Coll. Antropol. **35** (2011) Suppl. 2: 307–310
Review

The Role of Omega6 to Omega3 Ratio in Development and Progression of Age-Related Macular Degeneration

Tea Čaljkušić Mance[1], Damir Kovačević[1], Zvjezdana Alpeza-Dunato[1], Maja Novak Stroligo[1] and Gordana Brumini[2]

[1] Department of Ophtalmology, Rijeka University Hospital Center, Rijeka, Croatia
[2] Department of Medical Informatics, School of Medicine, University of Rijeka, Rijeka, Croatia

A B S T R A C T

The aim of this study is to investigate possible connection between omega-6/omega-3 fatty acid ratio and development and progression of Age-Related Macular Degeneration (ARMD). We examined 125 patients diagnosed with ARMD and divided into 5 groups of 25 patients according to CARMS (Clinical Age-Related Maculopathy Staging System). Control group consists of 51 patients with similar ages, without ARMD. All of them underwent stereobiomicroscopy, fundus photography and fluorescein angiography. Dietary fatty acids intake was measured using food frequency questionairre (FFQ). The FFQ was based on previously validated questionairre (DIETQ, Tinuviel Software, Warington, Ches, UK) and FFQ2 from Blue MountainEye Study. The data were analysed using food nutritient dana from McCance and Widdowson´s Food Composition Tables, supplemented with a food fatty acid content database (Foodbase, London, UK). We noticed statistically significant difference between omega-6/omega-3 ratio in neovascular ARMD (stage 5) and all other groups including control group (p=0.000020).The ratio in Stage 5 was about 11:1 like in Western diet. Stage 4-geographic atrophy (GA) has statistically significant difference in o-mega-6/omega-3 ratio compared with stage 1 (p=0.000571), stage 2 (p=0.000112) and stage 3 (p=0.000430). The ratio in first three groups is about 7–7.5:1 (greater then Mediteran-4–5:1, but lower then Western Diet-10–20:1). There is no statistically significant difference between first three stages (p>0.05) and stage 4 and control group (p=0.172388). Omega-6/omega-3 ratio is connected with development of neovascular ARMD. Decreased ratio protects against neovascular ARMD. On the contrary, GA seems to be connected with prolonged sunlight exposure (the ratio is about 6:1). It is good to know that changing nutrition habits someone can prevent development of severe neovascular form of ARMD because intravitreal anti-VEGF therapy limitations.

Key words: *age-related macular degenerations, omega-6 fatty acids, omega-3 fatty acids*

Introduction

Age-related macular degeneration (ARMD), a leading cause of visual loss in older adults in developed countries has limited terapeutic options[1]. Degenerative changes of macular arealead to damage of central vision and cause difficulties in reading, writing, driving, using PC and other aspects of normal quality of today human life[2]. Successful therapy is not yet available for the majority of patients, especially not for patients with severe form of »dry« ARMD. Before the introduction of anti-VEGF (Vascular Endothelial Growth Factor) medica-tions there was no known therapy for »wet« ARMD that can actually improve visual acuity.

Epidemiological studies over the last two decades have provided insights into the risk factors associated with ARMD including age, sex, nutritional status, smoking, hypertension, sunlight exposure and genetic markers. Therapies that focus on prevention through optimization of modifiable risk factors such as diet and nutritional status are key approaches to reducing the burden of disease. Methods that help to prevent development or progression of ARMD through nutritional supplementation will become especially important as our population increases in longevity and the number of individuals affected with ARMD continues to rise[1,3–5].

