J. Elem. s. 713–719 DOI: 10.5601/jelem.2012.17.4.13

DOES CHROMIUM (+3) DECREASE THE GLUCOSE CONCENTRATION IN EPILEPTIC CHILDREN?

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Abstract

Epilepsy is a common neurological disorder. It affects 50 million people worldwide, over half of which are children. Many children who suffer from epilepsy are also affected by metabolic disorders, characterized by obesity as well as intolerance and deficient transport of glucose. Recently, many researchers have indicated chromium (+3) as an essential trace mineral which probably plays an important role in metabolism of glucose and insulin. There are no data about chromium alterations in the body of epileptic patients. The purpose of this study was to find possible correlation between chromium (+3) concentration and the glucose level in children with epilepsy. Material and methods: Twenty-three untreated epileptic children with idiopathic generalized tonic-clonic seizures (9 girls and 14 boys) aged 13.4±2.7 years and 25 healthy children (sex-age-matched) served as a control were recruited to this study. The chromium blood and serum concentrations were determined as well as serum glucose level. Results: There were no statistically significant differences between epileptic and healthy children in the mean chromium (+3) blood concentration as well as according to sex in both analyzed groups of children. The mean serum chromium concentration in epileptic children was significantly lower than in healthy subjects generally ($p<0.001$), as well as in boys group ($p<0.001$) and girls ($p<0.001$). Although, the negative statistically significant correlation between serum glucose and chromium concentrations was found in epileptic children ($p<0.01$), we have not found so associations in whole blood and in healthy children. Conclusions: Our research has shown that during epilepsy the concentration of serum chromium was lower than in healthy subjects what was associated

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with glucose abnormalities. These preliminary results suggest that the detail research on the chromium in epilepsy are necessary.

Key words: glucose, chromium, epilepsy, children.

CZY CHROM OBNIŻA POZIOM GLUKOZY WE KRWI DZIECI Z EPILEPSJĄ?

Abstrakt

Epilepsja stanowi jedną z najczęstszych chorób neurologicznych. Ocenia się, że na całym świecie choroba ta dotyka ponad 50 mln ludzi, z czego ponad połowa to dzieci. Wielu dzieciom z epilepsją, w czasie ich rozwoju, towarzyszy także zespół metaboliczny, którego charakterystyczną cechą są otyłość i zaburzony metabolizm glukozy. W ostatnich latach wielu badaczy zwróciło uwagę na chrom (+3) jako niezbędny pierwiastek, który prawdopodobnie odpowiada za transport glukozy do tkanek przez stabilizowanie jej połączeń z insuliną. Rola chromu w tym aspekcie jest jednak wciąż niejasna. Brak jest również danych dotyczących zawartości chromu w organizmach dzieci z padaczką. W związku z powyższym celem pracy była ocena zawartości chromu (+3) w surowicy i pełnej krwi dzieci z padaczką oraz próba skorelowania jego zawartości z poziomem glukozy we krwi tych dzieci w odniesieniu do grupy kontrolnej. Badaniem objęto 23 dzieci ze świeżo rozpoznaną padaczką (9 dziewcząt i 14 chłopców) w wieku 13,4 ± 2,7 lat oraz 25 dzieci zdrowych odpowiadających grupie badanej strukturą wieku i płci. U wszystkich dzieci zmierzono stężenie chromu w surowicy krwi i pełnej krwi oraz ocenie poddano stężenie glukozy we krwi. Wykazano brak różnic w zawartości chromu (+3) w pełnej krwi, a także glukozy we krwi między grupą dzieci z padaczką a dziećmi zdrowymi, podobnie brak różnic w ocenie tych parametrów stwierdzono w odniesieniu do płci dzieci niezależnie od występowania choroby. Wykazano istotnie statystycznie niższy poziom chromu w surowicy krwi dzieci z padaczką w porównaniu z grupą kontrolną ($p<0,001$), jak też w surowicy chłopców i dziewcząt z padaczką w porównaniu z chłopcami i dziewczętami zdrowymi ($p<0,001$). Równocześnie zanotowano istotną ujemną zależność między stężeniem chromu w surowicy krwi dzieci z padaczką a stężeniem glukozy we krwi ($p<0,01$), przy czym nie zauważono podobnej zależności u dzieci zdrowych. Badania sugerują, iż istnieje możliwość związku między poziomem chromu (+3) u dzieci z padaczką a notowanymi w literaturze zaburzeniami transportu glukozy. Wydaje się uzasadnione rozwijanie tego tematu badań w dokładniejszych pracach, które mogłyby się przyczynić do głębszego zrozumienia padaczki.

