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Vitamin A status in different stages of schistosomal cases and the effectiveness of oral vitamin A therapy

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Summary: Thirty bilharzial patients were studied for their vitamin A status. Of the patients, 30 % were found to have low-fasting serum retinol level below the acceptable level of 20 μg/dl and one-third were presented with night blindness. Oral vitamin A therapy was effective in correcting the vitamin A deficiency among this group of patients.

Zusammenfassung: Dreißig an Bilharzie erkrankte Patienten wurden auf ihren Vitamin-A-Status hin untersucht. 30 % dieser Patienten hatten nüchtern gemessen einen sehr niedrigen Retinol-Serum-Spiegel, der noch unterhalb der Toleranzgrenze von 20 μg/dl lag. Ferner litt ein Drittel dieser Patienten an Nachtblindheit. Innerhalb dieser Patientengruppe erwies sich die orale Vitamin-A-Therapie als sehr effektiv, um den Vitamin-A-Mangel auszugleichen.

Key words: bilharzial patients, vitamin A status, serum retinol level, night blindness, oral vitamin A therapy

Schlüsselwörter: Bilharziose, Vitamin-A-Status, Retinol-Serum-Spiegel, Nachtblindheit, orale Vitamin-A-Therapie

Introduction

Schistosomes are parasitic helminths, which infect man and domestic animals. It is currently estimated that 200 million people are infected with Schistosomes throughout the tropical regions of the world (14). Schistosoma mansoni and Schistosoma haematobium are the main endemic parasites in Egypt, infecting 40–80 % of the farmers (2). Exposure of the bare feet to infected water is the major factor leading to infection by either cercariae, adult Schistosomes, ova, or their circulating metabolites (7). S. mansoni descend to the portal vein, reaching the mesentric veins in the intestinal walls, where the main egg-laying process takes place; whereas, S. haematobium matures in the liver, and adult worms find their way to the veins of the genitourinary organs (5). The main presenting symptoms of the established disease are direct nutrient losses from the body, resulting in lowered serum albumin level and general weakness. Hepatic Schistosomiasis is usually accompanied by liver malfunction, including eleva-

tions in the liver enzymes and progressive damage of liver cells, which may end up with ascites due to portal hypertension and hypoalbuminemia (1).

Patients with alcoholic cirrhosis (4, 15), cystic fibrosis (15), primary biliary cirrhosis (12), and (in children) cholestasis (17) frequently have depressed levels of serum vitamin A. Abnormal dark adaptation is commonly associated with the low serum vitamin A level in cirrhosis (3, 9, 13). The low level was attributed to different factors: failure to mobilize the vitamin from the liver, depleted vitamin A storage in the liver tissue, or others (16).

The present study was designed to assess vitamin A nutrition and abnormal dark adaptation in human patients with schistosomal liver affection, and their response to oral doses of vitamin A.

Materials and methods

The study included 30 hospitalized patients (16 males and 14 females) aged 19–70 years (mean 30.5 ± 3 years). The patients were examined clinically to determine the degree of liver enlargement. Sigmoidoscopy was performed to verify colonic polyposis. Morning-fasting blood samples were taken from each patient on admission for measurements of serum albumin, bilirubin, alanine amino transferase, and alkaline phosphatase using routine standard laboratory procedures (Boehringer Diagnostic kits). Night blindness was assessed by interviewing the patients.

Blood samples from 20 healthy staff members and their relatives, having similar age and sex as the patients and no history of Schistosomiasis, served as controls.

According to clinical and laboratory findings, the patients were divided into three groups, each consisting of ten patients: Group I, consisted of patients with early Schistosoma infection; Group II, consisted of infected patients with hepatomegaly (100 %), splenomegaly (80 %), and 20 % were presented with abnormal dark adaptation (night blindness); Group III, all patients belonging to this group were presented with ascites in addition to the hepatosplenomegaly. Night blindness was found in 40 % of the cases, and 20 % had hyperkeratosis.

Relevant data to all patient groups showed that of these 30 patients, 14 (47 %) had low plasma albumin levels (< 3.5 g/dl) and 5 (17 %) had elevated serum bilirubin levels (> 1.5 mg/dl). Serum alanine amino transferase (> 18 IU/l) and alkaline phosphatase activities (> 60 IU/l) were elevated in 10 % and 40 % of the cases, respectively, compared to normal levels.

Laboratory investigation of control subjects resulted the following mean values per liter of plasma: albumin 45.9 ± 1.6 g, bilirubin 5.0 ± 0.4 mg, alanine aminotransferase 8.7 ± 0.6 IU, and alkaline phosphatase 47 ± 1.9 IU, which were within the normal ranges.

