TOXICOLOGICAL STUDIES ABOUT THE SAFETY TREATMENT WITH NEUROTROPHIC DRUGS IN STROKE

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Abstract

The purpose of this study was to watch over the safety and efficacy of neurotrophic drugs at patients who had a stroke.

Cerebrolysin is a combination of biologically active fragments of the main endogenous neurotrophic factors .

This factors,in physiological conditions , contributed to maintain DNA expression at the cells level and preserving the functionality of neurovascular unit.

The main objective of this study was to evaluate the efficacy and safety of Cerebrolysine daily management, for 10 days in a dose of 50 ml / day. The process had to demonstrate that treatment, with Cerebrolysin in this form ,is safe and effective treatment patients with stroke .

Methods:

In this study we have two groups patients,with equal treatment, double-blind , placebo-controlled.For estimated efficacy of treatment we used Barthel Index . Duration of study was 20 days for each patient .The study included 120 patients , a total of 110 completed the study .

Results :

Generally, significant effects were observed on the individual visit.

Conclusion:

Differences from first day to 20.day are not statistically significant , ,but demonstrated that treatment with Cerebrolysin at patient,who had stroke,is safe and well tolerated .

Keywords: neurotrophisics , toxicity, stroke , Cerebrolysin

INTRODUCTION

Worldwide, stroke is the 2nd leading cause of death and considered the major medical emergency Stroke is a major health problem; and as the population ages, its significance will grow. A stroke is defined as an acute loss of neurological function due to an abnormal perfusion of brain tissue.

Treatment is:

- restore the arterial flow in the affected segment, by pharmacological or mechanical means
- increasing resistance of the affected brain tissue ;
- prevention of secondary complications ;
- neurorehabilitation ;
- recurrence prevention

Recent clinical studies demonstrate that adjuvant therapy in stroke should target different physiopathological mechanisms involved in the stroke,the effect of neuroprotective medication , with significant therapeutic benefits and efficacy .

MATERIAL AND METHODS

The methods used in the study, met all methodological requirement,and demonstrated the safety of treatment. Treatment of all patients was the standard treatment of stroke .

The study was conducted on 110 patients tested within 24 hours of stroke debut . There have been 4 assessment visits for patients enrolled.Patients who were suitable for participation in the study received initial assessment in the first day.

After this assessment patients received infusion with Cerebrolysin 50 ml for 10 days. From this sample , denoted as Lot . I participated 50 patients and the placebo group ,noted II, 60 patients .

Clinical efficacy visits were on day 5 (as the visiting No. 2) , day 10 (as the visiting No. 3 and the end of active treatment) and day 20 (as the visiting No. 4) .

To assess the patient's disability we used Barthel index.

All patients signed an application form. Patients wererecruited in 2011-2013 .

RESULTS AND DISCUSSION

Table I.Features of groups

	Cerebrolysin=50		**Placebo=60**		**p**
	Nr.	**%**	**Nr.**	**%**	
Male					
Men	31	62,0	35	58,3	0,457
Woman	19	38,0	25	41,7	
Urban	37	74,0	42	70,0	0,383
Rural	13	26,0	18	30,0	
Age					
<50 years	5	10,0	5	8,3	
50-65 years	16	32,0	18	30,0	0,710
>65 years	29	58,0	37	61,7	

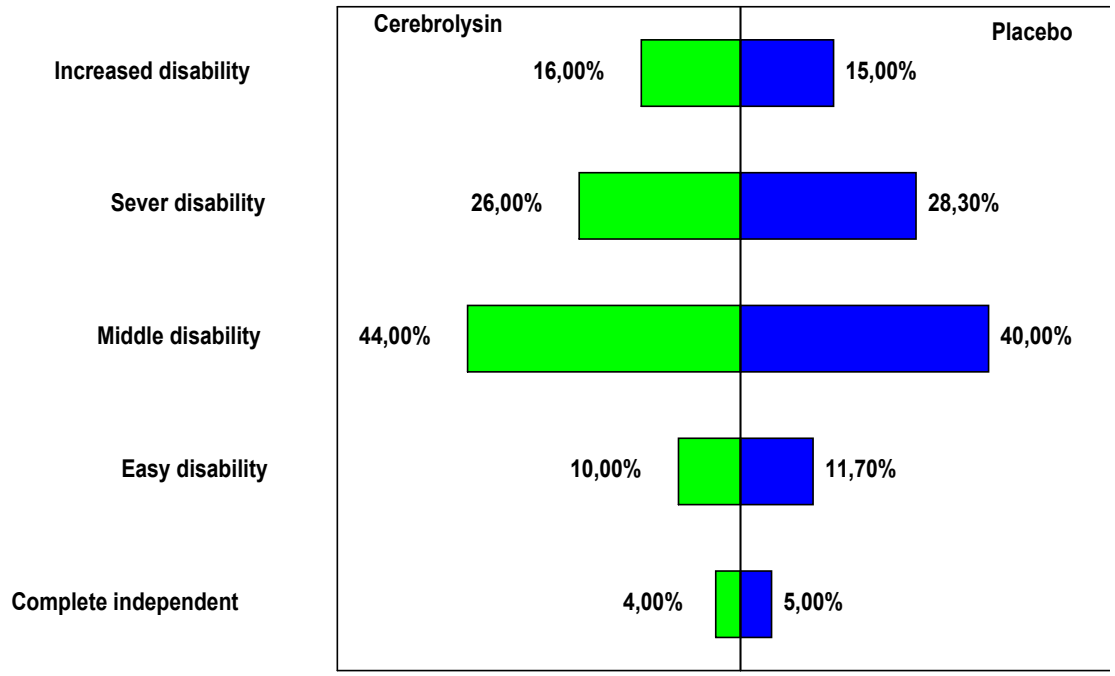
The most patients in each groups were male (62.0% and 58.3%) from rural areas (74.0% and 70.0%) over 65 years (58.0%, 61.7%) (Table I).

