ORIGINAL ARTICLE

Effect of occupational lead exposure on α- and γ-tocopherol concentration in plasma

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ABSTRACT

Objectives Changes in enzymatic antioxidant activity are frequently observed in workers occupationally exposed to lead. Few studies have investigated the influence of lead on the non-enzymatic antioxidant system. The aim of our study was to assess the influence of occupational exposure to lead on the plasma concentration of two hydrophobic forms of vitamin E: α-tocopherol and γ-tocopherol.

Methods A sample of 401 healthy men, aged 19–62, participated in the study. In total, 340 of these subjects were employed at the Mine and Metallurgical Plant in southern Poland. The workers who were occupationally exposed to lead were divided into quartiles (groups of 85 subjects). The lead concentrations in the blood of the subjects in the control group and in the lead exposure quartiles correspond to the following ranges: 10–72 μg/l (control group); 82–206 μg/l (Q1); 209–308 μg/l (Q2); 308–394 μg/l (Q3) and 395–644 μg/l (Q4), respectively.

Results Significant differences were observed only for the plasma concentration of γ-tocopherol, which differed between the control group and Q1 (by 24.1%, p=0.0368), between Q1 and Q3 (by −18.8%, p=0.0115) and between Q1 and Q4 (by −25.7%, p=0.0002). Multiple linear regression analysis showed that the statistically significant, predictive properties of the γ-tocopherol plasma concentration were as follows: triglycerides (β=0.440)> age (β=0.131)> whole cholesterol (β=0.117)> blood lead concentration (β=−0.108). For α-tocopherol, significant prognostic properties were triglycerides and total cholesterol (β=0.485 and β=0.399, respectively).

Conclusions Occupational exposure to lead is strongly correlated with the concentration of γ-tocopherol but not α-tocopherol.

What this paper adds

- Vitamin E plays a significant role in protection against oxidative stress, which may occur as the result of exposure to lead. However, previous studies have only investigated the α-tocopherol form.
- This study showed that exposure to lead is more strongly associated with the plasma concentration of γ-tocopherol than α-tocopherol.
- There is no need for vitamin E administration (α-tocopherol) in men who are occupationally exposed to lead.

INTRODUCTION

Lead emission in Poland has decreased considerably for the last 2 decades, mainly as a result of a ban on the use of leaded gasoline, limitation of the manufacturing of lead-containing paints and more efficient systems for the removal of lead containing dusts in industry. There was a substantial reduction in the percentage of workers in Poland with lead concentrations in the blood exceeding the biological action level of 500 μg/l from 1997 to 2005 (from 19% in 1997 to 1% in 2005).[1] However, there are still occupational groups working under conditions of lead exposure. It has been estimated that in Poland in 2005 approximately 26 500 workers were exposed to lead and its compounds in > 500 plants.[2] They were mainly men employed in the non-ferrous metals industry, the ceramic industry, storage battery manufacturing and in lead and zinc ore mining.

Occupational exposure to lead continues to be a significant health problem because lead adversely affects the central and peripheral nervous system, the kidneys and haematological, cardiovascular, reproductive, alimentary, osseous and immunological systems.[3 4] Such a wide spectrum of toxic lead activity is undoubtedly to a high degree the result of oxidative stress caused by that metal. Lead may generate reactive oxygen species (ROS) such as singlet oxygen, hydrogen peroxides and superoxide radical anion.[5] ROS formed as a result of lead exposure may oxidise nitric oxide present in the endothelial cells of the vessels, forming the highly reactive peroxynitrite anion ($ONOO^-$). That process is accompanied by arterial hypertension, DNA damage and intensification of lipid peroxidation.[6] The meta-analysis of 14 studies published in the years 1994–2008 shows significantly higher concentration of lipid peroxidation product, that is, malondialdehyde in serum, plasma and erythrocytes in people exposed to lead and lead compounds when compared with non-exposed individuals.[7]

