뇌신경재활
발표일시 및 장소 : **10 월 27 일(토) 14:10-14:20 Room C(5F)**

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The effect of cerebrolysin on disorders of consciousness due to acquired brain injury

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Introduction
Acquired brain injury (ABI) can cause disorders of consciousness (DOC), which is clinically very difficult to treat. While a variety of studies including clinical trial of medication have been conducted to improve cognition of patients with DOC, the effect of cerebrolysin on DOC has not been studied systematically. Therefore, in the present study, we investigated the efficacy of cerebrolysin on DOC.

Methods
This study is a retrospective study. Patients were recruited from department of rehabilitation center of university hospital between January 1, 2013 to November 30, 2017. The patients were divided into two groups (single therapy group (Amantadine) and dual therapy group (Cerebrolysin and Amantadine). Amantadine was administered orally twice a day with 100 mg in single and dual therapy group. Cerebrolysin was administered via intravenous route twice a day (10 mL per administration) in dual therapy group. The Coma Recovery Scale - Revised (CRS-R) assessment was conducted twice to evaluate consciousness state; the first before drug administration and the second within 3 days before drug discontinuation.

Results
A total of 101 enrolled patients were recruited. The average age was 61.46 years. And we enrolled 43 females. The enrolled patients consisted of 42 with hemorrhagic stroke, 28 with ischemic stroke, 21 with traumatic brain injury (TBI), 6 with hypoxic brain injury, one with encephalitis, and 3 with unspecified injury. The initial total score of CRS-R was 11.20, and the interval between onset of disease and treatment was 6.45 months. According to the CRS-R assessment, 22 patients were diagnosed in coma or vegetative state and 79 in minimally conscious state (MCS). There was a significant difference in age (single therapy group: 66.64 ± 14.99, dual therapy group: 56.37 ± 17.86, P=0.004), category of disease (P=0.016), initial total scores of CRS-R (single therapy group: 13.56 ± 4.45, dual therapy group: 8.88 ± 3.85, P<0.001), and category of DOC (P<0.001) in both groups. After

treatment, the change of CRS-R score tended to be higher in dual therapy group than single therapy group without significance (single therapy group; 2.46 ± 3.29, dual therapy group: 3.69 ± 3.30, P=0.056). The change in the patient's DOC category occurred after treatment. There were significant differences in the change of the DOC category (P=0.034) in both groups. In the comparison of responsiveness, the proportion of patients who received the drug before 6 months from onset or patients with TBI was higher in the subgroup responding to dual therapies, although not statistically significant.

Conclusions

The ratio of patients with change of DOC in dual therapy group was higher than single therapy group, with a significant difference. In dual therapy group, change of CRS tends to be higher than single therapy group. And the patients who started treatment earlier or with TBI tended to have better responsiveness in dual therapy group.

Table1. Characteristics of patients

Characteristics	Total (n=101)	Amantadine (n=50)	Cerebrolysin + Amantadine (n=51)	p-value
Age (years) [range]	61.46 ± 17.21 [21 - 92]	66.64 ± 14.99 [23 – 92]	56.37 ± 17.86 [21 – 88]	**0.004****
Sex (M / F) [n (%)]	58 / 43 (57.43% / 42.57%)	27 / 23 (54.00% / 46.00%)	31 / 20 (60.78% / 39.22%)	0.625
Category of disease [n] (Hemorrhagic stroke / Ischemic stroke) / Traumatic brain injury / Hypoxic brain injury / Encephalitis / Unspecified (including metabolic encephalopathy))	42 / 28 / 21 / 6 / 1 / 3	21 / 19 / 5 / 2 / 0 / 3	21 / 9 / 16 / 4 / 1 / 0	**0.016***
Interval between onset of disease and treatment (months)	6.45 ± 5.72 [1 - 39]	6.18 ± 6.38 [1 - 39]	6.71 ± 5.03 [2 - 26]	0.227
Initial CRS [range]	11.20 ± 4.75 [3 - 21]	13.56 ± 4.45 [6 - 21]	8.88 ± 3.85 [3 - 20]	**<0.001*****
Category of initial DOC [n (%)] (coma or vegetative / MCS / emergence from MCS)	22 / 79 / 0	6 / 44 / 0	16 / 35 / 0	**0.034***
Duration of treatment (days) [range]	32.52 ± 24.79 [6 - 211]	34.46 ± 32.25 [6 – 211]	30.63 ± 14.22 [8 - 109]	0.724
Cerebrolysin			27.04 ± 9.67 [8 - 64]	
Amantadine		34.46 ± 32.25 [6 – 211]	29.45 ± 15.03 [7 – 109]	
Concurrent (Cerebrolysin + Amantadine)			27.37 ± 13.98 [6 – 93]	
Follow-up CRS [range]	14.28 ± 4.87 [5 - 23]	16.02 ± 4.44 [5 - 23]	12.57 ± 4.70 [5 - 23]	**<0.001*****
Change of CRS [range]	3.08 ± 3.34 [-7 - 13]	2.46 ± 3.29 [-7 - 12]	3.69 ± 3.30 [-3 - 13]	0.056

