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VITAMIN A STATUS AND ITS DETERMINANTS IN PATIENTS WITH CYSTIC FIBROSIS*

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ABSTRACT

Background. Routine administration of vitamin A, recommended in CF patients, can help to prevent its deficiency. However, high vitamin A supplementation may lead to its excessive level and possible toxicity. Therefore, the aim of the present study was to assess the status of vitamin A and the determinants of its body resources in CF patients.

Material and methods. In 196 CF patients aged from 4 months to 47 years, the following parameters were analysed: nutritional status (standardized body weight and height, serum albumin concentration) and clinical expression of disease (lung function − spirometry; biochemical markers of liver function − ALT, AST, GGT; respiratory tract colonization by *Pseudomonas aeruginosa*; diabetes; cirrhosis, non-cirrhotic liver disease; exocrine pancreatic function − fecal elastase-1 concentration; blood clotting – INR and vitamin A supplementation).

Results. Median vitamin A concentration in the study group was 383.0 ng/ml (1st–3rd quartile: 316.5–457.0). Vitamin A deficiency was found in 32 (16.3%) subjects studied. Vitamin A concentrations above the reference range were observed only in 3 (1.5%) CF patients. CF patients with vitamin A deficiency were significantly older and had lower values of FEV1 compared to CF subjects with normal vitamin A status. Moreover, vitamin A deficiency occurred more frequently in CF patients with diabetes, *Pseudomonas aeruginosa* colonization, worse lung function and in those without vitamin A supplementation. However, in multiple linear regression analyses, none of the independent variables was documented to be important for predicting vitamin A status.

Conclusions. Vitamin A body resources in CF patients are mostly normal. Moreover, there are no good determinants of vitamin A status in these patients. Further studies targeted at exploring potential toxicity and deficiencies of vitamin A in CF patients are needed.

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INTRODUCTION

Vitamin A is a retinoid that includes organic compounds like retinol (alcohol form), retinal (aldehyde form), retinoic acid and carotenoids (provitamin A, which is converted to retinol) (Meissburger and Wolfrum, 2008). Retinoids play an important role in many biological processes in the human body (Olson, 1996). They are involved in normal tooth and bone growth, normal vision, immune system response, reproduction and healthy skin (Blomhoff and Blomhoff, 2006).

The deficiency of vitamin A has been observed in 11% to 33% of CF patients with vitamin A supplementation (Feranchak et al., 1999; Lindblad et al., 1997) and in 29% to 51% infants at the time of cystic fibrosis diagnosis (Bines et al., 2005; Lindblad et al., 1997). Patients with vitamin A deficiency suffer from eye diseases, such as abnormal dark absorption (night blindness), conjunctival and corneal xerosis, and Bitot's spot (Stapelton, 2006; West, 2003). Moreover, a weakening of the immune system response is observed, as are skin abnormalities. Therefore, vitamin A supplementation has been recommended in CF. The dosage of vitamin A is based on the individual and depends on age and annual serum retinol concentration (Brei et al., 2013). However, the current standard of supplementation may increase the risk of overdose and vitamin A toxicity (Graham-Maar et al., 2006). Hepatotoxicity and lower bone mineral density are observed as symptoms of an excessively high vitamin A concentration (Penniston and Tanumihardjo, 2006).

Therefore, the aim of the present study was to assess the status of vitamin A and the determinants of its body resources in CF patients.