The first line of defence against ROS is enzymatic antioxidants, and changes in antioxidant activities are observed in populations of people who are occupationally exposed to lead. The activation of the antioxidative system, resulting in increases in the gene expression activity of superoxide dismutase and glutathione peroxidase, has been observed in numerous studies.[8–11]

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The second line of defence against ROS is non-enzymatic antioxidants. Vitamin E, which contains α-, β-, δ- and γ-tocopherols, plays a particularly significant role in the protection of cell membranes against processes of lipid peroxidation. α-Tocopherol is the best known form of vitamin E and is found in the largest quantities in the blood and tissue. The main mechanism of action of α-tocopherol is based on the scavenging of ROS (superoxide radical anion, lipid peroxy free radical), which is responsible for lipid peroxidation. Recently, increasing evidence indicates that γ-tocopherol compared with α-tocopherol has unique bioactivities that may also be important for maintaining and improving human health. γ-Tocopherol has far more powerful anti-inflammatory actions than does the α form. γ-Tocopherol is a stronger inhibitor of cyclo-oxygenase, and possibly lipoxygenase, than α-tocopherol. Furthermore, γ-tocopherol traps reactive nitrogen species more efficiently than α-tocopherol.[12] In addition, γ-tocopherol inhibits the production of stress-related 'heat shock proteins' that result from inflammatory stimuli.[13] Several reports show a relationship between environmental lead exposure and α-tocopherol levels.[14 15] Furthermore, several studies have investigated the influence of occupational lead exposure on the vitamin E level in serum/plasma with a focus on the α-tocopherol form. There is however a lack of studies concerning γ-tocopherol. γ-Tocopherol has gained interest recently due to the role it may play in the prevention of cardiovascular diseases.[16]

The aim of this study was to determine the influence of occupational lead exposure on the plasma concentration of two hydrophobic antioxidants, the α-tocopherol and γ-tocopherol forms of vitamin E.

MATERIAL AND METHODS

Study object

The study group consisted of 401 healthy male volunteers aged 19–62, including 340 men employed for at least 2 years in the Boleslaw Mine and Metallurgical Plant S.A. in Bukowno (south Poland). The volunteers participated in the mining and processing of zinc and lead ores, the recovery of zinc-containing wastes from non-ferrous metals, steel working and storage battery processing. The control group consisted of 61 healthy male administrative workers without occupational exposure to lead and with no history of any chronic diseases. The group of subjects who were occupationally exposed to lead was divided into quartiles with respect to the exposure level (85 men in each). The blood lead concentration in the control group and in each quartile was as follows: 10–72 μg/l (control); 82–206 μg/l (Q1); 209–308 μg/l (Q2); 308–394 μg/l (Q3) and 395–644 μg/l (Q4).

A survey with questions related to the consumption of eight products rich in vitamin E (pea, carrot, lettuce, rapeseed and corn oil, eggs, margarine and mayonnaise) was administered to the participants. No statistically significant differences in the consumption of these products within the month preceding the study were detected. A second questionnaire concerned smoking habits, and requested the number of cigarettes smoked per day and the number of years of smoking. The participants stated that in the period of 3 months preceding the study, they did not take any pharmacological preparations containing vitamin E. The study excluded those whose creatine clearance test was higher than 140 ml/min and those with above normal concentration of aspartate aminotransferase and alanine aminotransferase. The study was conducted in the spring-summer period.

The Biomedical Ethics Committee at the Institute of Occupational Medicine and Environmental Health in Sosnowiec approved the study protocol.

Equipment

A high-pressure liquid chromatograph from Agilent Technologies 1200 series (USA), equipped with a set of pumps, a thermostat, an autosampler and a fluorescence detector, was used in the chromatographic study. The chromatographic system was controlled using the ChemStation for Liquid Chromatography computer software.

