Incidence of Low Serum Zinc in Noncirrhotic Patients (33614)

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(Introduced by D. F. Magee)

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A decreased serum zinc content is known to occur in a variety of diseases. Among these, myocardial infarction (1), hematologic disease (2), and alcoholic cirrhosis (3) have received the greatest attention. Recently zinc has been reported to be an effective therapeutic agent in the treatment of vascular disease (4) and to have a salutary effect on wound healing (5). Since the rationale for administration of zinc has rested, in part, upon lower than normal serum z nc levels, the incidence of this abnormality in hospitalized patients is worthy of further evaluation. The present study is concerned with depressed serum zinc levels in noncirrhotic and nonalcoholic patients. Various possible etiologic factors present in each group are compared in an effort to determine the processes producing the abnormality in serum zinc concentration in these as well as in cirrhotic patients. A low serum magnesium value is frequently found in the alcoholic and cirrhotic, suggesting a relation to the zinc abnormalities. An evaluation of this association is warranted in an attempt to understand the mechanisms producing these deviations from normal. The investigation desired specifically to determine the following:

1. Incidence of abnormal serum zinc in cirrhotics and in other categories of hospitalized patients.
2. The frequency with which magnesium and zinc abnormalities occurred simultaneously.
3. A comparison of urine and serum electrolytes in cirrhotics and noncirrhotics having low serum zinc levels.
4. An evaluation of serum protein content in relation to serum zinc concentration.

Materials and Methods. Serum zinc determinations were made within 48 hr of hospitalization in 195 consecutive admissions to Omaha VAH and in 30 alcoholics admitted to Douglas County Hospital Alcoholic Ward. Zinc, magnesium, and calcium determinations were performed by atomic absorption spectrophotometry (6, 7). When possible the concentration of electrolytes, zinc, and magnesium in a 24-hr urine specimen was determined. Urinary components are expressed per gram of creatinine. Serum protein was measured by refractometry and cellulose acetate electrophoresis. Patients designated as cirrhotics had varying degrees of hepatic dysfunction. The diagnosis was substantiated by liver biopsy with demonstration of typical pathology. Alcoholic patients had no evidence of hepatic dysfunction and were admitted for the most part because of withdrawal symptoms. Patients in the other disease categories met the usual clinical criteria for diagnosis.

TABLE I. Serum Zinc and Magnesium in Hospitalized Patients.*

	No. of samples	Zinc (μg/100 ml)	Magnesium (mg/100 ml)
All patients	225	67 ± 18	2.14 ± .34
Excluding cirrhotics and alcoholics	154	70 ± 16	2.17 ± .34
Normals		90 ± 10	1.92 ± .16

* Values are means ± SD.

Results. The mean values for serum zinc and magnesium for the entire group studied appears in Table I, in which the mean values are shown with and without the alcoholic and cirrhotic groups with a comparison to normal subjects.

It is apparent that serum zinc values in hospitalized patients are significantly lower than in healthy subjects. In an effort to delineate more clearly common factors which might be present in patients with lowered serum zinc, attention was focused on those with serum levels less than 60 μg/100 ml (3

TABLE II. Serum Zinc and Magnesium in Various Diseases.

