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New Therapies for the Treatment of Spastic Cerebral Palsy

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Research Article

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Abstract

Background: Cerebral palsy is a heterogeneous condition associated with a non-progressive lesion, but permanent disorder of movement with limited mobility. It is generally associated with gross motor developmental delay. In moderate to severe cases motor developmental milestones such as walking may never be achieved. There are no specific therapies for cerebral palsy, and treatment of spastic cerebral palsy is generally aiming at improving mobility through muscle relaxation and physiotherapy. This is a retrospective observational study describing the treatment of spastic cerebral palsy with individualized treatment plans providing a new combination of interventions including nutritional support, muscle relaxants and the use of oral pyritinol, intramuscular piracetam, citicoline (oral and injectable), intramuscular cerebrolysin, and intramuscular nandrolone decanoate. Treatment aimed primarily at improving motor development particularly standing and walking.

Patients and Methods: During the year 2018, six patients (3 girls and 3 boys) with spastic cerebral palsy and marked motor disability were treated. The patient age ranged from 22 months to three years. All patients were unable to stand or walk, and had poor speech development. Four patients (Patients 1, 4, 5, and 6) had severe cerebral palsy and were even not able to sit. The other two patients had moderately severe disorder and were unable to stand or walk. All the patients were not saying any word or were saying only few words.

Results: After treatment, all the patients experienced improvement in motor development without the occurrence of any side effect. Five patients were able to stand with support (patients 1,2,3,4, and 5), and four of them were also able to walk few steps with support. The sixth patient remained unable to stand and the limited benefit of treatment was attributed to some degree of deformity and muscle contracture. In all patients treatment was associated with initiation of speech development or improved speech. It was possible to demonstrate improvement in fine motor skills in three patients (Patient 2, 3, and 5).

Conclusion: The treatment of patients with spastic cerebral palsy (moderate and severe) with this individualized treatment plans was associated with a beneficial effect on motor development particularly standing and walking.

Keywords: Spastic Cerebral Palsy; Pyritinol; Piracetam; Citicoline; Cerebrolysin; Nandrolone Decanoate

Introduction

Cerebral palsy is a condition results from abnormal development or damage to the regions of the brain that control movement, balance, and posture. A minority of cases of cerebral palsy, about 2% could be attributed to an inherited genetic cause, and most inherited cases are expected to be autosomal recessive. The brain abnormalities in cerebral palsy cause a non-progressive, but permanent disorder of movement, posture, and limitation of mobility.

The movement disorder generally leads to gross motor developmental delay, and in moderate to severe cases motor developmental milestones such as walking may never be achieved. In addition to movement problems, patients with cerebral palsy may have cognitive impairment leading to difficulties with learning, and speech.

The spastic type of cerebral palsy is by far the most common type accounting for about 70% of all cases. In this type, mobility impairment is worsened by hypertonia caused by an upper motor neuron lesion in the brain and the corticospinal tract or the motor cortex.

Although the neurologic lesion in spastic cerebral palsy is non-progressive, secondary orthopedic complications are generally progressive and disabling because of the developments of joint deformities and joint contractures. In less severe cases, the patient can walk but experience gait difficulties mostly in the form of tip-toeing gait.

There are no specific therapies for cerebral palsy. Treatment of spastic cerebral palsy is essentially aiming at improving mobility through muscle relaxation and physiotherapy. Muscle relaxants are used to improve spasticity and prevent deformities and contractures. However, muscle relaxants have not been reported to have an important effect on motor development.

Many patients with moderate and severe spastic cerebral palsy develop flexion deformities especially equinus or planter deformity of the ankle [1-3]. Figure 1 shows a boy with spastic cerebral palsy who remained unable to stand or walk at the age of six years with the development of flexion deformities. The use of oral pyritinol with the judicious use of nandrolone decanoate given by intramuscular injection intermittently has been reported to be associated with a beneficial effect on motor development and learning [1,2].