A Perkin-Elmer 4100 ZL atomic absorption spectrometer equipped with stabilised-temperature platform graphite furnace and Zeeman background correction (Bodenseewerk Perkin-Elmer, Ueberlingen, Germany) was used for the metals determination, and an AVIV 206D hematofluorimeter from Biomedical Inc. (USA) was used for zinc protoporphyrin (ZPP) measurements.

Biochemical examinations

Blood for the biochemical analyses was obtained from the cubital vein into vacuum tubes (Vacuette; Greiner-Bio, Frickhausen, Germany) in the morning hours after 12 h of fasting. A portion of the blood was analysed for the content of ZPP in blood, and a portion of the plasma was used to determine the concentration of cholesterol, triglycerides and creatine. The remaining blood and plasma were stored at a temperature of −80°C until the spectrometric and chromatographic examinations.

α- And γ-tocopherols were simultaneously examined in the plasma using high-pressure liquid chromatograph method described elsewhere.[17] Briefly, a 5-μm LiChrospher 100 RP 18, 250×4 mm I.D. (Merck) chromatographic column was used for the separation and the separation was performed in an isocratic system in reverse phase. The elution mixture was an acetonitrile–butanol solution (95:5, v/v). The separations were conducted at a room temperature. A fluorescence detector was used for the detection of tocopherols with wavelengths of 285 nm (excitation) and 325 nm (emission).

The lead and cadmium concentrations in the blood were measured using electrothermal atomic absorption spectrometry on the basis of the methods described by Stoeppler and Brandt.[18 19] The blood samples were deproteinised with 0.8 M nitric acid mixed with blood in a 4:1 ratio. Calibration was performed using standard solutions prepared with whole blood.

Determination of an indicator of disturbances in haem synthesis as the earliest occurring effect of toxic lead activity was performed by determination of ZPP in blood using haematofluorometric method according to the manual of the instrument manufacturer.

Plasma cholesterol was measured by enzymatic method with an application of cholesterol esterase and oxidase, while triglycerides were measured using the method with phosphoglycerol oxidase and hydrogen peroxide determination (with peroxidase). Kinetic method with alkaline picrate was used for creatine analysis.

Statistical analysis

The statistical evaluation was performed using STATISTICA V.9.1 software by StatSoft Inc. (2010). The Kruskal–Wallis rank test comparing variable distributions in more than two groups was used for group comparison. Associations between the examined values were determined using Spearman's rank correlation coefficient (r_s). Those results for which $p<0.05$ were accepted as significant ones. All p values refer to two-sided hypotheses. To determine the predictive properties of independent variables (age, BMI, smoking status, the concentrations of lead, cadmium and ZPP in the blood and the concentrations of creatine, triglycerides and cholesterol in the plasma) on the dependent

variables (α-tocopherol or γ-tocopherol concentration), the multiple linear regression model was used in the calculations.

Box and whiskers charts were used for graphical interpretation of the results (α-tocopherol or γ-tocopherol concentration). These plots described the basic properties of variable distribution (median, IQR, range of non-outliers values, outliers and extremes values). Statistically significant differences between the quartiles and the control group were determined using a multiple comparisons test.

RESULTS

The examined physiological and biochemical parameters are presented in table 1.

Among the examined antioxidants, the Kruskal–Wallis test demonstrated high statistical significance only for γ-tocopherol ($p=0.0003$). The significance for α-tocopherol was close to the selected significance level ($p<0.05$), but did not exceed it ($p=0.0669$). The results of multiple comparisons indicated significant differences in the plasma γ-tocopherol concentration between the control group and Q1 (concentration increase of 24.1%, $p=0.0368$), between group Q1 and Q3 (concentration decrease of 18.8%, $p=0.0115$) and between group Q1 and Q4 (concentration decrease of 25.7%, $p=0.0002$) (figure 1). In specific groups, the differences in the plasma α-tocopherol concentration corresponded to that of γ-tocopherol, but the changes were not significant. The value of the significance level close to the assumed value of $p<0.05$ was only noted between the groups Q1 and Q4 (concentration decrease of 11.9%, $p=0.0520$) (figure 2). The Spearman's rank correlation coefficients for the examined population are shown in table 2.

