Section Editor: Peter Sandercock, MA, DM, FRCPE, FMedSci

Cerebrolysin for Acute Ischemic Stroke

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Cerebrolysin is a mixture of low molecular weight peptides and amino acids derived from pigs' brain, with potential neuroprotective and neurotrophic properties. It is widely used in the treatment of acute ischemic stroke in Russia, Eastern Europe, China, and other Asian and post-Soviet countries.

Material and Methods

Objectives

To quantify the potential benefits and harms of cerebrolysin in acute ischemic stroke.

Types of Studies

Randomized controlled trials.

Types of Participants

Patients admitted to hospital with acute ischemic stroke and started on treatment within 48 hours of stroke onset and continued for any time.

Types of Interventions

Cerebrolysin compared with placebo or no treatment added to standard treatment.

Primary Outcomes

All-cause death.

Secondary Outcomes

Poor functional outcome defined as death or dependence at the end of the follow-up period; early death (within 2 weeks of stroke onset); quality of life; and time to restoration of capacity for work.

Adverse Events and Effects

Serious adverse events (SAEs), as defined according to the International Council for Harmonization guideline:

- Total number of people with SAEs
- Total number of people with fatal SAEs
- Total number of people with nonfatal SAEs

Adverse effects specifically associated with cerebrolysin, such as hypersensitivity reactions; Total number of people with adverse events.

Results

We included 6 studies with a total of 1501 randomized patients: 3 were large multicentre trials, 2 were small in size and were judged to be of unclear quality, and 1 did not report numeric results. The manufacturer of cerebrolysin, pharmaceutical company EVER Neuro Pharma, supported 3 multicenter studies by providing either cerebrolysin and placebo, randomization codes, research grants, statisticians, or totally. None of the included studies reported on poor functional outcome or early death.

There was no difference in the number of all-cause deaths: 46/714 in cerebrolysin group versus 47/703 in placebo group; risk ratio was 0.91 (95% confidence interval, 0.61–1.35).

SAEs as reported by 3 large multicenter studies with 1335 participants: there was no significant difference in the total number of SAEs with cerebrolysin and risk ratio was 1.16 (95% confidence interval, 0.81–1.67). This comprised no difference in fatal SAEs with risk ratio of 0.90 (95% confidence interval, 0.59–1.38) and a >2-fold increase in the number of people with nonfatal SAEs (20/667 with cerebrolysin and 8/668 with placebo; risk ratio was 2.47 (95% confidence interval, 1.09–5.58; P=0.03; Figure).

There was no difference in the total number of people with adverse events: 308/667 in cerebrolysin group versus 307/668 in placebo group; risk ratio was 0.97 (95% confidence interval, 0.86–1.09).

Conclusions

Our results do not demonstrate clinical benefits of cerebrolysin for treating acute ischemic stroke. We found moderate-quality evidence that nonfatal serious adverse events may be more common with cerebrolysin use in acute ischemic stroke (Figure).

Implications for Practice

The review raises concerns about serious adverse events with cerebrolysin use in acute ischemic stroke with no clinical benefit.

Implications for Research

Future research, if any at all, should focus on well-designed randomized controlled trials to reliantly assess the benefits and harms of cerebrolysin in acute ischemic stroke.

Acknowledgments

This article is based on a Cochrane Review published in The Cochrane Library 2017, Issue 4 (see www.thecochranelibrary.com

Received April 28, 2017; final revision received May 19, 2017; accepted May 24, 2017.

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(*Stroke*. 2017;48:e245-e246. DOI: 10.1161/STROKEAHA.117.017841.)

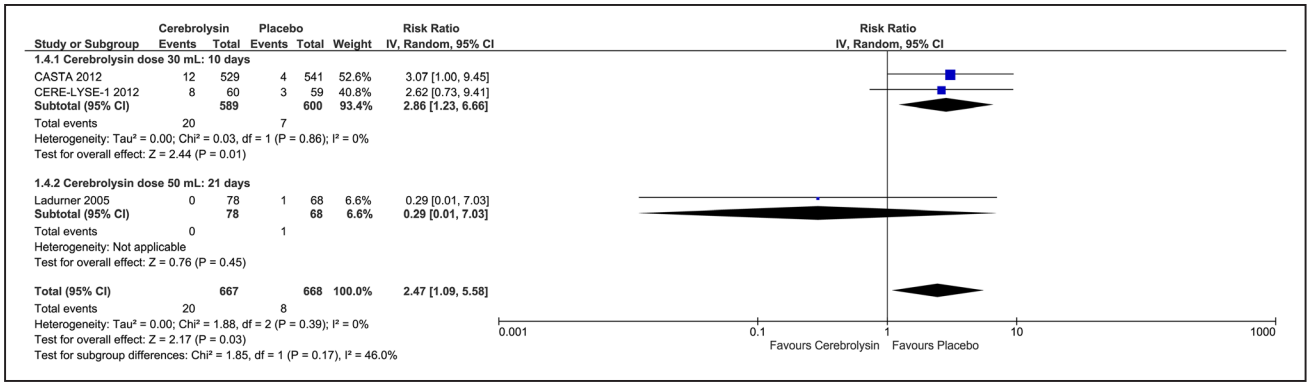

Figure. Nonfatal serious adverse events (SAEs). CI indicates confidence interval.

for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and The Cochrane Library should be consulted for the most recent version of the review.[1]

Sources of Funding

This review was developed according to the Russian Government Program of Competitive Growth of Kazan Federal University with support from the Cochrane Stroke Group and Cochrane Editorial Unit.

Disclosures

None.

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KEY WORDS: adverse drug event ■ all-cause death ■ amino acids ■ stroke

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Stroke. 2017;48:e245-e246; originally published online July 26, 2017;
doi: 10.1161/STROKEAHA.117.017841
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231

Print ISSN: 0039-2499. Online ISSN: 1524-4628