The use of oral pyritinol, intramuscular piracetam, citicoline (oral and injectable), intramuscular cerebrolysin, and intramuscular nandrolone decanoate has been reported to have a beneficial effect in a very severe form of spastic cerebral palsy associated with evidence of brain atrophy [3].

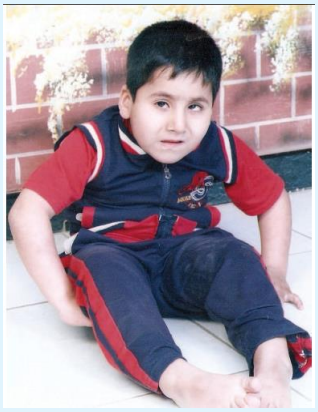

Figure 1: A boy with spastic cerebral palsy who remained unable to stand or walk at the age of six years with the development of flexion deformities.

The aim of this paper is to report a retrospective observational study describing the treatment of patients with spastic cerebral palsy with individualized treatment plans providing a new combination of interventions including nutritional support, muscle relaxants and the use of oral pyritinol, intramuscular piracetam, citicoline (oral and injectable), intramuscular cerebrolysin, and intramuscular nandrolone decanoate.

Treatment aimed primarily at improving motor development particularly standing and walking through: Controlling spasticity with use of muscle relaxants. Improving brain function with use of pyritinol, piracetam, citicoline, and cerebrolysin. Strengthening muscle with use of nandrolone decanoate. Improving the nutritional status with royal jelly, a natural dietary supplement. Treatment protocols for this research was approved by the scientific committee of Iraq headquarter of Copernicus Scientists International Panel, and conform to the provisions laid out in the Declaration of Helsinki (as revised in Edinburgh 2000).

Patients and Methods

During the year 2018, six patients (3 girls and 3 boys) with spastic cerebral palsy and marked motor disability were treated with individualized treatment plans providing a new combination of interventions. The

patient age ranged from 22 months to three years. All the patients were unable to stand or walk, and had poor speech development.

Four patients (Patients 1, 4, 5, and 6) had severe cerebral palsy and were even not able to sit. The other two patients had moderately severe disorder and were unable to stand or walk. All the patients were not saying any word or were saying only few words.

Patient-1

A girl with severe spastic cerebral who was seen at about the age of two years with markedly delayed motor development. She was unable to sit unsupported, and was not crawling She was treated with baclofen which was gradually increased to 30 mg daily. In addition, she received six courses of treatment (Table 1).

First course
Piracetam 2ml (400mg) given intra-muscularly every three days (4 doses). Citicoline 2ml (250mg) given intra-muscularly every three days (4 doses).
Second course
Oral Citicoline 2ml (200mg) daily for one month. Oral pyritinol 3ml (60mg) daily for one month. Nandrolone decanoate 12.5mg intramusular injetion.
Third course
Oral pyritinol 3ml (60mg) daily for one month. Nandrolone decanoate 12.5mg intramusular injetion.
Fourth course
Piracetam 3ml (600mg) given intra-muscularly every three days (10 doses). Oral Citicoline 2ml (200 mg) daily for one month given in the afternoon.
Fifth course
Cerebrolysin 1ml every third day, 10 dose were given over one month.
Sixth course
Cerebrolysin 3ml every third day, 10 given over one month. Oral Citicoline 3ml (300mg) daily for one month given in the afternoon.

Table 1: Course of treatment received by patient-1.

Patient-2

A two-year boy with spastic cerebral palsy and imaging studies showed mild brain atrophy presented as mild dilatation of the ventricular system. He had poor motor development and was not able to stand and had poor fine motor skills and was not saying any word. He was treated with Cerebrolysin 1ml every other day given by intramuscular injection (10 doses). Oral citicoline 2ml (200mg) in the morning.

Patient-3

A three-year old girl with spastic cerebral palsy who was unable to stand nor walk and had poor fine motor skills. She was not saying any word. She received four courses of treatment (Table 2).

