Cerebrolysin enhances cognitive recovery of mild traumatic brain injury patients: double-blind, placebo-controlled, randomized study

Chun-Chung Chen[1,2], Sung-Tai Wei[1], Shiu-Chiu Tsaia[1], Xian-Xiu Chen[3] and Der-Yang Cho[1,2]

[1]Department of Neurosurgery, China Medical University Hospital, Taichung, Taiwan; [2]College of Medicine, China Medical University, Taichung, Taiwan, and [3]Institute of Public Health, China Medical University, Taichung, Taiwan

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Introduction

Around 80% of the TBI are mild, and in adults, mild traumatic brain injury (MTBI) frequently results in impairments of cognitive functions. All these would lead to problems with learning, social adaptation and unfavorable social consequences in the nearest or more remote future. The aim of the study was to determine the efficacy and safety of Cerebrolysin in patients with MTBI who had abnormal image (intracranial contusion haemorrhage) while admission.

Methods

All patients were screened within 24 h after the onset of TBI. Patients were recruited if they: 1) were adults between 30 and 70 years; 2) had head injury within 24 h; 3) alert and conscious; 4) had intracranial contusion haemorrhage and did not need to received craniotomy; 5) only isolated head injury, no other body injury; 6) were able to offer written informed consent. Patients would be excluded if they presented status epilepticus and/or Grand mal; took full-dose or long-term anticoagulation therapy; coexisted systemic diseases such as terminal cancer, renal failure, cirrhosis, severe dementia or psychosis; participated in some other clinical trial within 3 months; and were alert and conscious but without intracranial haemorrhage (brain contusion). According to a balanced randomization, patients were randomized to receive Cerebrolysin (Group A, once daily intravenous infusion of 30 mL Cerebrolysin over a 60-min period for 5 days) or placebo (Group B, same dosage and administration of normal saline as Group A) treatments. The primary outcome measures were the differences in patients' scores on several clinical scales, between baselines and week 1 (7 ± 2 days), week 4 (28 ± 4 days), and between baseline and week 12 (84 ± 10 days). The scales we used were the measurement of cognition function including Mini-Mental Status Examination (MMSE) and Cognitive Abilities Screening Instrument (CASI). The scores of MMSE and CASI were assessed by an experienced research nurse.

Results

Thirty-two patients were recruited in this study. The baseline characteristics of Group A and Group B patients regarding gender, age and length of hospital stay were similar. A total of 32 patients completed the trial, 17 patients in Group A and 15 patients in Group B. The preliminary results demonstrated that the mean age of patient population was 44.8 ± 16.36 years (range, 30 – 75 years), length of hospital stay was 7.5 ± 2.1 days (5 –10 days), and the demographic characteristics of the patients in each group were not significantly different (Table 1).

Table. 1. Demographic and clinical data

	Total (n=32)	Placebo (n=15)	Cerebrolysin (n=17)	P value
Age	**44.8 ± 16.36**	**42.3 ± 14.05**	**47.1 ± 18.29**	**0.4238**
Gender				
Female	11 (0.34%)	5 (33.33%)	6 (35.29%)	
Male	21 (0.66%)	10 (66.67%)	11 (64.71%)	
Length of hospital stay	7.5 ± 2.1	7.1 ± 1.9	7.9 ± 2.3	0.9571

Primary outcome measures

The CASI scores at baseline were similar in the two groups, that is, 65.3 ± 27.2 for Group A and 75.1 ± 11.1 for Group B (p=0.1861; Table 2). The difference in CASI scores between baseline and week 12 was significantly greater in Group A than in Group B (21.0 ± 20.4 and 7.6 ± 12.1, respectively; p=0.0461) (Table 3; Fig 2. J,K).

Table. 2. Result of cognition test and comparison between Cerebrolysin-treated and placebo groups

