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EVOLUTION OF SPASTICITY IN POST STROKE PATIENTS TREATED WITH CEREBROLYSIN AND BFT

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ABSTRACT. The aim of our study was to monitor the evolution of spasticity in patients who have suffered a stroke and were treated with Cerebrolysin and BFT (balneophysiotherapy). The study was conducted over one year period in which patients were evaluated at the beginning of the period, at 6 months and at the final – at 12 months. Patients were divided into 2 groups, as follows: group I - 71 patients (Cerebrolysin was administered to them and they also did medical recovery) and group II - 68 patients (they only undergoing standard medical recovery procedures). The evolution of spasticity through the Ashworth scale shows progress both in the BFT + Cerebrolysin group and in the BFT group as well. Thus, if the BFT + Cerebrolysin group initially recorded a percentage of 43.66%, at the 6-months evaluation it decreased by 11.27%, reaching at the 12-months evaluation to a score of 25.35%. In the case of the BFT group the percentage at the initial assessment was 42.26%, decreasing by 7.04% at the 6 months assessment and another 5.63% at the 12-months assessment.
KEYWORDS: cerebrovascular accident (CVA), spasticity, Cerebrolysin, BFT, stroke;

INTRODUCTION

Cerebrovascular accidents are considered the second largest cause of death worldwide, in 2005 accounting for about 10% of the total deaths worldwide, a high percentage of 85% occurring in underdeveloped countries (Lopez et al., 2006). The incidence of stroke and the mortality caused by it are strongly marked by the population's life expectancy and the premature aging of the population as well as (Bonita et al., 1992). Due to their severity, their consequences and increasing numbers, vascular accidents are the most debated issues in brain pathology. Patients with vascular diseases should benefit from a thorough investigation and qualified medical assistance (Marcovici et al.,2004) Patients who suffer a stroke often remain with sequelae that persist for years, such as: sensory deficits, impairments in perception, deficiencies in maintaining balance, motor function paralysis, degeneration of cognitive functions (Asplung et al.,2003)

In most cases, home recovery cannot be done because, besides the disabilities caused by the neurological disease, coexisting sufferings such as hypertension, diabetes and heart disease are added. The latter complicates the application of recovery methods and determines increased dependence and social isolation (Francisco et al., 2012).

Ambulatory activities levels for patients with stroke are limited due to the side effects that the disease itself has on the walking function. This depreciation is a deviation from the normal functioning of the body with the loss of the physiological and anatomical structure (Arene et al., 2009). The disability refers to the inability to perform a task or function, occurrence of a stroke, thus determining more physical, mental and cognitive impairments that combined produce a disability (Langhorne et al., 2009). The time and intensity of rehabilitation are closely related to the time elapsed from the moment of the onset, the patient′s previous condition, the associated pathologies and last but not least, the available resources. Rehabilitation measures aim at reducing the symptoms that the lesion has caused, recovering the deficiencies and improving the quality of life. The therapeutical approach to rehabilitation focuses on the common interest of the therapist and the patient, this interest representing the desire to recover the deficiencies and transform the disability into ability (Uivaroșan, 2014). Studies on recovery models showed that there is no particular physiotherapy model to be superior in post-stroke recovery (Van Peppen et al., 2004; Polloch et al., 2007)

Spasticity, defined as the excessive increase of muscle tonus and stretch reflexes that occur mainly in various neurological diseases of the central nervous system, is frequently encountered in patients who have suffered stroke. Without proper treatment, spasticity results in contractions of the muscles and tendons causing deformation of the affected parts, pain, and malfunctions.

Neurotrophic factors sum up all the proteins involved in neuronal growth and survival during neuronal development. Growth is a characteristic feature of all living creatures, in the process of growth contributing a series of elements including trophic substances (Mureșanu, 2003). Growth factors are produced at the level of most tissues, including at the CNS level (Popescu, 2014). The efficacy of Cerebrolysin has been proved in numerous clinical trials and animal studies, in pathological conditions, this acting in the way of changing endogenous defense mechanisms, neuroprotection and neuroregeneration (Mureșanu, 2010). In vivo and in vitro experimental studies demonstrated the neuroprotective effect of Cerebrolysin and its multimodal mechanism of action (Alvarez et al., 2000) the intervention in neuroprotection taking place by simultaneous modulation at different levels of pathogenic molecular cascades involved in cerebral ischemia and neurodegeneration. Studies have shown that treatment with Crebrolysin did not increase the rate of adverse reactions compared to placebo treatment and did not demonstrate the existence of toxic effects (Bejenaru et al., 2010). The safety given by Cerebrolysin has been proved as result of randomized, controlled clinical trials and post-marketing surveillance studies (Hong et al., 2009). Controlled clinical trials with placebo do not report a greater incidence of adverse reactions in Cerebrolysin-treated groups, suggesting that safe administration can be made in patients with hemorrhagic stroke since the acute phase, which allows shortening the critical period from the beginning of treatment (Alvarez et al., 2006)

The objective of this study was to compare the evolution of spasticity in patients post stroke that benefited of BFT recovery versus those who had associated to BFT recovery the treatment with Cerebrolsin.

