Letter by Rezaei and Arjmand Regarding Article, “Cerebrolysin and Recovery After Stroke (CARS): A Randomized, Placebo-Controlled, Double-Blind, Multicenter Trial”

To the Editor:

We read with great interest and appreciation the article by Muresanu et al1 on the effects of cerebrolysin on the improvement of motor function in patients with acute ischemic stroke. Within the word count limitations of this letter, however, we would like to present a point that needs to be addressed and evaluated more in future experimental and clinical studies regarding the cerebrolysin mechanisms of action to improve ischemic stroke outcomes.

Cerebrolysin is a neuroprotective medication, which is a porcine brain–derived peptide that acts as a neurotrophic agent similar to growth and neurotrophic factors in the brain. It has been postulated that cerebrolysin implements its effect through the inhibition of apoptosis and the production of free radicals and lipid peroxidation, which can contribute to the inhibition of neuronal death and neuroinflammation, improvement of neuronal survival, and stimulation of neurogenesis.1,2

The majority of studies on this issue have demonstrated the recovery from functional or cognitive disabilities related to neurodegenerative diseases. In a randomized study, we showed, for the first time, that cerebrolysin led to a decline in the pulsatility index of the middle cerebral artery, as measured by a transcranial Doppler examination during a 90-day follow-up in patients who had experienced an acute ischemic stroke.3 This finding adds further scientific evidence of the cerebrolysin impact on ischemic stroke. As proved in previous reports, the pulsatility index reflects downstream peripheral resistance, which could be related directly to intracranial arterial resistance.4 Compared with arteries embedded in muscle, an increased resistance in distal small arteries in the brain may influence more proximal arteries. Therefore, it is of great value to investigate if cerebrolysin improves neurological function and via which pathophysiologic pathways: neuronal survival, increased cerebral blood flow, or both together. No clinical studies have focused on the hemodynamic effects promoted by cerebrolysin, which can, in some ways, explain its potential neuroprotective abilities in addition to previous findings.

We think that cerebrolysin has a pleiotropic effect on ischemic stroke, which is mediated mainly by 3 mechanisms: (1) neurogenesis and neuronal survival via inhibition of apoptotic pathways, (2) an anti-inflammatory role through inhibiting microglial activation, and (3) vasodilation caused by an undetermined mechanism. Further experimental and clinical studies on these issues, in particular the probable vasodilatory action, will give rise to more precise findings in predicting favorable clinical and functional outcomes in patients with acute ischemic stroke.

Disclosures

None.

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