

This article was downloaded by: [Uppsala University Library]

On: 11 September 2009

Access details: Access Details: [subscription number 786945401]

Publisher Informa Healthcare

Informa Ltd Registered in England and Wales Registered Number: 1072954 Registered office: Mortimer House, 37-41 Mortimer Street, London W1T 3JH, UK



Journal of Asthma

Publication details, including instructions for authors and subscription information:

<http://www.informaworld.com/smpp/title~content=t713597262>

Serum Vitamin A and -Carotene Levels in Children with Asthma

Abdulrahman M. Al Senaidy ^a

^a Department of Biochemistry, College of Science, King Saud University, Saudi Arabia

Online Publication Date: 01 September 2009

To cite this Article Al Senaidy, Abdulrahman M.(2009)'Serum Vitamin A and -Carotene Levels in Children with Asthma',Journal of Asthma,46:7,699 — 702

To link to this Article: DOI: 10.1080/02770900903056195

URL: <http://dx.doi.org/10.1080/02770900903056195>

PLEASE SCROLL DOWN FOR ARTICLE

Full terms and conditions of use: <http://www.informaworld.com/terms-and-conditions-of-access.pdf>

This article may be used for research, teaching and private study purposes. Any substantial or systematic reproduction, re-distribution, re-selling, loan or sub-licensing, systematic supply or distribution in any form to anyone is expressly forbidden.

The publisher does not give any warranty express or implied or make any representation that the contents will be complete or accurate or up to date. The accuracy of any instructions, formulae and drug doses should be independently verified with primary sources. The publisher shall not be liable for any loss, actions, claims, proceedings, demand or costs or damages whatsoever or howsoever caused arising directly or indirectly in connection with or arising out of the use of this material.

ORIGINAL ARTICLE

Serum Vitamin A and β -Carotene Levels in Children with Asthma

ABDULRAHMAN M. AL SENAIDY*

Department of Biochemistry, College of Science, King Saud University, Saudi Arabia

Background. Low serum levels of dietary antioxidants are associated with allergic diseases including asthma. Vitamin A and carotenoids are dietary antioxidants that are likely to play an important role against airway inflammation. **Methods.** This study included 433 asthmatic schoolchildren and 537 healthy control subjects, between 6 and 18 years of age. Serum β -carotene, vitamin A, cholesterol, and triglycerides levels were studied in all subjects. **Results.** Serum vitamin A concentration was significantly lower in asthmatic subjects than in healthy control subjects (19.4 ± 1.1 mg/dL vs. 28.9 ± 0.86 mg/dL) ($p < 0.001$). There were no significant differences in the levels of β -carotene, cholesterol, and triglycerides between the two groups. **Conclusion.** Reduction of vitamin A in asthmatic children may have etiological implications for the disease.

Keywords asthma, vitamin A, β -carotene, triglycerides, cholesterol

INTRODUCTION

The role of the environmental and nutritional factors in the pathogenesis of allergic diseases and airway obstruction has been recently the focus of investigation (1, 2). Dietary studies have suggested that there is an association between low intake of antioxidants and the development of asthmatic symptoms, such as bronchial inflammation and reduction of pulmonary function (3–5). Triggers of asthma, including allergens and viruses, lead to the recruitment and activation of airway inflammatory cells, which produce more oxygen-derived free radicals, resulting in oxidative damage (6). Lungs have several natural antioxidant defense systems that inhibit reactive oxidant propagation by scavenging hydroxyl radicals and singlet oxygen (7).

Vitamin A, C, E, and carotenoids belong to a group of antioxidants that are likely to play an important role in the respiratory tract by physiologically quenching singlet oxygen and inhibiting free radical chain reaction (8, 9). Several studies have supported the assumption that airway obstruction is probably associated with reduction in serum retinol (vitamin A) and carotenoids (10, 11). Retinoic acid, an active metabolite of vitamin A, is known to influence the development, maintenance, differentiation, and regeneration of lung epithelial cells (12). Lower vitamin intake is more prevalent among children with asthma, and vitamin A deficiency decreases the proliferation of airway mucus and basal cells, causing squamous metaplasia (13). Low intake of β -carotene due to reduced consumption of fresh fruits and fruit juice has been affiliated with diminished lung function (14, 15).