MATERIAL AND METHODS

Material

The study group was composed of 196 patients with CF – 95 (48.5%) females and 101 (51.5%) males aged from 4 months to 47 years. The diagnosis was based on accepted guidelines (Castellani et al., 2009; Turck et al., 2016). Mutations in one or both alleles of the *CFTR* gene were found in 189 patients (96.4%). The genotype could not be identified in 7 (3.6%) patients. The *CFTR* mutations of the group studied were as follows: F508del/F508del (n = 73); F508del/– (n = 24); F508del/3849 + 10 kbC > T (n = 8); F508del/CFTRdele2,3(21kb) (n = 7); F508del/1717-1G > A (n = 5); F508del/F508del/2143delT (n = 5); F508del/2183AA > G (n = 4); F508del/2184insA (n = 3); F508del/3272-26A > G (n = 3); F508del/N1303K (n = 3); F508del/R553X (n = 3); 3849 + 10 kbC > T/3600 + 1G > T (n = 2); A155P/3171insC (n = 2); F508del/3659delC (n = 2); F508del/K710X (n = 2); F508del/1078delT (n = 1); F508del/2721del11 (n = 1); F508del/296 + 1G > C (n = 1); F508del/3121-2A > G (n = 1); F508del/3171insC (n = 1); F508del/3600 + 2insT (n = 1); F508del/4374 + 1G > T (n = 1); F508del/D1152H (n = 1); F508del/dup1716 +51 – > 61 (n = 1); F508del/G27V (n = 1); F508del/G542X (n = 1); F508del/G551D (n = 1); F508del/IVS2 + 1G > T (n = 1); F508del/L467F (n = 1); F508del/R1158X (n = 1); F508del/R334W (n = 1); F508del/R347P (n = 1); F508del/R851X (n = 1); F508del/W1282X (n = 1); F508del/Y1092X (n = 1); G542X/- (n = 1); G542X/R553X (n = 1); N1303K/- (n = 1); N1303K/3272-26A > G (n = 1); N1303K/3849 + 10 kbC > T (n = 1); N1303K/CFTRdele2,3(21kb) (n = 1); N1303K/G551D (n = 1); Q1313X/- (n = 1); R553X/1717-1G-A (n = 1); S1196X/Q1382X (n = 1); T582I/2721del11 (n = 1); W1282X/CFTRdele2,3(21kb) (n = 1); 3849 + 10kbC > T/384910kbC > T (n = 1); 3849 + 10kbC > T/W1282X (n = 1); CFTRdele2,3(21kb)/F1052V (n = 1); 1524 + 1G > A/E585X (n = 1); 1717-1G-A/1717-1G-A (n = 1); 2183AA > G/- (n = 1); 2183AA > G/R117H (n = 1); 2184insA/2789 + 2insA (n = 1); 2184insA/622-1G > A (n = 1); 3659delC/- (n = 1); 3849 + 10kbC > T/1717-2A > G (n = 1).

In CF patients the following parameters were analysed: nutritional status (standardized body weight and height, serum albumin concentration) and clinical

expression of disease − lung function (spirometry); biochemical markers of liver function − ALT, AST, GGT; respiratory tract colonization by *Pseudomonas aeruginosa*; diabetes; cirrhosis, non-cirrhotic liver disease (Debray et al., 2011); exocrine pancreatic function − fecal elastase-1 concentration (Walkowiak et al., 2002); blood clotting (INR) and vitamin A supplementation. Clinical parameters in the study group were presented in Table 1.

Table 1. Clinical parameters in the study group

Parameters	Median (1st–3rd quartile)
Body weight (*Z*-score)	–0.63 (–1.23– –0.04)
Body height (*Z*-score)	–0.36 (–1.25–0.36)
Albumin, g/dl	3.88 (3.59–4.18)
AST, U/L	29.0 (22.8–39.0)
ALT, U/L	24.0 (16.8–34.0)
GGT, U/L	12.0 (9.0–19.0)
FEV1, %	79.0 (56.0–92.0)
INR	1.07 (1.00–1.14)
Vitamin A dose, IU/day*	5000 (2664–17250)**

*The calculated dose of vitamin A have also took account beta-carotene.

**Median and 1st–3rd quartile for vitamin A dose were calculated for all CF patients (receiving and not receiving vitamin A).

Body weight and height two standard deviation below the mean values for all patients studied were found in 13 (6.6%) and 19 (9.7%) subjects, respectively. Hypoalbuminemia was detected in 39 (19.9%) CF patients. Abnormal liver enzymes activities: ALT, AST and GGT were documented in respectively 18.9%, 15.8%, and 7.1% patients.

One hundred and sixty (81.6%) patients were pancreatic insufficient. Liver cirrhosis and other liver involvement were observed in 9 (4.6%) and 25 (12.8%) of the patients, respectively. Colonization by *Pseudomonas aeruginosa* was documented in 77 (39.3%) patients. Thirteen (6.6%) patients had diabetes.

One hundred and seventy-three (86.7%) patients had vitamin A supplementation. The dose ranged from 536 to 36 333 (mean ±SD: 10 654 ±9752; median: 5750; 1st–3rd quartile: 3340–18167). Twenty-three subjects were not supplemented with vitamin A, but only 12 of them were pancreatic sufficient.

The study was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from patients (>16 years old) and the patients' parents (patients under 16 years old). The project was approved by the Bioethical Committee at Poznan University of Medical Sciences (decision no. 244/2012).

