

The Use of Piracetam and Cerebrolysin in the Treatment of Agenesis of Corpus Callosum with Colpocephaly

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Abstract

Background: Corpus callosum is a large nerve tract consisting of a flat bundle of commissural fibers that runs below the brain cerebral cortex. It connects the left and right cerebral hemispheres. Absence of the corpus callosum because of failure of development is a rare congenital defect called "Agenesis of the corpus callosum".

Patients and Methods: Two Iraqi infants with non-syndromic agenesis of the corpus callosum were observed. One infant had the isolated type and the second infant had agenesis of the corpus callosum associated with colpocephaly.

Both infants had the clinical features of the syndrome resulting from the associated failure of neuronal migration including hypotonia with poor head control, no response to voice, not recognizing faces, and they didn't show any eye contact. They have never smiled and had poor spontaneous movements.

The patient with colpocephaly was a girl and, she was treated with courses of intramuscular piracetam and cerebrolysin for three months with aim of improving brain functions and accelerating her development. The second patient was a boy and he didn't receive any specific therapy.

Results: Treatment was not associated with any side effects, and after three months of treatment, the patient experienced improvements in feeding, muscle tone, alertness and response to voice, and movements.

The untreated patient didn't show any obvious improvement despite he didn't have colpocephaly.

Conclusion: Further studies enrolling a larger number of patients are recommended.

Keywords: Corpus Callosum Agenesis; Colpocephaly; Piracetam; Cerebrolysin Treatment

Introduction

Corpus callosum is a large nerve tract which consist of a flat bundle of commissural fibers that runs below the brain cerebral cortex. It connects the left and right cerebral hemispheres. Absence of the corpus callosum because of failure of development is a rare congenital defect called "Agenesis of the corpus callosum" [1,2].

Agenesis of the corpus can be:

- Isolated (Non-syndromic).
- Associated with colpocephaly (Non-syndromic).

- Associated with other abnormalities including the syndromic type which is associated with a well-known clinical syndrome such as Aicardi syndrome.

Clinical feature of the non-syndromic agenesis of the corpus callosum include two clinical syndromes [1,2]:

- The first syndrome is characterized by absence of mental retardation and the patients have normal motor functions. The only manifestation of the absence of the corpus callosum is the inability to transfer information from one cerebral hemisphere to the other hemisphere.
- Right handed patients may have difficulty in naming something placed in their left hand because of failure of transfer of information from the right sensory cortex to the speech areas in the left cerebral hemisphere.

The second clinical syndrome generally results from associated failure of migration of neurons, and its clinical features may include:

- Hypotonia, but some times spasticity is associated.
- Delayed development of motor milestones including head control, sitting, walking.
- Poor motor coordination.
- Impairment of vision or hearing.
- Feeding difficulties, difficulties in chewing and swallowing and gastro-esophageal reflux.
- Cognitive problems and mental retardation.
- Unusual social behavior during childhood that can be diagnosed as an autistic disorder.
- Seizures.

The diagnosis of agenesis of the corpus callosum is currently made by brain imaging studies including ultrasound, MRI and CT-scan [1,2].

Colpocephaly is a condition associated with disproportionate enlargement of the occipital horns of the lateral ventricles and it can be diagnosed early in life because of the development of seizures.

Sometimes colpocephaly is a nonspecific abnormality associated with other brain malformation including agenesis of the corpus callosum.

Colpocephaly is generally caused by neuronal migration disorders during early brain development. Clinical features of colpocephaly may include motor disabilities, spasticity and cerebral palsy, mental retardation, seizures and visual defects [3].

Patients and Methods

Two Iraqi infants with non-syndromic agenesis of the corpus callosum were observed. One infant had the isolated type and the second infant had agenesis of the corpus callosum associated with colpocephaly.

Both infants had the clinical features of the clinical syndrome resulting from the associated failure of neuronal migration including:

- Hypotonia with poor head control.
- No response to voice.
- Not recognizing faces even the face of the mother, and they didn't show any eye contact.
- They have never smiled.
- Poor spontaneous movements.
- Were not turning to sides, not crawling nor sitting.

