THE VITAMIN A , RETINOL - BINDING PROTEIN , β CAROTENE AND ZINC CONCENTRATIONS IN CHILDREN WITH INSULIN - DEPENDENT DIABETES MELLITUS

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SUMMARY : We investigated the serum vitamin A, β carotene, retinol binding protein (RBP) and zinc (Zn) levels in 24 children with insulin-dependent diabetes mellitus and 10 healthy subjects. The serum vitamin A and RBP levels were 27.5 ± 4.3 μg/dl and 27.8 ± 7.4 mg/L in the patients and 33.1 ± 4.6 μg/dl and 43.2 ± 8.0 mg/L in healthy subjects. The β carotene levels in the patients and the control subjects were 164.3 ± 36.3 and 106.0 ±14.6 μg/dl . The serum Zn concentrations in the patients and the control subjects were 86.9 ±16.5 and 118.1 ± 27.8 μg/dl respectively. There was a negative correlation between serum vitamin A and HbA 1C; serum RBP and HbA 1C levels; serum Zn and HbA 1C; a positive correlation between serum vitamin A and RBP levels in patients. The poorly controlled diabetic state may affect the serum vitamin A, β carotene, RBP and Zn concentrations in children with IDDM.

***Key Words :** Vitamin A, RBP, Beta carotene, Zinc, IDDM, Childhood.*

INTRODUCTION

Most of the diabetic complications; considering frequency, severity and progress were related not only to the duration of the disease, but also to the degree of the hyperglycemia and metabolic disorders (16). Vitamin A has some effects on the release of granules and secretion of hormones, especially effective glucose oxidation and insulin release (3).The previous studies revealed that insulin nondependent and dependent diabetic patients had lower retinol and RBP levels than the normal control subjects did (2, 20). In animal studies it was discovered that Zn deficiencies could cause insulin resistance in type II diabetes (11).

The patients with insulin-dependent diabetes mellitus (IDDM) we followed up had poor socioeconomical levels and their diabetic states were not excellent. This study was undertaken in patients with IDDM to assess serum vitamin A, RBP, β carotene and Zn concentrations.

MATERIALS AND METHODS

The study was conducted from February to June 1992 in The Pediatric Endocrinology Department of Medical Faculty, Erciyes University. The diabetic group consisted of 24 patients with IDDM and the nondiabetic group consisting of 10 healthy subjects. The patients were chosen among the diabetic patients who had been controlled regularly by our department.The diabetics were matched for age and gender with the ones in the control group. The patients who had any systemic disorders, vitamin deficiencies, malabsorption syndromes or any diabetic complications, except mild retinopathy, were excluded from the study. The children in the control

group did not have any systemic disorders, vitamin deficiencies, malabsorption syndromes, acute or chronic renal diseases. Name of the subjects in the study received any vitamin supplements. Urine analysis for protein was negative and the glomerular filtration rates were within normal limits in the patients.

Blood samples were taken postprandially in the morning and some of the separeted serum was used for routine biochemical analysis, the remaining was protected from light and frozen for later analysis. Simultaneous heparinized blood samples were taken for HbA_1C measurements. After the first urination the urine samples were collected for protein analysis. The glomerular filtration rate was calculated by collecting the 24-hour urine samples.

Vitamin A and β carotene levels were determined by the Neeld- Pearson Method (12). The normal values were 25-60 µg/ dl for vitamin A and 30-115 µg/ dl for β carotene. RBP levels were determined by Single radial immunodiffusion technique by using LC- Partigen immunodiffusion plaques (Behring Diagnostic, Marburg, FRG) (2). Normal limits were 30-60 mg /L. HbA_1C were determined by colorimetric manual method with 443 nm optic density (13). Serum Zn levels were determined by Hittachi 2-8000- polarized, Zeeman Atomic Absorption Spectrophotometer. The reference levels were 70 -150 µg/ dl (10).

Results were analyzed by the Student's t test, Mann - Whitney U test, correlation and regretssion analysis (7).

RESULTS

The clinical characteristics and laboratory findings of both diabetic and nondiabetic subjects are seen in Table 1. The mean serum vitamin A, β carotene, RBP and Zn levels in diabetic and nondiabetic subjects are shown in Table 2. Compared with the nondiabetics, vitamin A, RBP , Zn levels were significantly lower in the diabetic subjects. The serum β carotene levels in the diabetics were significantly higher than those of nondiabetic subjects. Linear regressions between HbA_1C and vitamin A, β carotene, RBP, Zn ; vitamin A and β carotene, RBP, Zn; RBP and Zn are shown in Table 2.

DISCUSSION

In diabetic patients, we observed that the serum vitamin A, RBP and Zn levels were lower, but serum β carotene levels were higher than those of controls. Serum vitamin A levels were correlated negatively with serum β carotene levels and positively with RBP and Zn levels in the patients. This decrease in retinol and increase in β carotene levels might be due to the impaired conversion of vitamin A to β carotene. Additionally the lower RBP levels of patients may have decreased vitamin A levels. This was the result of neither deficient absorption of vitamin A nor of malabsorption, because serum β carotene levels of our patients were higher than tho-