Method

The vitamin A concentration was analysed by high-performance liquid chromatography (HPLC). HPLC analysis was performed on the Hewlett Packard 1100 Series HPLC System (Wladbronn, Germany). For the separation of the retinol a Supelco C18 column (4.6 mm × 150 mm; 5 μm) was used. The mobile phase was methanol-butylated hydroxytoluene. The mobile phase flow rate was 1.4 ml/min. Detection with a UV detector was carried out at 326 nm.

Serum samples after protein precipitation with an equal volume of ethanol were extracted with a 10-fold increase in the volume of hexane. After centrifugation, the hexane layer was pooled, and then evaporated to dryness. The residue was dissolved in 100 ul of methanol. 20 ul of the solution was applied to a column. The final content of vitamin A in 1 ml of serum was calculated by comparing the peak area in the sample with the surface of the peak standard containing a known concentration of retinol in 20 μl (taking into consideration the dilution ratio and the performance of the analytical procedure which was assessed by using an internal standard).

A stock standard solution of vitamin A (1.5 ng/ml) was prepared by dissolving 25 mg of vitamin A (Sigma-Aldrich, Poznań, Poland) in 10 ml of ethanol absolute (≥99.8%). The working standard solution was prepared by diluting 5 μl of stock standard solution in10 ml of ethanol absolute.

A stock internal standard solution of retinyl acetate was prepared by dissolving 40 mg of retinyl acetate (Merck, Warsaw, Poland) in 10 ml of absolute ethanol. The working internal standard solution was prepared by diluting 20 μl of stock internal standard in 10 ml ethanol.

Statistical analysis

Data were assessed for normality of distribution using the Shapiro-Wilk and Lilierfors tests. The Mann-Whitney test, chi^2-test and the Fisher-Freeman-Halton test (for three categories of liver diseases) were used to assess the differences between the subgroups with normal and abnormal vitamin A statuses. The potential influence of the parameters studied on the occurrence of vitamin A deficiency was assessed using multiple linear regression analysis and multiple forward stepwise logistic regression analysis in two logistic regression models with different classifications of the *CFTR* gene mutations (F508del/F508del vs. other/other and severe/severe vs. other/other). The classification of *CFTR* gene mutations was based on consensus concerning the use and interpretation of cystic fibrosis mutation analysis in clinical practice (Castellani et al., 2009). The following independent variables were included in the regression models: age, *Z*-score for body weight and height, albumin concentrations, FEV1, vitamin A dose, vitamin A preparation (with or without) (AquADEKs and other than AquADEKs preparations – Vitaminum A – 50 000 IU/ml or 2500 IU/ml, Beta-Carotene, Vitaminum A+E, Vitaminum A+D3, Capivit A+E, ADEK, Multi Sanostol, Kinder Biovital, Vitaral, Centrum Junior, Centrum, Multivitamin, Vigor, Multi-Tabs, Vita-miner, Falvit, Visolvit), and the coexistence of the following: diabetes, liver cirrhosis, pancreatic insufficiency, *Pseudomonas aeruginosa* colonization and *CFTR* mutation. The level of significance was set at $p < 0.05$.

RESULTS

The median vitamin A concentration in the study group was 383.0 ng/ml (1st–3rd quartile: 316.5–457.0). Vitamin A deficiency (<200 ng/ml for infants, <250 ng/ml for children aged 1 to 4 years, <300 ng/ml for children over 4 years old and adults) was found in 32 (16.3%) of the subjects studied. Vitamin A concentrations above the reference range (>800 ng/ml) were observed only in 3 (1.5%) CF patients. A description of the clinical parameters in the subgroups of CF patients with low and normal vitamin A concentrations is presented in

Table 2. The distribution of low and normal vitamin A concentration depending upon clinical parameters in CF patients

Parameter		Vitamin A, ng/ml		*p*
		<300*	≥300	
Number of patients	*N* %	32 (16.3)	164 (83.7)	–
Age, year	Median (1st–3rd quartile)	18.0 (12.1–22.4)	10.5 (4.5–16.5)	0.000187
Body weight (*Z*-score)	Median (1st–3rd quartile)	–0.65 (–1.53– –0.42)	–0.58 (–1.20–0.04)	0.070176
Body height (*Z*-score)	Median (1st–3rd quartile)	–0.72 (–1.67–0.16)	–0.33 (–1.14–0.43)	0.128210
FEV1, %	Median (1st–3rd quartile)	56.00 (40.00–77.07)	84.00 (65.00–96.00)	0.000025
Albumin, g/dl	Median (1st–3rd quartile)	3.80 (3.57–4.01)	3.90 (3.59–4.21)	0.133511
Vitamin A dose, UI/day	Median (1st–3rd quartile)	3340 (0–18167)	5010 (3340–17250)	0.203203

* <200 ng/ml for infants, <250 ng/ml for children aged 1 to 4 years, <300 ng/ml for children over 4 years old and adults.

