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Beneficial effect of cerebrolysin on moderate and severe head injury patients: result of a cohort study

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Summary

Cerebrolysin is used as a neurotrophic agent for the treatment of ischemic stroke and Alzheimer's Disease. Exploratory studies in patients with post-acute traumatic brain injury have shown that this treatment might help improve recovery. Aim of this study was to investigate whether addition of Cerebrolysin to the initial treatment regimen of moderate and severe head injury patients would improve their outcome.

At 6 months, 67% of the patients (Cerebrolysin group) attained good outcome (GOS 3–5). The study group was compared with the historical cohort of patients from the hospital trauma data bank, with age, sex and admitting GCS matching. More patients tended to a good outcome in the Cerebrolysin group ($P = 0.065$). No significant side-effect requiring cessation of Cerebrolysin was noted.

It can be concluded that the use of Cerebrolysin as part of the initial management of moderate and severe head injury is safe and well tolerated. The results suggest that Cerebrolysin is beneficial in regard to the outcome in these patients, especially in elderly patients.

Keywords: Cerebrolysin; traumatic brain injury; clinical outcome.

Introduction

Traumatic brain injury is an important cause of morbidity and a costly disorder [5, 7, 12]. It also represents the most frequent reason for neurological illness after headache. Compared with other types of brain insult, traumatic brain injury produces more diffuse injury and more cognitive and neuropsychiatric disturbances [10]. Various drugs have been used in an attempt to improve the outcome of these patients.

Cerebrolysin is a peptide preparation produced by the biotechnologically standardized enzymatic breakdown of purified porcine brain proteins. It consists of approximately 15% peptides with a molecular weight not exceeding 10 kD and 85% amino acids, based on total nitrogen. The solution is free of proteins, lipids and antigenic properties.

The action mechanism is not clearly understood. It has been shown in animal studies to improve neuronal oxygen utilization, reduce cerebral lactic acid concentration and decreases free oxygen radical concentration. Cerebrolysin has produced significant improvement in cognitive function, non-cognitive psychiatric symptoms and daily activities in patients with Alzheimer's Disease and stroke [2, 8, 11].

In this study, we hypothesize that Cerebrolysin infusion during the acute phase of moderate and severe head injury improves functional outcome of patients [1], and second, our aim was to document its safety profile in these patients.

Patients and methods

Starting in March 2001, patients aged 18 years or above, with moderate or severe head injury within 48 hours prior to admission were recruited. Exclusion criteria included severe renal, liver, lung or cardiovascular disease, poor mental state due to drug or alcohol abuse, concomitant stroke, pregnancy or lactation, life-threatening multiple trauma, signs of brain stem failure, status epilepticus and grand mal fits. The study conformed to the Helsinki declaration. Written consent was obtained from suitable patients and their surrogate/guardian by one of the investigators.

All recruited patients received 50 ml Cerebrolysin through intravenous infusion over 15-minute-periods daily for 20 days. Data on age, sex, admission Glasgow Coma Score, hospital stay, 3-month Extended Glasgow Outcome Score and 6-month Extended Glasgow Outcome Score [3, 4] were prospectively collected.

Data were compared with a historical cohort of patients with moderate and severe head injury from the hospital trauma data bank. The historical control group was all matched by age, sex and admitting Glasgow Coma Score. Statistical analysis was carried out with SPSS for Window Release 10.

Results

Twenty one patients with moderate or severe head injury were recruited for this study between March

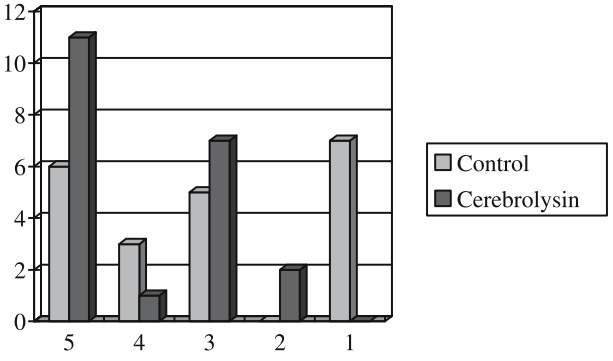

Fig. 1. Glasgow Outcome Score of the Crebrolysin group and cohort group. The X-axis represents the GOS and the Y-axis represents the number

2001 and March 2002. Mean age was 64 years, range from 28 to 82 years. The male to female ratio was 13 : 8. Results are charted in Fig. 1. At 6 months, 67% of patients had a good outcome as defined by Glasgow Outcome Score 3–5. They were compared with the historical cohort of patients from the trauma data bank of the same hospital. There was a trend of more patients with good outcome in the Cerebrolysin group ($P = 0.065$). No significant side-effects necessitating cessation of Cerebrolysin nor manifestation of allergy were noted.

Discussions

Previous studies have demonstrated that an important part of the recovery after traumatic brain injury occurs in the first six months after the injury [6, 7, 12]. A functional recovery is essential for the patient to return to society. Most of the moderate and severe head injury patients studied had cognitive and physical deficits, which hindered their eventual recovery [10].

The neurotrophic effects of Cerebrolysin are theoretically beneficial to traumatic brain injury patients, in particular when considering the cognitive function. With these data in mind, we performed this study to observe and record its clinical effect. The timing of Cerebrolysin treatment was designed to start within the first 48 hours and continue for 10 days to cover possible neuroprotective and neurotrophic effects. The results were encouraging with more patients attaining good outcome at six months in the Cerebrolysin group as compared to the historical control group.

No significant side effects were noted, as was also the case in the treatment of dementia patients [2, 8, 11]. The safety profile in head injury patients is confirmed with the current series.

The results suggest a beneficial effect of Cerebrolysin infusion in patients with moderate or severe head injury during the acute phase. It has also been shown in other studies to reduce EEG power ratio and enhance cognitive performance in tasks evaluating attention and memory functions [1]. This magnitude in terms of GOS improvement certainly is valuable to the patients and further studies to evaluate the role of Cerebrolysin in different neurological diseases are warranted.

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