However, the association between pulmonary function and vitamin A status, however, is not fully understood. The aim of this study was to compare the serum concentrations of vitamin A, β -carotene, cholesterol, and triglyceride in large groups of asthmatic children with non-atopic control subjects in a cross-sectional observational study.

MATERIALS AND METHODS

This study was conducted on schoolchildren, 6 to 18 years of age, living in the capital city Riyadh, Saudi Arabia. A total of 433 patients with controlled asthma took part in the study and were compared with 537 healthy control subjects with no respiratory problems. Diagnosis of asthma was based on a documented clinical history of recurrent cough and/or wheezing and previous demonstration of improvement of symptoms in response to asthma medication. The control subjects had never had any episode of breathlessness and had never used asthma medication. Exclusion criteria included previous or concurrent use of prescription medications or vitamins and upper respiratory tract infection within the past 30 days before the study. All subjects were screened by a physician. Information on the child's health was collected from parents by self-administered questionnaires.

Blood Collection

Fasting venous blood samples were collected from all the study subjects after informed parental consent and processed immediately. Blood was collected into Vacutainer (Beckton–Dickinson) tubes without anticoagulant that were centrifuged at 1700 g for 20 minutes at 4°C, and serum was stored at –70°C until analyzed. To avoid isomerization of vitamins, blood samples were protected from light as soon as they were drawn.

Test Methods

All analyses were performed in a single session; hence there were no multiple freezing and thawing cycles for serum samples. Aliquots (0.5 mL) of serum were extracted for vitamin A and β -carotene with hexane as described by Vuilleumier et al. (16). Vitamin A and β -carotene were determined by reverse phase high-performance liquid chromatography with UV-Vis detection at 300 and 436 nm, respectively (17). The mobile phase consisted of a mixture of acetonitrile, methylene chloride, and methanol (70/20/10, v/v/v). The coefficient of variation for the estimation of vitamin A and β -carotene were 3.3% and 1.8%, respectively.

*Corresponding author: Abdulrahman M. Al Senaidy, Department of Biochemistry, College of Science, King Saud University, P. O. Box 2455, Riyadh 11451, Saudi Arabia; E-mail: senaidy@ksu.edu.sa

Serum cholesterol and triglycerides were measured on a COBAS MIRA Clinical Analyzer (F. Hoffman-La Roche and Co., Basel, Switzerland) using commercial enzymatic kits (Roche Diagnostics).

Statistical Analysis. Data are reported as means $\pm$ SD. Statistical significance was determined by unpaired Student's *t* test, using GraphPad Software program (Prism 3.02; Graph-Pad Software, Inc., San Diego, CA). *p* values of <0.05 were considered to be statistically significant.

RESULTS

The main characteristics of the participants and levels of vitamin A, β -carotene, cholesterol, and triglycerides are outlined in Table 1. As shown, serum vitamin A level in the asthmatic group was significantly lower than in control subjects ($p < 0.05$). However, there were no significant differences between control subjects and asthmatic patients for serum levels of β -carotene, cholesterol, and triglyceride. We have also evaluated the serum biochemistry in the control subjects and asthmatic patients as a function of age, by distributing the subjects into six age groups: 6 to 8 years (20 asthmatics, 41 control subjects), >8 to 10 years (90 asthmatics, 81 control subjects), >10 to 12 years (87 asthmatics, 100 control subjects), >12 to 14 years (109 asthmatics, 115 control subjects), >14 to 16 years (90 asthmatics, 180 control subjects), and 16 to 18 years (37 asthmatics, 61 control subjects). Vitamin A levels were significantly lower ($p < 0.05$) in children with asthma as compared with the control subjects in all age categories (Figure 1). A decrease in β -carotene level, in the asthmatic group, is also presented in Figure 2, but the differences are less significant owing to the great individual variability of the data. However, there was no significant differences in the levels of cholesterol and triglycerides between asthmatics and control subjects irrespective of age factor within the groups (Table 2).

