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Cerebrolysin for acute ischaemic stroke

Ziganshina L., Abakumova T., Vernay L.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.Background: Cerebrolysin is a mixture of low-molecular-weight peptides and amino acids derived from pigs' brain tissue, which has potential neuroprotective and neurotrophic properties. It is widely used in the treatment of acute ischaemic stroke in Russia, Eastern Europe, China, and other Asian and post-Soviet countries. Objectives: To assess the benefits and risks of cerebrolysin for treating acute ischaemic stroke. Search methods: In May 2016 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. We also searched reference lists, ongoing trials registers and conference proceedings, and contacted the manufacturer of cerebrolysin, EVER Neuro Pharma GmbH (formerly Ebewe Pharma). Selection criteria: Randomised controlled trials (RCTs) comparing cerebrolysin, started within 48 hours of stroke onset and continued for any time, with placebo or no treatment in people with acute ischaemic stroke. Data collection and analysis: Two review authors independently applied inclusion criteria, assessed trial quality and risk of bias, and extracted data. Main results: We identified six RCTs (1501 participants) that met the inclusion criteria. We evaluated risk of bias and judged it to be unclear for generation of allocation sequence in four studies and low in two studies; unclear for allocation concealment in five studies and low in one study; high for incomplete outcome data (attrition bias) in five studies and unclear in one study; unclear for blinding; high for selective reporting in four studies and unclear in two; and high for other sources of bias in three studies and unclear in the rest. The manufacturer of cerebrolysin, pharmaceutical company EVER Neuro Pharma, supported three multi-centre studies, either totally, or providing cerebrolysin and placebo, randomisation codes, research grants, or statisticians. 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). All-cause death: we extracted data from five trials (1417 participants). There was no difference in the number of deaths: 46/714 in cerebrolysin group versus 47/703 in placebo group; risk ratio (RR) 0.91 95% confidence interval (CI) 0.61 to 1.35 (5 trials, 1417 participants, moderate-quality evidence). Serious adverse events: two trials reported on this outcome, with 90% confidence cerebrolysin increased the risks of serious adverse events by at least one third compared to placebo: 62/589 in cerebrolysin group versus 46/600 in placebo group; RR 1.37 90% CI 1.01 to 1.86 (2 trials, 1189 participants, moderate-quality evidence). Total number of people with adverse events: three trials reported on this. There was no difference in the total number of people with adverse events: 308/667 in cerebrolysin group versus 307/668 in placebo group; RR 0.97 95% CI 0.86 to 1.09, random-effects model (3 trials, 1335 participants, moderate-quality evidence). Authors' conclusions: The findings of this Cochrane Review do not demonstrate clinical benefits of cerebrolysin for treating acute ischaemic stroke. We found moderate-quality evidence suggesting that serious adverse events may be more common with

cerebrolysin use in acute ischaemic stroke.

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