Effects of Cerebrolysin® on Consciousness Level in Post-Stroke Minimally Conscious State(MCS)

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Introduction
The Porcine brain peptide(Cerebrolysin®) is composed of low molecular weight peptides and amino acids and has been shown to have potentially neuroprotective and neurotrophic properties. Cerebrolysin® has been reported to promote recovery of motor function in central nervous system disorders. However, the changes of cognitive function after Cerebrolysin® administration did not have been studied. Therefore, we aimed to examine the feasibility of Cerebrolysin® for the consciousness level in severe post-stroke patients with minimal conscious state through this retrospective study.

Method
75 patients with ischemic or hemorrhagic stroke who were admitted to Department of Rehabilitation Medicine from 2014 to 2017 were included in this retrospective study. They all met MCS criteria using JFK Coma recovery scale-Revised scores(CRS-R). The patients who missed CRS-R scores on admission and/or discharge or diagnosed as other brain disorders such as TBI(Traumatic Brain Injury) or HBI(Hypoxic Brain Injury) and etc. were excluded from this study (Fig. 1). All the medical records of a total 75 patients were reviewed. Among the 75 patients, 43 patients received Cerebrolysin® and the remaining 32 patients did not. In Cerebrolysin group, Cerebrolysin® was administered at a daily dosage of 10 ml for at least 20 days as an intravenous injection. Compared with Cerebrolysin group, control group received the same comprehensive rehabilitation treatment including physical therapy, occupational therapy except for only Cerebrolysin®. The CRS-R scores were assessed on admission and discharge. The difference of outcomes between two groups were compared by repeated measures ANOVA(Analysis of variance).

Result
The statistically significant differences were not found in baseline characteristics including age, sex, etiology of stroke, side of lesion, length of hospital stay, duration from onset and recurrence between two groups (Table 1). Compared with control group, Cerebrolysin group showed the significant improvements in CRS-R total scores (p=0.011), especially in oromotor (p=0.005) and arousal subscales (Fig. 2, Table 2), (p=0.038). However, the difference in CRS-R scores was not statistically significant depending on concomitant administration of other central nervous system(CNS) acting agents (p>0.05). Cerebrolysin® was safe and well tolerated.

Conclusion

This retrospective study suggested the possibility that intravenous administration of Cerebrolysin® in post-stroke patients with MCS may improve the consciousness levels of them. a well-designed double-blind placebo randomized controlled trial with Cerebrolysin® will be needed in future.

Table 1. Baseline characteristics of subjects.

	Cerebrolysin® (n=43, 58.1%)	Control (n=32, 41.9%)	p value
Age (years)	69.0±15.4	68.7±14.5	0.940
Sex (M/F)	23/20	22/10	0.236
Etiology (Hemorrhage/Infarction/Both)	18/22/3	8/23/1	0.205
Side of lesion (Rt./Lt./Bilateral)	2/24/17	3/10/19	0.090
Length of hospital stay (days)	50.1±13.7	64.0±45.0	0.776
Duration from onset (months)	2.9±2.7	4.8±5.7	0.160
Recurrence (1st /Recurrent onset)	34/9	25/7	1.000

Continuous variables are expressed as mean ± standard deviation.

Table 2. Comparison of JFK-CRS revised scores on admission and at discharge between Cerebrolysin® and control group.

JFK-CRS revised	Cerebrolysin® (n=43, 58.1%)		Control (n=32, 41.9%)		p value
	Admission	Discharge	Admission	Discharge	
Total	13.1±3.9	17.3±4.0	14.4±3.2	16.7±4.2	0.011*
Subscores					
Auditory	2.2±0.8	2.9±1.0	2.5±1.0	2.9±1.0	0.116
Visual	2.8±1.1	3.9±0.9	3.2±1.0	3.8±1.1	0.061
Motor	4.0±1.5	4.9±1.2	4.0±1.5	4.6±1.6	0.300
Oromotor	1.5±0.6	2.1±0.8	1.8±0.6	2.0±0.7	0.005*
Communication	0.5±0.5	1.0±0.7	0.7±0.5	1.0±0.6	0.351
Arousal	2.1±0.7	2.5±0.6	2.3±0.5	2.4±0.5	0.038*

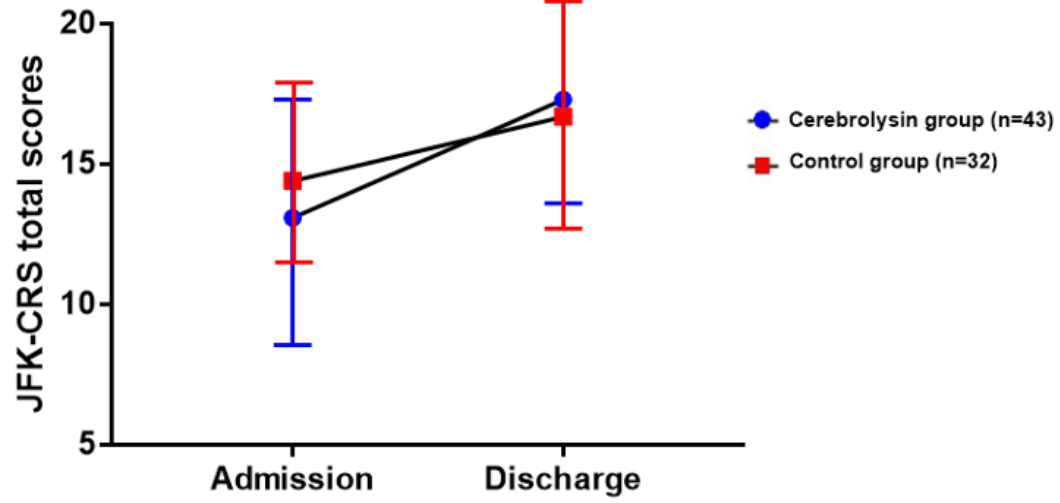The variables are expressed as mean ± standard deviation. * $p<0.05$

Figure 1. Changes of JFK-CRS scores in both groups from admission to discharge.