The patient without colpocephaly was a boy who was first seen at the age of eight months.

The patient with colpocephaly was a girl who was first seen at the age of nine months, and she was treated with courses of intramuscular piracetam and cerebrolysin for three months (Table 1) with aim of improving brain functions and accelerating her development.

First Month
First course
Piracetam 200 mg daily for 10 days (10 doses)
Second course
Piracetam 300 mg daily on alternate days over 20 days (10 doses)
Second Month
Third course
Cerebrolysin 1 ml daily for 10 days (10 doses)
Fourth course
Cerebrolysin 1 ml daily on alternate days over 20 days (10 doses)
Third Month
Fifth course
Cerebrolysin 1 ml given every third day (10 doses)

Table 1: Treatment courses of the girl with agenesis of the corpus callosum associated with colpocephaly.

Results

The treated patient experienced:

- Improvement in feeding.
- Improved muscle tone with good head control when pulled to sitting position.
- She was responding to voice.
- She was recognizing faces showed some eye contact.
- She began to smile.
- She began to shows spontaneous movements.
- She was turning head to sides.

The untreated boy didn't show any obvious improvement after three months of observation despite he didn't have colpocephaly.

Discussion

Syndromic agenesis of the corpus callosum occurs when the malformation is present as a part of a well-known clinical syndrome such as Aicardi syndrome. In 2010, Al Mosawi reported the novel occurrence of corneal opacity in association with first case of Aicardi syndrome in Iraq and in the Arab [2].

Non-syndromic agenesis of the corpus callosum has not been described or documented in Iraq [2].

In this paper, the first Iraqi infants with non-syndromic agenesis of the corpus callosum are described and the novel use of intramuscular piracetam and cerebrolysin in one of the patients is reported.

Piracetam (2-oxo-1-pyrrolidine acetamide) is a cyclic derivative of GABA (gamma-aminobutyric acid).

Piracetam can influence impaired brain function by:

- Improving neuronal and cognitive functions without acting as a sedative or stimulant.
- Increasing blood flow and oxygen consumption in the brain. Improving the function of the neurotransmitters and brain neurotransmission.
- Piracetam has no acute toxicity at the doses used in human studies.

The LD₅₀ is 5.6 g/kg in rats and 20 g/kg in mice, indicating extremely low acute toxicity.

Piracetam has no significant side effect. A large-scale, 12-week trial of high-dose piracetam showed that piracetam caused no adverse effects when compared to a placebo group. Several studies reported that piracetam was well tolerated [4-6].

Research papers have reported the safe use of piracetam in various childhood neurologic disorders including cerebral palsy, brain atrophy, and childhood idiopathic mental retardation.

Cerebrolysin is a peptidergic medicine which contains mainly biologically active neuro-peptides including brain-derived neurotrophic factor, glial cell line-derived neurotrophic factor, nerve growth factor, and ciliary neurotrophic factor. Cerebrolysin has a nerve growth factor like activity on neurons, and growth promoting efficacy in different neuronal populations from peripheral and central nervous system. Cerebrolysin solution contains free amino acids (85%) and low-molecular (MW < 10,000) weight amino acid sequences (15%). Cerebrolysin is associated with a relatively wide therapeutic time window. The therapeutic effects of cerebrolysin have been considered to be similar to the pharmacological activities of naturally occurring nerve growth factors [7-14].

The neuroreparative effects of cerebrolysin have been commonly attributed to [7-14]:

- 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.

The use of cerebrolysin has been reported to be beneficial and safe in the treatment of various pediatric neuro-psychiatric disorders including developmental and pervasive developmental disorders including autism and mental retardation, brain atrophy, cerebral palsy, Rett syndrome and myelomeningocele [7-9,13,14].

This study suggested that intramuscular piracetam and cerebrolysin is a promising agent for a new effective treatment of the non-syndromic agenesis of the corpus callosum associated with colpocephaly.

Conclusion

Further studies enrolling more patients are highly recommended.

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