Effects of Cerebrolysin on motor recovery in patients with severe motor impairment after stroke
Yun-Hee Kim, Deog Young Kim*, Yong-II Shin**, Myoung-Hwan Ko***, Won Hyuk Chang, Ahee Lee

Department of Physical and Rehabilitation Medicine, Center for Prevention and Rehabilitation, Heart Vascular and Stroke Institute, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul; **Department of Research Institute of Rehabilitation Medicine, Yonsei University College of Medicine, Seoul; ***Department of Rehabilitation Medicine, Pusan National University School of Medicine, Busan; **Department of Physical and Rehabilitation Medicine, Research Institute of Clinical Medicine of Chonbuk National University, Biomedical Research Institute of Chonbuk National Hospital, Jeonju, Korea

Poster presented during The European Stroke Organisation Conference 2015 in Glasgow, UK

Introduction
The aim of this study was to evaluate whether Cerebrolysin provides additional motor recovery in a group of rehabilitation therapy in the subacute stroke patients with moderate to severe motor impairment. The phase II trial was designed as a prospective, multicenter, randomized, double-blind, placebo-controlled, parallel-group study. The primary end point was the changes in Fugl-Meyer Assessment (FMA) scores (FMA-T, FMA-UL, and FMA-LL) at 3 weeks of treatment. Motor function at 3 months after stroke was also assessed. The secondary end point was the changes in diffusion tensor imaging (DTI) and with resting state functional magnetic resonance imaging (rsfMRI).

Methods
SUBJECTS
Induction criteria: the first cerebrovascular infarction at central or subcentral region (anterior, supra-sensory), confirmed by CT or MRI in patients, recruited at 7 days after stroke onset with moderate to severe motor function involvement – total of FMA-AT 44 and age between 18 and 80 years; (2) Inclusion criteria: severe subacute stroke patients with hemiparesis were included in this study from four centers in South Korea.

Written informed consent was obtained from all participants prior to inclusion in the study, and the study protocol was approved by the institutional review board.

EXPERIMENTAL DESIGN
A Phase II, prospective, multicenter, randomized, double-blind, placebo-controlled, parallel-group study.

Patients were randomized to receive a 21-day treatment course (Days 8-28) of either Cerebrolysin or placebo, given in addition to standard rehabilitation therapy. Assessments were performed at baseline, immediately after treatment, and 3 months after stroke onset.

Fugl Meyer assessment scores were used as primary endpoints, DTI and rsfMRI were obtained for neuropsychiatric assessment.

CHANGES OF MOTOR FUNCTION IN ALL PARTICIPANTS WITH A ITT DATA SET

In the ITT subgroup analysis of patients with severe motor impairment on T0 (n=37; Cerebrolysin n=20, placebo n=17; FMA-T at baseline <50), repeated measures ANOVA showed a significant interaction effect between time and type of intervention as measured by FMA scores (FMA-T, FMA-UL, and FMA-LL) at T3 between the groups. The improvement of FMA-T and FMA-UL tended to be higher in the Cerebrolysin group than in the control group, but without statistical significance.

Rehabilitation: 3 hours (NDT: 1 hour, Special PTx: 1 hour, OTx: 1 hour)/day (5 times/week for 21 days)

Test protocol, dose and mode of administration:
- Group 1: Cerebrolysin - 30 ml injection/day × 21 days with rehabilitation
- Group 2: Placebo (0.9% NaCl) 100 ml/day × 21 days with rehabilitation

Rehabilitation: 3 hours (NDT: 1 hour, Special PTx: 1 hour, OTx: 1 hour) /day (5 times/week for 3 weeks)

CHANGES OF DTI AND rsfMRI IN PATIENTS WITH SEVERE MOTOR IMPAIRMENT

In the ITT subgroup analysis of patients with severe motor impairment (T0; motor impairment (FMA<50) at baseline), T2 (1st follow-up, 2 months after stroke onset), and T3 (2nd follow-up, 3 months after stroke onset), it was found that Cerebrolysin treated patients showed significant improvement compared with placebo treated patients.

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Conclusions
The combination of standard rehabilitation therapy with Cerebrolysin treatment in the subacute stroke stage has shown additional benefit on motor recovery and plastic changes of the corticospinal tract in patients with severe motor impairment.

Cerebrolysin treatment as add-on to a rehabilitation program might be considered as a pharmacologic approach for motor recovery in ischemic stroke patients with severe motor impairment involvement at the subacute stage.

Related references

Supported by DAEI Novo Pharma GmbH and the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIP) (NRF-2016R1C1B1005132).

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