# The Accommodation Roles of Arginine in Cerebral Palsy Infants with Muscle Hypotonia

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**Abstract**: To analyze the relationship between arginine and blood ammonia, nutritional status, immunity, and to explore the regulating function of arginine in cerebral palsy infants with muscle hypotonia. We chose 96 cases with muscle hypotonia cerebral palsy from January 2009 to January 2012 in rehabilitation center of Zhengzhou children hospital as the research object, using the questionnaire survey to record the clinical symptoms, blood biochemical and blood tandem mass spectrum detection to understand arginine metabolism and biochemical indicators, and analyzed the relationship between blood arginine with nutritional status, immunity; also to analyze the regulating function of supplemental arginine in cerebral palsy infants with muscle hypotonia. In 96 cases, we detected 63 cases (65.63%) with reduced content of arginine; 52 of which include high blood ammonia, there is a negative correlation between them (r=-0.776,P=0.776); 42 of which with lower immunity, there is a positive correlation between them (r=0.351,P=0.351). There was statistical significance in the motor function, nutritional status, and the immunity function following supplement with arginine compared with the control group (P<0.05). Children with low blood arginine are often accompanied by high blood ammonia and low immunity. They also have symptoms, such as vomit, infection, and feeding difficulties, affecting the children's mental state, immune function and exercise tolerance ability. Supplement with arginine improves immune function, motor function and rehabilitation therapy.
[Jihua Z, Caiyun M, Guanghui L, Qing S, Jingjie L, Chao X. **The Accommodation Roles of Arginine in Cerebral Palsy Infants with Muscle Hypotonia**. *Life Sci J* 2014;11(6):698-703] (ISSN:1097-8135).
http://www.lifesciencesite.com. 106

**Key Words:** Arginine, Hypotonia, Cerebral palsy

## Introduction

Arginine is a kind of basic amino acid, currently the more common amino acid found in animal cells. It is not only an important raw material of protein synthesis, but also a precursor of muscle acid, polyamine and nitric oxide in the body. Arginine widely participates in tissue metabolism, and is closely associated with the body's immune function, protein metabolism, etc. It also can promote the blood ammonia into urea cycle, preventing ammonia intoxication. Arginine plays an important role in the process of nutrition metabolism and regulation of animal bodies, and it is an essential amino acid of children. Arginine is also the only substrate, synthesis of nitric oxide involved in the regulation of the immunity and blood vessel tension [1].In recent years, with accumulating research on arginine nutrition and physiological function, scholars focus on nutritional supplements, which improve sports, and promote the elimination of fatigue.

Muscle hypotonia cerebral palsy is one of the more common types of cerebral palsy with less effective rehabilitation. Patients mainly have clinical symptoms such as limb palsy, reduced muscle strength, less independent action with fatiguability, feeding difficulty, malnutrition and poor immunity. In the process of treating muscle hypotonia cerebral palsy, there exists long course, slow work, low exercise stamina, as well as poor fatigue resistance ability, resistance, and ineffective treatment, affecting not only the patient's clinical rehabilitation treatment, but also distinguishment from the genetic metabolic diseases. Whether there exists abnormal amino acid metabolism or not and how it influences children with muscle hypotonia cerebral palsy in the process of rehabilitation therapy. We did not see such research both at home and abroad. We detected amino acid metabolism of 96 children with muscle hypotonia cerebralpalsy in Zhengzhou children's hospital rehabilitation center hospital from January 2009 to January 2009, studying its relationship with blood ammonia, nutritional status and resistance, and the relationship between arginine and feeding difficulties, immunity, providing theoretical basis for further treatment.

