

Short communication

Decreased levels of coenzyme Q₁₀ in patients with bronchial asthma

Background: The contribution of free oxygen radicals in the pathogenesis of bronchial asthma is generally accepted. The modulation of antioxidative defence by supplementation with antioxidants represents additive therapy in complex management of disease. The aim of the study was to assess the levels of coenzyme Q₁₀, α -tocopherol, and β -carotene both in plasma and whole blood, and malondialdehyde (MDA) and eosinophil cationic protein (ECP) in plasma of asthmatics (As).

Methods: Fifty-six As (15 males and 41 females) aged from 19 to 72 years (mean age 46 years) suffering from allergic asthma were enrolled into the study. The control group comprised 25 healthy volunteers (16 males, 9 females) aged 25–50 years.

Results: The concentrations of CoQ₁₀ decreased significantly both in plasma and whole blood, compared with healthy volunteers ($0.34 \pm 0.15 \mu\text{mol/l}$ vs. $0.52 \pm 0.15 \mu\text{mol/l}$, $0.33 \pm 0.14 \mu\text{mol/l}$ vs. $0.50 \pm 0.13 \mu\text{mol/l}$, $P < 0.001$, $P < 0.001$, respectively). The levels of α -tocopherol were decreased both in plasma and whole blood in comparison with controls [$24.10 \mu\text{mol/l}$ (19.8; 30.5), vs. $33.20 \mu\text{mol/l}$ (28.25; 38.05), $17.22 \pm 6.45 \mu\text{mol/l}$ vs. $21.58 \pm 7.92 \mu\text{mol/l}$, $P = 0.006$, $P = 0.01$, respectively]. The levels of MDA were elevated over the reference range in both groups (reference range $< 4.5 \mu\text{mol/l}$). No changes were seen in β -carotene concentrations. Positive correlation was found between whole blood CoQ₁₀ and α -tocopherol concentrations.

Conclusion: Results of the study suggest a possible contribution of suboptimal concentrations of CoQ₁₀ on antioxidative dysbalance in As and provide a rationale for its supplementation.

F. Gazdík¹, A. Gvozdjaková²,
R. Nádvorníková³, L. Repická⁴,
E. Jahnová¹, J. Kucharská²,
M. R. Piják¹, K. Gazdíková¹

¹Department of Clinical Immunology, Institute of Preventive and Clinical Medicine, Bratislava;

²Pharmacobiochemical Laboratory of Medical Faculty, Comenius University, Bratislava;

³Out-patient Department of Allergy, Trenčín;

⁴University of Ss. Cyril and Methodius, Trnava, Slovak Republic

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František Gazdík, MD, PhD
Department of Clinical Immunology
Institute of Preventive and Clinical Medicine
Limbová 14
833 01 Bratislava
Slovak Republic

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Accumulating data indicate that asthma bronchiale is a chronic inflammatory disease. Airway inflammation and its control became a principal focus in asthma pathogenesis and treatment. The mechanisms underlying inflammation have not been fully clarified. Current understanding suggests that the dysbalance between increased production of free oxygen radicals, originating in the process of lipid peroxidation, and decreased antioxidative defence seems to be of importance. In this respect, the dysbalance could be considered as the important triggering factor as well as the factor responsible for the maintenance of chronic inflammation (1, 2). Antioxidative protective systems in humans are complex and comprises numerous substances possessing antioxidative effects, e.g., vitamins A, C, E, trace elements selenium and zinc, enzymes superoxide dismutase (SOD) and glutathion peroxidase. In clinical trials a disorder of antioxidative potential is well documented. Several authors reported decreased selenium status in asthmatics (3–5). Decreased levels of vitamins

A, C, E or decreased enzyme activity of SOD in asthmatics have been found (6, 7).

Coenzyme Q₁₀ (ubichinone), a vitamin-like substance, represents an important member of the antioxidative potential in humans. This substance plays a decisive role in the production of cell energy and in the scavenger activity of free oxygen radicals. Most concentrations of CoQ₁₀ represent tissues and organs with a high need of energy consumption (8).