Experimental design. Blood samples were collected from the antecubital vein after an overnight fast in coded clean glass tubes containing a few milligrams of Na_2-EDTA. All subjects were given seven capsules containing oily preparation of 50,000 IU vitamin A per capsule (Aviton, El-Kahira Pharmaceutical, Cairo, Egypt). A second blood sample was obtained after 4 h. The blood samples were stored in ice in the dark until transported to the laboratory.

Upon completion of the baseline tests, 12 patients received oral supplement of vitamin A according to the following schedule:

Day 1: Blood sampling after an overnight fasting.
Day 1: 7 × 50,000 IU vitamin A capsule.
Day 7: 1 × 50,000 IU vitamin A capsule.
Day 14: 1 × 50,000 IU vitamin A capsule.

Day 21: 1 × 50,000 IU vitamin A capsule.
Total 500,000 IU vitamin A.
Day 29: Blood sampling after an overnight fasting.

$$\text{Mean vitamin A intake/day} = \frac{500{,}000}{29 \text{ days}} = 17{,}000 \text{ IU}$$

Fasting and 4 h postprandial serum vitamin A determinations were made one month (28–30 days) after the initial baseline tests.

Plasma retinol was determined by a spectrophotometric procedure (11).

Results

Table 1 presents mean plasma retinol level distributed according to sex and disease state.

Highly significant mean plasma retinol level of 59.6 ± 6.1 μg/dl was obtained among the controls, compared to corresponding mean value of 25.5 ± 2.2 μg/dl ($P < 0.01$) found among the patients. None of the controls had fasting plasma retinol level below 20 μg/dl; whereas, 33 % of the patients had plasma retinol below the acceptable level of 20 μg/dl.

Sex differences were also observed with males having higher mean plasma retinol level. Mean values of 68 ± 10.5 μg/dl and 50 ± 5.5 μg/dl were found among healthy males and females, respectively, ($0.2 > P > 0.1$). Respective mean figures of 31.3 ± 2.0 and 18.9 ± 3.4 μg/dl were found among patients ($P < 0.05$).

Mean plasma retinol levels of 28.7 ± 4.0, 28.7 ± 3.0, and 19.2 ± 3.7 μg/dl were obtained among Schistosomal patients belonging to Groups I, II, and III, respectively. The last group had lower mean plasma retinol level ($0.1 > P > 0.05$) than Groups I and II.

After oral administration of a single dosage of vitamin A, maximum increase in plasma level was attained after 4 h. Therefore, throughout the course of this study blood sampling was collected 4 h after the oral intake of the vitamin. Figure 1 presents individual fasting and postprandial plasma-retinol levels among healthy controls and bilharzial patients. When the increase in postprandial plasma retinol was expressed in per-

Table 1. Mean fasting plasma vitamin A concentration (μg/dl) among the study group distributed per age and disease state.

Groups	Males			Females			Both sexes	
	N	$\bar{X}$	SE	N	$\bar{X}$	SE	$\bar{X}$	SE
Controls	11	68.5	10.5[b]	11	50.8	5.5[c]	59.6	6.1[b]
Bilharzial patients								
Group I	6	35.0	3.8[a]	4	19.1	5.6[a, b]	28.7	4.0[a]
Group II	5	28.8	3.6[a]	5	28.5	6.2[b]	28.7	3.4[a]
Group III	5	29.4	2.8[a]	15	9.1	1.3[a]	19.2	3.7[a]
All patients	16	31.3	2.0	14	18.9	3.4[a, b]	25.5	2.2[a]

Within the same column, mean values are significantly different ($P < 0.05$); if they don't share the same superscript (Student's t-test).

