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Changes in lipid metabolism in women with age-related macular degeneration

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Abstract Age-related macular degeneration (AMD) is one of the leading causes of visual loss among people aged 65 and older. At present the origin of AMD still remains unknown. The objective was to evaluate the chosen lipid and lipoprotein concentrations in blood of patients with AMD. Sixty women aged 55–71 (mean age 65.1±5.7) were treated in the outpatient ophthalmological clinic for more than two years because of AMD. We evaluated total serum cholesterol (TCH), triglycerides (TG), HDL-cholesterol (HDL), LDL-cholesterol (LDL), lipoprotein (a) (Lp(a)), apolipoprotein AI (Apo AI) and apolipoprotein B (Apo B) by direct spectrophotometry (Human and Randox standard kits, USA). We found a significant increase of TCH, LDL and TG (224.36±41.67 mg/dl, 159.02±39.66 mg/dl and 120.92±42.64 mg/dl), and a significant decrease of HDL (38.68±6.36 mg/dl) in the AMD patients when compared with the control group. We have not found a significant difference in the average TG level between the studied groups. The concentration of Apo B was markedly increased (164.66±46.46 mg/dl) and Apo AI concentration was markedly decreased (128.9±17.01 mg/dl) in the AMD patients when compared with the control group. There was no significant difference in the concentration of the Lp(a) between the two groups. The results of our present study could point to the fact that changes in the lipid metabolism could be one of the very important risk factors involved in the pathogenesis of AMD.

Key words AMD • Serum lipids • Serum lipoproteins

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Introduction

Due to the increasing average age among the European population, age-related diseases have become a real challenge for doctors of different specialisations.

Age-related macular degeneration (AMD) is one of the leading causes of visual loss among people aged 50 and older [1]. It is proposed to name all signs of age-related macular changes as age-related maculopathy (ARM). The late stages of ARM are called AMD and include both ‘dry’ (geographic) and ‘wet’ (disciform, exudative, neovascular)

forms. AMD is characterised by lipid deposits (drusen) beneath the retinal pigment epithelium (REP) and the atrophy of REP [2, 3].

In the disciform form, REP detachment and choroidal neovascularisation is present [3].

Although there are more effective and safer treatment methods for old age diseases including senility cataract, the effective treatment of AMD still remains a great challenge. A possible precise recognition of the risk factors of the AMD and a proper prevention in those people can play a decisive role in preventing the development of AMD. At present, the origin of AMD remains unknown.

In recent papers, low macular pigment level was identified as a risk factor [4, 5]. The other risk factors are genetic predisposition [6–9], cigarette smoking [10], postmenopausal oestrogen decrease [11] and excessive exposure to sunlight [12]. In the last decade, much interest has been devoted to the connection between the concentration of antioxidants and the presence of various disorders of old age. The authors have raised a point that oxidative stress is important in the aetiology of AMD and in the possible protective effect of antioxidants [13–16]. However, investigations so far are ambiguous and data are often contradictory. The latest papers widely discuss the problems of vascular diseases [17–21] and disturbances in lipid metabolism [11, 17, 19–23] as risk factors for AMD. The results of studies presented by various authors are often inconsistent and their interpretation is difficult.

Some studies have suggested a possible role of apo E polymorphism in the development of AMD [24, 25]. Apo AI is a major ingredient of high density lipoprotein. A decrease of Apo AI (and HDL cholesterol) is a very common symptom of an accelerated atherosclerosis. Most of the apolipoprotein B (Apo B) occurs in a LDL fraction where it makes up about 25% of particle mass. Disorders in Apo B metabolism are of great importance in the process of cholesterol deposition. Moreover, Apo B is a part of lipoprotein (a) (Lp(a)). The intensification of the Apo B production accompanies an increased production of cholesterol [26]. Lp(a) includes a protein called apoprotein (a) and an Apo B particle, the same as in LDL fraction [27].

The aim of the study was to evaluate the chosen lipid and lipoprotein concentrations in blood of patients with AMD.

Materials and methods

The participants of this study included 60 women aged 55–71 (mean age 65.1±5.7) with AMD. Because of probably different pathogenesis of the 'dry' and 'wet' form of AMD, studied cases included only patients with the 'dry' form of disease i.e., 43 patients with ARM, 17 patients with a more severe geographic degeneration. The control group consisted of 45 postmenopausal women aged 50–70 (mean 63.8±6.2) without ophthalmologic complications and family history of AMD reported to ophthalmologic outpatients clinic during routine tests and for glasses correction. Exclusion criteria were neovascular form of AMD, diseases other than AMD associated with neovascularisation, retinal detachment, severe ocular trauma, high myopia and intraocular inflammation.