In this respect, remains the unresolved question, whether a decreased level of CoQ₁₀ also contributes to antioxidative dysbalance linked with chronic mucosal inflammation in bronchial asthma.

The aim of a clinical pilot study was to assess, both in plasma and whole blood, the baseline levels of CoQ₁₀, α -tocopherol and β -carotene in As. The next aim was to assess the plasma levels of malondialdehyde (MDA), a marker of end-stage lipid peroxidation, and eosinophil cationic protein (ECP), a marker of inflammation.

Patients and methods

Fifty-six As of both sexes (males 15, females 41) aged 19–72 years were enrolled in the study. All of them fulfilled the criteria of allergic asthma (9). They suffered from mild to moderate forms of persistent asthma according to the criteria of GINA classification (10). Patients were regularly treated with inhaled corticosteroid (CS, beclomethasone propionate) and long acting β -agonists. The clinical status was stabilized. The control group comprised 25 healthy subjects (16 males, 9 females) aged 25–65 years. Informed consent was obtained from all subjects who entered the study.

A venous blood sample was taken after 12 h of fasting. The following parameters were assessed: plasma and whole blood concentrations of CoQ₁₀, α -tocopherol and β -carotene, by using the HPLC method, as described previously (11,12), on the machine HPLC, LKB, Sweden, with spectrophotometric detection. MDA was determined in plasma by spectrophotometry (13).

The levels of ECP were assessed by using the ELISA method/Ala STAT Microplate, DPC-Diagnostic Products Corporation, USA.

Baseline pulmonary function tests before administration of medications (forced vital capacity – FVC, Tiffenau index: the ratio of forced expiratory volume per first second – FEV₁ to FVC, peak expiratory flow – PEF and maximal expiratory flow in 25%, 50% and 25% to 75% of FVC – MEF₂₅, MEF₅₀, MEF_{25–75}, respectively) were examined using the spirometric machine Sano-scope (Ganzhorn Medizin Electronic, Germany).

The statistics

The measured values were statistically evaluated using parametric and nonparametric tests: *t*-test (coenzyme Q₁₀ in plasma and whole blood, α -tocopherol in whole blood and MDA in plasma), Wilcoxon test (α -tocopherol in plasma, β -carotene in plasma and whole blood, ECP in plasma), and Spearman's test for correlations. A *P*-value less than 0.05 was considered to be significant. The data analysis was carried out by using the program SPSS, version 8.0.

Results

Concentrations of CoQ₁₀ and α -tocopherol assessed in plasma and whole blood were significantly decreased in

comparison with healthy subjects ($P < 0.001$, $P < 0.001$, $P = 0.006$, $P = 0.01$, respectively) (Table 1).

The levels of β -carotene did not differ significantly between the investigated groups (Table 1). The levels of MDA in plasma were over the reference range (r.r. $< 4.5 \mu\text{mol/l}$) in both groups, but the changes between investigated groups were not significant (Table 1). The levels of ECP were significantly increased in As in comparison with controls ($P < 0.001$) (Table 1).

Parameters of functional pulmonary tests are shown in Table 2.

We found a positive correlation between the whole blood concentrations of CoQ₁₀ and the α -tocopherol (Spearman's correlation coefficient = 0.408, $P = 0.002$) (Fig. 1). No correlation was found between the levels of ECP, pulmonary functional tests and assessed antioxidants.

Discussion

In a pilot clinical study we found significantly decreased levels of CoQ₁₀, both in plasma and whole blood in As compared with controls. MDA levels were increased but did not differ between investigated groups. The concentrations of CoQ₁₀ in whole blood correlated positively with α -tocopherol levels. We did not observe any correlation between the concentrations of ECP and the levels of CoQ₁₀, α -tocopherol, β -carotene and pulmonary function tests.

The contribution of free oxygen radicals originating from the lipid membrane of accumulated cells in mucus of bronchi and decrease of antioxidative defence in pathogenesis of bronchial asthma is well documented (1, 2).

