

Association of alcohol consumption with total serum immunoglobulin E levels and allergic sensitization in an adult population-based survey

A. González-Quintela, F. Gude*, O. Boquete†, J. Rey†, L. M. Mejjide†, F. Suarez†, M. C. Fernández-Merino†, L. F. Pérez‡ and C. Vidal§

Departments of Internal Medicine and *Clinical Epidemiology, Complejo Hospitalario Universitario de Santiago, Santiago de Compostela, †Primary Care Unit, A-Estrada Pontevedra and Departments of ‡Biochemistry and §Allergy, Complejo Hospitalario Universitario de Santiago, Santiago de Compostela, Spain

Summary

Background Chronic alcoholism is associated with increased total serum IgE levels.

Objective The study aimed to investigate the relationship between alcohol intake and both total serum IgE levels and allergic sensitization in a general adult population.

Materials and methods A total of 720 subjects was randomly selected (stratified by age) from the population older than 18 years of A-Estrada (Spain) and invited to participate in the study. From 697 eligible subjects, 469 (67%, median age 54 years, range 18 to 92 years, 44% males, 75% of cases from a rural environment) agreed to participate. A battery of 13 skin prick tests to common aeroallergens was performed in all subjects. Cases with at least one positive test ($n = 121$, 26%) were considered to have allergic sensitization. The most frequent sensitizers were mites and pollens (24% and 10% of subjects, respectively). Total serum IgE was measured in 465 subjects (99%). Alcohol consumption was registered as the number of standard (approximately 10 g) drinking units habitually consumed per week. A total of 244 subjects (52%) were alcohol consumers (median intake, 14 units/week, range 1 to 147 units/week). Abstainers ($n = 225$, 48%) constituted the reference category.

Results Alcohol consumption of more than 14 units/week was associated with an increase in serum IgE levels after adjusting for age, gender, allergic sensitization and smoking ($P = 0.02$). Alcohol consumption was not significantly associated with either overall allergic sensitization or mite sensitization after adjusting for age, gender and smoking. However, alcohol consumption of more than 14 units/week was associated with an increased prevalence of pollen sensitization (adjusted OR 3.15, 95% CI 1.19 to 8.34, $P = 0.02$).

Conclusion Alcohol consumption above a certain threshold is associated with an increase in total serum IgE levels. Alcohol consumption may also be associated with an increased prevalence of pollen sensitization.

Keywords alcohol, allergic sensitization, atopy, ethanol, IgE, smoking

Submitted 27 May 2002; revised 13 September 2002; accepted 16 October 2002

Introduction

Total serum IgE levels and the predisposition to IgE-mediated (allergic) sensitization to common aeroallergens are under genetic control [1] but may be influenced by environmental factors. These factors may include cigarette smoking and alcohol consumption. Several studies have reported an association between smoking and an increase in total serum IgE levels [2–10]. However, smoking has been found to be associated with both a decreased incidence [11, 12] and a decreased prevalence [7, 13–15] of sensitization to common environmental allergens. The possible effect of smoking on allergic sensitization may vary depending on the allergen considered. In European studies, smoking is associated with a decreased risk of sensitization

to grass pollen [9, 13, 16], birch pollen [13] and cat [9, 16], but also with an increased risk of sensitization to house dust mites [9, 16].

Smoking is frequently linked to the consumption of alcohol [17], a powerful immunomodulatory drug [18]. Most previous studies that investigated the association of smoking with either serum IgE levels or allergic sensitization did not take into account the possible influence of concomitant alcohol consumption [2–14, 16]. A considerable amount of evidence indicates that chronic alcohol consumption is associated with increased serum IgE levels. Alcoholics have increased total serum IgE levels when compared with healthy controls [19–25]. Such an IgE increase is observed in both atopic and non-atopic cases [20, 24, 25]. In alcoholics, IgE levels decrease after alcohol abstinence [19, 20, 22]. Total serum IgE increase in alcoholics is unrelated to either hyperglobulinaemia (IgG, IgA or IgM increase) or liver dysfunction [21–23]. Moreover, normal or even low serum IgE values are observed in patients with non-alcoholic liver disease [21, 26, 27]. In mice,

Correspondence: A. González-Quintela, Department of Internal Medicine, Hospital Clínico Universitario c/Choupana sn, 15706 Santiago de Compostela, Spain. E-mail: mearturo@usc.es

experimental alcohol administration is followed by an early increase in total serum IgE levels [28]. Alcohol consumption in mothers during pregnancy is associated with an increase in cord blood IgE levels in their offspring [29]. Among patients studied in an allergy clinic, regular alcohol consumers of more than 70 g per week show higher total serum IgE levels than abstainers [30]. Moreover, *Dermatophagoides pteronyssinus*-specific serum IgE levels are higher in habitual alcohol consumers than in abstainers [30]. Furthermore, the prevalence of allergic sensitization may increase along with regular alcohol consumption [15].