MATERIALS AND METHODS

A number of 139 post-stroke patients hospitalized for treatment in the recovery clinic at Baile Felix Recovery Hospital and at the Oradea Neurology Hospital during 2011-2014 were included in the study. The study was conducted over one year period in which patients were evaluated at the beginning of the period, at 6 months and at the final – at 12 months.

The inclusion criteria were: ischemic or hemorrhagic stroke, time since stroke production at commencement of treatment less than or equal to 6 months, informed consent.

The exclusion criteria were: previous stroke , previous recovery program, recurrence of stroke during the study, not attending the 3 evaluations. The duration of a recovery series was 14 days, consistent with literature data.

As study medication Cerebrolysin was chosen, a combination of biologically active fragments of the major natural neurotrophic factors, having similar action with that of the endogenous neurotrophic factors, which was administered 10 ml / day, in single dose, for 10 days per month, infusibile solution, i.v. slowly after dilution with physiological saline to a volume of 100 ml, for one year prior to the final evaluation. The therapeutic means used in the recovery treatment were kinetotherapy, hydrokinetotherapy, masotherapy, electrotherapy, occupational therapy and thermotherapy.

The patients were divided into two groups: the first group with a number of 71 patients who did BFT + Cerebrolysin and the second group with 68 patients who only did BFT. Patients were randomly assigned into groups based on patient′s history, clinical characteristics and patient′s risk factors for stroke, with no significant differences between the two groups ($p > 0.05$).

Each patient included in this study signed an informed consent form, before the inclusion.

For the assessment of the pyramidal spasticity level, the modified Aschworth scale, which is a standardized scale demonstrating resistance to passive movement, was used. This system provides a gradual surveillance of the level of resistance experienced by the examiner. It includes 5 muscle tone severity degrees marked from 0 to 4. Bahanon changes the scale by entering level 1+. Interpretation of the Aschworth Score is presented in Table 1.

Table 1 Interpretation of the Aschworth Score

0	There is no increase in tonus
1	A slight increase in the tonus at the end or beginning of the motion arc
1+	A slight increase in the tonus manifested in the middle of the motion arc
2	The marked increase in tonus for most of the movement
3	Considerable increase in tone - difficult passive movements
4	Rigidly affected part in flexion or extension

The statistical analysis was made using EPIINFO, version 6. 0, a program of the Center of Disease Control and Prevention in Atlanta, adapted to the medical statistics processing. Parameter averages, frequency ranges, standard deviations, statistical significance tests were calculated using the Student method (t test) and $\chi 2$.

RESULTS AND DISCUTIONS

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In terms of gender distribution, age, stroke location, duration from stroke onset to clinical study and clinical characteristics of patients, there were no significant differences between groups (p> 0.05) at the beginning of the study.

The most common clinical sign in both BFT + Cerebrolysin group and BFT group was spasticity, being present in 92.96% of the patients from the study group and in 94.12% of the control group (p=0.782). At the initial assessment, there were no significant differences between the two groups regarding the Aschworth score. The evaluation of spasticity through the Aschworth scale shows good progress both in the BFT + Cerebrolysin group and in the BFT group (Table 2).

Table 2 Evolution of the Achworth index

Achworth index	Physiotherapy+Cerebrolysin group (n=71)					
	Baseline		At 6 months		At 12 months	
	No.	%	No.	%	No.	%
0	1	1.41	4	5.63	12	16.90
1	14	19.72	20	28.17	27	38.03
1+	25	35.21	24	33.80	14	19.72
2	14	19.72	10	14.08	8	11.27
3	9	12.68	7	9.86	6	8.45
4	8	11.27	6	8.45	4	5.63
Achworth index	Physiotherapy group (n=68)					
	Baseline		At 6 months		At 12 months	
	No.	%	No.	%	No.	%
0	1	1.41	4	5.63	10	14.08
1	12	16.90	11	15.49	17	23.94
1+	25	35.21	28	39.44	20	28.17
2	14	19.72	12	16.90	10	14.08
3	9	12.68	7	9.86	6	8.45
4	7	9.86	6	8.45	5	7.04

Initially at the BFT + Cerebrolysin group, the percentage of patients with a score ≥2 was of 43.66%, at 6 months it decreased by 11.27% (32.39%, p=0.168) and in the evaluation from 12 months with another 7.04% (25.35%, p=0.356), reaching 25.35% (p=0.022 to the baseline evaluation) (Figure 1).