Several authors reported a benefit of selenium supplementation on CS consumption, of both systemic and inhaled CS, in As (14, 15). Combined anti-inflammatory therapy is preferred in order to reduce the consumption

Table 1. Levels of coenzyme Q₁₀, α -tocopherol, β -carotene, MDA and ECP

	As (<i>n</i> = 56)		Controls (<i>n</i> = 25)		<i>P</i> §	<i>P</i> ¶
	Plasma	Blood	Plasma	Blood		
Coenzyme Q ₁₀ ($\mu\text{mol/l}$)	0.34 $\pm$ 0.15†	0.33 $\pm$ 0.14	0.52 $\pm$ 0.15	0.50 $\pm$ 0.13	< 0.001	< 0.001
α -tocopherol ($\mu\text{mol/l}$)	24.10‡ (19.8; 30.5)	17.22 $\pm$ 6.45 (28.25; 38.05)	33.20	21.58 $\pm$ 7.92	0.006	0.01
β -carotene ($\mu\text{mol/l}$)	1.42 (1.05; 2.36)	1.23 (0.90; 1.93)	1.56 (0.79; 3.66)	1.14 (0.57; 2.52)	NS	NS
MDA ($\mu\text{mol/l}$)	5.20 $\pm$ 0.63	–	4.88 $\pm$ 0.85	–	NS	–
ECP (ng/ml)	10.96 (7.58; 16.46)	–	5.41 (3.30; 7.79)	–	< 0.001	–

As, asthmatics; MDA, malondialdehyde; ECP, eosinophil cationic protein.

† Mean $\pm$ SD.

‡ Median (lower quartile; upper quartile).

§ Statistical significance between plasma levels.

¶ Statistical significance between whole blood levels.

NS, not significant.

Table 2. Pulmonary functional tests ($n = 56$)

Parameter	FVCexp L	FEV ₁ L/s	FEV ₁ /FVC %	MEF 50 L/s	MEF 25 L/s	MEF 25–75 L/s	PEF m/s
Median	3.2	2.70	82.0	3.53	1.37	3.42	5.44
Lower quartile	2.79	2.16	76.0	2.46	0.88	2.57	4.53
Upper quartile	3.93	3.25	87.0	4.36	1.77	4.13	7.29

n , number of patients; FEV₁, forced expiratory flow per second; FEV₁/FVC, ratio of forced expiratory flow per second to forced vital capacity; FVCexp, forced vital capacity; MEF50, maximal expiratory flow in 50% of FVCexp; MEF25, maximal expiratory flow in 25% of FVCexp; MEF 25–75, maximal expiratory flow between 25 and 75% of FVCexp; PEF, peak expiratory flow.

