Cochrane Library

Cochrane Database of Systematic Reviews

Cerebrolysin for acute ischaemic stroke (Review)

Ziganshina LE, Abakumova T, Hoyle CHV

Ziganshina LE, Abakumova T, Hoyle CHV.
Cerebrolysin for acute ischaemic stroke.
Cochrane Database of Systematic Reviews 2020, Issue 7. Art. No.: CD007026.
DOI: 10.1002/14651858.CD007026.pub6.

www.cochranelibrary.com

WILEY

[Intervention Review]

Cerebrolysin for acute ischaemic stroke

Liliya Eugenevna Ziganshina[1,2], Tatyana Abakumova[3], Charles HV Hoyle[1,4]

[1]Cochrane Russia, Kazan, Russian Federation. [2]Department of Pharmacology, Kazan State Medical University, Kazan, Russian Federation. [3]Department of Biochemistry, Biotechnology and Pharmacology, Kazan (Volga region) Federal University, Kazan, Russian Federation. [4]Deputy Editor-in-Chief, Kazan Medical Journal, Kazan, Russian Federation

Contact address: Liliya Eugenevna Ziganshina, lezign@mail.ru, lezign@gmail.com.

Editorial group: Cochrane Stroke Group.
Publication status and date: Edited (no change to conclusions), published in Issue 9, 2020.

Citation: Ziganshina LE, Abakumova T, Hoyle CHV. Cerebrolysin for acute ischaemic stroke. *Cochrane Database of Systematic Reviews* 2020, Issue 7. Art. No.: CD007026. DOI: 10.1002/14651858.CD007026.pub6.

ABSTRACT

Background

Cerebrolysin is a mixture of low-molecular-weight peptides and amino acids derived from porcine brain that has potential neuroprotective properties. It is widely used in the treatment of acute ischaemic stroke in Russia, Eastern Europe, China, and other Asian and post-Soviet countries. This is an update of a review first published in 2010 and last updated in 2017.

Objectives

To assess the benefits and harms of Cerebrolysin for treating acute ischaemic stroke.

Search methods

We searched the Cochrane Stroke Group Trials Register, CENTRAL, MEDLINE, Embase, Web of Science Core Collection, with Science Citation Index, LILACS, OpenGrey, and a number of Russian databases in October 2019. We also searched reference lists, ongoing trials registers, and conference proceedings.

Selection criteria

Randomised controlled trials (RCTs) comparing Cerebrolysin, started within 48 hours of stroke onset and continued for any length of time, with placebo or no treatment in people with acute ischaemic stroke.

Data collection and analysis

Two review authors independently applied the inclusion criteria, assessed trial quality and risk of bias, extracted data, and applied GRADE criteria to the evidence.

Main results

Seven RCTs (1601 participants) met the inclusion criteria of the review.

In this update we re-evaluated risk of bias through identification, examination, and evaluation of study protocols and judged it to be low, unclear, or high across studies: unclear for all domains in one study, and unclear for selective outcome reporting across all studies; low for blinding of participants and personnel in four studies and unclear in the remaining three; low for blinding of outcome assessors in three studies and unclear in four studies. We judged risk of bias to be low in two studies and unclear in the remaining five studies for generation of allocation sequence; low in one study and unclear in six studies for allocation concealment; and low in one study, unclear in one study, and high in the remaining five studies for incomplete outcome data. The manufacturer of Cerebrolysin supported four multicentre studies, either totally, or by providing Cerebrolysin and placebo, randomisation codes, research grants, or statisticians. We judged three studies to be at high risk of other bias and the remaining four studies to be at unclear risk of other bias.

All-cause death: we extracted data from six trials (1517 participants). Cerebrolysin probably results in little to no difference in all-cause death: risk ratio (RR) 0.90, 95% confidence interval (CI) 0.61 to 1.32 (6 trials, 1517 participants, moderate-quality evidence).

None of the included trials reported on poor functional outcome defined as death or dependence at the end of the follow-up period or early death (within two weeks of stroke onset), or time to restoration of capacity for work and quality of life.

Only one trial clearly reported on the cause of death: cerebral infarct (four in the Cerebrolysin and two in the placebo group), heart failure (two in the Cerebrolysin and one in the placebo group), pulmonary embolism (two in the placebo group), and pneumonia (one in the placebo group).

Serious adverse events (SAEs): Cerebrolysin probably results in little to no difference in the total number of people with SAEs (RR 1.15, 95% CI 0.81 to 1.65, 4 RCTs, 1435 participants, moderate-quality evidence). This comprised fatal SAEs (RR 0.90, 95% CI 0.59 to 1.38) and an increase in the total number of people with non-fatal SAEs (RR 2.15, 95% CI 1.01 to 4.55, P = 0.047, 4 trials, 1435 participants, moderate-quality evidence). In the subgroup of dosing schedule 30 mL for 10 days (cumulative dose 300 mL), the increase was more prominent: RR 2.86, 95% CI 1.23 to 6.66, P = 0.01 (2 trials, 1189 participants).