First course
Oral pyritinol 3ml (60 mg) in the morning daily for one month. Citicoline 2ml (250) given intra-muscularly every three days (10 doses).
Second course
Oral pyritinol 3ml (60 mg0 in the morning daily for one month. Nandrolone decanoate 12.5mg intra-muscularly.
Third course
Oral pyritinol 3ml (60 mg) in the morning daily for one month. Cerebrolysin 1ml every other day given by intramuscular injection (10 doses).
Four course
Amino acid supplementation Nandrolone decanoate 12.5mg intra-muscularly.

Table 2: Course of treatment received by patient-3.

Patient-4

A 22-month old girl with spastic cerebral palsy who had markedly delayed development. She was unable to sit alone and unable to stand, and she was not saying any word. She had squint of the right eye which was operated earlier for cataract. Brain ultrasound at the age of eighteen months showed evidence of mild dilation of both lateral ventricles and radiologist couldn't exclude periventricular abnormalities because of the limited visibility of brain. She was treated with baclofen which was gradually increased to 20 mg daily in two divided doses and cerebrolysin 1ml intra-muscularly on alternate days with 10 doses given over ten days.

Patient-5

A twenty-month old boy with extremely severe spasticity that markedly limited his movement. Most of the time, he looked miserable and in pain. His feeding was poor and he was, unable to turn to the sides, unable to creep or crawl, and unable to sit. CT-scan showed bilateral symmetrical hypodensity of the deep white matter of both hemispheres similar to the changes seen in leukodystrophy. He was treated with baclofen which was gradually increasing dose. In addition, he received five courses of treatment that were given over about seven months (Table 3).

First course (20 days)
Piracetam 2ml (400mg) every other day, he received eight doses. Oral citicoline 2ml (200mg) daily in the morning.
Second course (20 days)
Cerebrolysin 1ml given by intramuscular injection every other days. He received 10 doses. Oral citicoline 3 ml (300mg) daily in the morning.
Third course
Citicoline 3ml (375mg) given by intramuscular injection every third day in the morning over one month.
Fourth course (one month)
Piracetam 2ml (400mg) every other day, he received 10 doses. Oral citicoline 3 ml (300mg) daily in the morning.
Fifth course (50 days)
Oral diazepam 2mg per day given as single dose at night. Cerebrolysin 3ml given by intramuscular injection every fifth day. He received 10 doses. Oral citicoline 3 ml (300mg) daily in the morning. Oral amino acid supplementation. Nandrolone decanoate 12.5 mg given by intramuscular injection only once.

Table 3: Course of treatment received by patient-5.

Patient-6

A three-year old boy with severe spastic cerebral palsy and marked spasticity in all of his limbs causing significant limitation movements. He had poor feeding, and was not showing obvious alertness to environment and was not saying any word. He was unable to sit on a chair without slipping and couldn't control or move his head when put in the sitting position (Figure 8).

Treatment included baclofen in gradually increasing doses, and three courses of treatment (Table 4).

Figure 8: Patient-6 at about the age of three, he was unable to sit on a chair without slipping and couldn't control or move his head when put in the sitting position.

First course
Cerebrolysin 1ml given daily by intramuscular injection, received 10 doses.
Second course
Cerebrolysin 1ml given daily by intramuscular injection, received 10 doses. Oral citicoline 2ml (200mg) daily in the morning.
Third course
Citicoline 2 ml (250mg) given by intramuscular injection every third, received 10 doses.

Table 4: Course of treatment received by patient-6.

Results

After treatment, all patients experienced improvement in motor development without the occurrence of any side effect. Five patients were able to stand with support (patients 1,2,3,4,5), and four of them were also able to walk few steps with support. The sixth patient remained unable to stand and the limited benefit of treatment was attributed to some degree of deformity and muscle contracture. In all patients, treatment was associated with initiation of speech development or improved speech. It was possible to demonstrate improvement in fine motor skills in three patients (Patient 2,3,5).

Patient-1

After six treatment courses, the girl was able to sit and stand with support (Figure 2). Treatment was also associated with improved speech.