Table 3. The distribution of low and normal vitamin A concentration depending upon clinical parameters in CF patients

Parameter, N%		Vitamin A, ng/ml		*p*
		<300*	≥300	
Body weight (*Z*-score)	<–1	13 (20.6)	50 (79.4)	0.2614
	≥–1	19 (14.3)	114 (85.7)	
Body height (*Z*-score)	<–1	11 (18.3)	49 (81.7)	0.6136
	≥–1	21 (15.4)	115 (84.6)	
FEV1, %	<80	24 (30.8)	54 (69.2)	0.0013
	≥80	7 (9.6)	66 (90.4)	
Albumin, g/dl	<3.5	8 (20.5)	31 (79.5)	0.4598
	≥3.5	24 (15.6)	130 (84.4)	
Diabetes	yes	7 (53.8)	6 (46.2)	0.0002
	no	25 (13.7)	158 (86.3)	
Liver disease	cirrhosis	3 (33.3)	6 (66.7)	0.3234
	other liver involvement	3 (12.0)	22 (88.0)	
	no	26 (16.0)	136 (84.0)	
Pancreatic sufficiency	yes	2 (5.6)	34 (94.4)	0.0530
	no	30 (18.8)	130 (81.2)	
Ps. aeruginosa colonization	yes	21 (27.3)	56 (72.7)	0.0009
	no	11 (9.2)	108 (90.8)	
CFTR gene mutation	F508del/F508del	12 (16.4)	61 (83.6)	0.9740
	other/other	20 (16.3)	103 (83.7)	
	severe/severe	21 (16.8)	104 (83.2)	0.8119
	other/other	11 (15.5)	60 (84.5)	
Vitamin A supplementation	yes	23 (13.3)	150 (86.7)	0.0016
	no	9 (39.1)	14 (60.9)	

* <200 ng/ml for infants, <250 ng/ml for children aged 1 to 4 years, <300 ng/ml for children over 4 years old and adults.

Tables 2 and 3. CF patients with vitamin A deficiency were significantly older and had lower values of FEV1 compared to CF subjects with normal vitamin A status. Moreover, vitamin A deficiency appeared more frequently in CF patients with diabetes, *Pseudomonas aeruginosa* colonization, worse lung function and in those without vitamin A supplementation.

None of the regression models using multiple linear regression analysis was statistically significant (Table 4). On the basis on multiple forward stepwise logistic regression analysis (for regression model with *CFTR* gene mutations divided into severe/severe and other/other), we found that pancreatic insufficiency was a potential risk factor for vitamin A deficiency. However, the regression model with *CFTR* gene mutations

Table 4. Multiple linear regression analysis

Clinical parameters	Vitamin A, ng/ml	
	first model*	second model**
p model	0.50107	0.55693
Age	0.367890	0.298849
Body weight (*Z*-score)	0.748747	0.711096
Body height (*Z*-score)	0.545844	0.557277
Albumin, g/L	0.791325	0.819500
FEV1, %	0.274348	0.318429
Diabetes	0.209895	0.193192
Liver cirrhosis	0.538246	0.450301
PI/PS***	0.136856	0.110859
Pseudomonas aeruginosa colonization	0.509034	0.473791
CFTR gene mutation	0.416729	0.858039
Vitamin A dose, IU/day	0.316729	0.361404
Vitamin A preparation****	0.876570	0.966918

**CFTR* gene mutations were divided as follows: F508del/F508del, other/other.
***CFTR* gene mutations were divided as follows: severe/severe, other/other.
***Pancreatic insufficiency/sufficiency.
****With or without vitamin A preparation (AquADEKs and other than AquADEKs preparation).