Diag. group	No. in group	Zn (μg/100 ml)		Mg (mg/100 ml)		Zn <60 μg/100 ml
Cirrhotics	41	Mean	47.	Mean	1.98	28
		SD	$\pm$ 15.	SD	$\pm$ 0.40	
Myocardial infarction	33	Mean	71.	Mean	2.20	7
		SD	$\pm$ 14.	SD	$\pm$ 0.23	
Lymphoma	8	Mean	62.	Mean	2.15	4
		SD	$\pm$ 14.	SD	$\pm$ 0.40	
Proteinemia	10	Mean	62.	Mean	2.67	7
		SD	$\pm$ 21.	SD	$\pm$ 0.60	
Carcinoma	13	Mean	66.	Mean	2.03	6
		SD	$\pm$ 18.	SD	$\pm$ 0.30	
Psychobiologic reaction	8	Mean	70.	Mean	2.23	1
		SD	$\pm$ 20.	SD	$\pm$ 0.38	
Diabetes mellitus	13	Mean	72.	Mean	2.0	2
		SD	$\pm$ 17.	SD	$\pm$ 0.28	
Pneumonia and chronic lung disease	20	Mean	68.	Mean	2.13	5
		SD	$\pm$ 17.	SD	$\pm$ 0.26	
Acute alcoholism	30	Mean	71.	Mean	1.80	1
		SD	$\pm$ 20.	SD	$\pm$ 0.20	
Other	49	Mean	76.	Mean	2.16	5
		SD	$\pm$ 13.	SD	$\pm$ 1.00	

standard deviations below normal mean). Patients with such values have been categorized as having "low" serum zinc. Table II shows the mean serum zinc and magnesium values for nine specific diagnostic entities and a miscellaneous group. Thirty percent of the total have serum zinc values below 60 μg/100 ml.

The depression of serum zinc in myocardial infarciton and pneumonia may be related to concommitant changes in serum protein which are transient in nature. Patients with proteinuria have been noted to have larger urinary losses of zinc associated with loss of protein in the urine (8). The low values noted in the patients having renal disease, myocardial infarction, and infection are explicable on these bases. In the future analysis of factors common to the patients with low serum zinc, the patients with proteinuria or in whom transient alteration in serum proteins are known to occur have been excluded.

Serum zinc, magnesium, calcium, sodium, potassium, and serum protein were determined in five groups. The first consisted of 13 cirrhotics with normal serum zinc; the second, 23 cirrhotics with low serum zinc; third, 12 alcoholics with normal zinc; and the fourth, 10 patients in whom the low zinc levels were unexplained. This group of nonalcoholic–noncirrhotic patients having low serum zinc without demonstrable cause, was compared to cirrhotic and alcoholic patients. The data are shown in Table III.

The serum proteins were not obtained in sufficient number to allow evaluation of the alcoholic groups. Statistical p values greater than .10 are not shown in Table III.

Cirrhotic patients with low serum zinc also show significantly lower levels of serum calcium and magnesium than do cirrhotics with normal serum zinc. The low serum magnesium in the alcoholic patients occurs with normal zinc and probably results from the magnesium diuresis associated with recent ethanol ingestion. The patients with low serum zinc of undetermined cause have low calcium but normal magnesium. The differ-

ences in serum protein values suggest that low serum zinc in the cirrhotic as well as in the patient with low zinc of undetermined origin is associated with lower levels of serum albumin and α_2 globulin than in normals but are not significant. Calcium may share in this association, as in the cirrhotics with low serum zinc and the undetermined group. Magnesium, however, is clearly affected independently as demonstrated by the alcoholic groups.

In Table IV the relative levels of urine cation excretion and serum levels in the same four groups are compared. Again the p values greater than .10 are excluded in the table. Cirrhotics and the undetermined low zinc group excrete more zinc and less calcium than do the alcoholics. Cirrhotics also excrete less sodium. When compared to normals the zinc excretion of the cirrhotic and undetermined groups are distinctly elevated.

Discussion. Repeated studies have shown that ^{65}Zn is rapidly and tightly bound to serum proteins (9). Albumin and the alpha globulins (10) have been shown to bind the radioactive zinc. As it appears in the urine, however, zinc is completely dialyzable and not protein bound (9). The abnormalities of both zinc and magnesium metabolism occurring in cirrhosis and alcoholism have been characterized by a decrease in serum concentration of the cation accompanied by an increase in urinary excretion. The concommittant lowering of calcium, zinc, and magnesium in the second group of cirrhotic patients suggest a common etiologic mechanism. Comparison of serum protein levels between the two cirrhotic groups suggests a lower albumin level in those with low serum cations.