About 40% of the males and 72% of the females between 6 to 8 years of age had serum vitamin A level less than 10 $\mu\text{g/dL}$, which was an indication of vitamin A deficiency. In general, 67 (15%) of the males and 33 (7%) of the females asthmatic subjects had vitamin A deficiency (serum vitamin A $<10 \mu\text{g/dL}$); whereas 74 (17%) of the males and 60 (14%) of the females were found to be having serum vitamin A below the critical level (20 $\mu\text{g/dL}$) (Table 3).

DISCUSSION

The serum levels of vitamin A and β -carotene in the control group were similar to the levels previously reported (18, 19). Similarly, the level of serum cholesterol and triglycerides in the control group was also in agreement with earlier

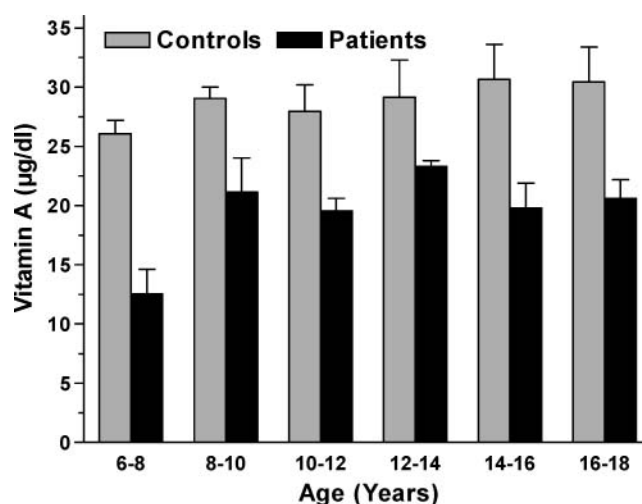


FIGURE 1.—Vitamin A level in serum of Asthmatics and Healthy subjects. Data are shown as mean $\pm$ standard deviation. Values with different letters were significantly ($P < 0.05$) different from each other.

published reports (20, 21). Several studies have shown associations between antioxidant vitamins and pulmonary function (3, 22). The present study demonstrated a significant decrease in serum level of vitamin A in asthmatic subjects compared with healthy controls. Serum β -carotene level showed no difference between the two groups. To explain the inconsistency of these findings, it is possible that serum concentrations of these biomarkers do not adequately reflect the specific conditions in the airway or that vitamin A has powerful antioxidant activity compared with β -carotene.

In agreement with our data, Riccioni et al. (23) reported decreased level of serum vitamin A concentration in patient group, while vitamin E and β -carotene level did not differ between patients and control subjects. Another study reported

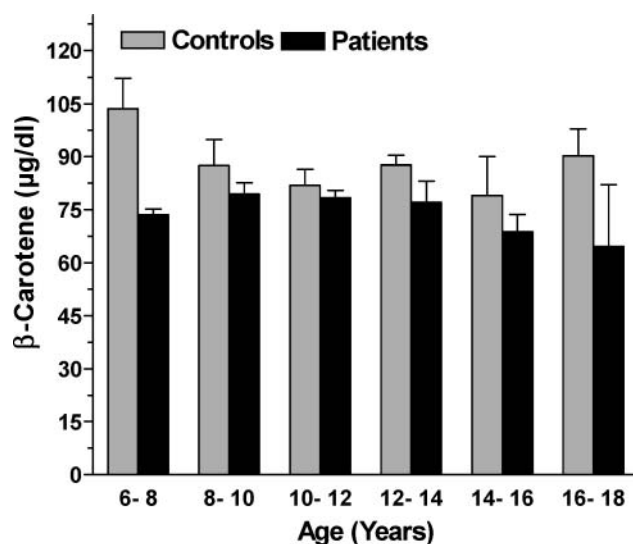


FIGURE 2.— β -Carotene level in serum of Asthmatics and Healthy subjects. Data are shown as mean $\pm$ standard deviation. None of the values were statistically different ($P < 0.05$).

TABLE 1.—Characteristics of patients and control subjects.