## Material and methods

96 cases with muscle hypotonia cerebral palsy in Zhengzhou children's hospital rehabilitation center hospital from January 2009 to January 2010 with

reference to the pediatric cerebral palsy definition, classification and diagnostic criteria **[2-3]** (1) the brain injury induced cerebral palsy not progressive;(2) the diseased region induced dyskinesia in brain;(3) symptoms appear in infancy;(4) complicating mental retardation, epilepsy, sense perception, communication disorders, abnormal behavior and other abnormalities;(5) low muscle tone, poor strength. We exclude serious structural diseases in the heart, liver, kidney. We distinguish muscle hypotonia cerebral palsy from myopathy, chromosome disease and inherited metabolic diseases according to poor treatment effect of clinical rehabilitation, easy fatigue, low immunity, feeding difficulties by electromyogram, chromosome and liquid chromatography tandem mass spectrometry. 28 female cases, 68 male cases, age from 5 months to 7 years old, average age of 1.1 years.

Liquid chromatography tandem mass spectrometry (LC/MS/MS API 3200, AB, USA), high performance liquid meter (APL2000,Agilent 1000, Applied Biosysterms,USA) were used to screen blood spectrum and acyl amino acids carnitine spectrum from 96 cases with muscle hypotonia cerebral palsy on the basis of literature [4-5], if organic acid hematic disease suspected, by gas chromatography/mass spectrometry of the urine. Using the questionnaire method, we investigated feeding conditions, susceptibility to respiratory infections, fatigue and rehabilitation therapy. Routine blood ammonia, immune function and kidney function were detected by our biochemical instruments (VITRQS350, Johnson &Johnson, USA).

1.2.4 Treatment Control group: normal arginine, 33 cases, using conventional comprehensive therapy, such as exercise therapy, massage, homework therapy, scalp acupuncture, muscle excitement therapeutic apparatus, brain nutrition drugs; Treatment group: low arginine, 38 cases, in addition to the above mentioned conventional comprehensive rehabilitation treatment, taking arginine after the consent from parents. Both groups with 30 d for a period of treatment, and treatment for 3 periods. Standard of curative effect: according to the literature[6], we evaluated comprehensively regarding muscle rigidity, strength, body stretch, joint stretch. Excellent: significant increase in muscle hardness and muscle strength, obvious diminution in body stretching, joint stretching. Effective: increase in muscle hardness and muscle strength, diminution in body stretching, joint stretching. Invalid: not obvious improvement in muscle hardness, strength, body stretching, joint stretching.

**1.3 Statistical analysis**

All values are presented as mean ± SEM using SPSS13.0 software. The numerical and classification variables were performed by correlation, associativity analysis. Values of $p<0.05$ were considered to be statistically significant.

**Results**

2.1 The general data: in 96 children with muscle hypotonia cerebral palsy, 58 cases with breastfeeding, 46 with low arginine, 38 with instruction of solid food including residency, 36 with mental retardation, 6 with epilepsy, 62 with language retardation, 47 with vomiting, 71 with abnormal head by CT/MRI , 18 with abnormal electroencephalogram, 88 in all with infection during hospitalization.

2.2 Blood tandem mass spectrometry screening and other special biochemical examination: in 96 cases with retardation, 63 with reduced arginine, accounting for 65.63%, 21 with decreased propionyl carnitine/free carnitine, propionyl carnitine/acetyl carnitine, 65 with increased hydroxyl palmitoyl carnitine, hydroxyl fatty acyl carnitine, 32 cases with decreased cysteine.

2.3 The relationship between arginine and blood ammonia: 52 cases with decreased arginine and elevated blood ammonia, accounting for 54.17%. There is a negative correlation between arginine and blood ammonia (r =- 0.776) (Table 1, Figure 1).