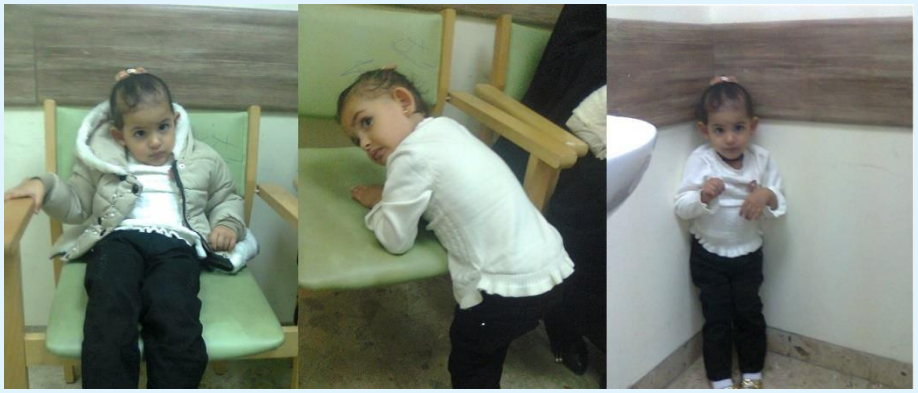

Figure-2: After the six treatment course, patient-1 was able to sit and stand with support.

Patient-2

After treatment, he was able to stand and walk with support and improved fine motor skills which enabled him holding small things (Figure 3). In addition, he started saying few words.

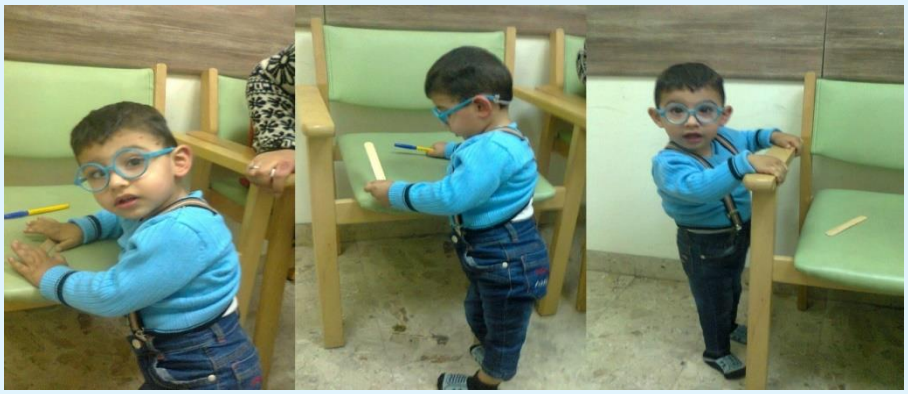

Figure 2: Patient-2 after treatment was able to stand and walk with support and improved fine motor skills enabled him holding small things.

Patient-3

After treatment (Figure 4), the girl was able to stand and walk holding furniture. She showed improved fine motor skills and was able to hold a pen to try to copy a circle, and she could copy a circle. Treatment was also associated with initiation of speech development.

Figure 4: Patient-3, after treatment was able to stand and walk holding furniture. She showed improved fine motor skills and was able to hold a pen to try to copy a circle, and she could copy a circle.

Patient-4

After treatment the girl was able to sit unsupported and stand and step with support holding hands or furniture (Figure 5).

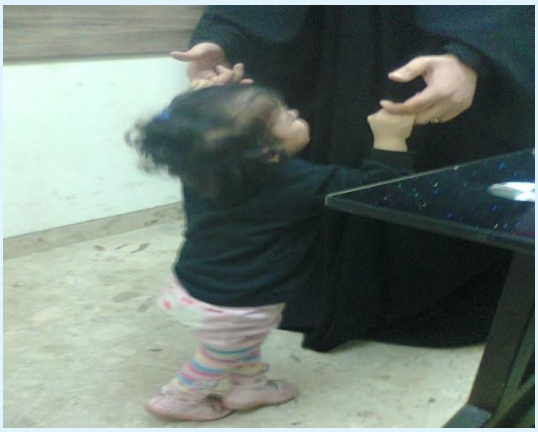

Figure 5: Patient-4, after treatment was able to sit unsupported and stand and step with support holding hands or furniture.