Variables	Controls (mean $\pm$ SD)	Patients (mean $\pm$ SD)	<i>p</i> value
Age (years)	12.3 $\pm$ 3.1	12.5 $\pm$ 3.1	—
Body mass index (kg/m ²)	19.68 $\pm$ 4.63	20.79 $\pm$ 5.79	—
Gender (% female)	48.7	40.8	—
Serum vitamin A (mg/dL)	28.9 $\pm$ 0.86	19.4 $\pm$ 1.1	0.0001
Serum β -carotene (mg/dL)	87.8 $\pm$ 3.2	75.1 $\pm$ 0.09	n.s
Serum cholesterol (mmol/L)	4.5 $\pm$ 0.83	4.2 $\pm$ 0.08	n.s
Serum triglycerides (mmol/L)	1.2 $\pm$ 0.05	1.1 $\pm$ 0.05	n.s

TABLE 2.—Lipid profile (mmol/L) in serum of asthmatic and healthy subjects.

Age group (years)	Control		Patients	
	Cholesterol	Triglycerides	Cholesterol	Triglycerides
6–8	4.6 ± 0.2	1.2 ± 0.1	4.0 ± 0.1	1.1 ± 0.1
>8–10	5.0 ± 0.1	1.3 ± 0.1	4.6 ± 0.2	1.3 ± 0.1
>10–12	4.7 ± 0.2	1.2 ± 0.1	4.3 ± 0.1	1.2 ± 0.2
>12–14	4.3 ± 0.1	1.1 ± 0.1	4.2 ± 0.2	1.2 ± 0.1
>14–16	4.2 ± 0.3	1.3 ± 0.2	4.1 ± 0.3	1.2 ± 0.1
>16–18	5.0 ± 0.2	1.5 ± 0.2	4.2 ± 0.2	1.2 ± 0.3

Data are shown as mean ± SD. None of the values were statistically different.
 $p < 0.05$.

that the severity of asthma is negatively correlated with the plasma level of retinol, and the children with vitamin A deficiency had more frequent and severe asthmatic attacks (24).

However, in contrast to our findings, in a recent experimental study, Gertrud et al. (25) reported aggravation of asthma by high dietary levels of vitamin A. Furthermore, it has been reported that earlier consumption of multivitamin supplements (26) as well as supplements containing only vitamins A and D have been linked with a high risk of asthma in later life (27). These adverse effects have been explained by the ability of vitamin A supplements to enhance immunity that increases the inflammatory response in the lungs (28).

Increased systemic production of free radicals is known to be a feature of chronic airway inflammation (29). Using a human bronchial epithelial cell line (BEAS-2B), Takamura et al. reported that retinoic acid may reduce eosinophilic airway inflammation. Oxidative burden has been suggested to be a potential mechanism linking airway inflammation to reduced pulmonary function. Neutrophils, macrophages, monocytes, eosinophils, and mast cells can generate oxygen free radicals and other reactive oxygen species (30, 31). Malondialdehyde (MDA) is a reactive aldehyde that has been evaluated as a biomarker of pulmonary oxidative stress attributed to air pollution exposure and changes in lung function (7). Excess lipid peroxides expressed as MDA has been found in exhaled breath condensate (32).

Enhanced production of lipid peroxides due to airway inflammation provides convincing evidence of cell membrane damage, which may induce cellular dysfunction and cause worsening of airway obstruction. Thus, it would be reasonable to assume that accumulation of free radicals is attributed to an impaired conversion of β -carotene to retinol, associated with a defect in the mobilization of stored retinol. Our results show that reduced level of vitamin A in asthma patients is probably caused by an increased utilization of this antioxidant in presence of excess free radicals, suggesting that

vitamin A appears to be more effective antioxidant. However, it is not clear from this study whether the low level of vitamin A is either a primary cause that is linked with the pathogenesis of asthmatic condition or is a secondary event due to the inflammatory process in asthma or a coincidence of low dietary intake and asthmatic condition.

The prevalence of asthma in Saudi Arabia has increased dramatically in recent years, with the highest prevalence in children below 18 years of age (33). Although vitamin A deficiency is not a public health problem in Saudi Arabia (34), the present study shows that serum retinol concentrations are markedly low in asthmatic school children, which was in sharp contrast to the normal concentrations found in nonasthmatic school children. Furthermore, we observed an increased lipid peroxides (i.e., serum MDA) in children with asthma. In summary, our results strengthen previous reports indicating that vitamin A plays a role in the evolution of asthma (10–13, 22–24). A detailed and comprehensive study of the effects of disease activity and treatment effects on antioxidant status is needed with a particular emphasis on vitamin A and other antioxidant vitamins.