Table 1 General characteristic and measured parameters for the control group and across the quartiles of blood lead concentration

Parameters	Control (n=61)	Q1 (n=85)	Q2 (n=85)	Q3 (n=85)	Q4 (n=85)	p Value*
Pb (μg/l)						
x±SD	32±16	147±33	262±31	354±24	473±62	<0.0001
Range	10÷72	82÷206	209÷308	308÷394	395÷644	
Median	30	146	271	357	453	
Age (years)						
x±SD	36.7±9.7	42.4±9.6	40.0±10.7	40.8±9.1	37.6±9.3	0.0026
Range	19÷61	23÷57	21÷62	20÷55	21÷55	
Median	37	44	39	40	35	
Smoking (%)	39.3	41.2	36.9	52.4	62.4	0.0046
BMI (kg/m^2)						
x±SD	27.0±3.7	27.2±4.0	27.3±3.9	27.2±3.9	27.1±3.8	0.9991
Range	21.0÷36.2	20÷43	19÷40	20÷40	19÷36.3	
Median	26.9	27	26.3	27	27	
Total cholesterol (mmol/l)						
X±SD	5.00±0.98	5.35±1.24	5.13±0.93	5.18±1.08	4.97±0.95	0.2575
Range	3.38÷7.54	3.50÷11.2	3.00÷7.50	3.30÷8.60	3.22÷8.03	
Median	5.02	5.20	5.20	5.00	4.83	
Triglyceryde (mmol/l)						
x±SD	1.48±1.07	1.68±0.92	1.70±1.15	1.64±1.19	1.41±0.81	0.1011
Range	0.49÷6.33	0.40÷4.69	0.46÷7.54	0.36÷7.59	0.34÷4.05	
Median	1.03	1.41	1.40	1.24	1.24	
Creatine (mmol/l)						
x±SD	80.2±14.4	83.4±13.1	81.4±10.4	78.1±11.1	77.7±11.8	0.0018
Range	38÷117	22÷109	57÷102	57÷108	49÷111	
Median	78.7	84.4	81.4	79.6	78.5	
Cd (μg/l)						
X±SD	1.28±1.58	1.61±1.41	1.90±1.67	2.40±2.23	2.93±2.56	<0.0001
Range	0.07÷8.76	0.23÷5.57	0.15÷6.86	0.33÷11.68	0.43÷15.1	
Median	0.66	1.00	1.22	1.47	2.15	
ZPP (μg/gHb)						
x±SD	2.13±1.02	2.21±0.72	3.13±1.81	4.27±2.29	6.37±3.88	<0.0001
Range	0.6÷7.5	0.5÷3.8	0.8÷10.8	0.9÷12.9	1.20÷25.6	
Median	2.0	2.1	2.7	3.9	5.6	
α-Tocopherol (μg/ml)						
x±SD	14.1±4.3	15.1±4.3	14.0±3.4	14.2±4.5	13.3±3.0	0.0669
Range	8.1÷28.2	8.1÷29.0	8.1÷25.9	7.32÷29.3	7.6÷22.7	
Median	13.1	14.1	12.9	12.8	13.1	
γ-Tocopherol (μg/ml)						
x±SD	1.16±0.48	1.44±0.60	1.29±0.62	1.17±0.52	1.07±0.44	0.0003
Range	0.46÷2.52	0.37÷3.30	0.59÷3.31	0.41÷3.07	0.36÷2.77	
Median	1.03	1.31	1.06	1.05	0.98	

*p Value is based on the Kruskal–Wallis test.
ZPP, zinc protoporphyrin.