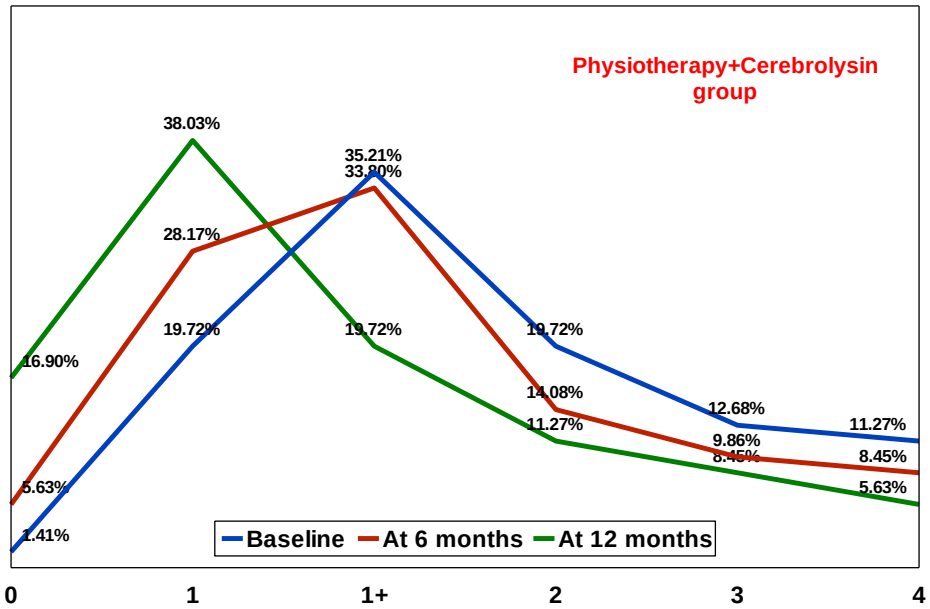

Fig.1 Evolution of the Aschoworth score- BFT + Cerebrolysin

In the BFT group, the percentage of patients with a score ≥2 was 42.26%, at 6 months it decreased by 7.04% (35.22%, p=0.401) and in the evaluation from 12 months with another 5.63% (29.59%, p=0.487), reaching 29.58% (p=0.125 to the baseline evaluation) (Figure 2).

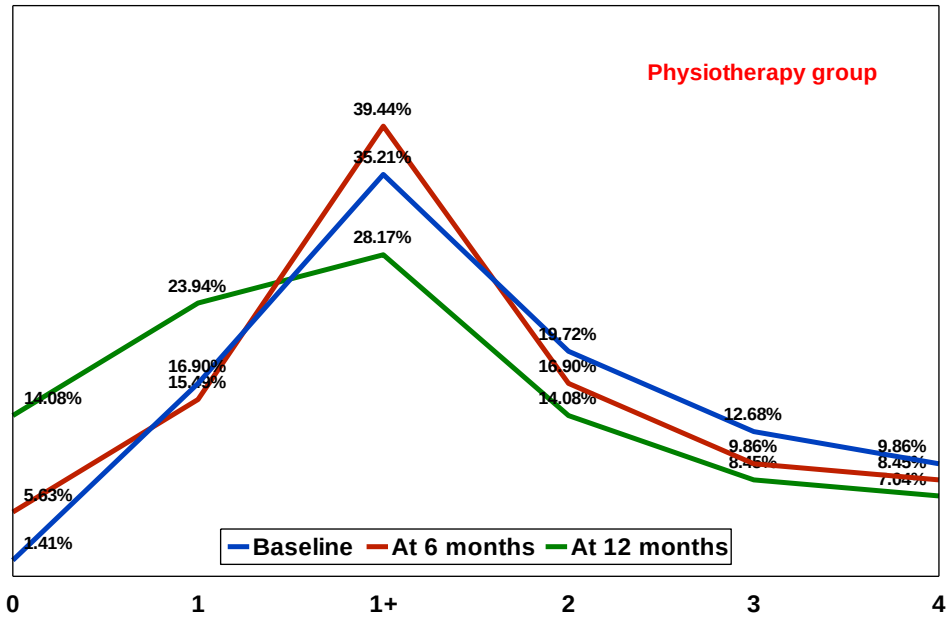

Fig.2 Evolution of the Aschoworth score- BFT

At 12 months, the percentage of patients with a score ≥2 in the BFT group decreased by 12.68%, compared to the BFT + Cerebrolysin group, where the reduction was 18.31% (p=0,145) (Figure 3).