Do not exists significant differences between the two groups in terms of demographic data.

Tab. II. Barthel index

	Cerebrolysin=50		**Placebo=60**	
	Nr.	**%**	**Nr.**	**%**
0-25 – increased disability	8	16,0	9	15,0
25-50 - sever	13	26,0	17	28,3
50-75 middle	22	44,0	24	40,0
75-99 – easy disab.	5	10,0	7	11,7
100- complete independent	2	4,0	3	5,0
Indice Bathel	**51,95±8,22**		**52,65±8,97**	

Barthel index indicates a moderate disability in each groups (51,95, or 52,65), in most cases Barthel index was in the range of 50-75 (44.0, respectively 40.0%) (p = 0894) (Table II).


Cerebrolysin
Placebo
Increased disability
16,00%
15,00%
Sever disability
26,00%
28,30%
Middle disability
44,00%
40,00%
Easy disability
10,00%
11,70%
Complete independent
4,00%
5,00%

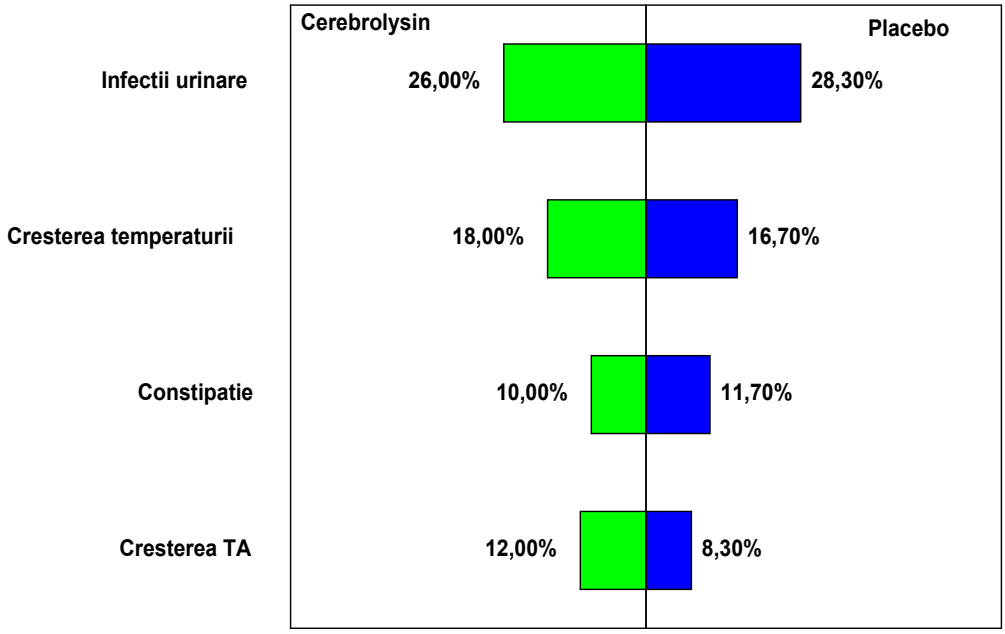


Table III. Adverse effects

	Cerebrolysin=50		Placebo=60		p
	Nr.	%	Nr.	%	
Urinary infections	13	26,0	17	28,3	0,605
Increasing temperatures	9	18,0	10	16,7	0,721
Constipation	5	10,0	7	11,7	0,571
High blood pressure	6	12,0	5	8,3	0,185
Total	**15**	**30,0**	**17**	**28,3**	**0,706**

Treatment with Cerebrolysin not increase the risk of toxicity or adverse reactions compared to placebo (p = 0.706) (Table III).

The most common adverse reactions were:

- Urinary tract infection (26.0% and 28.3%, p = 0.605);
- IncreasingTemperature (18% and 16.7%, p = 0.721);
- Constipation (10.0% and 18.3%, p = 0.571);

- Blood pressure (12% and 8.3%, p = 0.185).

After the study of laboratory parameters and ECG examinations, we do not found toxic substances, and we conclude that treatment with Cerebrolysin with dose up to 50ml is safe and well tolerated.
Therefore the test results in both groups do not showed significant differences, so we conclude that the therapy with Cerebrolysin not increase the incidence of adverse effects compared to treatment with placebo.
After analysis of laboratory parameters ,of vital signs ,ECG ,we can be said , that not exists toxic effect after the administration Cerebrolysine.

CONCLUSIONS

We conclude that treatment with Cerebrolysin in doses up to 50ml/zi is safe and well tolerated.

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