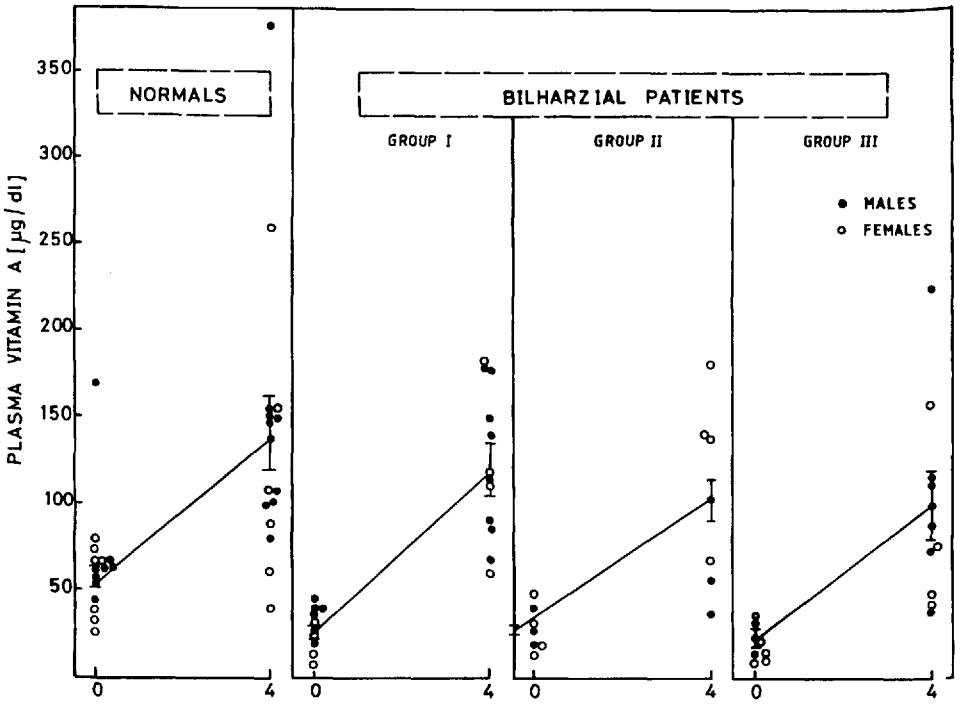

Fig. 1. Individual and mean plasma fasting and postprandial vitamin A level (four h after an oral dosage of 350,000 IU vitamin A) among normal and bilharzial patients.

cent of respective fasting level, the values fluctuated between 8.7 % and 77 % among the healthy controls, with mean value of 50 % ± 3.7 %; and between 22.3 % and 95.15 %, with mean value of 73 % ± 2.8 %, among the bilharzial patients. The latter percentage figure is higher ($P < 0.001$) than the normal mean.

In this study, eight patients were presented with manifestations of night blindness. Table 2 lists detailed description of age, sex, and biochemical blood analysis of those patients. It is interesting to note that all patients suffering from night blindness were females with hypoalbuminemia, having poor-to-low fasting plasma-retinol level below the acceptable level of 20 µg/dl (except patient No. 1), and very high percent of postprandial plasma vitamin A.

Individual fasting plasma vitamin A levels increased following therapeutic treatment for one month with vitamin A capsules (Table 2).

Discussion

Sex-dependent variation in plasma vitamin A level was apparent in the present study among healthy controls and bilharzial patients. Similar findings had been reported previously (4).

Table 2. Individual patient data in eight bilharzial liver-disease female patients with night blindness

Disease state	Age	Plasma albumin	Before treatment plasma vitamin A		After supplement plasma vitamin A	
		g/dl	Fasting µg/dl	Post-prandial	Fasting µg/dl	% increase
Group I	17	3.5	22.1	118.9	32.0	44.8
	17	3.0	6.7	60.3	–	–
Group II	22	3.8	12.6	61.8	27.9	121.4
	10	3.5	19.0	180.6	–	–
Group III	65	3.2	7.7	158.6	23.0	198.7
	45	3.2	14.0	39.6	28.5	103.6
	64	3.8	7.1	47.4	13.0	83.1
	30	3.2	9.0	74.9	–	–
Mean	33.7	3.4	12.3[a]	92.8	24.9[a]	110.32
SE	7.7	0.1[a]	2.0	18.9	3.3	25.51
Bilharzial patients with normal dark adaptation						
Group I						
$\bar{X}$	18.4	3.5	32.2[b]	125.1	56.3[b]	70.3
SE	3.0	0.2[a]	1.4	15.6	8.0	5.7
Group II						
$\bar{X}$	29.9	3.8	31.9[b]	102.0	51.2[b]	64.3
SE	5.9	0.2[a]	3.2	13.7	0.5	2.8
Group III						
$\bar{X}$	43.5	3.1	25.6[b]	112.9	48.6[a, b]	75.0
SE	6.6	0.2[a]	4.3	25.7	9.8	3.7
Normal	–	4.6	59.6[c]	141.6	–	–
	–	0.2[b]	6.1	22.2	–	–

Within the same column, mean values are significantly different ($p < 0.05$); if they don't share the same superscript (Student's t-test).

In the present study, low plasma concentration of vitamin A was found in patients with liver cirrhosis. Smith et al. (15) suggested that the low plasma vitamin A level is secondary to an abnormality in the secretion of vitamin A from the liver and the transport to extrahepatic tissues.

Mikhail and Mansour (8) analyzed the levels of vitamin A and components of its transport proteins complex: RBP and pre-albumin (PA) as well as zinc and its major binding proteins: albumin and α_2-macroglobulin in plasma of male Egyptian patients with active Schistosomal infection. According to their findings, the authors reported that the binding and transport of both zinc and vitamin A were adversely affected by Schistosomiasis and its various complications. The authors added that deficiencies of both zinc and vitamin A seem to be interrelated in this disease and suggested that the vitamin A transport system is largely dependent on the zinc status.

In cases with liver cirrhosis, impaired dark adaptation have been reported repeatedly. Many hypotheses have been postulated for explaining factors responsible for abnormal dark adaptation.

