ZINC IN TREATMENT OF PSORIASIS

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SUMMARY: Serum zinc and copper levels and the results of treatment with systemic zinc sulfate are presented in 10 demonstrative cases. All patients in this series complained of typical skin manifestations of psoriasis. In each case the diagnosis was proven histologically. Serum zinc levels (82.6± 1.93 μg/dl) were below that of normal controls at the first visit, gradually rose following oral treatment reaching to (99.3± 6.01 μg/dl) on the second month ($p<0.05$) and climbed to 103.6 μg/dl during the subsequent months. Simultaneously the clinical manifestations of psoriasis improved and finally disappeared. Serum copper levels were maintained within normal limits. The mean serum copper level was 107.8± 5.85 μg/dl at the beginning of the treatment. It was slightly reduced at the end of third month was later maintained near the initial level (109.3± 8.2 μg/dl, $p>0.05$). The improvement therefore of the clinical status of the patients was most likely because of restoration of serum zinc level to normal.

Key Words: Zinc deficiency, copper deficiency, erythrocyte zinc content, atomic absorption spectrophotometry.

INTRODUCTION

Psoriasis was described by Celsus 2000 years ago (1). Despite this long history of the ailment and the fact that nearly 3% of population in United States suffers from this disease (2), its etiology, pathogenesis and therefore its specific treatment are still unknown. With the presently encountered recurrences of over 90%, its prognosis can not be considered favorable (1-4).

The skin lesions of psoriatic patients are histologically similar to the lesions encountered in zinc deficient animals such as acanthosis and parakeratosis (5, 6). Common factor between the patient with psoriasis and animals with parakeratosis is, however, reduced serum zinc levels (7). It is furthermore known that by addition of zinc to the diet of the animals parakeratosis can be prevented (5-7). This observation led us to start a program of trace metal treatment on these patients the preliminary results of which are presented in this communication (8). In addition to this, review of the literature of the last 30 years confirms our impression that trace metals might have an important part in etiopathogenesis of psoriasis (9-16) and furthermore contribute significantly to its treatment.

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MATERIALS AND METHODS

All patients presented in this communication were known to have psoriasis who had been under treatment since several years but had not given a favorable response.

A detailed history was obtained from and a complete physical examination was performed on each patient upon arrival (Table 1). If the clinical impression supported the former diagnosis, a skin biopsy was done and pathologist consulted (Supported by Turkish Scientific and Technical Research Council and Anadolu Health and Research Foundation). No case was given our specified treatment until the diagnosis was histologically confirmed.

Routine CBC and urinalysis was performed for every patient. Enzymes related to zinc and copper were determined in addition to serum zinc and copper levels and zinc content of the erythrocytes and that of white blood cells.

Zinc and copper measurements were done using atomic

Table 1: Summary of clinical characteristics of the patients.

PRESENTING COMPLAINTS								
	Age	Sex	Duration of the disease (years)	Itching	Scaling	Localization of Lesions	% of skin involved	Former treatment
D.A.K. (576073)	33	M	2	+	+	Scalp, shoulders, back	15	Corticosteroid oinment
M.F. (574077)	58	M	5	+	+	Scalp, arms, elbows, knees, back	20	"
N.T. (1545379)	49	F	8	-	+	Scalp, arms, elbows, forehead, legs	10	"
H.P. (572959)	10	F	3	+	+	Scalp, forehead, left leg	15	"
N.Y. (1381327)	24	F	9	+	+	Scalp (post), arms, elbows, hips	20	Corticosteroids, antihistaminics
S.K. (1545272)	27	F	4	+	-	Scalp, abdomen, legs	20	Methetraxate, Corticosteroids
M.C. (576020)	40	M	-	-	-	Back, waist, legs, abdomen	15	Corticosteroid ointment
H.Ç. (1545551)	20	M	13	+	+	Hips, back, waist, abdomen	20	"
G.Ç. (1574027)	21	F	3	+	+	Scalp, knees, elbows, back, hips, legs	15	"
Z.K. (27842)	14	F	6	+	+	Left lateral tibial area, face, both elbows	15	"

absorption spectrophotometer Perkin Elmer, Model 103. The samples for trace element measurements were removed and processed with appropriate precautions to prevent contamination. The results were tabulated and statistically evaluated using student t-test (Table 2).

Case 1. N.T. was a 19-year old female (HU Prot No. 1545379) complaining of itching lesions at both lateral tibial areas. Her complaints started eight years ago on the lateral aspect of the I. tibia region. They were lesions of 8-10 mm in size at the beginning. They used to alleviate during summer months earlier but they persisted throughout the winter of 1989. Scaling lesions then appeared behind the ears and forehead. No other abnormalities were encountered in physical examination.