Słowa kluczowe: glukoza, chrom, padaczka, dzieci.

INTRODUCTION

Epilepsy is a common neurological disorder with the heterogeneous nature, which affects 50 million people worldwide, over half of which are children (Volpe et al. 2007). In about 25% patients with epilepsy the number of seizures is not greatly reduced even when two or three anti-epileptic drugs are used. As suggested by some authors (Volpe et al. 2007, Bertoli et al. 2006, Vianna et al. 2006), about 20 to 25% of patients administered the highest tolerated doses fail to control seizures.

More than 50% of epileptics are children. Metabolic disorders have frequently been demonstrated in children with epilepsy together with growth

retardation (Volpe et al. 2007) and intolerance and deficient transport of glucose (Vianna et al. 2006).

In the last years, it has been suggested that serum trace element concentrations in epileptic patients can show some abnormalities (Hirate et al. 2002, Verrotti et al. 2002, Johnson 2001, Ashraf et al. 1995). Balance of certain minerals is crucial for a healthy nervous system and neuronal susceptibility to excitability (Hamed et al. 2004). Several reports suggested that electrolytes (sodium, potassium, calcium) and the level of some trace elements (zinc, copper, iron) in the body play an important role in development of seizure condition (Hamed et al. 2004, Dudek 2001, Ikeda 2001, Pisacane et al. 1996, Smith, Bone 1982).

As suggested by Wallach (1985), the essential role of chromium in animal and human nutrition is now well accepted. Animal studies have shown that chromium deficiency occurs in diabetic-like states, impaired growth, elevated blood lipids, etc. In people, chromium deficiency has been demonstrated clearly only in just one clinical situation: patients on total parenteral nutrition without added Cr have been observed to have impaired glucose tolerance, hyperglycemia, relative insulin resistance, peripheral neuropathy and metabolic encephalopathy (Wallach 1985, Jeejeebhoy et al. 1977). The latest research indicates that Cr supplementation can improve glucose metabolism in glucose intolerance individuals, and Cr deficiency may be important in diabetes mellitus for stabilization of the insulin/glucose complex (Ali et al 2011). There are no data about chromium in epilepsy.

To sum up, the aim of this preliminary study was to assess chromium concentrations in blood and serum, and the glucose serum level in epileptic and healthy children.

MATERIAL AND METHODS

Twenty-three untreated epileptic children with idiopathic generalized tonic--clonic seizures (9 girls and 14 boys) aged 13.4±2.7 years and 25 healthy children (sex-age-matched) as the control were recruited to this study. The height and weight of all subjects (epileptic and healthy children) were within the normal range of the percentile growth charts for age and sex of children (between 50-75%, no overweight and obesity) (Kuczmarski et al. 2002). The characteristics of both populations are presented in Table 1. The study was approved by the Ethical Committee at the Poznan University of Medical Sciences. The parents of the patients, patients and the healthy subjects were under the care of the Department of Clinical Psychology at the Poznan University of Medical Sciences. The blood samples used in this research were obtained from the blood drawn for normal analytical procedures in the clinic. From each subjects, after an overnight fast, 5 ml venous blood was collected to 2 PP tubes;