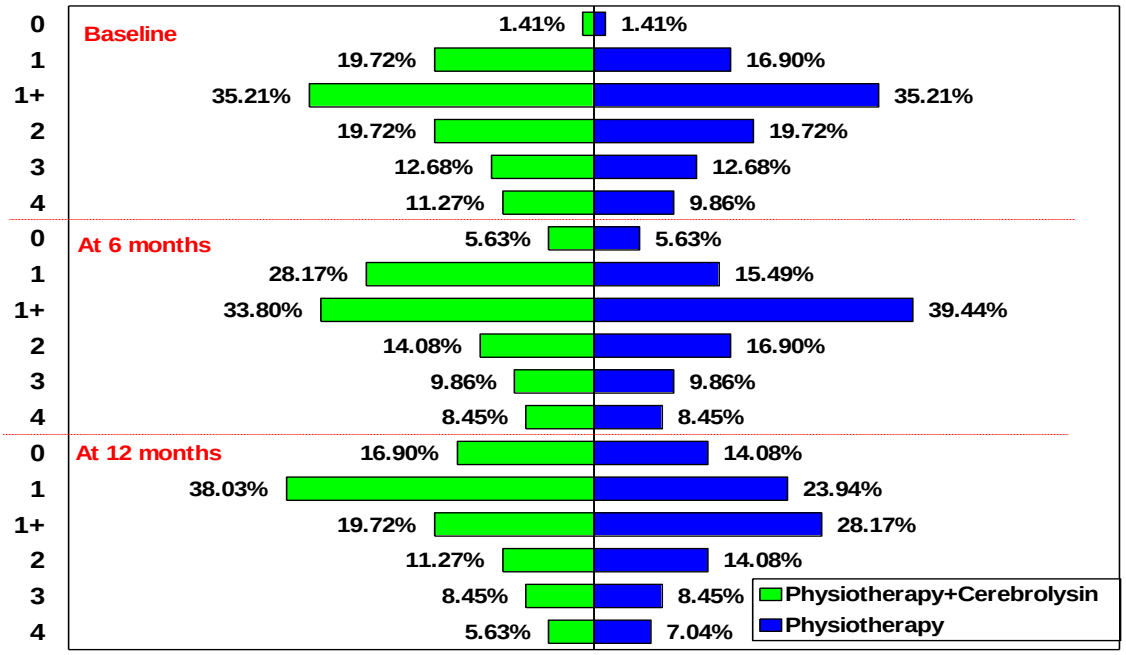

Fig.3 Evolution of the Aschoworth score - BFT + Cerebrolysin group compared to BFT group

Comparing the two groups we notice that as against the initial assessment, at 12 months, spasticity disappeared in 15.49% of the patients from BFT + Cerebrolysin group and in 13.24% of the BFT group (p = 0.707) and it decreased in 67,61% of the patients from BFT + Cerebrolysin group and in 41.18% of the BFT group (p = 0.002).

As a result of a stroke, a multitude of deficiencies occur in several systems, resulting in a disability complex (Fodor et al., 2018). Spasticity is the most common clinical sign both in the BFT + Cerebrolysin and in the BFT group, being an important element for diagnosis, evolution, and recovery program.

The time and intensity of rehabilitation are closely related to the time elapsed from the onset, the patient's previous condition, associated pathologies, and, last but not least, the available resources. Rehabilitation measures aim to reduce the symptoms that the lesion

has caused, to recover the deficiencies and to improve the quality of life. (Uivaroșan, 2016).

Post-stroke spasticity is usually accompanied by other symptoms and signs of superior motor neuron syndrome such as exhaustion, agonist/antagonist co-contraction and lack of coordination. In chronic phase this can negatively affect the quality of life indices (Francisco et al., 2012).

In order to control post-stroke spasticity, there should also be taken into account the influence of spasticity on the well-being, not just the decrease of muscle hypertonia.

Recovery will be considerably constrained if just spasticity is reduced without approaching the negative constituents of the upper neuron syndrome. In order to facilitate functional amelioration a combination of recovery techniques is required. Propitious functional results should be achieved by choosing the adequate post-stroke spasticity management objectives and treatment strategy (Francisco et al., 2012).

Techniques used by multidisciplinary physician teams to recover lost deficits are not fully understood and elucidated. Until now, we cannot accurately state that we have specific treatment methods, medications, or exact recovery schemes that can safely and obviously transform disability into these patients in abilities.

Recovery treatment of spasticity, to be successful, requires an interdisciplinary approach, consisting of conventional treatment for the recovery joined by the use of neurotrophic factors.

CONCLUSIONS

The results obtained from this study are conclusive evidence of the use of associated therapy between Cerebrolysin (neurotrophic factor) and classic medical treatment, in the view of reducing spasticity in patients with stroke. Recovery activity in a post-stroke patient is understood to be teamwork, where both the neurologist, the recovery doctor, the nurse and the social worker have the same important roles.

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