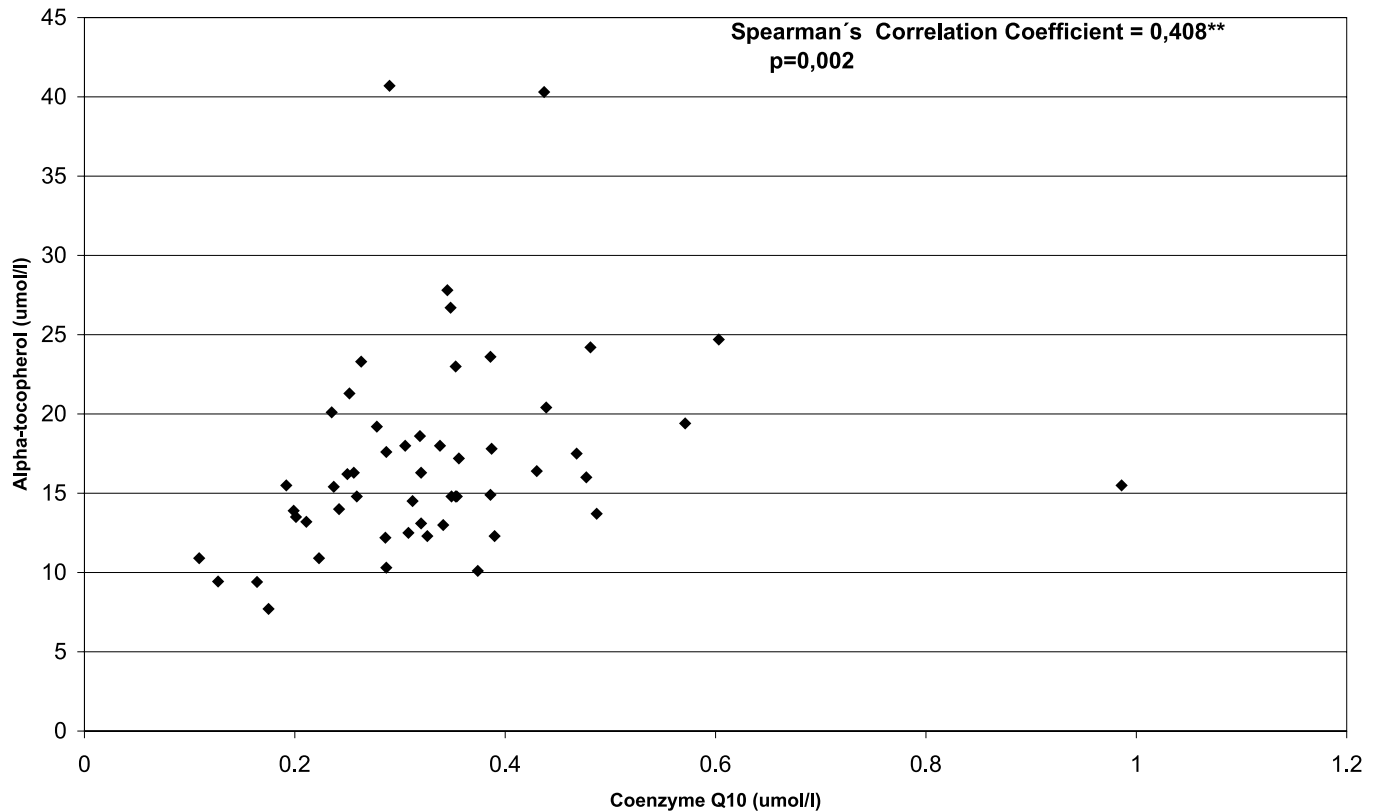


Figure 1. Correlation between coenzyme Q₁₀ and alpha-tocopherol levels. **Correlation is significant at the 0.01 level.

of CS. The rationale of such therapeutic approach is to minimize the manifestations of adverse reactions, especially in cases of long-term CS therapy. Presented results demonstrated decreased levels of both CoQ₁₀ and α -tocopherol in As and showed a rationale for its supplementation. We suppose that the suboptimal concentration of CoQ₁₀ would be considered as a possible risk factor participating in the total decrease of antioxidative potential in As. In this respect, no data have yet been published. Controlled studies are needed to show whether supplementation of CoQ₁₀ would be clinically relevant.

Supplementation of CoQ₁₀ in clinical medicine has been reported especially in cardiovascular diseases (8). Limited information regarding the influence of CoQ₁₀ on pulmonary functions has been reported. Protective

effects of CoQ₁₀ on pulmonary functions have been demonstrated in animal experiments. The levels of CoQ₁₀ are decreased in patients with chronic obstructive pulmonary disease (16).

Immunomodulating effects of CoQ₁₀ have been reported by several authors. In an experimental animal model CoQ₁₀ had protective effects against tumour growth and enhanced antiviral immunity. The immunostimulating effects of CoQ₁₀ on T cell mediated immunity, NK activity and antibody production have been documented (17–19).

Despite the clinically stabilized status of As, the levels of ECP differed significantly in comparison with healthy subjects. ECP is considered to be a marker of inflammation in As (20). In this respect, our results did not differ from those published already in the literature.

Conclusion

We demonstrated significantly decreased concentrations of CoQ₁₀, both in plasma and whole blood, in patients with allergic asthma in comparison with healthy controls. The contribution of CoQ₁₀ to antioxidative

dysbalance seems to be probable and could not be excluded. Additional studies are necessary in order to clarify the relevance of CoQ₁₀ supplementation on clinical response in respect of its anti-inflammatory potential.

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