Patient -5

After the fourth course, the improvement was slight, but undeniable. Speech development was initiated and the boy was saying few words. Spasticity was less and he was less miserable, more comfortable. All of his limbs remained in some flexion position, but he could sit on the chair (Figure 6). However, spasticity remained prominent and he needed more muscle relaxation to improve mobility.

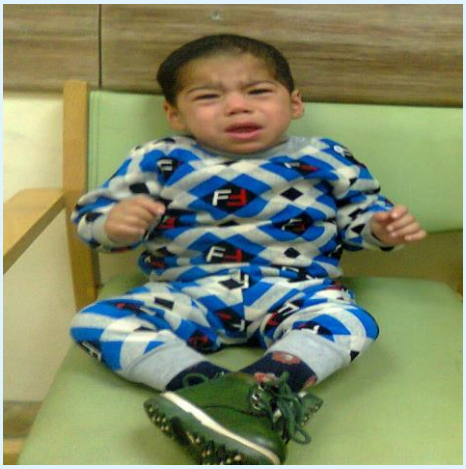

Figure 6: After the fourth course, the improvement was slight, but undeniable, and he could sit on the chair.

After the fifth course of treatment (Figure 7), he experienced significant improvement in speech, cognition, spasticity, fine and gross motor skills: He could sit comfortably on the chair for long time with only slight limb flexion. He could hold a bottle and feed himself. He could stand with support holding furniture and make few steps.

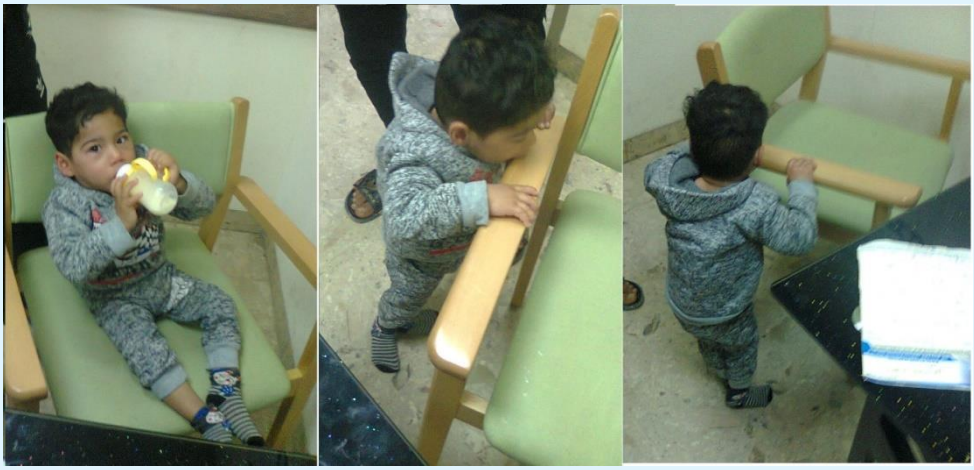

Figure 7: Patient-5 after the fifth course of treatment, he experienced significant improvement. He could sit comfortably on the chair for long time with only slight limb flexion. He could hold a bottle and feed himself .He could stand with support holding furniture and make few steps.

Patient-6

After treatment, obvious improvement was observed and included lessening of spasticity, improved alertness to the surroundings, and he could move his head when put in the sitting position without slipping (Figure 9). Speech was initiated and he was saying some words.

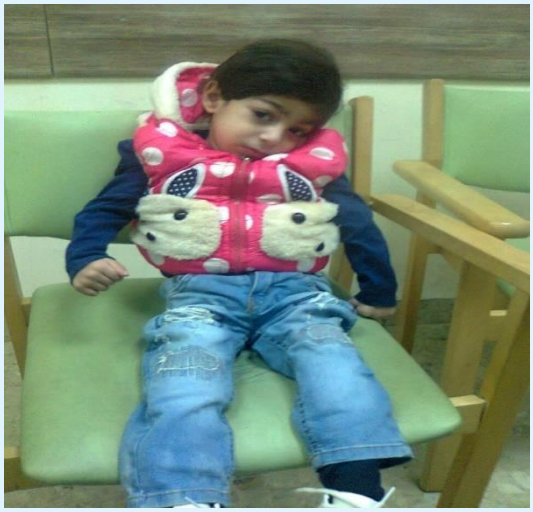

Figure 9: After treatment, patient-6 could move his head when put in the sitting position without slipping.