ACKNOWLEDGMENT

The author wishes to thank Mr. Mohammad A. Ismael for technical assistance. Financial support (grant Bio/2007/42) by research center, College of Science, King Saud University, is gratefully acknowledged.

REFERENCES

1. Salo PM, Arbes SJ Jr, Crockett PW, Thorne PS, Cohn RD, Zeldin DC. Exposure to multiple indoor allergens in US homes and its relationship to asthma. *J Allergy Clin Immunol* 2008; 121:678–684.e2.
2. Huang SL, Pan WH. Dietary fats and asthma in teenagers: analyses of the first Nutrition and Health Survey in Taiwan (NAHSIT). *Clin Exp Allergy* 2001; 31:1875–1880.
3. Hu G, Cassano PA. Antioxidant nutrients and pulmonary function: the Third National Health and Nutrition Examination Survey (NHANES III). *Am J Epidemiol* 2000; 151:975–81.
4. Riccioni G, Mancini B, Bucciarelli T, Ilio CD, D'Orazio N. Antioxidant vitamin supplementation in asthma. *Ann Clin Lab Sci* 2007; 37:96–101.
5. Nadeem A, Chhabra SK, Masood A, Raj HG. Increased oxidative stress and altered levels of antioxidants in asthma. *J Allergy Clin Immunol* 2003; 111:72–78.
6. Wood LG, Gibson PG, Garg ML. Biomarkers of lipid peroxidation, airway inflammation and asthma. *Eur Respir J* 2003; 21:177–186.
7. Van der Vliet A, O'Neill C, Cross CE, Koostra JM, Volz WG, Halliwell B, Louie S. Determination of low-molecular-mass antioxidant concentrations in human respiratory tract lining fluids. *Am J Physiol (Lung Cell Mol Physiol)* 1999; 276:289–296.
8. Raida IHK, Denis CM, Robert AW. Serum vitamin levels and the risk of asthma in children. *Am J Epidemiol* 2004; 159:351–357.
9. Wagner J, Jiang Q, Harkema JR, Ames BN, Illek B, Roubey RA, Peden DB. gamma-Tocopherol prevents airway eosinophilia and mucous cell hyperplasia in experimentally induced allergic rhinitis and asthma. *Clin Exp Allergy* 2008; 38:501–511.
10. Sies H, Krinsky NI. Antioxidant vitamins and β -carotene in disease prevention. *Am J Clin Nutr* 1995; 62 (suppl):1299S–1540S.
11. Chytil F. The lungs and vitamin A. *Am J Physiol* 1992; 262:517–527.
12. Gray T, Koo JS, Nettesheim P. Regulation of mucous differentiation and mucin gene expression in the tracheobronchial epithelium. *Toxicology* 2001; 160:35–46.

TABLE 3.—Distribution of the study groups according to the World Health Organization classification for vitamin A.

Group	< 10 μ g/dL N (%)	10–20 μ g/dL N (%)
Asthmatic:		
Male	67 (15)	74 (17)
Female	33 (7)	60 (14)
Control:		
Male	0	0
Female	0	0

Organization classification for vitamin A.