None of the patients were on antioxidant micronutrients supplementation and they all lived in the same industrial area. Because of the rather small numbers of patients in studied groups, we excluded diabetics and current or past smoking patients from the study. Both groups of patients were matched by age and sex.

The eye examination included visual acuity, biomicroscopy and ophthalmoscopy using either a 90-diopter lens or a direct ophthalmoscopy after papillary dilation, photography and fluorescein angiography of the retina.

In all cases the diagnosis of AMD and classification were based on reduction of visual acuity less than 20/20, ophthalmoscopy signs of disease, photography and fluorescein angiography of the retina. ARM was diagnosed in the eyes with clinically detectable pigment epithelial changes of hyper- or hypopigmentation and hard or soft druses appearance. The geographic atrophy was diagnosed in the eyes with a sharply delineated roughly round area of hypo- or depigmentation of at least one-third disc diameter in size, or an apparent absence of the RPE with choroidal vessels more visible than in the surrounding areas [1].

In the morning hours (after 8–12 h starvation), blood specimens for biochemical examination were collected.

In all patients we evaluated the body mass index (BMI) and in the peripheral blood we evaluated total serum cholesterol (TCH) and triglycerides (TG) using standard kits from Human company and cholesterol HDL and cholesterol LDL level with sets from Randox (Direct LDL and HDL) by direct spectrophotometric method.

The concentrations of Lp(a), Apo AI and Apo B were evaluated by direct spectrophotometry using a Human standard kit.

Studied parameters distribution between AMD patients and control group were calculated by Chi-square test. The statistical analysis was carried out using the 'Statistica 5.0 Pl' programme with Student's *t*-test for normal distribution of the results in the study groups or Mann-Whitney's *U*-test in other than normal distribution, assuming the levels $P<0.05$ as statistically significant.

The project was carried out with the permission of The Bioethics Board of the Medical University of Silesia (NN 013-653/I/99/2000). All subjects gave a formal consent before participating in the study, and research followed the tenets of the Declaration of Helsinki.

Results

The results obtained in the biochemical investigations in the AMD and control patients are presented in Tables 1 and 2.

We found a significant increase ($P<0.05$) in TCH and TG in the AMD patients (224.36±41.67 and 120.92±42.64 mg/dl) when compared with the control group

Table 1 Concentrations of the lipid parameters in the blood of the patients with AMD and the control group

	Means and standard deviation		*P* (Student's *t*)
	AMD (*n*=60)	Control (*n*=45)	
TCH mg/dl	224.36±41.67	190.86±23.55	*P*<0.05
HDL mg/dl	38.68±6.36	49.20±10.50	*P*<0.0001
LDL mg/dl	159.02±39.66	125.20±32.75	*P*<0.001
TG mg/dl	120.92±42.64	101.72±38.20	*P*<0.05

TCH, total serum cholesterol; *TG*, triglycerides; *HDL*, HDL-cholesterol; *LDL*, LDL-cholesterol

Table 2 Lipoprotein (a), apolipoprotein AI and B concentrations in the blood of the patients with AMD and the control group

	Means and standard deviation		*P* (Student's *t*)	*P* (Mann-Whitney *U*)
	AMD (*n*=60)	Control (*n*=45)		
Lp(a) mg/dl	19.48±22.03	12.21±6.58		NS, *P*=0.065
Apo AI mg/dl	128.9±17.01	160.32±22.22	*P*<0.05	
Apo B mg/dl	164.66±16.16	121.62±27.52	*P*<0.001	

Lp(a), lipoprotein (a); *Apo AI*, apolipoprotein AI; *Apo B*, apolipoprotein B; *NS*, not significant

(190.86±23.35 and 101.72±38.20 mg/dl). The average concentration of HDL (38.68±6.36 mg/dl) in AMD patients was markedly (*P*<0.0001) decreased when compared with the control group (49.20±10.50 mg/dl) and LDL concentration (159.02±39.66 mg/dl) was markedly (*P*<0.001) increased when compared with the control group (125.20±32.75 mg/dl) (Table 1).