Morrison et al. (10) related abnormal dark adaptation among cirrhotics to low serum zinc. The authors suggested that zinc may influence dark adaptation by affecting release or synthesis of retinol-binding protein (RBP) from the liver. Furthermore, the authors added that a decreased level of serum albumin in cirrhotics causes a shift in binding of zinc from macromolecular to micromolecular ligands, resulting in increased filtration of zinc at the renal glomerulus.

More recently, Fulton et al. (3) reported that cirrhotic patients with fasting retinol values below 15 μg/dl correlated significantly with scotopic thresholds. The authors could not state a limiting plasma retinol value below which the dark adapted threshold would be elevated. The fact that all patients in this study presented with night blindness were females raises the question about the possible presence of sex difference in the susceptibility to night blindness.

There was, however, no mention in the literature about sex-dependent susceptibility to night blindness. This observation still awaits further investigation.

Night blindness improved consistently and responded positively to supplementation. In the present work, all subjects also experienced a rise in serum retinol values after vitamin A supplement (500,000 IU over a period of four weeks), although variable individual responses were observed (Table 2). Generally, the response of our patients differ from those patients with alcoholic cirrhosis. After four weeks of 10,000 μg daily vitamin A intake (equivalent to 924,000 IU/four weeks) to eight subjects with alcoholic cirrhosis, only three patients experienced a rise in serum retinol values, two showed no change, while three had lower values than initial levels before supplementation; dark adaptation (night blindness) improved positively among the eight patients (9). The authors showed also that the proportion of circulating retinyl esters composed 20–50 % of the total serum vitamin A, suggesting that patients with severe liver dysfunction are less able to take up and store newly absorbed vitamin A. The same authors further recommended applying the RDR test as a useful predictor of vitamin A deficiency in patients with liver diseases.

References

1. El-Moufty A, Khattab M (1962) Hepato-splenic bilharziasis. Proc 1st Int Symp on Bilharziasis, Cairo II:79
2. Farid Z, Patwardhan VN, Darby WJ (1969) Parasitism and anemia. Am J Clin Nutr 22:498
3. Fulton AB, Hansen RM, Underwood BQ, Schwachman H, Barg DC (1982) Scotopic thresholds and plasma retinol in cystic fibrosis. Invest Ophthalmol Visual Sci 23:364
4. Haque T (1982) A survey of human liver reserves of retinol in London. Br J Nutr 47:165
5. Houba V (1980) Schistosomiasis. In: Houba V (ed) Immunopathological investigation of tropical parasitic diseases, 1st ed, vol 2. Churchill, London

6. Leo MA, Lieber CS (1982) Hepatic vitamin A depletion in alcoholic liver injury. N Engl J Med 307:597
7. Manson-Bahr, PEL, Apted FIC (1985) Manson's tropical diseases. 18th ed. English Language Book Soc, London
8. Mikhail MM, Mansour MM (1982) The interaction of zinc and vitamin A in human Schistosomiasis. European J Clin Invest 12:345
9. Mobarhan S, Russell RM, Underwood B, Wallingford J, Mathieson R, Al-Midani H (1981) Evaluation of the relative dose response test for vitamin A nutriture in cirrhosis. Am J Clin Nutr 34:2264
10. Morrison SA, Robert MD, Elizabeth AC, Carrey AB, Edwin V (1978) Zinc deficiency: a cause of abnormal dark adaptation in cirrhotics. Am J Clin Nutr 31:276
11. Neald JB, Pearson WN (1963) Macro- and micro-methods for determination of serum vitamin A using trifluoroacetic acid. J Nutr 79:452
12. Nyberg A, Berne B, Nordlinder H, Busch C, Eriksson U, Loof L, Vahlquist A (1988) Impaired release of vitamin A from liver in primary biliary cirrhosis. Hepatology 8:136
13. Russell RM, Morrison SA, Smith FR, Oaks EV, Carney EA (1978) Vitamin A reversal of abnormal dark adaptation in cirrhosis. Ann Intern Med 88:622
14. Simpson AJ, Ali PO, Yi X, Smithers SR (1988) Schistosome glycoconjugates as antigenes and their relevance in experimental and human Schistosomiasis. Biochem Soc Transactions 16:264
15. Smith ER, Underwood BA, Denning DR, Varma A, Goodman DS (1972) Depressed plasma retinol binding protein levels in cystic fibrosis. J Lab Clin Med 80:423
16. Smith FR, Goodman D (1971) The effects of diseases of the liver, thyroid and kidneys on the transport of vitamin A in human plasma. J Clin Invest 50:2426
17. Underwood BA, Denning CR (1972) Blood and liver concentrations of vitamin A and E in children with cystic fibrosis. Pediat Res 6:26

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