Total number of people with adverse events: four trials reported on this outcome. Cerebrolysin may result in little to no difference in the total number of people with adverse events: RR 0.97, 95% CI 0.85 to 1.10, P = 0.90, 4 trials, 1435 participants, low-quality evidence.

Non-death attrition: evidence from six trials involving 1517 participants suggests that Cerebrolysin results in little to no difference in non-death attrition, with 96 out of 764 Cerebrolysin-treated participants and 117 out of 753 placebo-treated participants being lost to follow-up for reasons other than death (very low-quality evidence).

Authors' conclusions

Moderate-quality evidence indicates that Cerebrolysin probably has little or no beneficial effect on preventing all-cause death in acute ischaemic stroke, or on the total number of people with serious adverse events. Moderate-quality evidence also indicates a potential increase in non-fatal serious adverse events with Cerebrolysin use.

PLAIN LANGUAGE SUMMARY

Cerebrolysin for acute ischaemic stroke

What did we want to know?

In this Cochrane Review, we wanted to find out how well a medicine called Cerebrolysin works to treat a stroke.

What is a stroke?

A stroke is a sudden attack of weakness that usually affects one side of the body. It happens when the flow of blood to part of the brain is cut off, stopping the supply of oxygen and nutrients to the brain cells. If the supply of blood to the brain is stopped, brain cells begin to die. This can lead to brain injury, disability, and possibly death.

Ischaemic strokes are the most common type of stroke. An ischaemic stroke happens when the flow of blood is blocked by a blood clot or a piece of fatty material in an artery.

Why is this review important?

Strokes are a medical emergency, and urgent treatment is essential. Ischaemic strokes are usually treated with a combination of medicines to prevent and dissolve blood clots, reduce blood pressure, and lower cholesterol levels.

Cerebrolysin is a mixture of proteins purified from the brains of pigs. Some of the proteins in Cerebrolysin are found naturally in the human brain and may help to protect and repair brain cells. Cerebrolysin is commonly used in some countries as a treatment for stroke.

What did we do?

We searched for studies looking at the use of Cerebrolysin to treat acute ischaemic stroke. We searched for randomised controlled studies, in which the treatment people receive is randomly decided, because these studies give the most reliable evidence about treatments.

Search date: We included evidence published up to October 2019.

What we found

We found seven studies in 1601 people who had had an acute ischaemic stroke. The studies looked at the effect of giving Cerebrolysin alongside medicines to prevent and dissolve blood clots (standard therapy) during the first 48 hours after a stroke. The studies compared this treatment with standard therapy alone or standard therapy plus a dummy treatment (placebo).

The studies were conducted in hospitals in Austria, Croatia, the Czech Republic, Hungary, Russia, Slovakia, Slovenia, China, Hong Kong, Iran, Myanmar, and South Korea, and lasted from 28 days to 90 days.

Results of our review

Adding Cerebrolysin to standard therapy probably makes little or no difference to the risk of dying from any cause after a stroke (6 studies; 1517 people).

Cerebrolysin added to standard therapy probably made little or no difference to:
• the total number of people who had serious unwanted effects (life-threatening effects that could result in death, disability, or a longer hospital stay) (4 studies; 1435 people);
• the number of serious unwanted effects that caused death (3 studies; 1335 people).

However, more people given Cerebrolysin plus standard therapy had serious unwanted effects that did not kill them than those who were given standard therapy (alone or with placebo) (4 studies; 1435 people).

Cerebrolysin may make little or no difference to the total number of people who had any less serious unwanted effects (4 studies; 1435 people).

We are uncertain whether adding Cerebrolysin to standard therapy made any difference to the numbers of people who dropped out of studies (6 studies; 1517 people).

We did not find enough evidence about how Cerebrolysin affected:
• risk of dying or needing continuing care at the end of the study;
• risk of dying within two weeks of having a stroke;
• the time taken for people to be able to go back to work; or
• people's well-being (quality of life).

Our confidence in the results

We are moderately confident (certain) in the results of this review. However, the evidence comes from a small number of studies. Four studies involved a pharmaceutical company that makes Cerebrolysin, which may have affected how those studies were designed, carried out, and reported. Our conclusions are likely to change if results from further studies become available.

Conclusions

Adding Cerebrolysin to standard therapy after an ischaemic stroke probably:
• does not reduce the risk of dying;
• does not affect how many people have serious unwanted effects overall; but
• increases the number of serious, non-fatal unwanted effects.