The possible relationship of alcohol consumption and IgE responses may be relevant as both IgE-mediated diseases and alcohol intake are common in many communities. The present study was aimed at evaluating the relationship of alcohol consumption to total serum IgE levels and allergic sensitization in an adult population-based survey.

Subjects and methods

Study design and setting

This cross-sectional study was performed in the municipality of A-Estrada, in northern Spain. The municipality covers an area of 282 km² and had an adult population (18 years and older) of 19 346 when the study was begun. About a quarter of the population lives in the main village (A-Estrada, 43°40' N, 8°30' W), and the remainder live in a rural environment.

Subjects

An age-stratified random sample of the population 18 years and older was drawn from the National Health System Registry, which covers more than 95% of the population and contains the name, birth date and address of every person to be attended in primary care. The sample was stratified in age groups as follows: 18 to 29 years, 30 to 39 years, 40 to 49 years, 50 to 59 years, 60 to 69 years, 70 to 79 years, and 80 years and older. A computer program generated a random sample of equal numbers ($n=100$) of subjects in each age group, except for the first group (18 to 29 years), which comprised a larger age period than the other groups and included 120 subjects. These 720 individuals were invited to participate in the study by a personal letter. From this initial sample, those unable to give informed consent were considered ineligible to participate in the study. This included patients with dementia ($n=12$), mental retardation ($n=5$), cerebrovascular disease ($n=2$), terminal cancer ($n=3$), and an inability to communicate ($n=1$). From the remaining eligible 697, a total of 469 subjects agreed to participate in the study (overall participation rate, 67%). Participation was lower in the youngest and in the oldest age groups (Table 1). Median age of the sample studied was 54 years (range 18 to 92 years). Two hundred and six were males (44%) and 263 were females (56%). The mean participation rate was 66% for men and 68% for women. Most subjects lived in a rural environment (352 cases, 75%), and the remainder lived in the A-Estrada village. There were no significant differences in age, gender and residence (rural/urban) between subjects who agreed to participate in the study and those who did not. From February to December 2000, all subjects were successively convened for one day in the Primary Care Centre for evaluation, including:

Table 1. Participation rates in the study

Age group (year)	Source population (n)	Randomly selected (n)	Eligible for participation (n)	Participated in the study (n)	Participation rate (%)
18–29	3792	120	119	71	60
30–39	2842	100	100	61	61
40–49	2377	100	99	74	75
50–59	2594	100	96	77	80
60–69	2792	100	100	70	70
70–79	2297	100	95	69	73
> 80	1656	100	88	47	53
Total	18350	720	697	469	67

(a) an interviewer-administered structured questionnaire that included demographic data as well as the registration of alcohol consumption and smoking; (b) skin prick testing to a standard battery of aeroallergens; and (c) fasting venous blood sampling. A blood sample was not available in four cases (1%) for technical reasons. Sera were stored at -20°C until tested.

Alcohol consumption

Alcohol intake was registered in each subject by adding up the total number of standard drinking units (one bottle of beer, one glass of wine, or one unit of spirit, all of them approximately equivalent to 10 g of ethanol) habitually consumed per week. Alcohol consumption recorded in this way showed a significant correlation with serum gammaglutamyl-transpeptidase (sGGT, a surrogate marker of alcohol consumption) determined in an Olympus AU-400 analyser in the same subjects (Spearman's correlation coefficient 0.443, $P<0.001$). Among alcohol drinkers ($n=244$, 52%), median weekly alcohol consumption was 14 units (range one to 147 units/week). Among habitual alcohol drinkers, 215 (88%) consumed alcohol on a daily basis, and 29 (12%) were irregular consumers, mostly as weekend drinking. Subjects were classified according to alcohol intake into three groups as follows: (a) abstainers ($n=225$, 48%); (b) light drinkers (consumers of one to 14 units/week, median consumption seven units/week, $n=144$, 31%); and (c) heavy drinkers (consumers of more than 14 units/week, median consumption 28 units/week, $n=100$, 21%). Subjects who had stopped alcohol consumption during the last 12 months after years of alcohol use were still considered drinkers. Alcohol consumption was significantly linked to male gender. Eighty-eight (88%) drinkers of more than 14 units/week were males, compared with 56 (39%) drinkers of one to 14 units/week and 62 (28%) alcohol abstainers ($P<0.001$).

