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Original article

Study of serum copper and ceruloplasmin levels in Egyptian autistic children

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ABSTRACT

Background: Autism is a behaviorally defined neurodevelopmental disorder of unknown etiology.
Objective: To assess serum copper and ceruloplasmin levels in Egyptian autistic children patients.
Subjects and methods: 40 participants have been subjected to thorough history taking, complete clinical examination, IQ assessment, estimation of serum copper and ceruloplasmin levels.
Results: A statistically significant difference was found between patients and controls as regards stereotypic movements, absent eye contact, delayed motor development, delayed speech and IQ ($p < 0.01$ for each item). Mean level of copper was significantly higher in patients than in controls ($P < 0.001$), also mean level of ceruloplasmin was significantly higher in patients than controls ($P = 0.009$).
Conclusion: Serum copper level may have a role in the pathogenesis of autism.

1. Introduction

Autism is a syndrome characterized by impairments in social relatedness, communication, repetitive behavior, abnormal movements and sensory dysfunction [1].

Copper, an essential trace mineral, is vitally important for both physical and mental health. Copper is critical for energy production in the cells. It is also involved in nerve conduction, connective tissue, the cardiovascular system and the immune system. Copper stimulates production of the neurotransmitters epinephrine, norepinephrine and dopamine. It is also required for monoamine oxidase, an enzyme related to serotonin production [2].

Ceruloplasmin is the major copper-carrying protein in blood, and in addition plays a role in iron metabolism. First described in 1984, ceruloplasmin carries about 70% of the total copper in human plasma while albumin carries about 15% [3].

Autistic children are frequently subjected to oxidative stress; hence the levels of major antioxidant serum proteins like ceruloplasmin (copper-binding protein) are decreased in children with autism. Heavy metals –including copper– are found at higher values in serum of autistic individuals than their normal peers [4].

2. Aim of the work

To assess serum copper and ceruloplasmin levels in Egyptian autistic children patients.

3. Subjects and methods

The present study was designed to be of a case control type. It enrolled 20 cases with autism diagnosed by ICD-10 (International Classification of disease, 10th edition) and the Childhood Autism Rating Scales (CARS), with no other medical disease. The patients were 15 males and 5 females. Their ages ranged from 2 to 13 years with mean of 6.15 ± 3.133 years. They were recruited from the psychiatric clinic of pediatric department and psychiatric department, Ain Shams University, during the period from December 2011 to April 2012.

The control group enrolled 20 apparently healthy children, matched to the patients' age and sex. They were recruited from the outpatient clinic, children's hospital, Ain Shams University. Their ages ranged from 4 to 17 years with a mean of 9.05 ± 3.605 years.

All patients were subjected to:

1. Thorough history taking laying stress on social interactions, impairment of language, age, gender, age of onset of clinical manifestation, presence or absence of perinatal problems and family history of psychiatric disorders.

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2. Complete clinical examination with special emphasis on neurological examination.
3. Psychiatric evaluation including:
   a- IQ assessment using Stanford-Binet Intelligence Scale (1986) [5].
   b- Assessment of the severity of autistic symptoms using Children Autism Rating Scale (CARS) [6].
4. Laboratory investigations including serum copper and ceruloplasmin levels [7].

3.1. IQ assessment

Using Stanford-Binet Intelligence Scale (1986) was carried out by clinical psychologists at the psychiatry department, Ain Shams University Hospitals. IQ was calculated using the following equation:

$$IQ = \frac{Mental\ age\ (MA)\ assessed\ using\ the\ proper\ test}{Chronological\ age\ (CA)} \times 100$$

Ranges of IQ: 20–30 severe mental retardation, 31–49 moderate mental retardation, 50–70, mild mental retardation, 71–89 below average IQ, 90–109 normal IQ, 110–12 above average IQ and 125–140 genius.

Items of the CARS are: relating to people, imitation, emotional response, body use, object use, adaptation to change, visual response, listening response, taste, smell and touch response and use, fear or nervousness, verbal communication, non verbal communication, activity level, level and consistency of intellectual response and general impressions.

3.2. Collection of blood samples

Specimen collection and storage: The usual precautions for puncture were observed and followed. Blood samples were collected by a syringe with a wide bore needle 5 ml. All samples were drawn from non fasting individuals. Evacuation of the sample was done after removal of the needle very slowly over the side of the test tube to avoid hemolysis without anticoagulant. Don't shake the tube to avoid hemolysis. The samples were stored at room temperature for 2 h then centrifugation was done for serum separation. Serum was then collected at eppendorf tube and frozen at −20 C for storage.

3.3. Statistical methods

IBM SPSS statistics (V. 20.0, IBM Corp., USA, 2011) was used for data analysis. Data were expressed as Mean ± SD for quantitative parametric measures in addition to both number and percentage for categorized data. Student *t* test was used to compare between two independent mean groups for parametric data, person correlation test was done to study the possible association between each two variables among each group for parametric data. Chi-square test was done to study the association between each 2 variables or comparison between 2 independent groups as regards the categorized data.

The probability of error p value = 0.05 or less was considered significant.

4. Results

A statistically highly significant difference was found between patients and controls as regards stereotypic movement, delayed motor development (90% of patients), absent eye contact (85% of patients), all our patients have abnormal speech and low IQ ($p < 0.01$). The difference between patients and control groups was statistically insignificant ($P > 0.05$) as regards convulsions (5% of patients). All patients and controls have taken M.M.R vaccine (Table 1).

There was statistically highly significant difference between mean level of copper in patients and controls ($P < 0.001$). Copper

Table 1
Statistical comparison between patients and controls as regards clinical data.

Variable		Cases n = 20		Controls n = 20		Value	P	Sig.
		No	%	No	%			
Stereotypic movements	Negative	2	10	20	100	32.727[a]	0.000	HS
	Positive	18	90	0	0			
Absent eye contact	Negative	3	15	20	100	29.565[a]	<0.01	HS
	positive	17	85	0	0			
Delayed motor development	Negative	2	10	20	100	32.727[a]	<0.001	HS
	Positive	18	90	0	0			
Normal speech	Negative	20	100	0	0	40.000[a]	<0.001	HS
	Positive	0	0	20	0			
Convulsions	Negative	19	95	20	100	1.026[a]	>0.05	IS
	Positive	1	5	0	0			
M.M.R vaccination	Negative	0	0	0	0		>0.5	NS
	Positive	20	100	20	100			

IS: insignificant. HS: High significance. NS: non significant.

Table 2
Statistical comparison between patients and controls as regards copper, ceruloplasmin levels and IQ.

Parameter	Case Mean ± SD	Control Mean ± SD	t	P	Sig.
Copper 70–140 μg/dl	132.15 ± 28.019	105.46 ± 15.607	−3.72	0.001	HS
Ceruloplasmin 20.4–40.7 mg/dl	35.175 ± 8.748	29.04 ± 4.481	−2.79	0.009	HS
IQ	52.7 ± 4.846	100.75 ± 2.468	39.51	0	HS

HS: High significance.