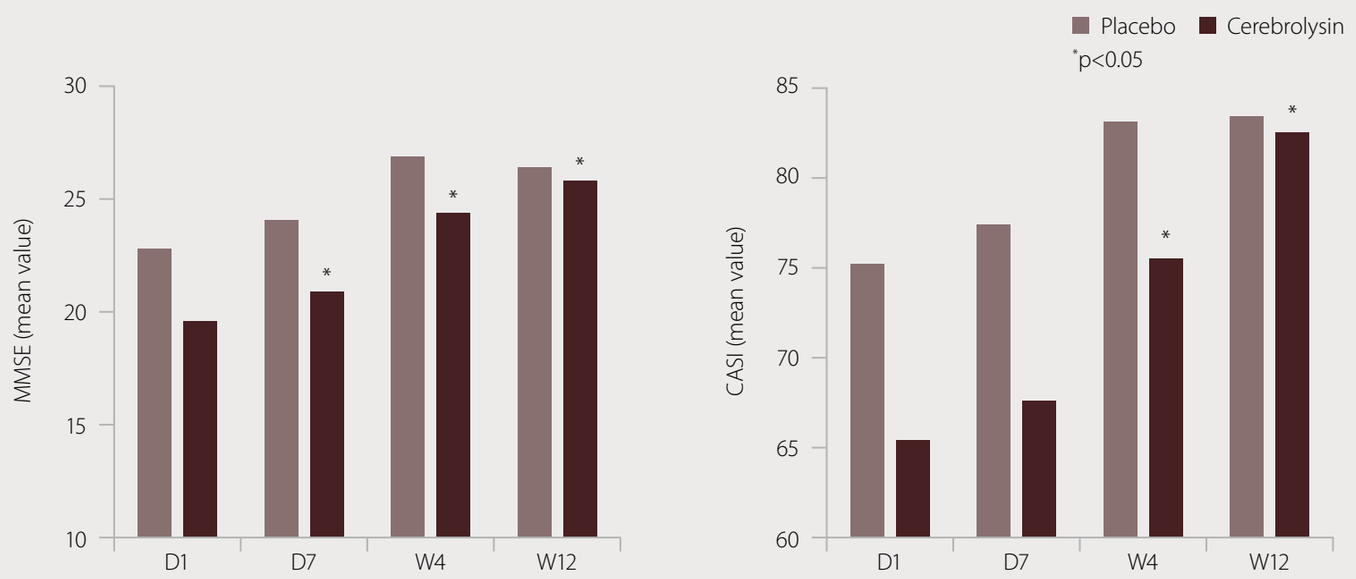
	Placebo mean ± SD	Cerebrolysin mean ± SD	P value
MMSE			
D1	22.8 ± 2.5	19.6 ± 8.3	0.1431
D7	24.1 ± 3.3	20.9 ± 8.8	0.2168
W4	26.9 ± 1.3	24.4 ± 5.6	0.1237
W12	26.4 ± 3.0	25.8 ± 3.6	0.6513
CASI			
D1	75.1 ± 11.1	65.3 ± 27.2	0.1861
D7	77.4 ± 9.7	67.6 ± 29.6	0.2532
W4	83.1 ± 5.5	75.6 ± 20.2	0.2034
W12	83.4 ± 6.9	82.5 ± 11.6	0.8089

Table. 3. The result of the cognition function difference between baseline (first day) after 7 days and 4 weeks and 12 weeks

	Placebo mean ± SD	Cerebrolysin mean ± SD	P value
MMSE			
D7-D1	1.2 ± 2.8	1.9 ± 2.7	0.5431
W4	4.1 ± 2.5	5.4 ± 4.3	0.3494
W12	3.5 ± 3.8	6.8 ± 6.5	0.111
CASI			
D7	1.6 ± 6.8	5.2 ± 8.9	0.2361
W4	7.9 ± 11.6	13.3 ± 14.5	0.2809
W12	7.6 ± 12.1	21.0 ± 20.4	0.0461