Table 1

The characteristics of the analyzed populations

Characteristic of subjects	Mean ± SD (range)
Age (years)	
Epileptic Girl Boys	13.4 ± 2.7 (9-17) 14.1 ± 2.4 (9-16) 13.0 ± 2.8 (9-17)
Control Girl Boys	14.2 ± 2.6 (9-16) 13.9 ± 2.8 (9-16) 14.7 ± 2.1 (9-16)
Sex (girls/boys)	
Epileptic	9/14
Control	10/15
Duration of illness (months)	
Epileptic	2.1 ± 1.7 (0.4-6)

one tube from each subject was allowed to stay at room temperature and was centrifuged at 5000 rpm for 10 minutes, afterwards the serum was stored frozen at –20ºC until chromium analyses. The second tube with a blood sample, mixed with heparin, was stored at –20ºC until the chromium analyses. The glucose concentration was measured immediately by the colorimetric method using an Accu-Check Active glucometer (Roche).

The serum and blood concentrations of chromium were determined by the Atomic Absorption Spectrometry method with a graphite furnace spectrometer (AAS-5, Zeiss), having diluted the samples with de-ionized water as required. The accuracy of the method was assessed by comparison with the certified serum control (Human Serum, Merck).

There are no reference values for serum chromium concentrations.

The data are presented as arithmetic means ± standard deviation (SD) and statistically significant differences were determined by *t*-test and Wilcoxon test using Excel 2007 and Statistica ver. 7.0. Statistical significance was defined as $p<0.05$.

RESULTS AND DISCUSSION

Childhood epilepsy is the most common neurological disorder in children. More than 50% of the 50 millions of epileptic patients are children. The metabolic syndrome is an aggregate of metabolic and cardiovascular

abnormalities including obesity, impaired glucose tolerance, dyslipidemia, and cardiovascular morbidity (Grundy et al. 2005). As suggested Daniels et al. (2009), children with epilepsy usually have a high rate of obesity at initial presentation, as a consequence of metabolic abnormalities. In our study, however, we did not observe body mass abnormalities in the children with epilepsy, or different glucose concentrations (Table 2) compared to healthy subjects (epileptic – 87 mg dL^{-1}; healthy – 93 mg dL^{-1}). On the other hand, animal (Lee et al. 2011) as well as human studies (Vianna et al. 2006) show that glucose intolerance is common during epilepsy, especially in children, and can be associated with the metabolic syndrome, which can result in increased hippocampal pathology and more freuqnet seizures. In the last years, it has been suggested that serum trace element concentrations in epileptic patients can show some abnormalities (Hirate et al. 2002, Verrotti et al. 2002, Johnson 2001, Ashraf et al. 1995). Balance of certain minerals is crucial for a healthy nervous system and neuronal susceptibility to excitabil-

Table 2

The mean serum and blood levels of chromium and blood glucose level in control and epileptic children

Total	Control, n=25 mean ± SD (range)	Epileptic, n=25 mean ± SD (range)	
Blood Cr (ng dL^{-1})	261.6 ± 38.2 (123.0-345.2)	254.1 ± 44.2 (153.0-328.3)	ns
Serum Cr (ng dL^{-1})	181.3 ± 23.4 (64.6-243.2)	113.0 ± 28.0 (41.0-151.8)	P=0.000
Blood glucose (mg dL^{-1})	87.0 ± 18.2 (65.0-117.0)	92.8 ± 17.1 (70.0-134.0)	ns
Girls	control, n=10 mean ± SD (range)	epileptic, n=9 mean ± SD (range)	
Blood Cr (ng dL^{-1})	254.2 ± 46.3 (123.0-321.9)	259.1 ± 29.8 (217.9-301.2)	ns
Serum Cr (ng dL^{-1})	182.4 ± 19.9 (64.6-223.4)	116.2 ± 18.3 (93.7-151.2)	P=0.000
Blood glucose (mg dL^{-1})	97.4 ± 21.3 (74.0-117.0)	89.0 ± 11.8 (76.0-112.0)	ns
Boys	control, n=15 mean ± SD (range)	epileptic, n=14 mean ± SD (range)	
Blood Cr (ng dL^{-1})	267.7 ± 67.2 (132.7-345.2)	250.9 ± 52.3 (153.0-328.3)	ns
Serum Cr (ng dL^{-1})	191.2 ± 34.6 (71.3-243.2)	111.0 ± 33.2 (41.0-151.8)	P=0.000
Blood glucose (mg dL^{-1})	78.4 ± 19.2 (65.0-99.0)	95.3 ± 19.8 (70.0-134.0)	ns