Table2. Change of DOC

Characteristics	Total (n=101)	Amantadine (n=50)	Cerebrolysin + Amantadine (n=51)	p-value
Initial CRS [range]	11.20 ± 4.75 [3 - 21]	13.56 ± 4.45 [6 - 21]	8.88 ± 3.85 [3 - 20]	**<0.001*****
Category of DOC – initial [n (%)] (coma or vegetative / MCS / emergence from MCS)	22 / 79 / 0	6 / 44 / 0	16 / 35 / 0	**0.034***
Follow-up CRS [range]	14.28 ± 4.87 [5 - 23]	16.02 ± 4.44 [5 - 23]	12.57 ± 4.70 [5 - 23]	**<0.001*****
Category of DOC – follow-up [n (%)] (coma or vegetative state / MCS / emergence from MCS)	7 / 94 / 0	3 / 47 / 0	4 / 47 / 0	1.000
Change of CRS [range]	3.08 ± 3.34 [-7 - 13]	2.46 ± 3.29 [-7 - 12]	3.69 ± 3.30 [-3 - 13]	0.056
Patients with change of DOC category – total [n (%)]	15 / 86 (14.85% / 85.15%)	3 / 47 (6.00% / 94.00%)	12 / 39 (23.53% / 76.47%)	**0.028***
Patients with change of DOC category [n (%)] (from coma or vegetative state to MCS)	15 / 7 (68.18% / 31.82%)	3 / 3 (50.00% / 50.00%)	12 / 4 (75.00% / 25.00%)	0.544

Table 3. Comparison of responsiveness for patients of coma or vegetative state in dual therapy

Characteristics	Total (n=16)	Patients with no change of DOC category (n=4)	Patients with change of DOC category (n=12)	p-value
Age (years) [range]	61.50 ± 14.87 [24 – 82]	55.75 ± 23.89 [24 – 82]	63.42 ± 11.39 [46 – 79]	0.574
Sex (M / F) [n (%)]	9 / 7 (56.25% / 43.75%)	2 / 2 (50.00% / 50.00%)	7 / 5 (58.33% / 41.67%)	1.000
Category of disease [n] (Hemorrhagic stroke / Ischemic stroke) / Traumatic brain injury / Hypoxic brain injury / Encephalitis / Unspecified (including metabolic encephalopathy))	6 / 1 / 7 / 2 / 0 / 0	2 / 1 / 1 / 0 / 0 / 0	4 / 0 / 6 / 2 / 0 / 0	0.229
Interval between onset of disease and treatment (months)	6.94 ± 4.96 [2 - 19]	10.00 ± 2.83 [6 - 12]	5.92 ± 5.18 [2 - 19]	0.075
Initial CRS [range]	5.25 ± 1.13 [3 - 7]	5.25 ± 1.71 [3 - 7]	5.25 ± 0.97 [4 - 7]	0.845
Duration of treatment (days) [range]	28.50 ± 11.9 [8 - 64]	29.25 ± 5.44 [25 - 37]	28.25 ± 13.59 [8 - 64]	0.951
Cerebrolysin	27.62 ± 11.78 [8 - 64]	26.25 ± 4.11 [21 - 30]	28.08 ± 13.55 [8 - 64]	0.952
Amantadine	27.88 ± 12.07 [8 – 64]	29.25 ± 5.44 [25 – 37]	27.42 ± 13.77 [8 –64]	0.584
Concurrent (Cerebrolysin + Amantadine)	27.00 ± 11.90 [8 – 64]	26.25 ± 4.11 [21 – 30]	27.25 ± 13.72 [8 – 64]	0.903
Follow-up CRS [range]	9.69 ± 3.32 [5 - 17]	6.25 ± 0.96 [5 - 7]	10.83 ± 3.01 [6 - 17]	**<0.001*** **