The Apo B concentration (164.66±16.16 mg/dl) was markedly (*P*<0.001) increased when compared with the control group (121.62±27.52 mg/dl) and Apo AI concentration (128.9±17.01 mg/dl) was markedly (*P*<0.05) decreased when compared with the control group (160.32±22.22 mg/dl). There was no statistical difference in the Lp(a) concentration because of the huge standard deviation of the results in the AMD patients (Table 2). The mean concentration of Lp(a) in the AMD group (19.48±22.03 mg/dl) was two times higher than the mean concentration in the control group (12.21±6.58 mg/dl) and a number of results exceeding the limits assumed as a norm for Lp(a) were significantly higher within the study group.

In the AMD group we found that an average BMI index (28.5±5.3 kg/m^2) was higher when compared with control patients (25.9±4.1 kg/m^2), which is consistent with results presented by other authors [19, 23, 28].

Discussion

Increased frequency of AMD with increasing age has been observed in several studies [28, 29], but knowledge of other possible risk factors is controversial. It is possible that in different populations the relative role of individual risk factors may vary.

It is difficult to interpret connections between lipid changes and the development of AMD. Atherosclerotic vascular disease, due to its influence on choroidal circulation, has been hypothesised as a possible pathogenetic factor for development of AMD. However, the study of the relationship of lipid changes and/or atherosclerosis and the development of AMD has not presented uniform results [11, 17–21, 23, 28, 29].

Some studies have found an increased risk of AMD with a past cardiovascular event [30, 31], systemic hypertension [17, 21, 32] and increased blood cholesterol levels [11, 23], although other studies have found no association with vascular events [19, 23, 33], systemic hypertension [19, 23, 33, 34] or blood lipid levels [19–21, 33–36].

Results of our study are consistent with results of some previous studies correlating AMD with lipid and lipoprotein disturbances.

Belda Sanchis et al. [36], in a group of 25 patients with AMD, found a significant increase in Apo B, TCH, TG and cholesterol LDL.

Hirvela et al. [28] found that high BMI was associated with AMD, supporting the theory that excessive caloric intake increases the risk of AMD. The authors also found an association of AMD with the presence of severe arteriolar sclerosis of the retinal vessels, however, the role of local vascular factors in the pathogenesis of AMD is not known. Ikeda et al. [20], in a population with neovascular AMD, found an increased concentration of both total cholesterol and TG and a decrease of HDL in peripheral blood but no significant dif-

ference when compared with healthy people. The authors also have not found a significant difference in concentration of Apo AI and Apo B between the studied groups.

In a recent study, Vingerling et al. [30] found that macular degeneration was associated with atherosclerosis determined by the presence of plaques in the carotid bifurcation and common carotid artery. Data from the National Health and Nutrition Examination Survey also showed that persons with a positive history of atherosclerotic vascular disease had a higher prevalence of AMD [37]. The Eye Disease Case-Control Study [11] has found a positive relationship between TCH and development of AMD.

Hyman et al. [17] found positive association between neovascular AMD and higher cholesterol intake and elevated serum HDL cholesterol. In this study neither AMD type was related to serum cholesterol, TG or LDL cholesterol. Similarly, a positive relationship was found with high serum HDL cholesterol and an inverse with total cholesterol-HDL ratio by other authors [21].

The interpretation of these results is difficult and inconsistent with the hypothesised connection of AMD to the lipid changes and cardiovascular disease. Although scientific literature documented multiple aetiologic theories and pathophysiologic abnormalities in patients with AMD, blood lipid abnormality and atherosclerotic process could play an important role in AMD development by affecting the flow of choroidal vessels, but the mechanism for this process is unclear [18].

Some of the differences in results among the various studies may be due to differences in populations with completely different nutritional habits, or to methodological issues.

One of the serious restrictions in establishing the role of lipid metabolism in the development of AMD is a lack of direct possibility for its measurement in the retina vessels. In interpreting the results it must be assumed that the concentration in the peripheral blood correlates with the concentration in the eye.

In our opinion, apart from genetic conditions, a very large group of risk factors is involved in the development of AMD. It seems that changes in lipid metabolism could play a pathogenic role, especially at the very beginning of natural history of the AMD development and could have a damaging influence also on choriocapillaris. It can be the reason for ischaemia of the avascular macular zones and disorders in the physiologic balance of angiogenic and antiangiogenic factors, which might consequently lead to neovascularisation of the macular region.

In conclusion, the results of our present study could point to the fact that changes in the lipid and lipoprotein metabolism are one of the risk factors involved in the pathogenesis of AMD.

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