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Zinc and Copper Concentration in Serum of Patients with Congenital Ichthyosis, Spastic Di- or Tetraplegia and Mental Retardation (Sjögren-Larsson Syndrome)

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ABSTRACT

Serum zinc and serum copper were examined in 18 patients with the Sjögren--Larsson syndrome (congenital ichthyosis, spastic di- or tetraplegia and mental retardation), in four patients with congenital ichthyosis and mental retardation, of whom three had alopecia, and in nine healthy controls. No indication of disturbed zinc or copper metabolism in these groups of patients was found.

INTRODUCTION

The Sjögren-Larsson syndrome (SLS) is a genetically determined syndrome with autosomal recessive inheritance, characterized by the three cardinal symptoms congenital ichthyosis, spastic di- or tetraplegia and mental retardation (6, 7, 8). An additional symptom, glistening dots in the retina of the eye, was recently reported by Jagell et al. (3). The basic etiology is unknown, but SLS has been thought to be related to an inborn error involving either metabolism of lipids or organic acids. Holmgren et al. (to be published) found no abnormalities in the urine excretion of amino acids or other organic acids in SLS patients. In another recent study, however Hernell et al. (to be published) observed that the total products of Δ6 desaturation of polyunsaturated fatty acids were low, indicating the possibility of a defect metabolism of long chain fatty acids. Possibly, Δ6 desaturase activity might be decreased due to zinc deficiency.

Hair and skin changes may be related to zinc deficiency. Patients with acrodermatitis enteropathica have low levels of zinc in serum (5) and zinc therapy reverses the skin symptoms of the disease. The cutaneous manifestations typical of acrodermatitis enteropathica have also been observed in acuired zinc deficiency of different causes (4).

In order to investigate the possibility that symptoms in SLS might be related to zinc deficiency, the concentration of zinc in the serum of SLS patients and in patients with ichthyosis and mental retardation but without neurological disorders were studied. The serum concentration of copper was also measured, as

there is an inverse relationship between zinc and copper concentrations in serum (1). Furthermore, some patients with low serum zinc concentrations were selected for treatment with oral zinc to evaluate the clinical effects of the treatment.

MATERIALS

Patients

Eighteen patients (seven females and 11 males) with SLS and four patients (three females and one male) with ichthyosis and mental retardation but no neurological disorder - named "non-SLS" in this report -, of whom three also had alopecia, and nine healthy controls (five females and four males) were studied. The four "non-SLS" patients, of whom two were siblings, probably represent three different clinical entities with autosomal recessive inheritance. Clinical data are given in Table 1.

TABLE 1. Clinical and familial data on the 18 SLS patients and the four "non-SLS" patients studied.

No.[1]	Patient	Sex	Born in year	Ichthyosis	Mental retardation	Spasticity	Glistening dots	Alopecia
SLS								
11	IA	F	1907	+	+	+	+	-
21	GB	M	1920	+	+	+	+	-
22	EN	F	1921	+	+	+	+	-
26	AN	F	1927	+	+	+	+	-
33	NH	M	1939	+	+	+	+	-
37	BM	M	1952	+	+	+	+	-
38	EL	F	1956	+	+	+	+	-
39	TJ	M	1957	+	+	+	+	-
40	AL	M	1957	+	+	+	+	-
43	AA	M	1960	+	+	+	+	-
44	UG	M	1960	+	+	+	+	-
49	IG	F	1963	+	+	+	+	-
50	AL	F	1964	+	+	+	+	-
51	AU	M	1965	+	+	+	+	-
52	KL	M	1969	+	+	+	+	-
55	MJ	M	1973	+	+	+	+	-
56	MJ	F	1973	+	+	+	+	-
58	MP	M	1977	+	+	+	+	-
"Non-SLS"								
	GK	F	1919	+	+	-	-	+
	BR	M	1939	+	+	-	-	+
	BR	F	1945	+	+	-	-	+
	KL	F	1965	+	+	-	-	-

[1] Number according to Jagell et al (2)
+ Present
- Absent

METHODS

Venous blood was obtained by cubital vein puncture in the morning after an overnight fast. Zinc and copper concentrations in the serum were determined by atomic absorption spectrophotometry (Varian AA-6DB) as described by Hallmans (1978). Neurological and dermatological examinations were performed on all patients except the healthy controls. Skin biopsies were taken for histological examinations and photographs for documenting ichthyosis and hair. These investigations will be reported elsewhere.