Table 1. The relationship between arginine and blood ammonia in children with low muscle tone

| arginine | Blood ammonia | | Total | $X^2$ | P | r |
|---|---|---|---|---|---|---|
| | high | normal | | | | |
| Low | 52 | 11 | 63 | 18.439 | 0.00 | 0.401 |
| normal | 13 | 20 | 33 | | | |
| Total | 65 | 31 | 96 | | | |

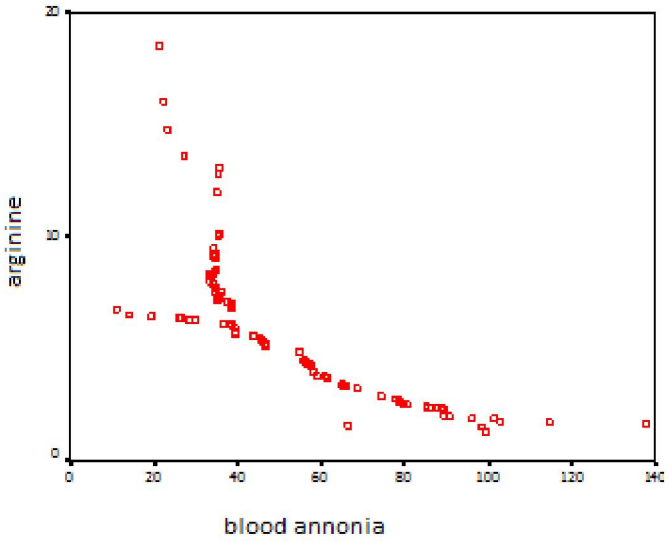


Figure 1. The relationship between arginine and blood ammonia in children with muscle hypotonia cerebral palsy

2.4 The relationship between arginine and nutritional status: 47 cases with decreased arginine, swallowing difficulties, poor appetite, diarrhea, not increased body weight, accounting for 48.96%, suggesting the correlation between arginine and nutritional status in children with muscle hypotonia cerebral palsy ($P < 0.01$, $r = 0.372$) (Table 2).

Table 2. The relationship between arginine and nutritional status

| arginine | swallowing difficulties, poor appetite, diarrhea, not increased body weight, etc | | Total | X2 | P | r |
|---|---|---|---|---|---|---|
| | Yes | No | | | | |
| Low | 47 | 16 | 63 | 15.423 | 0.00 | 0.372 |
| normal | 11 | 22 | 33 | | | |
| Total | 58 | 38 | 96 | | | |

2.5 The relationship between arginine and immunity: 42 cases with decreased arginine and immunity, accounting for 43.75%, suggesting the correlation between arginine and the immunity in children with muscle hypotonia cerebral palsy ($P < 0.01$, $r = 0.351$) (Table 3).

Table 3. The relationship between arginine and the immunity in the body

| arginine | immunity | | Total | $X^2$ | P | r |
|---|---|---|---|---|---|---|
| | Low | normal | | | | |
| Low | 42 | 21 | 63 | 13.496 | 0.00 | 0.351 |
| normal | 9 | 24 | 33 | | | |
| Total | 51 | 45 | 96 | | | |

2.6 Contrasting clinical curative effects between two groups of children with muscle hypotonia cerebral palsy: total effective rate was 76.32% in the treatment group in the clinical curative effect of movement functions; 60.61% in the control group. The treatment group was 73.68% in improving nutritional status, and the treatment group was 68.42% in improving immunity. There is statistical significance between the two groups in total effective rate, nutrition and immunity ($P < 0.05$).(Table 4).

Table 4. Contrasting clinical curative effects between two groups of children with muscle hypotonia cerebral palsy

| group | Number | Motor function effect （%） | | | | Nutritional status | Improve immunity |
|---|---|---|---|---|---|---|---|
| | | Excellent | Effective | Invalid | Effective rate | | |
| control | 33 | 8 | 12 | 13 | 60.61 | 20 | 15 |
| treatment | 38 | 12 | 17 | 9 | 76.32* | 28* | 26* |

Note: compared with control, * P ＜ 0.05

**Discussion**

Arginine, mainly sinistral arginine plays a physiological role in the body. Under normal circumstances, arginine partly derives from dietary, partly from ornithine synthesis via citrulline by the synergy among several organs. In the body, all organizations utilize arginine to synthesize plasmosin and nucleoprotein, promoting protein synthesis in muscle. At the same time, arginine is also the only provider of amidine, and further synthesizes creatine[7]. Arginine is an important carrier of nitrogen transport and storage in the body, and very important in the metabolism of muscle. Arginine improves not only nitrogen balance, but also the body's immune status. Arginine mainly participates in the urea cycle in addition to constructing protein in the body. Due to the particularity of arginine in the urea cycle, it plays an important role in the process of eliminating ammonia poisoning (Figure 2).

