Retrospective Evaluation of Routine Biochemical Blood Parameters in Children with Cerebral Palsy

Serebral Palsili Çocuklarda Rutin Biyokimyasal Kan Parametrelerinin Retrospektif Olarak Değerlendirilmesi

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ABSTRACT

Objective: Cerebral palsy (Cp) is a persistent developmental disorder that is common in childhood and affects movement and posture throughout life. Along with motor dysfunction, which is the main finding of the disease; Sensory cognitive problems, epilepsy, communication perception problems, oral motor failure and related nutritional problems, behavioral disorders, orthopedic disorders, neurological dysfunctions, convulsions, chronic lung problems and sleep problems are common. The prevalence of Cp is approximately 2- 3.5 per 1000 live births. The aim of this retrospective study was to evaluate the biochemical blood parameters of children with Cp.
Materials and Methods: The study included 50 children with Cp aged between 0 and 18 years and 50 healthy children as a control group. The Cp group was selected from the children with Cp diagnosis in the Department of Pediatric Neurology at Gazi University Faculty of Medicine between 2018-2019 and the control group was selected from the Children's Health Unit. Control group; was selected from patients who were in the same age range as the Cp group and who did not have any neurological disease. For the study, the ethics committee permission was obtained from Gazi University Clinical Research Ethics Committee (decision number: 430). In two groups, routine biochemical parameters were evaluated retrospectively.
Results: According to our study; creatinine, calcium, phosphorus, sodium, folic acid, albumin, ferritin ratios were significantly different between Cp and control group ($p<0.05$).
Conclusions: In children with Cp there may be bone metabolism disorders. This quality of life in chronic monitoring of children so that these disorders can be corrected early it is important to be noticed and treated.

Keywords: Cerebral palsy, Biochemistry, Blood parameters

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ÖZET

Amaç: Serebral palsi (Cp), çocukluk çağında sık görülen, yaşam boyu hareket ve postürü etkileyen kalıcı bir gelişimsel bozukluktur. Hastalığın ana bulgusu olan motor fonksiyon bozukluğu ile birlikte; duyusal-bilişsel sorunlar, epilepsi, iletişim-algı sorunları, oral motor yetmezlik ve buna bağlı beslenme sorunları, davranış bozuklukları, ortopedik bozukluklar, nörolojik işlev bozuklukları, konvülsiyonlar, kronik akciğer sorunları ve uyku bozuklukları sık görülür. Cp prevalansı yaklaşık 1000 canlı doğumda 2-3.5'dir. Bu retrospektif çalışmanın amacı, Cp'li çocukların biyokimyasal kan parametrelerini değerlendirmektir.
Yöntem: Çalışmaya 0-18 yaş arası Cp'li 50 çocuk ve kontrol grubu olarak 50 sağlıklı çocuk alındı. Cp grubu 2018-2019 yılları arasında Gazi Üniversitesi Tıp Fakültesi Çocuk Nörolojisi Anabilim Dalı'nda Cp tanısı alan çocuklardan, kontrol grubu ise Çocuk Sağlığı Birimi'nden seçildi. Kontrol grubu; Cp grubu ile aynı yaş aralığında olan ve herhangi bir nörolojik hastalığı olmayan hastalardan seçildi. Çalışma için Gazi Üniversitesi Klinik Araştırmalar Etik Kurulu'ndan etik kurul izni (karar numarası: 430) alındı. İki grupta rutin biyokimyasal parametreler retrospektif olarak değerlendirildi.
Bulgular: Çalışmamıza göre; kreatinin, kalsiyum, fosfor, sodyum, folik asit, albümin, ferritin oranlarında Cp ve kontrol grubu arasında anlamlı fark bulundu ($p<0.05$).
Sonuç: Cp'li çocuklarda kemik metabolizması bozuklukları görülebilmektedir. Bu bozuklukların erken dönemde belirlenmesi, tedavi edilebilmesi ve yaşam kalitesi için çocukların düzenli izlenmesi önemlidir.

Anahtar Sözcükler: Serebral palsi, Biyokimya, Kan parametreleri

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INTRODUCTION

Cerebral palsy (Cp) ; It is a permanent motor dysfunction, posture and movement disorder that develops as a result of injury in the prenatal, natal and postnatal periods in the developing brain, which is not progressive but can change with age and restricts movement (1).