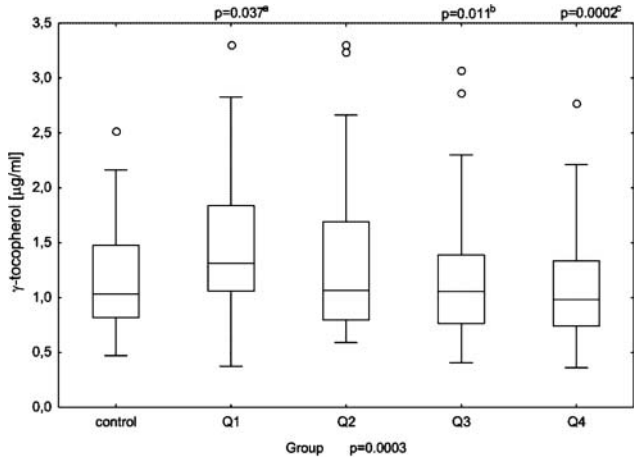

Figure 1 γ-Tocopherol in the blood plasma related to the blood lead concentration (categorised) in a population study. The boxes depict the 25th, 50th and 75th percentiles and whiskers represent the minimum and maximum, excluding outliers (circle). p Value for Kruskal–Wallis test with multiple comparisons ([a]Control vs Q1, [b]Q1 vs Q3, [c]Q1 vs Q4).

It may be concluded that both α- and γ-tocopherols are significantly correlated with age, BMI, total cholesterol, triglycerides and creatine concentration. However, among these two forms of vitamin E, only γ-tocopherol is significantly correlated with blood lead concentration (p=0.008 vs p=0.095, respectively). The strongest predictive properties of plasma α- and γ-tocopherol concentration, based on the β-coefficient values, were the triglyceride concentration (β=0.485 vs β=0.440, respectively) and the total cholesterol concentration (β=0.399 vs β=0.117, respectively). These are only independent variables that were significantly correlated to α-tocopherol. For γ-tocopherol, a significant prognostic value was also demonstrated for age (β=0.131) and blood lead concentration (β=−0.108) (table 3).

DISCUSSION

Attempts to explain the prooxidative lead activity are based on both direct and indirect mechanism of enhancing lipid peroxidation. The direct hypothesis is based on the increased formation ROS, such as hydroxyl radical, superoxide anion radical, hydrogen peroxide or singlet oxygen. The indirect hypothesis proposes that because lead leads to an increase in the δ-aminolevulinic acid concentration, it causes disorders in haem biosynthesis and consequently leads to modifications of cell membrane structures, which influences the system that protects the cell against ROS.[20] Thus, disorders in antioxidative defence may occur in conditions of lead exposure. An influence of occupational lead exposure on various markers of oxidative stress (eg, superoxide dismutase, catalase, glutathione peroxidase, glutathione reductase, malondialdehyde) has been analysed in previously published studies.[21 22] The effect of lead exposure on non-enzymatic antioxidant mechanisms was also investigated in several studies. A number of compounds, such as glutathione, ascorbate, uric acid (hydrophilic antioxidants), β-carotene, bilirubin, α-lipoic acid, coenzyme Q and α-tocopherol (hydrophobic antioxidants), participate in the non-enzymatic antioxidant system in humans. In previous studies, the lead concentration in the blood showed a negative correlation with glutathione levels and a positive correlation with the bilirubin concentration.[7] Many clinical investigations have indicated that in subjects with symptoms of gout, high concentrations of lead in the blood were observed. A significant risk of hyperuricaemia (OR=1.74; 95% CI 1.12 to 2.61) is associated with exposure to lead when the lead concentration in the blood exceeds 400 µg/l.[23]

Vitamin E appears to be one of the most important non-enzymatic antioxidants. It is the main, lipid-soluble antioxidant in biological membranes and amphipathic sheath of plasma lipoproteins.[24]

α-Tocopherol is a form of vitamin E that is most abundant in the human body and demonstrates the highest biological activity. Therefore, it is often considered as vitamin E.