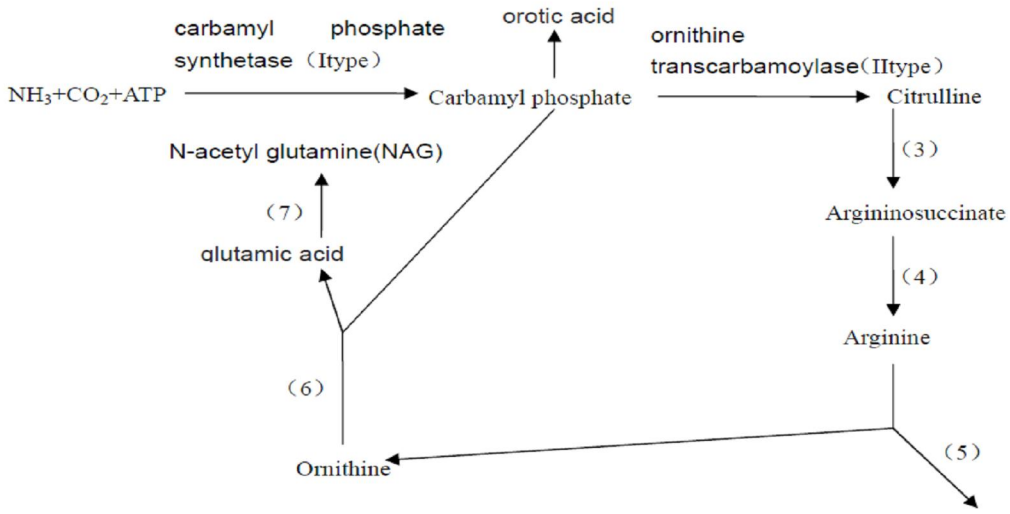


Figure 2. Schematic urea cycle where (3) indivates argininosuccinate synthetas; (4) indicates argininosuccinaseal and (5) for arginase, (6) for Ornithine, (7) for N-acetylglutamate synthetase Hyperammonemia.

Muscle hypotonia cerebral palsy is found mainly in infants and young children. The limb muscle relaxation is attenuated by encountered resistance when the limbs move, and the limb muscle relaxes due to lack of muscle belly and normal toughness, thus muscle hypotonia occurs. When we lie on our back, limbs take on the position of abduction-external rotation like a frog, but the head can't lift when in the prone position, mainly with lower muscle tone significantly, a vertical head later, difficult standing,