Prematurity and low birth weight are important risk factors for Cp; besides, there are many other factors associated with increased risk of Cp, including maternal infections and multiple pregnancy. In most Cp cases, the first injury to the brain occurs during early fetal brain development; Intracerebral bleeding and periventricular leukomalacia are the main pathological findings found in preterm babies who develop Cp. The diagnosis of Cp is primarily based on clinical findings. Early diagnosis is possible by reviewing the clinical history, based on the use of standard neuromotor evaluation and magnetic resonance imaging (MRI) findings. MRI scan has been shown to outline the extent of brain lesions and identify congenital brain malformations (2).

Frequently, motor dysfunction, which is the main finding of the disease; sensory cognitive problems, epilepsy, communication perception problems, oral motor failure and related nutritional problems, behavioral disorders, orthopedic disorders, neurological dysfunctions, convulsions, chronic lung problems, and sleep problems are common. The fact that different systems are affected at the same time requires multi-disciplinary impression of children with cerebral palsy. In individuals with cerebral palsy, the clinical picture may change over time, eg spasticity or involuntary movements may replace the initial hypotonia (3).

Children with Cp with moderate to severe functional can be vulnerable to low bone mineral density (BMD) due to reduced mobility, decreased growth rate, in adequate nutrition, low vitamin D levels, and irregularities in pubertal and skeletal maturation (4).

Patients with neurological disorders are at risk of developing osteoporosis because they have multiple risk factors leading to low bone mineral density (5). These factors include inactivity, less exposure to sunlight, poor nutrition, and use of drugs or treatments that can cause lower bone mineral density, such as antiepileptic drugs and glucocorticoids (6, 7).

Cerebral palsy registries from developed countries suggest its prevalence is 2–3 per 1000 live births. The prevalence is significantly higher in children born prematurely: 40–100 per 1000 live births for those born below 28 weeks gestation. (8).

Children with Cp are smaller than healthy children with peers and have a certain body composition. Decrease in bone mineral density, muscle mass, fat mass; are the features that distinguish them from healthy children. Malnutrition is common in children with Cp due to nutritional barriers such as chewing, sucking, swallowing, gastroesophageal reflux disease, constipation, or changes in appetite caused by anticonvulsant medications that prevent the development of seizures used in the treatment of many types of epilepsy. The etiology of Cp is diverse and multifactorial. It is usually caused by injury to the brain before or at birth. This is the major causative factor. It can also happen between the ages of 3–5 y. There are three predominant Cp syndromes (spastic, dyskinetic and ataxic). Hypotonic Cp, though described earlier, is absent from the contemporary classifications. Majority of patients with “hypotonic Cp” in early infancy later develop spastic, dyskinetic or ataxic Cp. However, some children may continue to be hypotonic due to involvement of cerebro-cerebellar circuits or the extrapyramidal circuity (9, 10).

Most children with Cp have nutritional difficulties and are particularly prone to malnutrition (11). Studies evaluating the micronutrient status of children with Cp found that deficiencies for iron, zinc, copper, vitamin D, carnitine, folic acid, and vitamin B12 were common and their incidence ranged between 10% and 55% (12, 13).

Calcium and vitamin D play a critical role in the mineralization of bone. Children with neurological disorders are at greater risk of poor dietary calcium and vitamin D intake (6). Bone loss in adulthood Cp increases not only the risk of fractures but also the risk of medical complications (14). Children with Cp generally have lower mineral intake than healthy children. In this population; Low food intakes have been noted, including energy, calcium, iron, folate, niacin, vitamin E, vitamin D and fatty acids (15-19).

Diagnosis of cerebral palsy requires a complete history, physical examination, and ancillary investigations. The history should include a detailed account of gestation and perinatal events and documentation of the attainment of developmental milestones. In addition to a general physical inspection, the examination should assess station (pelvic and leg alignment during stance), spinal alignment, gait (if applicable), active and passive range of motion of joints, sensibility, motor power, muscle tone (spasticity), type and extent of movement disorders, and presence of limb deformity. Cranial ultrasonography, MRI, CT, and other specialised tests are used to assess the extent of the CNS insult (20).

The aim of this retrospective study was to evaluate the biochemical blood parameters of children with Cp.