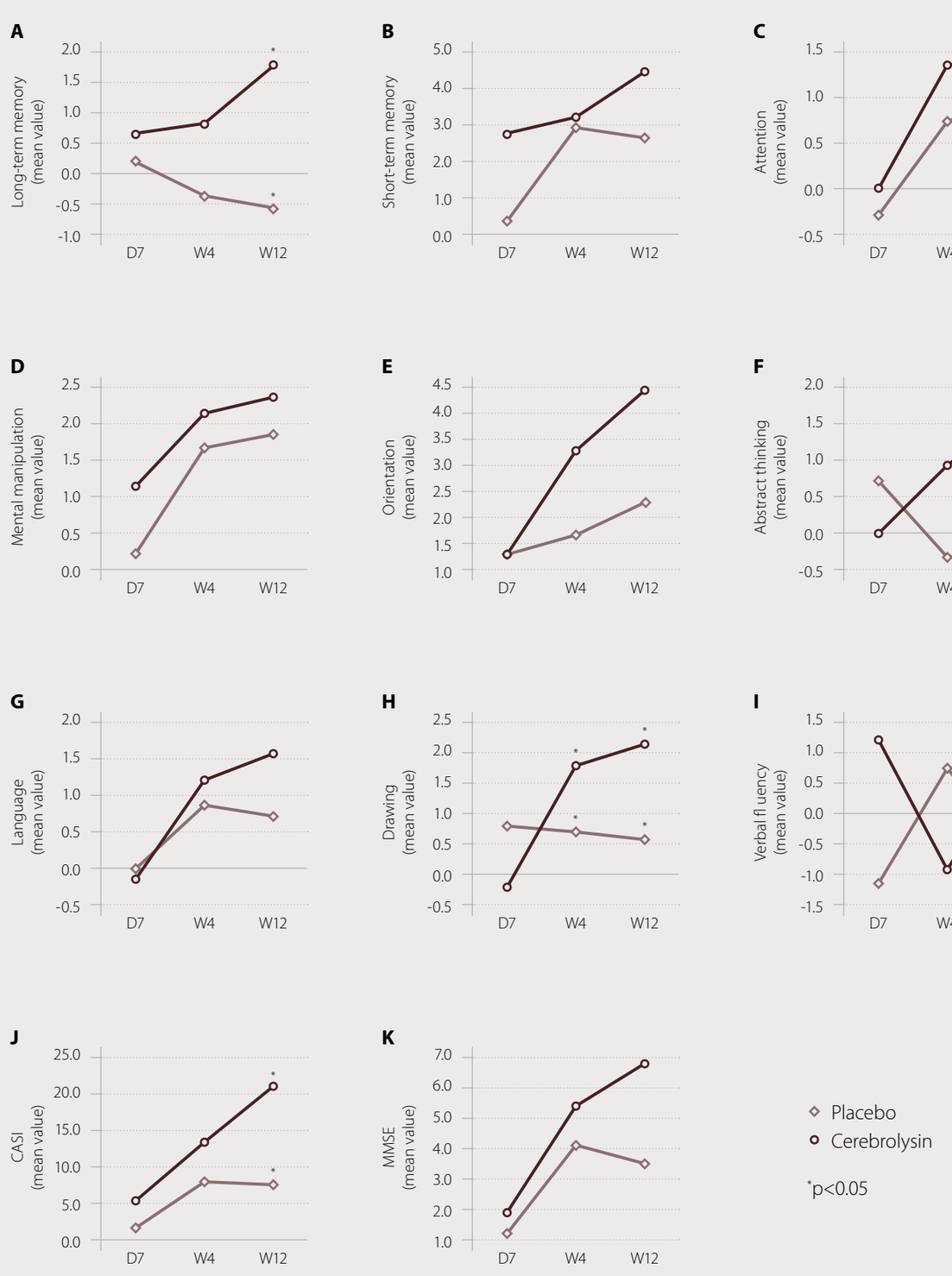
Figure 1 shows the comparison of the cognition function difference between the baseline and other check points. There were significant differences in MMSE test while we compared the D7, W4, and W12 with the baseline (D1) in the Cerebrolysin – treated group, p=0.024, p<0.001 and p=0.001, respectively. And while we compared the W4 and W12 with the baseline in the Cerebrolysin – treated group, p=0.005 and p=0.003, respectively, in CASI test.

Fig. 1. The comparison of the cognition function difference between the baseline and other check points within treatment groups



The findings shown in Figure 2 indicate that Group A achieved significantly greater score changes than did Group B in several CASI domains. Group A achieved a significantly greater difference than Group B for the subscale 'drawing', between baseline and week 4 (p=0.0066), and between baseline and week 12 (p=0.0472). Group A also achieved a significantly greater difference than Group B for the subscale 'long-term memory', between baseline and week 12 (p=0.0256). The score differences for other subscales are summarized in Figure 2. No statistically significant difference was found between the two groups' CASI subscales scores, at baseline, for the following subscales: attention, orientation, short-term memory, language abilities, verbal fluency, abstract thinking and mental manipulation (Fig. 2).

Fig. 2. The result of the CASI domains difference between baseline (first day) after 7 days and 4 weeks and 12 weeks



Conclusions

Our results indicated that Cerebrolysin therapy started within 24 h after the onset of MTBI with intracranial contusion haemorrhage can improve patients' CASI scores; this finding suggests that Cerebrolysin may enhance cognitive recovery after MTBI. We believe that MTBI with intracranial contusion haemorrhage patients can benefit from supplementary treatment with Cerebrolysin in addition to the usual medical treatment for this condition.

Related references

1. Original article: BR J NEUROSURG. 2013 DEC;27(6):803-7