It has been long believed that γ-tocopherol, as opposed to its homologue α-tocopherol, does not play any significant role in biochemical processes. This assumption was based on its lower antioxidative activity and lower concentration in the plasma when compared with α-tocopherol. Recently, more studies have focused on the role of γ-tocopherol and its metabolite, γ-carboxyethyl hydroxychroman, in the pathogenesis of various diseases.[25–27]

In healthy subjects, the value of the ration of the concentration of α-tocopherol to γ-tocopherol in serum is highly variable.

Table 2 Spearman's rank correlation coefficient (r_s) between the independent variables and plasma tocopherol levels in the study subjects (n=401)

	α-Tocopherol		γ-Tocopherol	
Variables	r_s	p Value	r_s	p Value
Age (year)	0.2391	<0.0001	0.2482	<0.0001
BMI (kg/m^2)	0.1500	0.003	0.2180	<0.0001
Pb (µg/l)	−0.0843	0.095	−0.1327	0.008
ZPP (µg/gHb)	−0.0702	0.166	−0.0325	0.522
Cd (µg/l)	−0.0247	0.630	−0.0377	0.463
Triglycerides (mmol/l)	0.5724	<0.0001	0.4580	<0.0001
Total cholesterol (mmol/l)	0.6280	<0.0001	0.3849	<0.0001
Creatine (mmol/l)	0.1406	0.005	0.1457	0.004
Cigarettes/day	0.0381	0.451	0.0212	0.676

ZPP, zinc protoporphyrin.

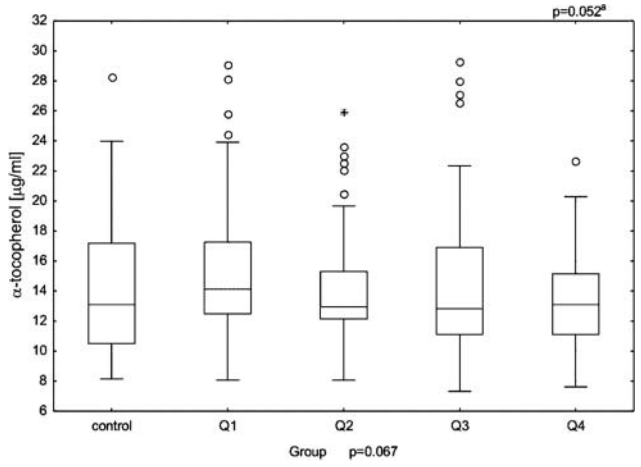

Figure 2 α-Tocopherol in the blood plasma related to the blood lead concentration (categorised) in a population study. The boxes depict the 25th, 50th and 75th percentiles and whiskers represent the minimum and maximum, excluding the outliers (circle) and extremes (asterisk). p Value for Kruskal–Wallis test with multiple comparisons ([a]Q1 vs Q4).

Table 3 Multiple linear regression analysis of variables that may be linked to plasma α-tocopherol and γ-tocopherol (n=401)

	α-Tocopherol		γ-Tocopherol	
	β Coefficient	95% CI (β)	β Coefficient	95% CI (β)
Adjusted R-square	0.5566		0.3082	
Age (year)	0.045	−0.030 to 0.120	0.131	0.038 to 0.224
BMI (kg/m^2)	−0.039	−0.115 to 0.038	0.059	−0.036 to 0.155
Pb (μg/l)	−0.046	−0.120 to 0.029	−0.108	−0.201 to −0.015
Cd (μg/l)	−0.051	−0.148 to 0.046	0.019	−0.101 to 0.140
Triglycerides (mmol/l)	0.485	0.406 to 0.565	0.440	0.340 to 0.539
Total cholesterol (mmol/l)	0.399	0.320 to 0.479	0.117	0.017 to 0.216
Creatine (mmol/l)	0.070	−0.002 to 0.142	0.027	−0.063 to 0.117
Cigarettes/day	−0.003	−0.099 to 0.087	−0.003	−0.120 to 0.114