Zinc therapy

Zinc was administered orally as zinc sulphate (Solvezink ^{R}, Tika AB, Lund, Sweden) for at least three months in four SLS patients with serum zinc levels below 12 µmol/l. Patients with a body weight of 30 kg or more received 400 mg daily, corresponding to 90 mg Zn^{++}, divided into two doses. Those with a lower body weight received half that dose.

Statistics

Differences of different variables were tested for significance by means of Student's t-test for unpaired observations. The test was modified if the variances were significantly different ($p < 0.01$: F-test).

RESULTS

The SLS patients had, as a group, a slightly lower serum zinc concentration than the control group (Table 2). Four SLS patients (Nos. 37, 39, 44, 51) with low serum zinc concentrations were given zinc therapy orally for three months. The serum zinc levels were normalized during this therapy, but no improvement of the mental, neurological or skin symptoms was observed in these patients. No differences in copper concentrations was found between the groups (Table 3).

TABLE 2. Serum zinc and copper concentrations in SLS patients and controls. The results are given as mean values ± S.E.M. T-test results in relation to controls are indicated.

	No. of subjects	Age range (years)	Serum zinc µmol/l	Serum copper µmol/l
SLS	18	2 - 56	11.9 ± 0.5$^{\times}$	18.0 ± 0.8
Controls	9	5 - 77	13.7 ± 0.5	17.3 ± 1.3

$^{\times}$ = $p < 0.05$

TABLE 3. Zinc and copper values in serum of the 18 SLS patients and the four "non-SLS" patients studied.

No.[1]	Before zinc treatment		After zinc treatment				
	Zn	Cu	Zn	Cu		Zn	Cu
SLS	µmol/l	µmol/l	µmol/l	µmol/l	"Non-SLS"	µmol/l	µmol/l
11	10.8	18.7			GK	10.1[4]	25.9[4]
21	21.0	19.5			BR	15.4	16.5
22	13.2	15.4			BR	13.0	20.2
26	14.0	13.8			KL	13.0	15.3
33	12.0	13.5					
37	8.1	13.1	16.4	12.7			
38	11.7	22.6					
39	9.4	18.7	14.0	12.8			
40	11.0	11.7					
43	13.2	15.2					
44	6.5	20.2	11.1[2]	23.0			
49	13.6	16.4					
50	11.7	16.2					
51	11.0[3]	27.0[3]	17.0	15.3			
52	13.8	17.0					
55	11.9	24.1					
56	15.1	24.1					
58	15.4	17.1					

[1] Number according to Jagell et al (1981). [2] Low dose treatment because of gastric complaints. [3] Examined at a different laboratory. [4] Non-fasting value.

DISCUSSION

The four SLS patients who were given oral zinc had low serum zinc concentrations of unknown cause. Their dietary intake of zinc was normal. Poor absorption was suspected in two of them (Nos. 39, 44), as they were very thin in spite of a large food intake. Both had severe spastic tetraplegia and severe mental retardation. The other two SLS patients (Nos. 37, 51) treated with zinc had more severe ichthyosis. However, the zinc therapy appeared to have no effect on any of these symptoms in the four SLS patients. Thus, the results of this study did not support the hypothesis that zinc or copper deficiency may play a part in the pathogenesis and symptomatology of SLS or in "non-SLS" patients with ichthyosis and mental retardation.

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