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Blood lead and cadmium in age related macular degeneration in a Turkish urban population

Elif Damar Güngör[a,*], Fatma Yülek[a], Utku Serkant[b], Yasin Toklu[a], Asım Hocaoğlu[c], Şaban Şimsek[a]

[a] Ophthalmology Department, Ataturk Training and Research Hospital, Yildirim Beyazit University, Ankara, Turkey
[b] Ministry of Health, Ankara, Turkey
[c] Pharmaceutical and Medical Device Establishment, Ankara, Turkey

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ABSTRACT

Purpose: To evaluate the blood lead (Pb) and cadmium (Cd) levels in age related macular degeneration (AMD) in a turkish urban population.

Methods: Blood Pb and Cd levels of 31 AMD patients and 24 age and gender matched controls with no sign of AMD were measured using dual atomic absorption spectrophotometer system (AAS). History of hypertension, diabetes mellitus, cigarette smoking, myocardial infarction and stroke were obtained from all subjects. Degree of AMD was grade 4 according to the Age-Related Eye Disease Study grading system. Median blood Pb and Cd levels were compared by using Students' *t*-test.

Results: Demographic properties like smoking status, presence of diabetes mellitus or hypertension, cerebrovascular occlusion history, serum cholesterol and lipid levels were not significantly different between groups except history of ischemic heart disease (3.22% vs 25% in AMD and control groups respectively, p = .022). Overall in AMD group blood Pb level was 2.83 ± 0.15 μg/l and it was 2.63 ± 0.23 μg/l in control group (p = .36). The Cd level was 3.25 ± 0.20 μg/l in AMD group and 3.11 ± 0.25 μg/l in control group (p = .67). The mean Pb (2.38 ± 0.88 μg/l vs 2.91 ± 1.37 μg/l for AMD vs control, p = .61) and Cd levels (3.06 ± 1.34 μg/l vs 3.35 ± 1.26 μg/l for AMD vs control, p = .56) in current and previous smokers with AMD were not significantly different from those of the current and previous smokers in control group.

Conclusion: Blood Pb and Cd levels which reflect short term exposure were not significantly different in AMD patients and the control group. The difference was not significant either after involvement of previous or current smoker subjects.

1. Introduction

Heavy metal toxication has become a serious global issue regarding its deleterious effects on health [1]. Lead and Cd are the two common types found in the environment because of their abundant sources and widespread distribution. Anthropogenic activities such as combustion of coal and mineral oil, smelters, mining and alloy processing units, paint industries, vehicular emissions besides the natural sources contribute to Pb and Cd pollution [2–6]. Cadmium is also absorbed and concentrated in tobacco plant and enters the body via inhalation of tobacco smoke [7].

Due to their long half-lives both metals accumulate in tissues of many organ systems such as central and peripheral nervous system [8], haemopoietic system [9], cardiovascular system [10], reproductive system [11], kidney [12] and liver [13]. Oxidative stress and inflammation seem to play the main role in this toxicant induced tissue damage [14–16].

Some age related diseases like hypertension [17–19], peripheral artery disease have been associated with Pb and Cd exposure. Recent postmortem studies proved that human retinal tissues with AMD had increased concentrations of Pb and Cd [20–22]. Adult macular degeneration is a common cause of blindness in elderly population. It is presented with drusen formation, hyperplasia of retinal pigment epithelial(RPE) cells, geographic atrophy and choroidal new vessel formation involving macular region. Aging is the major risk factor for AMD. Aged RPE cells and choroid are faced with some biochemical changes such as decreased catalase activity and vitamin E level, membrane blebbing, increased lipofuscin content of RPE and decreased

* Corresponding author at: Kahramanmaraş Necip Fazıl Şehir Hastanesi Yörükselim Ek Hizmet Binası, Gaziantep Yolu 12. Km Karacasu Kırım Mah, Dulkadiroğlu/Kahramanmaraş, Turkey.
E-mail addresses: elif.damargungor@saglik.gov.tr (E. Damar Güngör), fyulek@ybu.edu.tr (F. Yülek), utku.serkant@saglik.gov.tr (U. Serkant), ytoklu@ybu.edu.tr (Y. Toklu), asim.hocaoglu@titck.gov.tr (A. Hocaoğlu).