ns – non-significant

ity (Hamed et al. 2004). The micronutrient chromium is of interest as it can potentially improve glucose tolerance by reducing insulin resistance (Ali et al. 2011, Krejpcio et al. 2007). There are no data about the role and concentration of chromium in epilepsy. Table 2 shows the determined concentrations of chromium in the blood and serum of epileptic and healthy children. However, we did not observe significant differences between epileptic and healthy children in the blood chromium concentration (~260 ng dL^{-1}), whereas the serum chromium level was significantly lower ($p<0.001$) in epileptic total (~113 ng dL^{-1}), girls (~116 ng dL^{-1}), and boys (~111 ng dL^{-1}) than in healthy total (~181 ng dL^{-1}), girls (~182 ng dL^{-1}) and boys (~191 ng dL^{-1}). A significantly higher level of chromium in hair of epileptic male and female patients in Pakistan compared to healthy subjects was described earlier by Ashraf et al. (1995). In Nigeria, Nsonwu et al. (2005) obtained similar levels of chromium (~250 ng dL^{-1} vs. ~265 ng dL^{-1}, respectively) in type 2 diabetics and non-diabetics.

The association between chromium and glucose in epileptic patients can prove significant correlation between the glucose level and chromium concentration in epileptic children (Figure 1), although not correlated in healthy subjects. It has been suggested that chromium plays an important role not only in diabetes mellitus but also in epilepsy. In conclusion, once the role of chromium and other metals in epilepsy is clearly explained, it should help us combat this disease more successfully and perhaps stop neural deficits caused by the metabolic syndrome and other epilepsy associated dysfunctions.

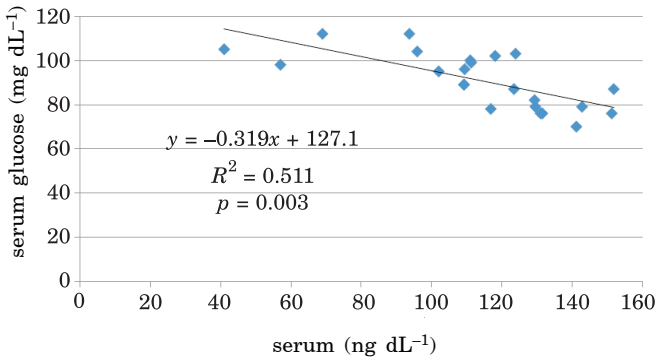

Fig. 1. Correlation between the serum chromium level and blood glucose concentration in epileptic children

REFERENCES

Ali A., Ma Y., Reynolds J., Pierce Wise J. Sr., Inzucchi S.E., Katz D.L. 2011. *Chromium effects on glucose tolerance and insulin sensitivity in persons at risk for diabetes mellitus.* Endocr. Pract., 17: 16-25.

Ashraf W., Jaffar M., Mohammed D., Iqbal J. 1995. *Utilization of scalp hair for evaluating epilepsy in male and female groups of the Pakistan population*. Sci. Total Environ., 164: 69-73.

Bertoli S., Cardinali S., Veggiotti P., Trentani C., Testolin G., Tagliabue A. 2006. *Evaluation of nutritional status in children with reflactory epilepsy.* Nutr. J., 5: 14-23.

Daniels Z.S., Nick T.G., Liu C., Cassedy A., Glauser T.A. 2009. *Obesity is a common comorbidity for pediatric patients with untreated, newly diagnosed epilepsy.* Neurology, 73: 658-664.

Dudek F. E. 2001. *Zinc and epileptogenesis.* Epilepsy Curr., 1: 66-70.