MATERIALS and METHODS

The study included 50 children with Cp aged between 0 and 18 years and 50 healthy children as a control group. 32 of the children with Cp were boys and 18 were girls. The control group children were 29 boys and 21 girls. The Cp group was selected from the children with Cp diagnosis in the Department of Pediatric Neurology at Gazi University Faculty of Medicine between 2018-2019 and the control group was selected from the Children's Health Unit. Control group; was selected from patients who were in the same age range as the Cp group and who did not have any neurological disease. For the study, the ethics committee permission was obtained from Gazi University Clinical Research Ethics Committee (decision number: 430). In two groups, routine biochemical parameters were evaluated retrospectively. Children with Cp and control groups participated in the study; BUN, Creatinine, Calcium, Phosphorus, ALP, Sodium, Potassium, İron, Ferritin, TSH, T4, D, AST, ALT, Folic acid, Cholesterol, Triglyceride, Chlorine, B12, Albumin values were analyzed retrospectively.

Ferritin, TSH, T4 Vitamin D, B12 tests were run on Beckman Coulter DXI 800 autoanalyser. All of these tests use the paramagnetic particle chemiluminescence immunoassay method for the quantitative determination of these tests in human serum.

Creatinine: Jaffe, Calcium: Arsenazo III, AST, ALT: Enzymatic, Sodium, Potassium, Chlorine: Indirect ISE (Ion Selective Electrote), Total Cholesterol: The spectrophotometric measurement of the absorbance of the chromophore formed after enzymatic destruction of cholesterol esters with Cholesterol Esterase, Trigiliserid: It is based on the spectrophotometric measurement of the absorbance of the chromophore formed by a series of enzymatic reactions with the enzymatic destruction of triglyceride with Lipase. All these above measurements were carried out on Beckmac Coulter AU 5800 autoanalysers.

Data were analyzed using SPSS 25.0 statistical package program. Descriptive statistics (frequency, percentage distribution, mean, median etc.) were used for statistical analysis. Subgroups were formed according to different characteristics and it was examined whether the quantitative variables fit the normal distribution. $p < 0.05$ was considered statistically significant.

RESULTS

Fifty (50) children with Cp and 50 healthy controls aged between 0 and 18 years were included in the study. 32 of the children with Cp were boys and 18 were girls. The control group children were 29 boys and 21 girls.Children with Cp and control groups participated in the study; BUN, Creatinine, Calcium, Phosphorus, ALP, Sodium, Potassium, İron, Ferritin, TSH, T4, D, AST, ALT, Folic acid, Cholesterol, Triglyceride, Chlorine, B12, Albumin values were analyzed retrospectively.

According to our study, the BUN average of the Cerebral palsy group was 11.4067 (mg/dL) and the control group was 10.0703 (mg/dL) , there was no sıgnıfıcant difference between the two groups.While the average of creatinine in the Cp group was 0.3022 (mg/dL), it was 0.4028 (mg/dL) in the control group, the difference was statistically significant ($p<0.05$).In our study the difference between calcium levels of Cp and control group was statistically significant $p = 0.031$ ($p<0.05$). The average calcium levels of children diagnosed with Cp was Mean=9.9112 (mg/dL) , while the average calcium levels of the control group was Mean=10.2245 (mg/dL).

The difference between phosphorus levels of Cp and control group was statistically significant ($p<0.05$). The average levels of phosphorus children diagnosed with Cp was Mean=4.5174 (mg/dL) , while the average phosphorus levels of the control group was Mean=5.3086 (mg/dL).While the average sodium in the Cp group was 140.1079 (mmol/L), it was 138.7188 (mmol/L) in the control group, the difference was statistically significant ($p<0.05$).Potassium mean was 4.4722 (mmol/L) in the Cp group and 4.4594 (mmol/L) in the control group, there was no significant difference between the two groups.

The mean iron was 53.9833 (µg/dL) in the Cp group and 59.4286 (µg/dL) in the control group, there was no significant difference between in the two groups.The average of ferritin in the Cp group was 106.8056 (ng/mL) and 25.9375 (ng/mL) in the control group, the difference was statistically significant (p<0.05).