The group of nonalcoholic, noncirrhotic patients with low serum zinc, appear to have a lower serum albumin but not at a significant level. The urinary excretion of zinc in this idiopathic group, however, is strikingly lower than the cirrhotic groups. In this aspect they resemble the zinc deficiency syndrome associated with dwarfism as observed by Prasad (11).

Magnesium appears to be affected independently of zinc and calcium as manifested by

TABLE III. Serum Cations and Protein in Cirrhosis.

Patient group	No. cases		Serum Zn (μg)	Ca (μg)	Mg (mg/100 ml)	Na (mEq)	K (mEq)	Cl (mEq)	Protein (g/100 ml) Total	Alb.	Glob.	α_1	α_2	β	γ
I Cirrhotics	13	Mean	0.76	83.4	2.13	135	4.91	99	6.95	3.15	3.80	0.32	0.69	0.89	1.83
normal Zn		SD	± 0.16	5.95	0.28	4.2	0.78	5.7	0.89	0.54	0.64	0.08	0.14	0.16	0.63
II Cirrhotics	23	Mean	0.44	79.4	1.99	134.2	4.07	96.5	6.8	2.81	4.02	0.34	0.75	0.89	1.79
low Zn		SD	± 0.12	12.6	0.45	6.9	0.93	8.6	1.40	0.89	1.14	0.20	0.46	0.30	0.53
III Alcoholics	12	Mean	0.77	84.2	1.78	142.7	4.4	101.8							
normal Zn		SD	± 0.18	4.2	0.15	2.9	0.5	2.8							
IV Other diag.	10	Mean	0.48	69.3	2.07	136	3.7	97.4	6.70	3.09	3.60	0.26	0.73	0.76	1.82
low Zn		SD	± 0.13	8.4	0.34	6.2	0.5	4.4	1.20	0.64	0.98	0.10	0.31	0.35	0.65
Group comparison															
p value	I to II			<.05	<.001	<.001									
	I to III														
	II to IV														

TABLE IV. Urinary Zinc and Magnesium Excretion in Cirrhosis.

Patient group	No. cases		Serum Zn (μg)	Urine/g of creatinine Zn (mg)	Ca (mg)	Mg (mg)	Na (mEq)	K (mEq)
I Cirrhotics	13	Mean	0.76	0.74	28.7	80.1	81.1	83.1
normal Zn		SD	± 0.16	0.41	24.9	50.9	42.7	48.4
II Cirrhotics	23	Mean	0.44	0.67	29.5	100.2	63.0	47.9
low Zn		SD	± 0.12	0.43	21.6	101.0	45.1	18.4
III Alcoholics	12	Mean	0.77	0.37	117.4	54.0	132.7	41.9
normal Zn		SD	± 0.18	0.18	80.4	38.5	70.7	16.7
IV Other diag.	10	Mean	0.48	1.00	15.0	65.6	101	65.8
low Zn		SD	± 0.13	0.92	10.7	47.2	80	34.4
Group comparisons								
p value I to II								<.01
I to III				<.01	<.002		<.05	<.01
II to IV					<.05			<.05

the alcoholic group in which very low serum magnesium levels occurred with normal zinc and calcium levels.

Summary. A survey of serum zinc concentration in 225 hospitalized patients indicated that 68% of cirrhotics and 21% of other patients had zinc levels 3 standard deviations below the normal mean. Magnesium and calcium were also lower in the serum of cirrhotics with low zinc but appeared independent of zinc concentration in the other groups. Urinary excretion of zinc and magnesium were comparatively great in cirrhotics despite decreased serum concentration. A group of patients with low serum zinc of uncertain etiology had diminished zinc excretion. Despite the presumed stability of protein binding of zinc, the occurrence of low serum levels of zinc, calcium, and magnesium in the cirrhotic patients with abnormally low serum albumin and α_2 globulin suggests that the decreased serum content is related to diminished serum proteins.

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