Depending on the region, this ratio ranges from 11 for men in Ireland to 32 in Spain.[28] In some regions of the USA, γ-tocopherol is a predominant form of dietary vitamin E.[29] Moreover, γ-tocopherol, not α-tocopherol, may play a key role in the prevention of some forms of cancer and blood vessel and heart diseases.[30 31]

The presented study showed the lack of a significant relationship between the lead concentration in the blood and the α-tocopherol level in the plasma. The only difference in α-tocopherol concentration in the plasma of the exposed worker that was close to an assumed significance level was between the Q1 and the Q4 groups (p=0.0502). In contrast, a statistically significant difference in the γ-tocopherol concentration was noted between most of the examined groups (figure 1). Unexpectedly, in the Q1 group, an increase in the concentration of both forms of vitamin E was observed when compared with the control group, and a decrease in the α- and γ-tocopherol concentrations was observed with an increase in blood lead concentration. We propose that this may be associated with an increase of antioxidative activity within the body. The body activates protective mechanisms by increasing antioxidant concentrations, including that of vitamin E, as a response to oxidative stress caused by exogenous factors. One hypothesis suggests that an event causing oxidative stress can initiate chain reactions, cause lipid peroxidation and protein oxidation, generating bioactive molecules, and deplete the antioxidants at the target sites. These events would activate signal transduction pathways that in turn might lead to antioxidant mobilisation if the body's antioxidant stores are high. In this case, tolerance, repair and recovery may occur. However, if antioxidants are deficient and the antioxidant capacity is limited, injury will progress and direct or indirect damage and organ dysfunction will occur.[32]

Spearman's rank correlation coefficient for the relationship between blood lead concentration and the plasma concentration of α- and γ-tocopherols was negative in all cases, but it was statistically significant only for the γ form. High correlation coefficients which were determined for the relationship between the total cholesterol concentration and the triglyceride concentration, and the α- and γ-tocopherol concentrations are a result of contribution of lipoproteins to their transport in the blood plasma.

Quite unexpectedly, no relationship was observed between the tocopherol concentration and a number of cigarettes smoked per day. In fact, the influence of tobacco smoking on the level of α-tocopherol has been well documented, and divergent data exist concerning γ-tocopherol only.[33] We believe that the reason for discrepancy between our findings and the results reported in other studies may be related to the assessment of smoking habit based on a questionnaire only and not on more objective methods, such as assessment of the cotinine concentration in urine/plasma. Moreover, the passive or former smokers were not considered separately, which would also affect the results obtained.

Additionally, no relationship between the cadmium concentration in blood and the level of the discussed tocopherols was noted. Consideration of cadmium in the present study resulted first from the fact that workers may be exposed to cadmium when mining and processing zinc and lead ore. Second, cadmium exposure may also be a cause of oxidative stress.[34]

We observed the lack of a relationship between ZPP concentration and tocopherol concentration in the plasma. ZPP is an index that reflects lead exposure over a longer period than lead concentration in blood. To some degree, this may support the hypothesis about antioxidative mobilisation within the body, which is the result of current exposure rather than long-term exposure.

The results of the multiple regression analysis demonstrate that the highest prognostic value for the level of both tocopherol forms can be attributed to the concentration of triglycerides and total cholesterol, which is a consequence of tocopherol transport by lipoproteins in blood. In turn, among the other independent variables selected for multiple regression, age was observed to have prognostic value for γ-tocopherol concentration (positive), as was lead concentration in the blood (negative). BMI and creatine level, which were also positively correlated with plasma tocopherol level, lost their significant correlation after total cholesterol and triglycerides were included in the multiple regression analysis. Because age influenced the γ-tocopherol levels, it may have also contributed to the significant elevation of γ-tocopherol in the Q1 group, which was characterised by a higher mean age than the control group and the other quartiles. However, it should be kept in mind that the differences in age in the specific groups were relatively small, and the age range was similar in each studied group. Recent studies on age-dependent plasma or serum tocopherol level in a European population revealed slight changes among the adult population, whereas a pronounced increase in tocopherol level was observed in older subjects aged ≥65 years.[35 36]