The mean TSH was 2.6356 (µIU/mL) in the Cp group and 2.8010 (µIU/mL) in the control group. The mean T4 in the Cp group was 0.9521 (ng/dL) and in the control group it was 0.9572 (ng/dL). The average vitamin D in the Cp group was 27.4553 (µg/L) , and 25.1285 (µg/L) in the control group. AST mean 38.8711 (U/L) in the Cp group and 35.1714 (U/L) in the control group. The ALT mean in the Cp group was 21.1261 (U/L) , in the control group it was 18.4941 (U/L) . There was no significant difference between the two groups in terms of these values.

The difference between folic acid levels of Cp and control group was statistically significant p = 0.018 (p<0.05). The average folic acid levels of children diagnosed with Cp was Mean=16.7033 (ng/mL) , while the average folic acid levels of the control group was Mean=9.5714 (ng/mL).

The mean cholesterol in the Cp group was 169.600 (mg/dL) , and 171.0917(mg/dL) in the control group. The mean triglyceride in the Cp group was 118.1000 (mg/dL), and 93.8667 (mg/dL) in the control group. The mean chlorine in the Cp group was 105.5365 (mmol/L) and 105.0952 (mmol/L) in the control group. There was no significant difference between the two groups in terms of these values.

In our study the difference between albumin levels of Cp and control group was statistically significant p = 0.038 (p<0.05). The average albumin levels of children diagnosed with Cp was Mean=4.5715 (g/dL) , while the average albumin levels of the control group was Mean=4.1504(g/dL).

Table 1. Comparison of study and control groups in terms of biochemistry laboratory examination results

	Cp Group N=50 Mean± SD	Control Group N=50 Mean± SD	P Value
Albumin g/dL	4.1504±0.54094	4.5715±0.80989	0.038*
Creatinine mg/dL	0.3022±0.09242	0.4028±0.19959	0.030*
D µg/L	27.4553±9.46148	25.1285±8.28166	0.335
T4 ng/dL	0.9521±0.19995	0.9572±0.16822	0.912
Calcium mg/dL	9.9112±0.68038	10.2245±0.47606	0.031*
AST U/L	27.2542±10.47660	31.4545±15.26817	0.504
Sodium mmol/L	140.1079±3.41851	138.7188±1.87056	0.039*
Potassium mmol/L	4.4722±0.68304	4.4594±0.40667	0.926
Phosphorus mg/dL	4.5174±0.66984	5.3086±0.97455	0.001*

Notes: Student t-test was used for parametric data and Mann–Whitney U test was used to compare the non-parametric data. N (Number of people)=50 Cp group, N (Number of people)=50 control group. D=Vitamin D, T4=Thyroxine, AST=Aspartate Aminotransferase.

According to our study; creatinine, calcium, phosphorus, sodium, folic acid, albümin, ferritin ratios were significantly different between Cp and control group (p<0.05). However, there was no significant difference between the two groups in terms of BUN, ALP, potassium, iron, TSH, T4, vitamin D, AST, ALT, cholesterol, triglyceride, chlorine, vitamin B12 values.

DISCUSSION

Children with cerebral palsy may have unique nutritional needs due to poor growth, poor oral food or fluid intake, dependence on tube feeding, and micronutrient deficiencies. Nutritional evaluations are generally specified in this patient population and include attention to growth charts, physical examination, evaluation of food diaries and laboratory monitoring. Interventions may include dietary supplementation using oral supplements, calorie boosting techniques, tube feeding adjustments, and mineral and vitamin supplementation (21).

In children with Cp, undernutrition contributes to poor somatic growth, diminished bone mineral density, abnormal pubertal development, and poor general health (22). Body composition may have different effects on general health (such as resistance to infection) and a child's ability to function (eg mobility and social interaction), thus affecting the quality of life of the child and the family (23).

Bone loss is a serious clinical problem in patients with cerebral palsy (14). According to the study conducted by Taşdemir et al.; this study was performed in 24 children (16 boys, eight girls) aged from 10 months to 12 years (mean (±SD) age 4.1±2.9 years) with Cp who were admitted to the Department of Pediatrics in the Faculty of Medicine of Atatürk University and Nineteen children (age- and sex-matched) without any disease affecting bone turnover were considered as the control group. Differences in serum 25OHD3, PTH and ALP concentrations between the patient and control groups were not statistically significant. However, Ca (calcium) and P (phosphorus) levels of children with Cp were significantly higher than those of controls (p<0.05) (24).

Proper bone growth in an individual requires sufficient calcium intake. Calcium is required for adequate mineralization of the bone matrix, and there is a positive correlation between calcium intake and bone mass in individuals of all ages (6).