13. Morabia A, Menkes MJS, Comstock GW, Tockman MS. Serum, retinol and airways obstruction. *Am J Epidemiol* 1990; 132:77–82.
14. Kassaye T, Becklake MR, Receveur O, Hanley JA, Johns T. Association between vitamin A status and lung function level in children aged 6–9 years in Wukro Wereda, Northern Ethiopia. *Int J Epidemiol* 2001; 30:457–464.
15. Misso NLA, Brookes-Wildhaber J, Ray S, Vally H, Thompson PJ. Plasma concentrations of dietary and nondietary antioxidants are low in severe asthma. *Eur Respir J* 2005; 26:257–264.
16. Vuilleumier JP, Keller HE, Gysel D, Hunziker F. Clinical chemical methods for the routine assessment of the vitamin status in humans. Part I: The fat-soluble vitamin A and E and β -carotene. *Int J Nutr Res* 1983; 53:265–272.
17. Arnaud J, Fortis I, Blachier S, Kia D, Favier A. Simultaneous determination of retinol, α -tocopherol and β -carotene in serum by isocratic high performance liquid chromatography. *J Chromatogr* 1991; 572:103–116.
18. KÜÇÜKbay H, Yakincin C, KÜÇÜKbay FZ, Turgut M. Serum vitamin A, β -carotene levels in children with recurrent acute respiratory infections and diarrhea in Malatya. *J Trop Pediatr* 1997; 43:337–340.
19. Malvy JMD, Burtshy B, Dostalova L, Amedee-Manesme O. Serum retinol, β -carotene, α -tocopherol and cholesterol in healthy French children *Int J Epidemiol* 1993; 22:237–246.
20. Meistes S, Buffone GJ, Cheng MH. In: *Pediatric Clinical Chemistry. Reference (normal) values*. 3rd ed. Washington, DC: AACC press, 1989:239–294.
21. Lokitch G, Halstead AC, Wadsworth L. Age and sex specific pediatric reference intervals and correlation for zinc, copper, selenium, iron, vitamin A and E and related proteins. *Clin Chem* 1988; 34:1625–1628.
22. Holger J, Schünemann, Brydon J. B. Grant, Jo L. Freudenheim, Paola Muti, Richard W. Browne, Julie A. Drake, Robert A. Klocke, Maurizio Trevisan. The relation of serum levels of antioxidant vitamins C and E, retinol and carotenoids with pulmonary function in the general population. *Am J Respir Crit Care Med* 2001; 163:1246–1255.
23. Riccioni, G., Bucciarelli, T., Mancini, B., Ilio CD., Della Vecchia R., D'Orazio N. Plasma lycopene and antioxidant vitamins in asthma. The PLAVA Study. *J Asthma* 2007; 44:429–432.
24. Arora P, Kumar V, Batra S. Vitamin A status in children with asthma. *Pediatr Allergy Immunol* 2002; 13:223–226.
25. Gertrud US, Nicholas JK, Charles BS. Vitamin A deficiency decreases and high dietary vitamin A increases disease severity in the mouse model of asthma. *J Immunol* 2008; 180:1834–1842.
26. Milner JD, Stein DM, McCarter R, Moon RY. Early infant multivitamin supplementation is associated with increased risk for food allergy and asthma. *Pediatrics* 2004; 114:27–32.
27. Kull I, Bergstrom A, Melen E, Lilja G, Van Hage M, Pershagen G, Wickman M. Early-life supplementation of vitamins A and D, in water soluble form or in peanut oil, and allergic diseases during childhood. *J Allergy Clin Immunol* 2006; 118:1299–1304.
28. Stephensen CB, Franchi LM, Hernandez H, Campos M, Gilman RH, Alvarez JO. Adverse effects of high dose vitamin A supplements in children hospitalized with pneumonia. *Pediatrics* 1998; 101:E3.
29. Huseyin Vural H, Aksoy N, Ceylan E, Gencer M, Ozguner F. Leukocyte oxidant and antioxidant status in asthmatic patients. *Arch Med Res* 2005; 36:502–506.
30. Takamura, K, Yasuyuki N, Motoko K, Tomoko B, Yoko T, Ichiro K, Etsuro Y, Satoshi M, Robert PS, Masaharu N. Retinoic acid inhibits interleukin-4-induced eotaxin production in a human bronchial epithelial cell line. *Am J Physiol Lung Cell Mol Physiol* 2004; 286:777–785.
31. Barnes PJ. Reactive species and airway inflammation. *Free Radic Biol Med* 1990; 9:235–243.
32. Romieu I, Barraza-Villarreal A, Escamilla-Nunez C, Almstrand AC, Diaz-Sanchez D, Sly PD. Exhaled breath malondialdehyde as a marker of effect of exposure to air pollution in children with asthma. *J Allergy Clin Immunol* 2008; 121:903–909.
33. Al Frayh AR, Shakoor Z, Gad El Rab MO, Hasnain SM. Increased prevalence of asthma in Saudi Arabia. *Ann Allergy Asthma Immunol* 2001; 86:292–296.
34. Al Senaidy AM. Serum Concentration of retinol, β -carotene, cholesterol, and triglycerides in Saudi school children. *J Trop Pediatr* 2000; 46:163–167.