’ tPA due to ‘bypassing’ its metabolism by the liver. This may result in the exposure of the clot to a larger concentration of tPA. If this mechanism is believed to work, then we may make some minor attempts to augment the passage of more blood (with more tPA) through the RLS. Repeated performance of the valsalva maneuver during IV-tPA infusion may not be possible in all acute stroke patients. Alternatively, changing the body position may increase the passage of more venous blood through RLS. We have recently demonstrated that the change of body positioning from the supine to sitting up position increased substantially the number of air microemboli (from a median of 20 in the supine to a median of 72 in the sitting position) detected during RLS detection by TCD. However, by sitting upright, patients may lose the advantages of improved residual blood flow to ischemic brain as seen in the ‘head-down’ position (with a zero-degree elevation of the head).

The details of hemodynamics effects of RLS are unclear. However, passage of larger number of microembolic signals in bigger RLS may indicate some increase in the amount of blood flow (hence tPA) also through it. If escaping ‘first pass through the liver’ due to RLS results in delivering a higher amount of tPA to the occluded intracranial artery, then the ‘size’ of the RLS as well as its ‘functional-potential’ should play an important role and contribute, at least to some extent, toward higher rates of recanalization and clinical recovery. It would be interesting if the authors could present the relationship between the ‘size’ or ‘functional grading’ of RLS and the rates dramatic clinical recovery.

If these hypotheses and speculations are deemed feasible, then a quick testing for the presence of RLS in acute ischemic stroke patients may be considered. Only a couple of minutes are needed for detecting the presence of RLS by TCD. Patients having an RLS may then be subjected to some of the maneuvers to augment the blood flow through the shunt with an aim to deliver a larger amount of tPA to the clot. One possible argument against such an approach could be the possibility of increasing the rates of intracranial hemorrhage due to the delivery of a ‘higher dose of tPA’ to the ischemic brain. Some information can be gathered from retrospective analyses, especially at centers where sufficient number of IV-tPA–treated patients underwent an active screening for RLS at some point of time during their follow up. These possibilities become especially important because the benefits of an RLS can be offered to a significant number of cases, as RLS are seen in almost a quarter of the general population. However, this approach would need to be tested prospectively in a larger cohort.

Lastly, the role played by RLS in acute stroke still remains controversial. Kimura et al could not find the thrombi in the leg veins in patients with RLS to account for the source of cerebral embolization. Establishing such associations is often difficult due to various methodological and temporal issues. Doppler ultrasonography of deep veins in the legs may not demonstrate the thrombus because it might have already migrated proximally. Although it may not always contribute toward the clinical management, an imaging study (contrast venography or magnetic resonance venography) of the pelvic veins might prove more fruitful.

Disclosures

None.

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