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Clinical Study

Role of Cerebrolysin in cervical spondylotic myelopathy patients: a prospective randomized study

Ahmad Fouad Abdelbaki Allam, MD, MRCS[a], Tarek Abdalla Ahmed Abotakia, MD[a], Wael Koptan, MD[b,*]

[a]*Orthopaedic Department, Minia University, Agricultural Rd, Minia, 61512, Egypt*
[b]*Orthopaedic Department, Faculty of Medicine, Cairo University, 71 Kasr Alainy St, Cairo, 11562, Egypt*

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Abstract

BACKGROUND CONTEXT: Cerebrolysin is a mixture containing 85% free amino acids and 15% biologically active low–molecular weight peptides that is believed to mimic the effects of endogenous neurotrophic factors to interact with the pathologic process cascade of neurodegenerative diseases. No study has examined the effect of Cerebrolysin on cervical myelopathic patients.
PURPOSE: The objective of this study was to evaluate the effect of Cerebrolysin as a conservative modality on cervical spondylotic myelopathic patients.
STUDY DESIGN: This is a prospective randomized study.
PATIENT SAMPLE: A total of 192 patients with cervical spondylotic myelopathy (CSM) were subdivided blindly into two equal groups.
OUTCOME MEASURES: Followed-up was performed at 1, 3, and 6 months comparing the recovery rate Japanese Orthopaedic Association (JOA) score for cervical myelopathy between the two groups.
METHODS: Group I received Cerebrolysin and Group II received placebo for 4 weeks; both groups received celecoxib 200 mg for 4 weeks.
RESULTS: Myelopathy improved in 92% and 52% of patients at 1 month in Groups I and II, respectively; these changed at 6 months to 87% and 33%; the remaining 13% in Group I neither improved nor deteriorated, whereas 60% in Group II neither improved nor deteriorated and 7% deteriorated with statistically significant differences when comparing the mean JOA recovery rate between the 2 groups at 1, 3, and 6 months.
CONCLUSIONS: Cerebrolysin over 4 weeks is safe and effective for the improvement of CSM as compared with placebo, with no reported cases of neurologic deterioration over 6 months of follow-up.

Keywords: Cerebrolysin; Cervical canal stenosis; Cervical myelopathy; Cervical spondylosis; Conservative; Neurotrophin mixture

FDA device/drug status: Although Cerebrolysin is approved for use in many European countries, it is yet to be approved by the Food and Drug Administration for use in the United States.

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All the authors declare that they have no conflict of interest.

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This study was approved by the Research Ethics Committee of Cairo University.

As this is the first study on this entity, a larger study with a longer follow-up is advised for more evaluation of Cerebrolysin for cervical spondylotic myelopathy.

The authors recommend the use of Cerebrolysin after surgical decompression for cervical spondylotic myelopathy to study its added benefit on postoperative recovery.

* Corresponding author. Orthopaedic Surgery, Faculty of Medicine, Cairo University, 71 Kasr Alainy St, Cairo 11562, Egypt. Tel.: 002 012 3118522.
E-mail address: waelkoptan@yahoo.com (W. Koptan)

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Introduction

Cervical spondylosis can cause spinal canal stenosis and spinal cord compression with subsequent cervical spondylotic myelopathy (CSM). Cervical spondylotic myelopathy is a common dysfunctional spinal disorder in patients over the age of 55 years. Surgical decompression is indicated for patients with moderate to severe disease [1].

Cerebrolysin is a mixture prepared by enzymatic lysis of lipid-free pig brain products. It contains 85% free amino acids and 15% biologically active low–molecular weight peptides that can readily cross the blood-brain barrier. It is believed to mimic the effects of endogenous neurotrophic factors and to block the pathologic cascade of neurodegenerative diseases and cerebrovascular disorders [2].

Cerebrolysin has been used in a large number of neurologic conditions such as stroke, Alzheimer disease, other cognitive disorders, and dementia, resulting in significant improvement, with no reported significant adverse reactions except for allergies and seldom central nervous system excitability enhancements [3–5].

No study has examined the effect of Cerebrolysin on cervical myelopathic patients as a conservative modality.