The present study is the first to examine the influence of occupational lead exposure on plasma γ-tocopherol concentration. Few papers describe an influence of occupational lead exposure on the α-tocopherol concentration in plasma/serum, presenting diverse results. Antonowicz *et al*[37] examined 141 workers at a copper plant. A multiple linear regression analysis did not show statistically significant differences in the serum

α-tocopherol concentration in workers divided into two groups due to lead concentration in the blood (>400 and <400 μg/l). A report concerning lead exposure in men working in a garage was published recently.[11] The concentration of α-tocopherol in the plasma between the group of exposed workers (n=25; Pb concentration in blood 79±5 μg/l) and the control group (n=24; Pb concentration in blood 26±2 μg/l) differed by 30.8%. Similar changes in the plasma α-tocopherol concentration were shown by Filho *et al*.[38] In the group of workers exposed to the incineration of solid residues from health facilities (lead concentration in urine 4.47 vs 2.20 μg/l in urine of the control group), a decrease in the plasma α-tocopherol concentration of 34.1% was observed, while in the group supplemented with vitamin E the concentration increased by 28.5% when compared with the control group. However, the examined population was small as each of the groups was composed of just 20 individuals.

The use of vitamin E as a medicine to provide a protective role against atherosclerosis progression and the occurrence of acute coronary syndromes has been affected by the results of multi-centre clinical studies. The studies of HOPE (*Heart Outcomes Prevention Evaluation*), SECURE (*The Study to Evaluate Carotid Ultrasound changes in patients treated with Ramipril and vitamin E*), GISSI Prevenzione, *Heart Protection Study* and *The Physicians Health Study II* did not confirm a protective effect of vitamin E on an occurrence of acute coronary syndromes and atherosclerosis progression based on the thickness of the internal and central membrane in the internal carotid arteries by USG examination. Vitamin E was administered in various combinations with other medicines, for example, with ACE inhibitors (HOPE). Moreover, it has been suggested that high doses of vitamin E (above 400 UI/day) may increase the death rate and should not be used.[39]

The results that we obtained did not confirm the validity of the application of vitamin supplementation in people occupationally exposed to lead activity. It seems that a well-balanced diet is enough to maintain the plasma tocopherol concentration in the normal range in people who are occupationally exposed to lead. This finding is in accordance with the recommendation of American Heart Association.[40] Considering the toxic effects of lead on the non-enzymatic antioxidative system, an explanation of the role that γ-tocopherol plays requires further research.

Contributors AP and AS participated in the design of the study, acquisition of data, analysis and interpretation of data and preparation of the manuscript. They are the guarantors. MS and JK participated in acquisition and analysis of data and carried out chromatographic and spectrometric studies. EA initiated and coordinated the study and participated in the design of the manuscript. ZO participated in the design of the study. MR and NP collected the samples, participated in acquisition of data and preparation of the manuscript. PO and IS-B participated in acquisition of data and analysis and interpretation of the results.

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Competing interests None.

Patient consent Obtained.

Ethics approval Biomedical Ethics Committee in Institute of Occupational Medicine and Environmental Health in Sosnowiec.

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Effect of occupational lead exposure on α- and γ-tocopherol concentration in plasma

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Corrections

A Prokopowicz, A Sobczak, M Szuła *et al*. Effect of occupational lead exposure on α- and γ-tocopherol concentration in plasma. *Occup Environ Med* 2013;**70**(6):365–371. During the production process, all instances of 'creatinine' were replaced by 'creatine' which is incorrect. All instances of 'creatine' should be replaced by 'creatinine'.

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