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Iodine in autism spectrum disorders

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ABSTRACT

Objective: The aim of our study was to assess the iodine status of Polish boys with severe autism compared to their healthy peers and evaluate the relationship between urinary iodine, thyroid hormones, body mass index and Autism Spectrum Disorder (ASD) symptomatology.
Subjects and methods: Tests were performed in 40 boys with ASD and 40 healthy boys, aged 2–17 from the same geographic region in Poland. Urinary iodine (UI), free triiodothyronine (fT3), free thyroxine (fT4), thyroid stimulating hormone (TSH), BMI, and individual symptoms measured by the Childhood Autism Rating Scale (CARS) were correlated.

Validated ion chromatography method with pulsed amperometric detection was applied for the determination of urinary iodine after optimized alkaline digestion in a closed system assisted with microwaves.
Results: 19 out of 40 children with ASD had mild to moderate iodine deficiency. Statistically significant lower levels of UI, fT3 and fT4 and higher levels of TSH were found in the autistic group when compared with the control group. Concentration of iodine in urine was negatively associated with clinician's general impression for children between 11 and 17 years. Emotional response, adaptation to environmental change, near receptor responsiveness, verbal communication, activity level, and intellectual functioning are more associated with UI than other symptoms listed in CARS.
Conclusion: The severity of certain symptoms in autism is associated with iodine status in maturing boys. Thyroid hormones were within normal reference ranges in both groups while urinary iodine was significantly lower in autistic boys suggesting that further studies into the nonhormonal role of iodine in autism are required.

1. Introduction

Autism spectrum disorders (ASD) and iodine deficiency disorders (IDDs) are both global health problems. Autism spectrum disorder has no single known cause [1]. The major challenge facing progress in research into the etiology of autism is the complex interplay between many factors (environmental, genetic, social) and their poorly understood effect on the function and development of the autistic brain. ASD are developmental disorders that become evident during early childhood. Usually they are evidenced by problems forming relationships, difficulty communicating with other people and certain abnormal behavioral patterns. ASD is an umbrella term that was outlined by diagnosis criteria presented in the Diagnostic and Statistical Manual of Mental Disorders (DSM), currently in its 5th edition [2] and encompasses what were previously recognized as distinct subtypes including autistic disorder, Asperger syndrome, childhood disintegrative disorder and pervasive developmental disorder-not otherwise specified. The exact number of children affected by ASD in Poland is hard to quantify. Up until 2010 the healthcare & disability coding system did not distinguish between persons affected by autism disorders and other psychiatric or neurological problems. However, we do know that the global trend of increasing ASD diagnosis is consistent with the increasing incidence here in Poland [3,4]. The best estimates indicate that around 30,000–50,000 children in Poland are affected by ASD [5].

Although the exact etiology of ASD is unknown, the subject is one of much recent inquiry. Numerous studies have documented statistically significant nutritional and metabolic aberrations in persons affected by ASD when compared to normal populations [6,7]. Abundant effort has been devoted to determining the content

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of elements that may contribute to the development of ASD, even if their exact mechanism or roles in the disorder remain unclear.

Iodine is a particularly important microelement in human physiology—it plays a crucial role as a component of thyroid hormones and deficiency at any stage of life can cause significant clinical manifestations [8–13]. The most critical time for proper iodine status, however, is early in life—hypothyroidism due to iodine deficiency which can lead to impaired neurodevelopment. Adequate levels of thyroid hormones are especially important for myelination, cell migration, differentiation and maturation of the fetal brain [14–16]. IDD are caused primarily by insufficient dietary iodine intake and/or inadequate iodine utilization due to, for example, the presence of goitrogens [17,18].

In one study performed in Egypt, 54% of tested autistic children were found to be iodine deficient [19]. Another study performed in USA found 45% lower iodine content in hair of children with autism when compared with healthy controls [7]. Up until now, such studies have not yet been performed in Poland. There is also a lack of current data assessing the effectiveness of iodine prophylaxis in Polish children between the ages of 2 and 17 years and whether iodine consumption is at a satisfactory level. Although significant steps have been taken in Poland to eliminate iodine deficiency and the resulting disorders [20], the situation still requires constant monitoring. Measurements of thyroid hormone levels and thyroid stimulating hormone levels are important in the assessment of thyroid function. The majority of dietary iodine, however, ends up in the urine, so although it is not a direct measurement of function, urinary iodine (UI) level is a great indicator of recent iodine intake and low values demonstrate a population is at risk for deficiency [14,21,22].