Received for publication May 30, 2011

Given the considerable public health burden imposed by ARMD, much effort has been directed towards discovering principles of pathogenesis in order to identify risk factors and develop preventive measures and treatments. Together with epidemiological evidence linking cardiovascular risk factors with ARMD risk and basic science work examing the role of lipid metabolism in ARMD, numerous human studies have assayed a potentional relationship between dietary lipids and development of ARMD[6]. Lipids and lipid metabolites have long been known to play biological roles that go beyond energy store and membrane structure. In ARMD dysregulation of lipid metabolism is closely associated with disease onset and progression. The topics of lipoprotein modulation and omega-3 fatty acid intake receive special attention[6,7]. A large study involving researchers and patients from eight European countries now report that regular consumption of oily fish my reduce risk of developing ARMD by 53%. The reaserchers observed a strong correlation between fish intake and dietary intake of the two main component of fish oil-EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) which is omega-3 fatty acids[8]. Omega-6 and omega-3 are polyunsaturated fatty acids and they are essential because our organism cannot produce them and we musts get them food. For most of the time human have been on earth we have eaten foods containing omega-6/omega-3 ratio of about 1–2:1. However, over the last 50 years in Western diet, the ratio has changed to 10–20:1. Our diet now includes huge amounts of oils that are extracted from plants and used for cooking or in prepared food. These oils (such as sunflower and corn oil) are primarily omega-6. Omega-3 is found in oily fish, in whole grains and beans. So, today we have excessive amounts of omega-6 fatty acids compared with diet on which human beings envolved and their genetic patterns were established. Excessive amounts of omega-6 and a very high omega-6/omega-3 ratio, as is found in today´s Western diets, promote the pathogenesis of many chronic diseases, including cardiovascular, cancer, and autoimmune diseases, whereas increased levels of omega-3 exert suppressive effect. In our organism omega-6 has proinflamatory and omega-3 antiinflamatory effect. It is possible i that optimal ratio may vary with disease under consideration[9,10].

ARMD is also chronic disease and it is multigenic and multifactorial. We try to discover values of omega-6/omega-3 ratio in patients diagnosed with different stages of ARMD and influence of that ratio on development and progression of ARMD.

Materials and Methods

The study group included 125 patients (125 eyes) divided into 5 groups according to CARMS (Clinical Age-Related Maculopathy Staging System)[11]. The first 3 stages represent different form of »dry« ARMD, 4th represent geographic atrophy (GA)-developed »dry« form and 5th represent neovascular form of ARMD. The control group included 51 patients without any signs of ARMD with similary ages as study group. All the patients were examined in Department of Ophtalmology in Rijeka University Hospital.They underwent stereobiomicroscopic examination, fundus photography and fluorescein angiography. Dietary fatty acids intake was measured by using food frequency questionairre (FFQ). The FFQ was based on a previously validaded questionairre (DIETQ, Tinuviel Software, Warington, Ches, UK) and FFQ2 which had been used in Blue Mountin Eye Study. The FFQ and weighed records were analysed using food nutritient dana from McCance and Widdowsons Food Composition Tables, suplemented with a food fatty acid content database (Foodbase, London, UK)[12,13].

Statistical analysis of dana was performing by using Statistica for Windows, release 8.1 (StaSoft, INC, Tulsa, OK, USA). The dana of omega-6/omega-3 ratio were presented as the mean±standard deviation (SD) or median and range (5th–95th percentile boundaries), depending on the normality of distribution. We used one-way analysis of variance (one-way ANOVA) to test the differences between the group according to omega-6/omega-3 ratio. For post hoc analysis Tukey´s test were used. All statistical values were considered significant at the p-level of 0.05.

Results

We noticed folowing results of omega-6/omega-3 ratio in five different stages of ARMD and control group (Table 1). Total number of examined patients were 176, 125 diagnosed with ARMD and 51 in control group. In the first three groups (Stages 1, 2 and 3) we counted ratios 7.65±0.77, 7.76±0.65 and 7.67±0.70 (mean±SD) which represent stages of mild or moderate »dry« form of ARMD. In the stage 4-GA omega-6/omega-3 ratio was 6.44±0.68 and in the stage 5 (neovascular ARMD) ratio was 11.52± 1.83 (mean±SD). Control group has ratio of 7.04±1.05 (mean±SD). As we can see patients with neovascular ARMD had greater values of omega-6/omega-3 ratio and patients with GA mild lower than other groups.