In our study the difference between calcium levels of Cp and control group was statistically significant p = 0.031 (p<0.05). The average calcium levels of children diagnosed with Cp was Mean=9.9112 (mg/dL) , while the average calcium levels of the control group were Mean=10.2245 (mg/dL). The difference between phosphorus levels of Cp and control group was statistically significant (p<0.05). The average levels of phosphorus children diagnosed with Cp was Mean=4.5174 (mg/dL) , while the average phosphorus levels of the control group were Mean=5.3086 (mg/dL).

According to the study conducted by Papadopoulos et al.; studied 108 patients (55 males, 53 females) ranging between 8 and 29 years that were hosted in a specialized institute in Thessaloniki, Greece, due to cerebral palsy. In most cases, cerebral palsy resulted from perinatal hypoxemia; other causes included craniocerebral traumas, infections of the central nervous system and hereditary disorders. Approximately 33% of patients suffered from hypochromic anemia, whereas 38% were iron deficient. Folic acid and B12 levels were within normal range in all cases (25).

In our study, there was no significant difference between the two groups in terms of iron and vitamin B12 but the difference between folic acid levels of Cp and control group was statistically significant p = 0.018 (p<0.05). 69 Cp patients with ages between 2 and 21 years old were included in the study conducted by Roy et al. According to this research; Albuminaemia was normal in all patients. Mean 25(OH)D level was 24.3 ± 8.8 ng/mL; 33 patients (47.8%) had insufficiency and 21 (30.4%) deficiency; 36 patients (52.2%) had low ferritin levels (26) (4, 27). According to the study by Akpinar that examined the levels of vitamin D of children with cerebral palsy: Serum 25 (OH) D levels of 235 children with Cp were measured. There were 79 children at the 25(OH)D level ≤12 ng/ml, regarded as vitamin D deficiency; 62 children at the 25(OH)D level 12-≤20 ng/ml, considered as vitamin D insufficiency, 43 children at the 25(OH)D level 20-≤30 ng/ml, considered as vitamin D sufficiency, and 15 children at the 25(OH)D level >30 ng/ml. A total of 36 children were already taking vitamin D supplements (28).

In our study the difference between albumin levels of Cp and control group was statistically significant p = 0.038 (p<0.05). The average albumin levels of children diagnosed with Cp was Mean=4.5715 (gr/dl) , while the average albumin levels of the control group was Mean=4.1504(gr/dl). In our study, there was no significant difference in vitamin D levels between the two groups.

In the study by Vrhovsek et al; the aim of this study was to determine the effect of vitamin D and calcium substitution on bone mineral density (BMD) in a group of children with Cp in full-time care. Twenty children with the most severe form of Cp (spastic quadriplegia) who had been treated with anti epileptic drugs for a relatively long period of time were included in the study. Thirteen patients were treated for 9 months with 1,25-dihydroxy-cholecalciferol vitamin D (0.25 mcg daily) and with calcium (500 mg daily). Seven control children were used for observation only. BMD greatly increased in the treated group, while children with Cp in full-time care who did not receive vitamin D and calcium substitution continued to lose their bone mass. It can be concluded that the addition of vitamin D and calcium increases BMD in children with the most severe form of Cp, who are receiving anti epileptic drugs (29).

Eventually, according to our study; creatinine, calcium, phosphorus, sodium, folic acid, albümin, ferritin ratios were significantly different between Cp and control group (p<0.05).

However, there was no significant difference between the two groups in terms of BUN, ALP, potassium, iron, TSH, T4, vitamin D, AST, ALT, cholesterol, triglyceride, chlorine, vitamin B12 values.

In order to interpret the results of the study more accurately, groups should be investigated in various factors such as drug use status, whether they are receiving intravenous therapy or not. Relationships between calcium phosphorus and vitamin D levels should be investigated in more detail. Since our research is a retrospective study, there was limitations at these points.

CONCLUSION

In children with cerebral palsy there may be bone metabolism disorders. This quality of life in chronic monitoring of children so that these disorders can be corrected early it is important to be noticed and treated.

We think that further studies should be conducted with larger patient groups on the bone metabolism, nutritional status, effects of vitamin supplementation to the process.

Conflict of interest

No conflict of interest was declared by the authors.

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