The primary aims of our study were to compare iodine excretion in ASD children with those of their normally developing peers and to correlate iodine status with fifteen common diagnostic criteria for ASD from the Childhood Autism Rating Scale (CARS) in order to check which items on the scale are mostly affected by iodine status. The data were also interpreted to identify whether or not there were any relationships between age, BMI, the severity of individual symptoms of ASD, thyroid hormones and urinary iodine. To the best of our knowledge, studies of iodine status in relation to specific items from the scale measuring the severity of autism are lacking not only in Poland but are also very rare in the entire world.

2. Materials and methods

2.1. Patients and samples

Our studies have been carried out in accordance with the code of ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans. The study protocol was reviewed and approved by the Ethics Committee of the Medical University of Lublin, Al. Racławickie 1, 20-059 Lublin, room 128, tel.: +48 81448 5213, Poland KE 0254/12/2014. Informed written consent was signed by the parents or legal guardians of the studied subjects Tests were performed in 80 male children who constituted the studied group 40 boys (age 2–17 years, the average age: 7.2 years) and the control group, i.e., 40 healthy boys (age 2–17 years, the average age: 9.9 years) from the same geographic region (i.e., the south–east, unindustrialized region surrounding Lublin, Poland—a city of approximately 400 thousand residents). Socioeconomic status of all children was similar. Autistic children were recruited from the I Department of Psychiatry, Psychotherapy and Early Intervention of the Independent Public Hospital No. 1 in Lublin, Poland. Among autistic children, 21 were nonverbal, and 19 were verbal (echolalic speech, i.e., repeating words or phrases spoken by others). The patients fulfilled the diagnostic criteria of autism described in the 4th edition of the Diagnostic and Statistical Manual of Mental Disorders.[23]

The control group was comprised of 40 healthy children who were unrelated to the autistic patients. The control group was carefully selected from children who visited the medical center to have regularly scheduled check-ups, performed as part of regular procedure. They were not receiving any medical treatment and were not admitted to the hospital. Children were screened for any indications of infectious disease, thyroid pathologies, neurological disorders and psychiatric disorders and excluded from the study if they presented with any symptoms. All participants had normal results for routine urine analysis. Both ASD and healthy children did not take any mineral and vitamin supplements before the samples for analysis were collected. Children who were taking regular medications including stimulants, anticonvulsants, and atypical antipsychotic drugs were excluded from our study. They were not on any special diets prior to the tests—patients on casein-free, gluten-free diets and vegetarians were excluded from the study.

Characteristic of autistic and healthy children are included in Table 1.

2.2. Autism severity scale

Childhood Autism Rating Scale (CARS) is a test that combines parent reports and direct observations made by the clinician. The CARS score, which is a measurement of the severity of the disorder, rates the child on a scale from one to four in each of fifteen areas: 1—relationships with people, 2—imitation, 3—emotional response, 4—body use, 5—relation to non-human objects, 6—adaptation to environmental change, 7—visual responsiveness, 8—auditory responsiveness, 9—near receptor responsiveness (taste, smell), 10—anxiety reaction, 11—verbal communication, 12—nonverbal communication, 13—activity level, 14—intellectual functioning and 15—the clinician's general impression. Children who score between 30 and 36 are diagnosed with mild to moderate autism, while those who score between 37 and 60 points are diagnosed with severe autism[24,25]. The assessments are based not only on frequency of the behavior, but also on its intensity, peculiarity, and duration. All autistic children in our study had severe autism (total score >37).

The individual CARS scores of the study group are presented in Table 2.

2.3. Sample collection

24-h urine samples were collected for three consecutive days. Samples were collected in acid washed polyethylene containers. Samples were defrosted at room temperature and divided into aliquots. The aliquots were either directly measured or stored at −25 °C until analysis.

2.4. Biochemical analysis

Measurements of serum free triiodothyronine (fT3), free thyroxine (fT4) and thyroid stimulating hormone (TSH) were performed by accredited diagnostic labs (Lublin, Poland) holding certificates according to PN-EN ISO 9001:2009 standards.

2.5. Measuring urinary iodine concentration

Studies of total iodine content in urine (UI) of ASD and healthy children were performed using ion chromatography with pulsed amperometric detection (IC-PAD). The validated analytical method and optimized sample preparation procedure (i.e., microwave assisted alkaline digestion in a closed Teflon vessels with the use of tetramethylammonium hydroxide (TMAH) solution together