Statistically significant difference was noticed between omega-6/omega-3 ratio in neovascular ARMD group (stage 5) and ratios in all other groups including control group ($p=0.000020$) (Table 2). Besides that patients in stage 4 (GA) has statistically significant difference in omega-6/omega-3 ratio compared with patients in stage 1 ($p=0.000571$), stage 2 ($p=0.000112$) and stage 3 ($p=0.000430$). There is no statistically significant differences between omega-6/omega-3 ratio in first 3 stages of ARMD ($p>0.05$) and between stage 4 and control group ($p=0.172388$).

Discussion and Conclusion

Omega-6/omega-3 ratio in mild and moderate form of ARMD is about 7–7.5:1. This ratio is greater than in Mediteran Diet (4–5:1) but lower than in Western Diet (10–20:1)[9,10]. In group with neovascular ARMD ratio is about 11:1 and it is like in Western Diet. Maybe it is answer on question we have in our last year epidemiological

TABLE 1
OMEGA-6/OMEGA-3 FATTY ACIDS RATIO ACCORDING TO STAGES OF ARMD (MEAN SD)

	Level of – Factor	N	–Mean±SD	–Std.Err	–95,00%	+95,00%
Total		176	7.87±1.86	0.14	7.60	8.15
group	Stage 1	25	7.65±0.77	0.15	7.34	7.97
group	Stage 2	25	7.77±0.65	0.13	7.50	8.04
group	Stage 3	25	7.67±0.71	0.14	7.38	7.96
group	Stage 4	25	6.44±0.68	0.14	6.16	6.73
group	Stage 5	25	11.52±1.83	0.37	10.76	12.27
group	Control	51	7.04±1.05	0.15	6.75	7.34

ARMD – age-related macular degeneration, SD – standard deviation

TABLE 2
COMPARISON OF OMEGA-6/OMEGA-3 RATIO AMONG DIFFERENT STAGES OF ARMD AND CONTROL GROUP (p values)

Group	I.	II.	III.	IV.	V.	VI.
1		0.998767	1.000000	0.000571	0.000020	0.153041
2	0.998767		0.999508	0.000112	0.000020	0.047719
3	1.000000	0.999508		0.000430	0.000020	0.127637
4	0.000571	0.000112	0.000430		0.000020	0.172388
5	0.000020	0.000020	0.000020	0.000020		0.000020
6	0.153041	0.047719	0.127637	0.172388	0.000020	

ARMD – age-related macular degeneration

study when we noticed greater prevalence of neovascular ARMD in Gorski kotar where people rare consume oily fish (omega-3) and consume great deal of plant oil (omega-6) and saturated fats[14]. We think that besides genetics, nutritional habits,also, has important roles in conversion from moderate form of ARMD into severe neovascular form. It confirmes datas from several studies that decreased omega-3/omega-6 ratio protects against neovascular ARMD and acts like natural anti-VEGF factor because decreases VEGF in blood[10].

Lower omega-6/omega-3 ratio, about 6–6.5:1 was noticed in stage 4 (GA). It is possible that in that variant of severe form of ARMD, which in our last study was more frequent in islands, greater influence in conversion from moderate to severe form has long time of sunlight exposure[15,16].

No significant difference between group 1 and 3 and control group was noticed and we think that is possible that optimal ratio may vary with disease under consideration but we have to know that we cannot tell for sure in what way and why patients with moderate form develop severe form.

However, we can conclude that omega-6/omega-3 ratio has important role in development of neovascular form of ARMD. It is good to know in prevention of disease because intravitreal therapy with anti-VEGF medications has limitations.