Grundy S.M., Cleeman J.I., Daniels S.R., Donato K.A., Eckel R.H., Franklin B.A., Gordon D.J., Krauss R.M., Savage P.J., Smith S.C. Jr., Spertus J.A., Costa F. 2005. *Diagnosis and management of the metabolic syndrome: an American Heart Association/National Heart, Lung, and Blood Institute Scientific Statement.* Circulation, 112: 2735-2752.

Hamed S.A., Abdellah M.M., El-Melegy N. 2004. *Blood levels of trace elements, electrolytes, and oxidative stress/antioxidant systems in epileptic patients.* J. Pharmacol. Sci., 96: 465-473.

Hirate M., Takeda A., Tamano H., Enomoto S., Oku N. 2002. *Distribution of trace elements in the brain of EL (epilepsy) mice.* Epilepsy Res., 51: 109-116.

Ikeda M. 2001. *Iron overload without the C282Y mutation in patients with epilepsy.* J. Neurol. Neurosurg. Psychiatry, 70: 551-553.

Jeejeebhoy K.N., Chu R.C., Marliss E.B., Greenberg G.R., Bruce-Robertson A. 1977. *Chromium deficiency, glucose intolerance, and neuropathy reversed by chromium supplementation, in a patient receiving long-term total parenteral nutrition.* Am. J. Clin. Nutr., 30: 531-536.

Johnson S. 2001. *Micronutrient accumulation and depletion in schizophrenia, epilepsy, autism and Parkinson's disease?* Med. Hypoth., 56: 641-645.

Krejpcio Z., Kuryl T., Dembski B., Wojciak R.W. 2007. *Effect of dietary supplementation with fructans and chromium (III) on blood glucose and insulin and beta-oxidation in lymphocytes of type 1 diabetic rats.* Med. Wet., 63: 1494-1496.

Kuczmarski R.J., Ogden C.L., Guo S.S. *CDC growth charts for the United States: Methods and development.* National Center for Health Statistics. Vital Health Stat, 11: 1-189.

Lee E.B., Warman G., Dhir R., Ahima R.S. 2011. *Metabolic dysfunction associated with adiponectin deficiency enhances kainic acid-induced seizure severity*. J. Neurosci., 31: 14361--14366.

Nsonwu A.C., Usoro C.A. O., Etukudo M.H., Usoro I.N. 2005. *Serum and urine levels of chromium and magnesium in type 2 diabetics in Calabar, Nigeria.* Mal. J. Nutr., 11: 133-142.

Pisacane A., Sansone R., Impagliazzo N., Coppola A., Rolando P., D'Apuzzo A., Tregrossi C. 1996. *Iron deficiency anaemia and febrile convulsion: case-control study in children under 2 years.* B.M.J., 313: 343-344.

Smith W. G., Bone I. 1982. *Copper, zinc and magnesium plasma levels in epilepsy.* J. Neurol. Neurosurg. Psychiatry, 45: 1072-1073.

Verrotti A., Basciani F., Trotta D., Pomilio M.P., Morgese G., Chiarelli F. 2002. *Serum copper, zinc, selenium, glutathione peroxidase and superoxidase levels in epileptic children before and after 1 year of sodium valproate and carbamazepine therapy.* Epilepsy Res., 48: 71-75.

Vianna J.B.M., Atallah A.N., Prado G.F., Valente O., Duarte-Barros M.L., Vianna E.C.S., Mello L.E.A.M. 2006. *The oral glucose tolerance test is frequently abnormal in patients with uncontrolled epilepsy.* Epilepsy Behav., 9: 140-144.

Volpe S.L., Schall J.I., Gallagher P.R., Stallings V.A., Bergqvist A.G.C. 2007. *Nutrient intake of children with intractable epilepsy compared with healthy children.* J. Am. Diet. Assoc., 107: 1014-1018.

Wallach S. 1985. *Clinical and biochemical aspects of chromium deficiency.* J. Am. Coll. Nutr., 4: 107-120.