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blood flow in choriocapillaris that are associated with cumulative oxidative injury [23–26]. Pathogenesis of AMD is still unclear but oxidative stress and inflammation affecting aged retinal tissues seem to play important role in disease progression [27,28]. Lead and Cd also cause oxidative stress and inflammation in the tissues they accumulate [29–33]. Retinal accumulation of these metals can be in association with AMD pathogenesis. Current study was designed to compare the blood Pb and Cd levels in subjects with AMD and normal subjects in a Turkish urban population where load of heavy metals may be high due to living conditions. If the blood level of these metals is high, modifications in life style may be suggested for the patients.

2. Methods

This study was carried out in accordance with the Declaration of Helsinki after approval by the institutional review board. Informed consent was obtained from all of the patients. Thirty one patients who were followed up with the diagnosis of AMD were enrolled in this study. Color stereoscopic fundus photographs of the patients were obtained (TRX 50DX, Topcon Medical Systems) and severity of AMD was graded by the same observer specialized in retinal diseases in a randomized fashion. Age-Related Eye Disease Study (AREDS) methods were used when obtaining the photographs and grading AMD [34,35]. All the patients in AMD group had grade 4 disase having either geographic atrophy involving the centre of the macula or neovascular AMD. Control group was made up with the 24 patients that had no sign of AMD like RPE changes, drusen formation, pigment epithelial atrophy or retinal hemorrhage. All the subjects were questioned for history of hypertension, diabetes mellitus, cigarette smoking, myocardial infarction(MI) and stroke. Patients with previous history of occupational metal exposure, glaucoma and previous ocular surgery were excluded.

The procedure we used to determine Pb and Cd levels in blood was Kayaaltı et al. method [36]. To determine Pb and Cd levels 3 ml of venous blood sample was collected from patients with the use of a closed system (vacutainer) into the heparinated tubes. Next, the blood sample was transported in refrigerating units to Ankara Occupational Diseases Hospital in Ankara. Lead and Cd levels were measured in the laboratory of toxicology. A microwave system (CEM Mars Xpress) was utilized for digestion of the samples with concentrated nitric acid solution. The analysis was carried out with a dual atomic absorption spectrophotometer (AAS) system (Varian 240). 1 ml of whole blood samples were dissolved in 10 ml of nitric acid, after which all samples were transferred to teflon tubes and digested in microwave at 200 °C for 20 min. Digested sample solutions were diluted before being introduced to a graphite furnace. AAS equipped with a graphite furnace and Zeeman background correction system was used for Cd and Pb determination. The quality of measurements performed in this centre is systematically verified by certified reference materials (Seronorm Trace Elements Whole Blood Level 2–3). Certified materials used in our studies have Cd element's target value designated as 5,1 μg/L for level 2, where accepted range is between 2,8–7,4 μg/L. In different instances of our study, level 2 control sample has been identified as 4,6 μg/L lowest and 5,91 μg/L highest, which are in the indicated accepted range. For Cd elements Level 3 control sample, target value is identified as 9,9 μg/L, where accepted range is between 7,9–11,9 μg/L. In our studies Level 3 findings were determined as 8,4 μg/L lowest and 10,5 μg/L highest, which also are in the accepted range. The target value for Pb element's 2nd level is designated as 396 μg/L, where the accepted range is between 296–469 μg/L. In our studies, we determined this value 310 μg/L as lowest and 390 μg/L as highest. For Level 3 control sample, the target value is 437 μg/L, referenced range is between 412–462 μg/L. Along in our studies, we identified this control sample as 418 μg/L lowest and 440 μg/L highest.