obvious body swinging and joints stretching, thus the pathological reflex appears, often accompanied by mental retardation, language barriers, etc. In this study, in 96 cases with muscle hypotonia cerebral palsy, children with mental retardation account for 37.50%, epilepsy 6.25%, and language retardation 64.58%. Improving muscle tone and enhancing muscle strength are the key in treatment of muscle hypotonia cerebral palsy. At present, when treating muscle hypotonia cerebral palsy mainly rehabilitation exercise therapy is utilized, but work is slow and the course is long. In this study, of 96 cases with muscle hypotonia cerebral palsy, 63 had arginine reduced, suggesting arginine is perhaps associated with low muscle tone. Scholars abroad in sports medicine are combining arginine with the regulating mechanism in the movement, recovery after exercise, and treatment after sports trauma[8], in order to further reveal the relationship between movement and the body. A large number of studies[9-12] show that exogenous L - arginine can improve aerobic exercise ability, extend the time of exercise, reduce muscle damage, and delay fatigue. In this study, 96 cases with muscle hypotonia cerebral palsy,79.31% of which with breastfeeding and lower arginine, 34.21% with assistant food and lower arginine. However, with arginine treatment in 38 cases, the total effective rate is higher compared with the control group, and the difference is statistically significant. It prompts us to consider that supplement with exogenous arginine can raise muscle strength, muscular tension and muscle movement endurance, and enhance the athletic ability of children with muscle hypotonia cerebral palsy. Domestic scholars[13-14] found different content changes of sinistral arginine in serum when sports may be associated with exercise intensity, exercise time and the function status in the body. Studies have found that after heat stress, 17 kinds of free amino acids in the serum except arginine decreased, the rest is higher, may be due to the reason that high temperature accelerates urea cycle, leading to increased decomposition of sinistral arginine for urea to elimin-ate the toxicity of ammonia, helpful to prevent fatigue[15]. Foreign scholars [16-17] found that the sinistral arginine improves the movement capacity of the body, and the mechanism may be due to the reason that increased ammonia lowers athletic ability, suggesting that the supplement with arginine can promote ornithine cycle, thus too much ammonia as the result of the sports consumption of protein is converted to urea, preventing the increase of blood ammonia, thus improving exercise capacity[18]. Consistent with the abovementioned literature at home and abroad, we found in this study that there was a negative correlation between arginine and blood ammonia in 96 cases with muscle hypotonia cerebral palsy, demonstrating that increased blood ammonia is associated with decreased arginine in the body. However, this study also found that there are 13 cases with normal arginine and increased blood ammonia, mainly consisting of the older children with adding assistant food, considering arginine can be obtained from food to supply arginine consumption in the body, which can guide us to add assistant food rich in arginine for reducing blood ammonia accumulation in the body.

When we do sports, the body produces increased free radicals and lipid peroxidation, leading to fatigue or some diseases[19]. In the present study, 91.67% of 96 cases with muscle hypotonia cerebral palsy had infection symptoms when hospitalized, perhaps associated with low immunity. Some scholars found that supplement with a certain dose of arginine can enhance the immune function of the organism[20-22]. However studies have also reported long-term and heavy load training can inhibit the immune function. Long-term heavy load training can reduce the content of arginine in serum, but after long-term heavy load training, supplement with arginine can adjust and improve the body's immune function[23]. In movement state, the demand for arginine increases. Providing with sufficient arginine can reduce the loss of nitrogen, and help protein synthesis in the body. Arginine can also promote the activity of the natural killer cells, regulate and strengthen the body's immune function. In this study, we found that there are statistically significant in nutritious status and and immunity between two groups with muscle hypotonia cerebral palsy about clinical curative effect. Thus, for rehabilitation treatment of muscle hypotonia cerebral palsy, we advocate appropriate exercise and supplement with exogenous arginine, maybe it is an effective method to avoid lowering immunity under the premise that rehabilitation treatment effect is guaranteed. With rapid developments in the theory and methods of immunology, research on the effects of amino acids on the immune function has been developed to study the specific organ specificity or the specific individual amino acids. Arginine plays an important role in immune defense, regulation, maintenance, and protection of the intestinal mucous membrane function and tumor specific immune. Muscle hypotonia cerebral palsy is one of the more common types of cerebral palsy with less effective rehabilitation. In the process of treatment on muscle hypotonia cerebral palsy, there exists serious clinical symptoms, long course, slow work, affecting not only the patient's clinical rehabilitation treatment, but also parents' confidence in clinical treatment. Administration with arginine enhances the body's immune function, and improves children's sports endurance, which is of great significance in helping to improve the effect of rehabilitation therapy in children,

to shorten the rehabilitation treatment, to enhance the confidence of the parents, and to reduce the economic burden on parents and communities.

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6/12/2014