Cerebrolysin in Steel: Richardson-Olszewski Syndrome

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Citation

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Abstract

Objectives: The authors investigated the effectiveness of Cerebrolysin, a neurotrophic factor, in 6 patients with Steel-Richardson-Olszwski (Progressive supranuclear palsy) also known by Opthalmo-facial-cervical dustonia. Methods: 6 patients (mean age 67.8 years) with progressive supranuclear palsy (PSP), mean duration of disease 3.8 years, were treated with Cerebrolysin 10 ml intravenous infusion on a daily basis for 20 days to be repeated every 2 months for a total of 6 months. Progressive supranuclear palsy rating scale and staging system (PSPRS) were assessed at baseline and after 6 months. Results: Five patients continued the study period; 5 patients showed modest improvement on (PSPRS) score. Side effect of Cerebrolysin was negligible. Conclusion: This study showed that Cerebrolysin has modest effect in the treatment and delaying progression in patients with PSP.

INTRODUCTION

Progressive Supranuclear Palsy (PSP) described by Steel – Richardson- Olszewski syndrome in 1964 (SROS) is a neurodegenerative disorder of unknown etiology. Pharmacological therapy has been disappointing [1,2].

PSP usually presents itself in the seventh decade with early postural instability, vertical supranuclear gaze palsy(affectinf chiefly vertical gaze), pseudobulbar palsy, dysarthria,dystonic rigidity of the neck and upper trunk, frontal subcortical dementia, and parkinsonism. Clinical symptoms started between 48 and 51 years of age with slow progression during 2 to 4 years. Many of the symptoms present in PSP do not respond to dopamine stimulation. The potential benefits of these compounds are restricted to akinesia and rigidity[3]. Also the effectiveness of dopamine agonist is similar3.

Cerebrolysin is a peptidergic solution containing free amino acids and biologically active peptides with proven neuroprotective and neurotrophic effect[4] . This drug has previously been used in the treatment of brain dementia4, Parkinson disease[5], and stroke[6].

METHODS

Six patients with PSP entered the open label study. Patients were recruited for the study during their routine outpatient visit to King Hussein Medical Center. All patients fulfilled the National Institute of Neurological Disorders and Stroke (NINDS) clinical criteria for the diagnosis of PSP. No levodopa or any dopamine agonist was allowed during the study period. Cerebrolysin was given 10 ml intravenous infusion on a daily basis for 20 days to be repeated every 2 months for a total of 6 months. Progressive supranuclear palsy rating scale and staging system were assessed at baseline and after 6 months.The Ethical committee of the King Hussein Medical Center approved this study.

RESULTS

One of the six patients died 2 months after starting treatment due to myocardial infarction. Five patients (mean age 67.8 years, mean duration of disease 3.8 years) continued on Cerebrolysin for 6 months. There was modest improvement in the Progressive supranuclear palsy rating scale and staging system as seen in table 1. There was slowing in progression in our treated group according to (PSPRS) score in 2 patients. The remaining 3 patients had slight worsening in their PSPRS from baseline, but we still consider their condition as improved, since their PSPRS were lower than their expected PSPRS at 6 months. Side effects of Cerebrolysin was negligible.

Figure 1

Patient	Age	Disease duration	Baseline PSPRS	PSPRS at 6 months	Baseline PSP staging	PSP staging system at 6 months	Expected PSPRS at 6 months
Number 1	69	4.1	64	62	3	3	70
Number 2	63	2.9	51	50	2	2	57
Number 3	72	3.7	58	-	3	-	64
Number 4	67	4.3	72	75	1	1	78
Number 5	69	3.5	61	62	2	1	67
Number 6	71	4.4	69	62	4	4	75

DISCUSSION

Cerebrolysin has been used in parkinson's disease where improvement of symptoms was observed5, and was also found effective-among others conditions- in dementia and stroke6,[7]. , It has also been shown to be effective in the treatment of Alzheimer's disease in earlier trials. Cerebrolysin (Cere) is a compound with neurotrophic activity that cause neuronal differentiation (sprouting of axons and dendrites,) and maintains the functional integrity of the nerve cell4.

The (PSPRS) has a range of scores from 0 (normal) to 100. The PSPRS includes questions on activities of daily living ascertained historically and examination items on behavior, bulbar function, eye and eyelid movement, limb movement and midline movement/gait. The mean rate of progression from the time of symptom onset to the first administration of the PSPRS was .98 point per month for men and .85 points per month for women[8].

As with all parkinsonian disorders, levodopa is always tried in order to ameliorate the symptoms of rigidity and bradykinesia, but as with the other non-PD neurodegenerative parkinsonisms, response is generally poor3,[9,10] .

Dopamine receptor agonists are likewise unhelpful[11] and trials of pramipexole (Mirapex) have not borne out success[12] . Despite the severe cholinergic deficit in PSP, cholinergic drugs have been used without benefit[13,14,15].

Zolpidem (Ambien) has been reported to help parkinsonism and eye movements but the benefit was brief[16] .

Tricyclics have modest beneficial effect, mainly Amitriptyline, on gait disorder and eyelid apraxia3 . Despite the severe cholinergic deficit in PSP, cholinergic drugs have been used without significant benefit13 . Amantadine, which has also anticholinergics effects, was found to have modest benefit in PSP3. Electroconvulsive therapy (ECT) was of limited value in PSP[17].A new compound being tested in Japan, tadospirone citrate, a partial serotonin (5-HT 1A) receptor agonist, has recently been reported to be effective[18,19].

In this open label trial patients did demonstrate modest efficacy of cerebrolysin, and in delaying progression in patients with PSP. The true mechanism by which this drug work in such a degenerative disease is still unknown, but probably the neuronal differentiation (sprouting of axons and dendrites) and the maintenance of the functional integrity of the nerve cell play a major role in the improvement encountered in this trial.

The side effect of cerebrolysin was negligible, so the absence of adverse effect in cerebrolysin treated patients confirms an extreme wide margin of safety for this drug, however longterm efficacy and safety of Cerebrolysin in SROS' patients should be evaluated in the future. A prostective investigation using this compound on a biggest number of patients with similar presentation of SROS should be done in a randomized, double-blind, placebo controlled trial.

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