Discussion

Spastic cerebral palsy is a heterogeneous condition and patients generally show variable responses to various therapeutic interventions. Therefore, the attempt to treat all patients with spastic cerebral palsy with the same therapeutic plan or intervention seems far for being practically useful [1-3].

In this study, treatment of patients with spastic cerebral palsy (moderate and severe) with individualized treatment plans providing a new combination of interventions including nutritional support, muscle relaxants and the use of oral pyritinol, intramuscular piracetam, citicoline (oral and injectable), intramuscular cerebrolysin, and intramuscular nandrolone decanoate was associated with a beneficial effect on motor development particularly standing and walking. Piracetam is a safe racetam that may improve brain functions by increasing cerebral blood flow and improving the function of neurotransmitters [3]. Citicoline is a safe neuro-protective agent that may improve brain functions through the following mechanisms [3-13].

Preservation of cardiolipin and sphingomyelin. Preservation of arachidonic acid content of phosphatidylcholine and phosphatidylethanolamine. Partial restoration of phosphatidylcholine levels. Stimulation of glutathione synthesis and glutathione reductase activity. Reduction of phospholipase A2 activity.

Increasing glucose metabolism in the brain. Increasing cerebral blood flow. Reducing oxidative stress and preventing excessive inflammatory response in the brain by inhibiting the release of free fatty acids and reducing

blood brain barrier breakdown. Enhancing cellular communication by increasing the availability of neurotransmitters, including acetylcholine, norepinephrine, and dopamine. Lowering increased glutamate concentrations and increasing the decreased ATP concentrations induced by ischemia.

Increases dopamine receptor densities. Pyritinol is a pyrithiothixine derivative that may improve brain functions through increasing cerebral blood flow and improving nerve cell metabolism. It is safe and available over the counter in many countries [1-3]. Nandrolone decanoate is an anabolic steroid that can strengthen muscles and should be used judiciously in childhood disorders only by the experts [1-3,14,15]. Cerebrolysin is a neuroprotective agent consisting mainly of biologically active neuro-peptides including brain-derived neurotrophic factor, glial cell line-derived neurotrophic factor, nerve growth factor, and ciliary neurotrophic factor. It has a nerve growth factor like activity on neurons, and growth promoting efficacy in different neuronal populations from peripheral and central nervous system.

Cerebrolysin can improve brain functions through [16-21]. Inhibition of apoptosis. Improving synaptic plasticity and induction of neurogenesis. Augmenting the proliferation, differentiation, and migration of adult subventricular zone neural progenitor stem cells, contributing to neurogenesis. Induction of stem-cell proliferation in the brain.

Conclusion

The treatment of patients with spastic cerebral palsy (moderate and severe) with individualized treatment plans providing a new combination of interventions including nutritional support, muscle relaxants and the use of oral pyritinol, intramuscular piracetam, citicoline (oral and injectable), intramuscular cerebrolysin, and intramuscular nandrolone decanoate was associated with a beneficial effect on motor development particularly standing and walking.

References

1. AJ Al Mosawi (2008) Dramatic effect of nandrolone decanoate on motor development in cerebral palsy. Arch Dis Child 93(2): A338-A339.

2. Al Mosawi AJ (2017) A novel therapeutic approach for the treatment of cerebral palsy. LAP Lambert Academic Publishing, Germany.

3. Al Mosawi AJ (2017) A novel therapeutic approach for the treatment of brain atrophy. LAP Lambert Academic Publishing, Germany.