We aimed in the present study to evaluate the effect of Cerebrolysin as a conservative modality on cervical spondylotic myelopathic patients.

Methods

This prospective randomized multicenter study was carried out in patients with CSM who were surgical candidates and refused to have surgery; these patients were divided into two equal groups.

After approval of the Research Ethics Committee, an initial pilot study was conducted to determine the sample size required for the study. Using G Power 3.1.9.2 software (Universität Kiel, Kiel, Germany), a total sample size of 192 patients (96 in each group) was determined to provide 95% power for a two-tailed *t* test, with effect size=0.5241067, at the level of 0.05 significance.

Inclusion criteria were CSM with motor weakness, gait disturbance, and magnetic resonance imaging evidence of spondylotic cervical canal stenosis.

All patients with comorbidities such as diabetes mellitus, rheumatoid arthritis, alcoholism, immunosuppressive treatment, and combined cervical and lumbar canal stenosis were excluded.

Clinical and neurologic examination and scoring using Japanese Orthopaedic Association (JOA) score for cervical myelopathy were done for all patients.

Cervical radiographs were done including dynamic views; there were no cases of fixed kyphosis, no cases of cervical instability, and no cases of ossified posterior longitudinal ligament. Magnetic resonance imaging scan was done for all patients for the assessment of neural compression. The affected levels of canal stenosis in Group I were 5 single levels, 18 double levels, 34 triple levels, 37 quadruple levels, and 2 quintuple levels, whereas the affected levels in Group II were 6 single levels, 12 double levels, 31 triple levels, 41 quadruple levels, and 3 quintuple levels (p=.41).

After signing their written informed consent, all patients were asked to choose one of shuffled sealed envelopes with treatment allocations inside.

The patients and the outcome assessors were blinded to the treatment.

In Group I, there were 61 women and 35 men, whereas in Group II, there were 53 women and 40 men (p=.22). The mean age in Group I was 58.3±7.2 (range 45–75 years), and the mean age in Group II was 61.03±7.6 (range 45–80 years) (p=.014).

Group I included 96 patients who had received Cerebrolysin 5 mL IM injection for 5 d/wk for 4 weeks, whereas Group II included 96 patients had received placebo IM injection for 5 d/wk for 4 weeks. Both groups had received oral celecoxib 200 mg as a single, after-meal daily dose for 4 weeks.

Follow-up was done at 1, 3, and 6 months in the form of clinical examination, JOA scoring, and calculation of JOA recovery rate percentage that is equal:

$$\frac{\text{Follow-up score}-\text{initial score}}{(\text{full score}-\text{initial score})\times 100}.$$

Collected data were analyzed using SPSS software, version 20 (SPSS Inc, Chicago, IL, USA) and Megastat software version 10.1 (McGraw-Hill, New York City, New York, USA). p-Values less than .05 were considered statistically significant.

Results

No one missed the follow-up in Group I. The mean follow-up period in Group II was 5.8±0.85 months as three patients discontinued participation in the study without causes.

Descriptive statistics was done firstly for all variables and showed that the data were normally distributed as the data had a kurtosis value that ranged within −1.0 to 1.0; so, independent *t* test for parametric quantitative data, chi-square test for categorical data, and one-factor analysis of variance tests were used, and the numbers of patients within the groups were established as n=96 for Group I and n=93 for Group II for the statistical analysis.

The mean pretreatment JOA score in Group I was 11.5±1.2 (range 8.5–14) and that in Group II was 11.3±1.2 (range 9–14) (p=.28).

In Group I, the mean JOA score improved to 14.1±1.4 (range 10–16) at 1 month (p<.0001), then became 14.09±1.3 (range 10–16) at 3 months (p<.0001), and finally reached 13.9±1.3 at 6 months (range 10–16) (p<.0001). There were insignificant differences when comparing the mean post-treatment JOA scores at 1, 3, and 6 months (Fig. 1).

In Group II, the mean JOA score improved to 12.02±1.2 (range 9–14) at 1 month (p=.0121), then became 11.9±1.22 (range 9–14) at 3 months (p=.0020), and finally reached 11.8±1.23 at 6 months (range 9–14) (p=.0004). There were