REFERENCES

1. KRISNADEV N, MELETH AD, CHEW EY, Curr Opin Ophtalmol, 21 (2010) 184. — 2. SYNEK S, VOJNIKOVIĆ B, PAHOR Đ, Coll Antropol, 34 (2010) 25. — 3. SEDDON JM, GEORGE S, ROSNER B, Arch Ophtalmol, 124 (2006) 995. — 4. TAN JS, WANG JJ, FLOOD V, MITCHELL P, Arch Ophtalmol, 127 (2009) 656. — 5. SEDDON JM, COTE J, ROSNER B, Arch Ophtalmol, 121 (2003) 1728. — 6. KISHAN AU, MODJATAHEDI BS, MARTINIS EN, MODJATAHEDI BS, MORSE LS, Surv Ophtalmol, 56 (2011) 195. — 7. SIMOPOULOS AP, Biomed Pharmacother, 60 (2006) 502. — 8. AUGOOD C, CHAKRAVARTHY U, YOUNG I, VIOQUE J, DE JONG P, BENTHAM G, RAHU M, SELAND J, SOUBRANE G, TOMAZZOLLI L, TOPOUZIS F, VINGERLING JR, FLETCHER AE, Am J Clin Nutr, 88 (2008) 398. — 9. SIMOPOULOS AP, Biomed Pharmacother, 56 (2002) 365. — 10. SIMOPOULOS AP, Exp Biol Med, 233 (2008) 674. — 11. SEDDON JM, SHARMA S, ADELMAN RA, Ophtalmol, 113 (2006) 260. — 12. BROADFIELD E, McKEEVER T, FOGARTY A, BRITTON J, Br J Nutr, 90 (2003) 215. — 13. ORTHON HD, SZABO NJ, CLARE SALZER M, NORIS JM, Eur J Clin Nutr, 62 (2008) 733. — 14. ČALJKUŠIĆ-MANCE T, KOVAČEVIĆ D, NOVAK-STROLIGO M, ALPEZA-DUNATO Z, Coll Antropol, 34 (2010) 109. — 15. NJIRIĆ S, MIŠLJENOVIĆ T, MIKULIČIĆ M, PAVIČEVIĆ L, Coll Antropol, 31 (2007) 107. — 16. VOJNIKOVIĆ B, VOJNIKOVIĆ D, Coll Antropol, 34 (2010) 5.

T. Čaljkušić-Mance

Department of Ophthalmology, Rijeka University Hospital Center, Krešimirova 42, 51000 Rijeka, Croatia
e-mail: teamance@hotmail.com

ULOGA OMJERA UNOSA OMEGA-6 I OMEGA-3 MASNIH KISELINA U ORGANIZAM U RAZVOJU I PROGRESIJI SENILNE MAKULARNE DEGENERACIJE

S A Ž E T A K

Cilj ove studije bio je ispitati moguću povezanost omjera unosa omega-6 i omega-3 masnih kiselina u organizam sa razvojem i progresijom senilne makularne degeneracije (SMD). U tu svrhu pregledali smo 125 pacijenata s dijagnozom SMD te ih podijelili u 5 skupina po 25 pacijenata prema stupnju težine bolesti. Kontrolnu skupinu činio je 51 pacijent slične dobi bez SMD. Svima je učinjena stereobiomikroskopija, fundus fotografija i fluoresceinska angiografija. Unos masnih kiselina u organizam ispitan je pomoću upitnika prehrambenih navika. Statistički značajna razlika zabilježena je kod neovaskularnog oblika SMD u odnosu na sve ostale skupine uključujući i kontrolnu grupu ($p=0,00002$). Grupa 4 – geografska atrofija (GA) se statistički značajno razlikuje od prve 3 skupine koje predstavljaju blaži oblik SMD ($p<0,05$). Omjer unosa kod neovaskularnog oblika je oko 11:1 i odgovara zapadnjačkom tipu prehrane dok je niži kod ostalih skupina (oko 7–7.5:1), a najniži u skupini 4 (oko 6:1). Primjećujemo izrazitu povezanost povećanog omjera unosa omega-6/omega-3 sa razvojem neovaskularnog oblika SMD, dok smanjeni omjer djeluje protektivno. To saznanje može biti korisno u prevenciji ovog teškog oblika SMD, jer intravitrealna terapija ima svoja ograničenja.