Table 5. Multiple forward stepwise logistic regression analysis

p model	R^2	Adjusted R2 for model	Dependent variable	Independent variable	b ±standard error	*p*
0.06251*	–	–	vitamin A, ng/ml	PI/PS***	50.4911 ±30.24256	0.097169
				diabetes	–55.1466 ±42.59641	0.197506
				FEV1	0.5756 ±0.46984	0.222486
				CFTR gene mutation	24.9938 ±24.37098	0.306809
0.04777**	0.05260455	0.03313752	vitamin A, ng/ml	PI/PS***	58.1134 ±29.32025	0.049354
				diabetes	–57.2590 ±42.55413	0.180532
				FEV1	0.4981 ±0.46381	0.284578

R^2, adjusted R2, regression slope coefficient ±standard error of regression slope coefficient were presented only for the statistically significant model.
**CFTR* gene mutations were divided as follows: F508del/F508del, other/other.
***CFTR* gene mutations were divided as follows: severe/severe, other/other.
***Pancreatic insufficiency/sufficiency.

divided into F508del/F508del and other/other was not statistically significant (Table 5).

DISCUSSION

In the past, available evidence mainly indicated the possibility of vitamin A deficiency in CF patients (Duggan et al., 1996; Huet et al., 1997; Lindblad et al., 1997). Nowadays, routine administration of vitamin A recommended in CF patients, especially in those who are pancreatic insufficient, can help to prevent its deficiency (Kalnins and Wilschanski, 2012; Graham-Maar et al., 2006). However, high vitamin A supplementation may lead to its excessive level and possible toxicity, manifested by liver disease and bone complications (Graham-Maar et al., 2006). Therefore, routine measurements of vitamin A concentrations in CF are recommended (Turck et al., 2016). However, it is worth trying to establish what determinants may affect its body resources.

In the present study vitamin A deficiency was found in 32 (16.3%) CF patients. Twelve of them received vitamin A in a dose ranging from 11 500 to 36 333 IU/day, which was above the previously recommended dose in Europe – 4000–10 000 IU/day (Sinaasappel et al., 2002). The most recent recommendations do not define the supplemental dose of vitamin A, although they suggest that the aim of vitamin A supplementation should be achieving a normal range of serum retinol concentrations characteristic of healthy people (Turck et al., 2016). Thirty of the 32 patients with vitamin A deficiency were pancreatic insufficient, and 2-pancreatic sufficient. Twenty-two of the 30 subjects with pancreatic insufficiency received vitamin A supplementation (median, 1st–3rd quartile: 14375, 2833–18167). One of the two pancreatic sufficient patients received 3340 IU of vitamin A daily. Previously, vitamin A deficiency was frequently reported in CF patients (Duggan et al., 1996; Huet et al., 1997; Lindblad et al., 1997). Duggan et al. (1996) documented vitamin A deficiency in 8 (22.9%) out of 35 CF patients with acute exacerbations. Lindblad et al. (1997) found 5 (33%) out of 15, and Huet et al. (1997) 9 (90%) out of 10 CF subjects with retinol concentrations below reference values. However, in recent years, some studies have showed that vitamin A deficiency in CF patients appeared rarely or was absent (Brei et al., 2013; Maqbool et al., 2008; Rana et al., 2014; Woestenenk et al., 2016). Brei et al. (2013) showed that none of the 32 CF patients with pancreatic insufficiency receiving vitamin A in a dose of 0 to 20 000 IU/day had its deficiency. The same results were documented by Maqbool et al. (2008). They studied 78 CF patients with pancreatic insufficiency and a vitamin A dose ranging from 0 to 30 627 IU/day. Rana et al. (2014) presented a low retinol concentration in 80 (15.2%) out of 526 CF children receiving vitamin A (dose range 625–1250 μg/day). According to the latest research, vitamin A deficiency was documented in 17 (2%) out of 862 CF children and adolescents – the supplemental dose ranged from 1169 ±500 ug RAE/day to 1546 ±817 ug RAE/day (Woestenenk et al., 2016).

On the other hand, some available evidence highlighted the possible toxicity of vitamin A in supplemented CF patients (Graham-Maar et al., 2006; Maqbool et al., 2008). Graham-Maar et al. documented significantly higher serum retinol concentration in CF children (52 ±13 μg/dL, range: 26–98 μg/dL) in comparison with healthy children (reference population included 8.0–11.9 year-old children from the National Health and Nutrition Examination Survey – NHANES) 37 ±10 μg/dL, range: 17–63 μg/dL (Graham-Maar et al., 2006; Ervin et al., 2004). The supplemental dose of vitamin A was 2720 ±1120 IU/day in CF patients (Graham-Maar et al., 2006). Moreover, Maqbool et al. (2008) showed that as many as 58% of CF patients aged 8 to 25 years had retinol concentrations above 72 μg/dL (the upper limit of the NHANES reference range of 30 to 72 μg/dL). The dose of vitamin A supplement ranged from 0 to 30 627 IU/day, whereas the total vitamin A dose from food and supplement amounted to between 1457 and 41 597 IU/day. In the present study, based on the NHANES reference range for vitamin A, only 6 (3.1%) participants have high retinol levels without any clinical symptoms of vitamin A hypervitaminosis.

