Cerebrolysin

Cerebrolysin, a peptide preparation mimicking the action of neurotrophic factors, has beneficial effects on neurodegenerative diseases and brain injuries.

Human Studies

Poon et al. evaluated the safety and efficacy of Cerebrolysin as an add-on therapy to local standard treatment protocol in patients after moderate-to-severe traumatic brain injury.

The patients received the study medication in addition to standard care (50 mL of Cerebrolysin or physiological saline solution daily for 10 days, followed by two additional treatment cycles with 10 mL daily for 10 days) in a prospective, randomized, double-blind, placebo-controlled, parallel-group, multi-centre phase IIIb/IV trial. The primary endpoint was a multidimensional ensemble of 14 outcome scales pooled to be analyzed by means of the multivariate, correlation-sensitive Wei-Lachin procedure.

In 46 enrolled TBI patients (Cerebrolysin 22, placebo 24), three single outcomes showed stand-alone statistically significant superiority of Cerebrolysin [Stroop Word/Dots Interference ($p = 0.0415$, Mann-Whitney(MW) = 0.6816, 95% CI 0.51-0.86); Color Trails Tests 1 and 2 ($p = 0.0223/0.0170$, MW = 0.72/0.73, 95% CI 0.53-0.90/0.54-0.91), both effect sizes lying above the benchmark for “large” superiority ($MW > 0.71$)]. While for the primary multivariate ensemble, statistical significance was just missed in the intention-to-treat population ($pWei\text{-}Lachin < 0.1$, MWcombined = 0.63, 95% CI 0.48-0.77, derived standardized mean difference (SMD) 0.45, 95% CI -0.07 to 1.04, derived OR 2.1, 95% CI 0.89-5.95), the per-protocol analysis showed a statistical significant superiority of Cerebrolysin ($pWei\text{-}Lachin = 0.0240$, MWcombined = 0.69, 95% CI 0.53 to 0.85, derived SMD 0.69, 95% CI 0.09 to 1.47, derived OR 3.2, 95% CI 1.16 to 12.8), with effect sizes of six single outcomes lying above the benchmark for “large” superiority. Safety aspects were comparable to placebo.

This trial suggests beneficial effects of Cerebrolysin on outcome after TBI. Results should be confirmed by a larger RCT with a comparable multidimensional approach [1].

A retrospective cohort study being performed during a 2-year period in a level I trauma center in Southern Iran including all the adult patients (>16years) with severe disability (GOS of 2 and 3) 1-month after trauma.

They excluded those with posttraumatic seizures and those with meningitis or current infections. Some patients received cerebrolysin (n=65) and some did not (n=64). Cerebrolysin was administered intravenously in 10mL dosage daily for 30days. Patients in two study groups were matched regarding the baseline characteristics including age, gender, GCS on admission, pupil reactivity and Rotterdam score. The administered cerebrolysin dosage was 10mL intravenously daily for 30days. The 3- and 6-month Glasgow Outcome Scale Extended (GOSE) was recorded. The outcome scales were compared between two study groups.

Overall we included 129 patients with severe disability 1-month after TBI. The baseline characteristics were comparable between groups. We found that GOSE at 3-month ($p=0.017$) and 6-month ($p=0.009$) was significantly higher in those receiving cerebrolysin. Cerebrolysin administration was associated

with lower mortality rate, and higher good recovery after 6 month of therapy (p=0.024). Cerebrolysin administration was also associated with higher favorable and lower unfavorable outcome (p=0.043). Cerebrolysin was associated with higher seizure rate (p=0.042).

Cerebrolysin administration in patients with severe disability after TBI is associated with improved functional recovery, decreased mortality rate and increased favorable outcome. Seizure is important side effect of cerebrolysin administration in TBI patients [2].

Animal Studies

A study investigated the long-term effects of Cerebrolysin treatment on cognitive function in rats after mTBI.

Rats subjected to closed-head mTBI were treated with saline (n = 11) or Cerebrolysin (2.5 ml/kg, n = 11) starting 24 hours after injury and then daily for 28 days. Sham animals underwent surgery without injury (n = 8). To evaluate cognitive function, the modified Morris water maze (MWM) test and a social odor-based novelty recognition task were performed after mTBI. All rats were killed on Day 90 after mTBI, and brain sections were immunostained for histological analyses of amyloid precursor protein (APP), astrogliosis, neuroblasts, and neurogenesis.

Mild TBI caused long-lasting cognitive memory deficits in the MWM and social odor recognition tests up to 90 days after injury. Compared with saline treatment, Cerebrolysin treatment significantly improved both long-term spatial learning and memory in the MWM test and nonspatial recognition memory in the social odor recognition task up to 90 days after mTBI ($p < 0.05$). Cerebrolysin significantly increased the number of neuroblasts and promoted neurogenesis in the dentate gyrus, and it reduced APP levels and astrogliosis in the corpus callosum, cortex, dentate gyrus, CA1, and CA3 regions ($p < 0.05$).

These results indicate that Cerebrolysin treatment of mTBI improves long-term cognitive function, and this improvement may be partially related to decreased brain APP accumulation and astrogliosis as well as increased neuroblasts and neurogenesis [3].

1)
Poon W, Matula C, Vos PE, Muresanu DF, von Steinbüchel N, von Wild K, Hömberg V, Wang E, Lee TMC, Strilciuc S, Vester JC. Safety and efficacy of Cerebrolysin in acute brain injury and neurorecovery: CAPTAIN I-a randomized, placebo-controlled, double-blind, Asian-Pacific trial. Neurol Sci. 2019 Sep 7. doi: 10.1007/s10072-019-04053-5. [Epub ahead of print] Erratum in: Neurol Sci. 2020 Jan 6;:. PubMed PMID: 31494820.
2)
Khalili H, Niakan A, Ghaffarpasand F. Effects of cerebrolysin on functional recovery in patients with severe disability after traumatic brain injury: A historical cohort study. Clin Neurol Neurosurg. 2016 Nov 15;152:34-38. doi: 10.1016/j.clineuro.2016.11.011. [Epub ahead of print] PubMed PMID: 27871029.
3)
Zhang Y, Chopp M, Meng Y, Zhang ZG, Doppler E, Winter S, Schallert T, Mahmood A, Xiong Y. Cerebrolysin improves cognitive performance in rats after mild traumatic brain injury. J Neurosurg. 2015 Jan 23:1-13. [Epub ahead of print] PubMed PMID: 25614944.