In accordance with the guidelines of the laboratory, Pb concentration in full blood was regarded normal if its average level was below 100 μg/l. In 1991, this value was accepted as a limit by the World Health Organization (WHO) [37]. According to Tietz normal value for blood lead level is less than < 25 μg/l [38]. Nevertheless, studies carried out during the last 20 years show undeniably that this value cannot be regarded as safe. Whether a safe limit can be established or not is a very disputable question. In accordance with criteria of Tietz, a normal cadmium level in blood is 0,3–1,2 μg/l for nonsmokers and it is 0,6–3,9 μg/l for smokers.

The software package used for statistical analysis was SPSS Version 15.0 for Windows (SPSS Inc, Chicago, IL). The difference of two groups for Cd and Pb levels was evaluated with Students' *t*-test. A two-tailed probability of 0.05 was considered statistically significant.

Table 1
The demographic characteristics of patients.

		Group		p value
		SMD	Control	
Smoking status	Currently smoking	5 (16.13%)	6 (25%)	.49
	Not smoking	20 (64.52%)	13 (54.17%)	
	Previous smoker	6 (19.35%)	5 (20.83%)	
History of ischemic heart disease (number and percent)		1 (3.22%)	6 (25%)	.022
Hypertension (number and percent)		20 (64.52%)	11 (45.83%)	.13
Diabetes mellitus (number and percent)		2 (6.45%)	3 (12.5%)	.38
History of cerebrovascular occlusion (number and percent)		3 (9.68%)	1 (4.17%)	.41
LDL level (mean–SEM)		51.35–11.43	72.21–12.61	.23
HDL level (mean–SEM)		21.53–5.04	25.34–4.38	.58
Cholesterol level (mean–SEM)		88.71–19.25	89.38–20.59	.98

3. Results

There were 31 patients (22 male, mean age-SEM: 69–1.46) in AMD group and 24 patients (18 male, mean age-SEM: 68.12–8.34) in the control group. The demographic characteristics of patients are summarized in Table 1. None of the properties like smoking status, presence of diabetes mellitus or hypertension, history of ischemic heart disease, cerebrovascular occlusion, serum cholesterol and lipid levels were significantly different between groups except history of ischemic heart disease (Table 1, p = .022, 3.22% vs 25% in AMD and control groups respectively). In AMD group blood Pb level was 2.83 ± 0.15 μg/l and it was 2.63 ± 0.23 μg/l in control group (p = .36). The Cd level was 3.25 ± 0.20 μg/l in AMD group and 3.11 ± 0.25 μg/l in control group (p = .67). The heavy metals levels were compared in AMD patients and control patients with previous or current smoking habit. Similarly the mean Pb (2.38 ± 0.88 μg/l vs 2.91 ± 1.37 μg/l for AMD vs control, p = .62) and Cd levels (3.06 ± 1.34 μg/l vs 3.35 ± 1.26 μg/l for AMD vs control, p = .56) in current and previous smokers with AMD were not significantly different from those of the current and previous smokers in control group. The mean levels of Pb and Cd in non smokers without AMD were 2.40 ± 0.24 μg/l and 2.91 ± 0.35 μg/l respectively. The mean levels of Pb and Cd in nonsmokers with AMD were 2.40 ± 0.19 μg/l and 3.36 ± 0.22 μg/l respectively. The difference was not statistically significant for Pb (p = .99) and Cd (p = .18) among nonsmokers for AMD and control groups.

4. Discussion

The effects of two heavy metals Pb and Cd have been studied in human retinal tissues especially in neural retina, RPE and the choroid [20–22]. Cadmium toxicity on cultured RPE cells have been reported with increased level of reactive oxygen species and alterations in cellular morphology after Cd exposure which were prevented by antioxidant N-acetylcysteine [21,22].

Lead accumulation in retinal tissues increase as a function of age [20]. Even in low tissue concentrations Pb has toxic effects including