In some studies, discussed below, the researchers attempted to analyze the correlation between retinol concentration and different clinical parameters (Aird et al., 2006; Brei et al., 2013; Duggan et al., 1996; Greer et al., 2004; Rivas-Crespo et al., 2013; Woestenenk et al., 2015). However, these results are very often ambiguous. Some data suggested significant positive correlations between vitamin A concentration and FEV1

in children, adolescent and young adults with CF (Aird et al., 2006; Rivas-Crespo et al., 2013). Rivas-Crespo et al. established that 90% of CF patients with a serum retinol concentration up to 110 μg/dL had FEV1 ≥ 80% (Rivas-Crespo et al., 2013). However, Woestenenk et al. (2015) in their longitudinal study did not find such a relationship in children and adolescents with CF (n = 228). Similarly, Brei et al. (2013) did not document any positive correlation between FEV1 and retinol concentration (Maqbool et al., 2008). Our results indicate that vitamin A deficiency appeared more frequently in patients with FEV1 < 80%.

In the present study, we also found that vitamin A deficiency appeared more frequently in patients with *Pseudomonas aeruginosa* colonization. Feuillet-Fieux et al. (2009), comparing antioxidant markers concentrations – including vitamin A in healthy subjects (n = 9) and CF patients infected (n = 12) and uninfected (n = 24) *Pseudomonas aeruginosa* – found no significant differences in vitamin A levels between groups.

Maqbool et al. (2008) showed that serum retinol levels were negatively correlated with standardized body weight and height, and not associated with age, gender or vitamin A intake (from food, supplement or both). Duggan et al. (1996) found positive correlations between plasma retinol concentrations and age, weight, body mass index, triceps-skinfold-thickness percentile, midupper arm circumference percentile, plasma vitamin E and RBP concentration. These results suggest that CF patients with better nutritional status had more optimal vitamin A body resources. In the present study, we found that patients with vitamin A deficiency were older. On the other hand, CF patients with vitamin A deficiency and its normal status did not differ significantly in terms of standardized body weight and height.

Furthermore, in our study we established that vitamin A deficiency appeared more frequently in CF patients not receiving vitamin A, and in those with diabetes. There are no data concerning the correlation between vitamin A deficiency and diabetes in CF patients.

In the present study, using multiple linear regression analysis, none of the regression models were statistically significant. On the basis on multiple forward stepwise logistic regression analysis (for regression model with *CFTR* gene mutations divided into severe/severe and other/other) we found that pancreatic insufficiency was a potential risk factor for vitamin A deficiency. However, using our regression model we were able to explain only about 3% of the variation of retinol concentration. Available evidence documenting the potential predictors of vitamin A level in CF patients is scarce. Greer et al. (2004), whose study was the only one to use multiple linear regression analysis, found that CRP concentration, vitamin E and 1.25 $(OH)_2D_3$ concentration, the existence of liver disease, the number of admissions and age, but not FEV1, standardized body weight, number of hospitalizations or exacerbations were predictive factors of vitamin A status. The regression model explained 49% of the variation in retinol concentration.

In our study, we analyzed vitamin A status based only on serum retinol concentration, and the following parameters were not included: retinol binding protein (RBP), zinc and C-reactive protein (CRP) concentrations, which is a limitation of this study. Retinol concentration is a marker of liver vitamin A storage and remains normal until the hepatic resources are depleted. However, the serum retinol concentration is decreased by acute inflammatory processes without affecting vitamin A liver resources. Moreover, infection leads to a decrease in negative acute-phase proteins, including RBP (Morton, 2011; Stephenson and Gildengorin, 2000). RBP is also decreased by zinc deficiency (Morton, 2011). This protein plays an important role in transporting retinol from the liver to the peripheral tissues. In the bloodstream, retinol is bound to the RBP-transthyretin complex, from which it is released (Mrugacz et al., 2005).

To sum up, vitamin A body resources in CF patients are mostly normal. Moreover, there are no good determinants of vitamin A status in these patients. Further studies targeted at exploring the potential toxicity and deficiencies of vitamin A in CF patients are needed.

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