Her CBC, urinalysis, fasting blood sugar, BUN, lipids and cholesterol were within the limits of normal. Sedimentation rate was 37 mm/h. A biopsy was performed report of which revealed 'psoriasis'.

All the skin lesions disappeared at the end of the first month of treatment. During the second month 10x7 mm lesion at the I. molar region, and during the third month 10x15 mm lesion at the I. lypochondrium were observed both of which disappeared following continued treatment.

Case 2. H.P. was a 10-year old school girl (H.U. Prot. no. 572959). She first complained of itching and scaling lesions at both pre-tibial skin 3 years ago following; which typical scaling psoriatic lesions appeared gradually extending to the prepateller regions and to both upper arms. Several ointments all containing cortisone derivatives were prescribed by physicians without much success. Patient noticed a spontaneous remission during summer months.

The physical examination and routine laboratory procedures did not uncover any further abnormalities. Biopsy specimen was interpreted as 'psoriasis'.

No changes occurred in the lesions during the first month of treatment. Itching disappeared, scaling was reduced during the second month, and the lesions appeared hyperemic. Nearly 50% reduction in the size of the lesions during the third month was observed. Only few 3x4 mm lesions remained at the end of fourth month. They disappeared subsequently.

One important point to be stressed concerning these patients is the fact that in no case classical or newly proposed antipsoriasis medicaments were prescribed.

DISCUSSION

Psoriasis was treated with arsenic 100 years ago. Turpentine, anthimony, cantharides and phosphorus were also used (1). Local therapy to cure the scales consisted of soap, B naphthol, thymol, pyrogallic acide, mercury salts and later chryarobin (3-methyl dithianol) (3). In 1915 tar was considered standard treatment (4). X-rays were later proposed to treat psoriasis. This method was soon discarded however, because of its well known side effects.

Table 2: Serum zinc, copper, erythrocyte zinc levels and zinc content of 10^{10} erythrocytes.

	Before Treatment				During Treatment												Mean values of subsequent visits			
					First month				Second month				Third month							
Cases	Serum Zn	10^{10} E Zn	E Zn	Serum Cu	Serum Zn	10^{10} E Zn	E Zn	Serum Cu	Serum Zn	10^{10} E Zn	E Zn	Serum Cu	Serum Zn	10^{10} E Zn	E Zn	Serum Cu	Serum Zn	10^{10} E Zn	E Zn	Serum Cu
D.A.K. (576073)	88	16.0	1440	110	98	11.0	1056	114	80	13.2	1296	114	98	14.9	1224	86	91	14.1	1344	82
M.F. (574077)	78	13.5	1104	120	78	15.1	1272	100	80	12.3	1176	124	86	13.7	1368	108	99	14.3	1272	120
N.T. (1545379)	78	14.1	1296	110	96	11.0	1032	110	102	12.6	1008	124	100	14.1	1296	116	96	14.8	1080	116
H.P. (572959)	78	12.5	1272	140	86	12.0	1032	180	88	13.5	1272	140	92	10.7	984	128	94	10.6	936	138
N.Y. (1381327)	82	14.7	1176	86	112	13.1	1392	86	130	11.1	1248	100	102	15.4	1296	102	112	12.1	1029	101
S.K. (1545272)	86	10.7	1008	130	104	12.3	1152	160	100	11.8	1008	140	72	15.1	1392	152	118	10.5	876	164
M.C. (576020)	84	12.0	1080	96	90	9.4	960	80	100	11.7	1080	82	90	11.0	1080	60	93	11.5	1128	88
H.Ç. (1545551)	92	12.0	1128	96	108	16.4	1512	86	126	11.7	960	92	92	12.3	1032	90	-	-	-	-
G.Ç. (1574027)	74	11.5	1080	100	86	-	-	104	88	11.0	1032	94	106	9.0	888	94	110	10.5	1032	92
Z.K. (27842)	74	9.5	1008	100	86	10.8	888	104	76	12.7	1224	110	74	11.3	1104	92	70	9.8	984	86
Mean	81.4	12.6	1161	108.8	94.4+	12.3	1144	112.4	97.0+	12.2	1130	112.0	91.2+	12.7	1166	102.8	98.1	12.0	1076	109.7
Standard Error	1.9	10.62	43.9	5.33	3.50	0.74	69.3	10.32	5.92	0.27	39.9	6.35	3.58	0.69	54.6	7.98	4.74	0.63	50.7	9.19

+ $p<0.05$, E Zn:Erythrocyte zinc, 10^{10} E Zn: Zinc content of 10^{10} ery throcytes

It was observed nearly 300 years ago that the sun had beneficial effects on the skin diseases. This was further confirmed when it was noted that the patients suffering from psoriasis became somewhat better during the summer. This has been the rationale of ultraviolet rays (UVR) therapy (2, 17-19).