4. Giménez R, Raïch J, Aguilar J (1991) Changes in brain striatum dopamine and acetylcholine receptors induced by chronic CDP-choline treatment of aging mice. British Journal of Pharmacology 104(3): 575-578.

5. López-Coviella I, Agut J, Savci V, Ortiz JA, Wurtman RJ (1995) Evidence that 5'-cytidinediphosphocholine can affect brain phospholipid composition by increasing choline and cytidine plasma levels. Journal of Neurochemistry 65(2): 889-894.

6. D'Orlando KJ, Sandage BW (1995) Citicoline (CDP-choline): mechanisms of action and effects in ischemic brain injury. Neurological Research 17(4): 281-284.

7. Alvarez XA, Sampedro C, Lozano R, Cacabelos R (1999) Citicoline protects hippocampal neurons against apoptosis induced by brain beta-amyloid deposits plus cerebral hypoperfusion in rats. Methods and Findings in Experimental and Clinical Pharmacology 21(8): 535-540.

8. Wurtman RJ, Regan M, Ulus I, Yu L (2000) Effect of oral CDP-choline on plasma choline and uridine levels in humans. Biochemical Pharmacology 60(7): 989-992.

9. Warach S, Pettigrew LC, Dashe JF, Pullicino P, Lefkowitz DM, et al. (2000) Effect of citicoline on ischemic lesions as measured by diffusion-weighted magnetic resonance imaging. Citicoline 010 Investigators. Annals of Neurology 48(5): 713-722.

10. Hurtado O, Moro MA, Cárdenas A, Sánchez V, Fernández-Tomé P, et al. (2005) Neuroprotection afforded by prior citicoline administration in experimental brain ischemia: effects on glutamate transport. Neurobiology of Disease 18(2): 336-345.

11. Secades JJ, Lorenzo JL (2006) Citicoline: pharmacological and clinical review, 2006 update. Methods and Findings in Experimental and Clinical Pharmacology 28(B): 1-56.

12. Saver JL (2008) Citicoline: update on a promising and widely available agent for neuroprotection and neurorepair Reviews in Neurological Diseases 5(4): 167-177.

13. Overgaard K (2014) The effects of citicoline on acute ischemic stroke: a review. Journal of Stroke and Cerebrovascular Diseases 23(7): 1764-1769.

14. Al-Mosawi AJ (2005) Experience with refractory vitamin D-resistant rickets and non-17α alkyl testosterone derivative anabolic agent. Therapy 2(1): 91-94.

15. Al-Mosawi AJ (2006) Dramatic effect of non-17 alpha alkyl testosterone derivative anabolic agent on growth in a child with achondroplasia on the short term. Therapy 3(5): 605-607.

16. Windisch M, Gschanes A, Hutter-Paier B (1998) Neurotrophic activities and therapeutic experience with a brain derived peptide preparation. J Neural Transm Suppl 53: 289-298.

17. Shankaran S, Laptook AR, Ehrenkranz RA, Tyson JE, McDonald SA, et al. (2005) Whole-body hypothermia for neonates with hypoxicischemic encephalopathy. N Engl J Med 353: 1574-1584.

18. Schauer E, Wronski R, Patockova J, Moessler H, Doppler E, et al. (2006) Neuroprotection of cerebrolysin in tissue culture models of brain ischemia: post lesion application indicates a wide therapeutic window. J Neural Transm 113(7): 855-868.

19. Zhang C, Chopp M, Cui Y, Wang L, Zhang R, et al. (2010) Cerebrolysin enhances neurogenesis in the ischemic brain and improves functional outcome after stroke. J Neurosci Res 88(15): 3275-3281.

20. Masliah E, Díez-Tejedor E (2012) The pharmacology of neurotrophic treatment with cerebrolysin: brain protection and repair to counteract pathologies of acute and chronic neurological disorders. Drugs Today 48(A): 3- 24.

21. Chen CC, Wei ST, Tsaia SC, Chen XX, Cho DY (2013) Cerebrolysin enhances cognitive recovery of mild traumatic brain injury patients: double-blind, placebo-controlled, randomized study. Br J Neurosurg 27(6): 803-807.