	Diabetics (n =24)	**Nondiabetics (n =10)**	**p**
Age (year)	12.12 ± 3.50*	12.30 ± 3.20	> 0.05
Sex (M / F)	7 / 17	3 / 7	
Body weight (kg)	37.42 ± 12.79	43.70 ± 14.40	< 0.05
Height (cm)	139.75 ± 18.28	147.10 ± 14.81	< 0.05
Diabetic age (year)	4.4 ± 3.4	-	
Blood glucose (mg/dl)	211.9 ± 121.2	96.4 ± 8.0	< 0.01
HbA_1C (%)	14.2 ± 4.0	5.3 ± 0.4	< 0.01
BUN (mg / dl)	13.38 ± 4.03	12.90 ± 3.14	> 0.05
Creatinin (mg / dl)	0.67 ± 0.14	0.62 ± 0.19	> 0.05
GFR (ml / min)	116.6 ± 19.8	-	
AST (U /L)	19.04 ± 6.91	18.10 ± 7.01	> 0.05
ALT (U / L)	17.42 ± 6.95	16.80 ± 3.01	> 0.05
Total protein (g /dl)	7.02 ± 0.70	7.20 ± 0.42	> 0.05
Albumin(g / dl)	4.36 ± 0.39	4.39 ± 0.24	> 0.05

* : X ± SD ; GFR: Glomerular filtration rate; BUN: Blood urea nitrogen;
AST : Aspartate aminotransferase; ALT: Alanine aminotransferase,

Table 1 : Clinical characteristics and laboratory findings of diabetic and nondiabetic subjects.

	Diabetics (n =24)		Nondiabetics (n =10)		p
Vitamin A (µg/dl)	27.5 ± 4.3*		33.1 ± 4.6		< 0.01
ß Carotene (µg/dl)	164.3 ± 36.3		106.0 ± 14.6		< 0.01
RBP (mg/L)	27.8 ± 7.4		43.2 ± 8.0		< 0.01
Zn (µg/dl)	86.9 ± 16.5		118.1 ± 27.8		< 0.01
Linear regressions were as below :					
	Diabetics			**Nondiabetics**	
Vitamin A / HbA_1C	r = -0.69	p < 0.001	r = 0.18		p > 0.05
ß Carotene / HbA_1C	r = 0.66	p < 0.001	r = 0.01		p > 0.05
RBP / HbA_1C	r = -0.73	p < 0.001	r = 0.18		p > 0.05
Zn / HbA_1C	r = -0.81	p < 0.001	r = -0.03		p > 0.05
ß Carotene / Vitamin A	r = -0.63	p < 0.001	r = 0.80		p > 0.01
RBP / Vitamin A	r = 0.88	p < 0.001	r = 0.94		p > 0.001
Vitamin A / Zn	r = 0.58	p < 0.01	r = 0.12		p > 0.05
RBP / Zn	r = 0.54	p < 0.01	r = 0.33		p > 0.05

* Mean ± Standart deviation.

Table 2 : Serum mean vitamin A, ß carotene, RBP, Zn concentrations in diabetic and nondiabetic subjects and lenear regressions.

se of the control subjects. Basu et al (2) demonstrated that the levels of serum vitamin A and RBP were significantly lower in patients with IDDM than those of control subjects. On the other hand Cinaz et al (5) found that serum vitamin A levels were higher, but β carotene levels lower than those of control subjects. Wako et al (20) demonstrated that reduced or normal plasma levels of retinol were accompanied by significantly increased concentrations of retinyl esters in patients with IDDM. It was shown that the diabetics had carotenemia in both blood and skin (6,9). An experimental trial in diabetic rats revealed that the conversion of β carotene to vitamin A in intestinal mucosa cells was insufficient (15). We observed that HbA_1C levels were correlated negatively with serum vitamin A, RBP and Zn; and positively with serum β carotene levels. The poor diabetic control may have a role in this situation.

The mobilization and transport of vitamin A from liver stores require hydrolysis of the retinyl esters followed by conjugation of the free retinol with RBP which is produced in the liver. Vitamin A mobilization from the liver is regulated by factors that control the rates of RBP production and secretion. Retinol deficiency specifically blocks the secretion of RBP. Delivery of retinol to peripheral tissues appears to involve specific cell surface receptors for RBP (8). By using Zn and vitamin A deficient animals, it had been demonstrated that Zn was necessary for normal mobilization of vitamin A from the liver (18). The plasma RBP levels of Zn-deficient rats were lower than those of control rats fed on a Zn-sufficient diet. The Zn deficiency interferes with both the synthesis of RBP by the liver and probably the synthesis of some other plasma proteins as well (19). The levels of vitamin A in patients with the lung cancer were significantly correlated with serum concentrations of RBP and Zn (1).

Animal studies related to the effects of vitamin A on membranes revealed that retinol regulated the stability of the rat liver lysosome, the rat erythrocyte membrane and normalized the shape of the rat erythrocyte, probably through a membrane effect and regulated the binding of membrane-bound ATPase (14). Chertow and Baker (3) tested the effects of vitamin A, a membrane surface-active agent, on glucose-induced biphasic insulin release from collagenase-isolated rat islets. It revealed that whereas vitamin A at high concentrations inhibited the insulin secretion, it stimulated the insulin secretion at low concentrations, and at normal concentrations there were not any effect on the insulin secretion. Later Chertow et al (4) demonstrated that retinol in high concentrations inhibited the second phase insulin release induced by glucose, glyceraldehyde and leucine mediated in part through impairement of mitochondrial function and intracelluler glucose oxidation. Vitamin A had decreased the volume of secretory granules and increased the volu-

me of material within the rough endoplasmic reticulum. Vitamin A suplementation in diabetic rats did not alter glucose levels in the blood or in the urine (17).

During the clinical course of type I diabetes, changes in serum vitamin A, β carotene, RBP and Zn may develope. The severity of these changes may be higher in poorly controlled diabetics and can affect the diabetic care in a negative way. Serum vitamin A, β carotene, RBP and Zn levels in diabetic patients should be measured periodically and especially Zn supplementation should be given. The nutritional disorders which were effective in the metabolism of glucose and insulin should be corrected by giving the deficient nutrients. However, because there is no definite knowledge about vitamin A supplementation, and even vitamin A could be harmful, it must be careful with supplementation. Further investigation will determine the mechanism of reduced vitamin A levels in diabetics.

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