LETTER TO THE EDITOR

The synergistic effect of exposure to alcohol, tobacco smoke and other risk factors for age-related macular degeneration

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Age-related macular degeneration (AMD) is the leading cause of severe visual loss among people aged 50 years and older in the developed world [1]. Cigarette smoking, hypertension, inflammation and alcohol consumption, have been shown to be associated with AMD in some, but not all studies [2–4]. In our study we have evaluated the synergistic effect of alcohol and tobacco smoking with other risk factors in the risk of developing AMD.

The investigation adhered to the Declaration of Helsinki and was approved by the Ethics Committee. We recruited patients, providing written informed consent, with AMD (the phenotype was early AMD, both the drusen and the pigmentary changes) during the period between August and November 2011 from the Center Maculopathy of the Department Sense Organs Sapienza University of Rome, Teaching Hospital Umberto I.

The controls, matched to cases by age and sex, consist of two distinct groups:

a) patients with eye diseases (unrelated with AMD);

b) individuals belonging to the Clinic Orthopedic of the Teaching Hospital Umberto I, Rome.

A questionnaire was administered to cases and controls for collecting data including thirty-five questions divided into five sections. The first section asked for demographic data regarding age, gender, occupation, education level, weight, height, eyes colour. The second section asked for AMD family history (any relative), cardiovascular disease,

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hypertension, hypercholesterolemia, diabetes, cataract surgery. The third section ascertained whether the patients are ever smokers. The fourth section asked if the patients drink wine, beer or hard liquor. The last section tested how many times a week, patients eat the following foods: bread, pasta, legumes, fruit, vegetables, red meat, white meat, cheese, fish, sweets.

The possible interaction between sociodemographic variables was tested using the synergism index, calculated as follows: $S = [OR11 - 1]/([OR01 + OR10] - 2)$, where OR11 is equal to OR of the joint effect of two risk factors and OR10 and OR01 are equal to OR of each risk factor in the absence of the other. A value of S equal to unity was interpreted as indicative of additivity, whereas a value greater than unity was indicative of superadditivity and synergism [5].

A total of 122 cases and 124 controls were enrolled. The median age in the case group was 75, whilst in the control group was 74. Alcohol intake is the same in both groups (2.4 grams per day); as regards smoking condition, we found that 61.5 % (75 persons) in the case group are ever smokers, in the control group they are 41.9 % (52 persons).

Table 1 shows OR for each variables AMD-related. There was an indication for the additivity and synergism between many risk factors (Table 2): family history AMD and ever smokers (S = 1.51; 95 %CI 0.11–20.69), hypercholesterolemia and ever smokers (S = 1.77; 95 %CI 0.44–7.10), finally from hypercholesterolemia and alcohol intake (S = 1.64; 95 %CI 0 −>999). Moreover, we found out a synergistic interaction for Obesity with Ever smokers (1.54; 95 %CI 0.24–9.63) and Alcohol intake (4.2; 95 %CI 0 −>999).

Our findings suggest that many risk factors are associated to the development of AMD, some of them have a

Table 1 Odds Ratio for the outcome AMD

Variables	OR (95 % CI)
Family history AMD	4.49 (1.45–13.8)
Cardiovascular disease	0.64 (0.38–1.06)
Hypertension	1.40 (0.82–2.38)
Hypercholesterolemia	1.29 (0.78–2.51)
Diabetes	0.70 (0.40–1.24)
Cataract surgery	0.57 (0.33–0.98)
Obesity	1.23 (0.61–2.48)
Ever smokers	2.20 (1.32–3.68)
Alcohol intake	0.97 (0.58–1.62)

Table 2 Synergistic interaction between various variables in influencing age-related macular degeneration

Variables		Synergistic interaction (95 %CI)
Family history AMD	Ever smokers	1.51 (0.11–20.69)
Cardiovascular disease	Ever smokers	1.07 (0.05–23.07)
Hypertension	Ever smokers	0.96 (0.32–2.86)
Hypercholesterolemia	Ever smokers	1.77 (0.44–7.10)
Diabetes	Ever smokers	0.84 (0.08–8.07)
Cataract surgery	Ever smokers	0.19 (0–4.85)
Family history AMD	Alcohol intake	Nc
Cardiovascular disease	Alcohol intake	Nc
Hypertension	Alcohol intake	Nc
Hypercholesterolemia	Alcohol intake	1.64 (0 —>999)
Diabetes	Alcohol intake	0.72 (0.17–3.07)
Cataract surgery	Alcohol intake	0.62 (0.25–1.56)
Alcohol intake	Ever smokers	0.49 (0.09–2.54)
Obesity	Ever smokers	1.53 (0.24–9.63)
Obesity	Alcohol intake	4.2 (0 —>999)

synergistic interaction. First of all we found a highly interaction between family history of AMD and ever smokers condition, as reported in other studies [6]. Smoking resulted in a great risk factor influencing the developed of AMD too: it is possible that smoking itself may be a risk indicator for other factors that have been associated with age-related maculopathy such as alcohol consumption [7]. The hypertension influences the development of AMD increasing the risk especially when we stratified for females. The association between smoking and hypertension has not showed a synergistic interaction to increase this risk. Independently, each single factors as age, cigarette smoking, hypertension and alcohol consumption resulted associated with AMD in some, but not all studies [8]. A previous work found that obesity and cardiovascular disease were both risk factors for AMD, especially for the late stage disease [9]. In particular in our

study we found a synergistic interaction between obesity and ever smokers in the development of AMD and a significant synergistic interaction between obesity and alcohol intake. In addition, there was an indication for additivity between smoking condition and cardiovascular disease and a synergistic interaction with hypercholesterolemia, and between hypercholesterolemia and alcohol intake. As regards the synergistic interaction between alcohol intake and the status of ever smokers in our study, we found no additive effects and this is in contrast with other study that combined smoking/drinking by persons and with this pathological condition [10]. Identification of factors exacerbating AMD can facilitate development and adoption of effective preventative measures for this disease. So, the control of these risk factors, that are the same for the cardiovascular disease, can reduce the prevalence of early AMD. Therefore, the prevention of cardiovascular related disease risks (such as obesity, hypertension, hypercholesterolemia) and a regular eye examination are needed especially in middle-age and elderly persons.

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