In 1950 corticosteroids were first utilized for treatment of psoriasis. During the following years systemic ACTH, and cortisone, preparations and local hydrocortisone ointments were widely acclaimed. It was later noted that ACTH and cortisone, besides leading to severe side effects, were actually not very influential in treatment of psoriasis (2). In 1960, following several reports showing that the local hydrocortisone therapy was also not effective in treatment of psoriasis ACTH and cortisone therapy was completely rejected by some investigators (3).

Peckham and his associates conducted a wide scale study inquiring about the then current therapy of psoriasis in 1976. Of the 510 dermatologists contributing, 52% stated that methotrexate was the most frequently utilized chemotherapeutic agent (18). During the last 10 years the most favorable treatment has been methotrexate with or without phototherapy using ultraviolet A rays (PUVA) (19). But because of carcinogenic effects of ultraviolet rays and ocular and immunological complications this method has recently fallen into disfavor (20, 21).

Several combinations of the above methods of treatment have been tried among which methotrexate and UVB, methotrexate and PUVA or UVB and PUVA have most commonly been proposed (22-24).

Vitamin A has been another reasonable proposal for treatment of psoriasis due to its role in preservation of epithelial tissues. But its side effects during the long periods of treatment has widely precluded its application (25, 26). Vitamin D also has been favored for treatment of psoriasis by some authors (27) to be followed by cyclosporine (28-30).

One of the latest developments in treatment of psoriasis involves trace elements. Review of literature from this point reveals many communications assigning a significant role to trace metals in pathogenesis of psoriasis (9-16). In fact several authors in the past have reported low serum zinc levels in patients with psoriasis, while others have found it within normal limits. Some investigators

have correlated zinc levels with the extent of lesions, claiming that the larger is the lesion the more impressive is the drop of serum zinc (31).

It should be stressed that all of our cases were referred to us after failure of the currently available remedies. After clinical and laboratory studies a biopsy of one of the lesions was made in each case. The serum zinc levels were determined (Table 2) following which the patient was prescribed oral zinc sulfate ($7H_2O$) 50-200 mg three times per day. Since rising serum zinc however induced a significant reduction on serum copper levels in few days recurrence of symptoms may soon be observed. We were therefore obliged to administer up to 5 mg copper sulfate ($5H_2O$) 2-3 times per day together with zinc sulfate (32, 33). With this regimen it has become possible to maintain the copper levels within the normal limits (Table 2). It is important to add that outside the occasional nausea and vomiting no significant complications occurred in a series of over two thousand patients on this treatment, all patients were maintained on monthly evaluations. At each visit the subjects were given a physical examination, blood samples were taken for CBC, trace metal measurements and several enzymes related to trace metals. Under these precautions in no case an undue rise of serum zinc or copper to toxic levels was observed. Our problem was rather delayed response of the zinc levels which frequently attributed to improper absorption by the intestinocytes.

It was observed that the lesions in most cases revealed a moderate degree of improvement during the first month of treatment. This became more impressive during the second month at which time itching disappeared. Scaling frequently disappeared or was markedly reduced simultaneously. The first case was completely revealed of lesions during the third month while the other patients experienced striking relief. On the subsequent months the other cases improved further and became free of symptoms.

It is important to note that the serum zinc levels were significantly above that of the initial visit at the end of the first, second and third months ($p<0.05$). Zinc content of the red cells were not however statistically different from the pretreatment levels ($p>0.05$). Another words improvement in the clinical status of the patients began before zinc content of the erythrocytes rose. We observed at other cases however when the serum zinc content rose to or above 15-16 mg/dl the most persistant cases responded favorably.

Increased serum copper levels have been reported by several investigators (34, 35). The further claimed that this rise was secondary to that fraction of copper which was not bound to ceruloplasmin. In our series serum copper levels were within normal except in one case where it was reduced and remained low throughout the observation period. In some of our cases the serum copper levels were below normal values (Table 1). Since we intended to restore them to normal, copper supplementation was resorted to (32, 33), which permitted this parameter to remain almost identical to that of the pretreatment level ($p>0.05$). Despite this the patients were relieved of symptoms. This may indicate that copper in our cases had no relation to genesis of psoriasis nor to its treatment.

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