Smoking habit

Tobacco smoking was registered in each subject as the number of cigarettes regularly consumed per day. Among smokers (consumers of at least one cigarette per day, $n=100$, 21%), median cigarette consumption was 17 cigarettes/day (range one to 80 cigarettes/day). Subjects were classified according to smoking habit into three groups as follows: (a) non-smokers ($n=369$, 79%); (b) light smokers (consumers of one to nine cigarettes/day, median consumption four cigarettes/day, $n=21$, 4%); (c) and heavy smokers (consumers of more than nine cigarettes/day, median consumption 20 cigarettes/day,

$n = 69$, 17%). Subjects who had stopped smoking during the last 12 months after years of tobacco consumption were still considered smokers. Cigarette smoking was significantly linked to heavy alcohol drinking. Thirty-three (33%) drinkers of more than 14 units/week were smokers, compared with 25 (17%) drinkers of 1 to 14 units/week and 42 (19%) alcohol abstainers ($P = 0.01$).

Skin prick tests

All subjects underwent a battery of skin prick tests (SPT) to 13 aeroallergens commonly found in the studied area, including mites (*Dermatophagoides pteronyssinus*, *Lepidoglyphus destructor*, *Tyrophagus putrescentiae*), pollens (*Lolium perenne*, *Plantago lanceolata*, *Betula alba*, *Parietaria judaica*), moulds (*Alternaria alternata*, *Aspergillus* spp., *Penicillium notatum*, *Cladosporium herbarum*) and animal danders (dog and cat) (ALK-Abelló, Madrid, Spain). SPT were performed on the volar side of the lower arm by the same two nurses throughout the study. Weals greater than 3 mm after 15 min were judged positive [31]. Cases with at least one positive SPT were considered to have allergic sensitization.

Total serum IgE

Total serum IgE was determined by chemiluminescent enzyme immunoassay (Immulate, Diagnostic Products Corporation, Los Angeles, USA). Normal reference values for IgE are 0 to 170 IU/mL with this method.

Statistical analysis

Continuous variables are expressed as median and interquartile range. Categorical variables are expressed as absolute numbers and percentages, approximated to their entire values. Statistically significant differences between proportions were determined by the chi-square test (with linear by linear correction where appropriate). The Mann–Whitney and the Kruskal–Wallis tests were employed for comparison of continuous variables. Spearman's rank test was employed for evaluation of correlation between continuous variables. Linear regression analysis was employed to estimate the relationship between IgE and alcohol consumption. For that purpose, IgE values were transformed into their natural logarithm to meet the assumption of linearity between IgE and covariates. Graphical methods, including scatter and residual vs. predicted plots, were used to assess linearity and normality. Logistic regression analysis was employed to estimate the relationship between alcohol consumption and allergic sensitization. In regression models, age (in years) entered the equation as a continuous variable. The remaining variables were categorical and entered the equation as '1' ('present' or 'yes') or '0' ('absent' or 'no'). In regression models, alcohol abstainers and non-smokers were the reference categories for the analysis of the influence of alcohol intake and smoking, respectively. To account for the stratified sampling, a design-based analysis was performed and all regression models were weighted to give unbiased estimates. The sampling procedures used in the study departed from unequal probability selection. Compensatory weights were developed to obtain estimates from the original target population in the study area [32]. The Stata software (StataCorp, College Station, USA) was employed to compute appropriate standard

errors for the weighted analyses. Two-tailed P -values lower than 0.05 were considered statistically significant.

Ethical considerations

The study conformed to the principles of the Helsinki 1975 declaration, and was reviewed and approved by the local research committee.

Results

Total serum IgE levels

Total serum IgE levels in the sample studied ranged from 3.1 to 4312 IU/mL (median, 59 IU/mL). The distribution of total serum IgE values according to gender, age, allergic sensitization, smoking habit and alcohol consumption is represented in Table 2. Serum IgE levels were higher in males than in females and decreased with age. IgE levels were higher in cases with allergic sensitization than in cases without it. Smokers of more than nine cigarettes/day had the highest IgE levels when compared with other categories of tobacco consumption. Drinkers of more than 14 units/week had the highest IgE levels when compared with other categories of alcohol consumption (Table 2). Lighter alcohol drinkers had similar IgE values than abstainers. The relationship of alcohol intake with serum IgE levels was similar in patients with and without allergic sensitization, but it was statistically significant in only the non-allergic group (Table 3).

In order to further elucidate the influence of variables that could be associated with both alcohol consumption and serum IgE levels, a multivariate analysis was performed. Age, gender,

Table 2. Total serum IgE values according to gender, age, allergic sensitization, smoking habits and alcohol consumption

Factor	Total serum IgE (IU/mL)	P -value*
Gender		
Males ($n = 205$)	69.1 (27.6–165)	0.003
Females ($n = 260$)	49.6 (17.6–114)	
Age group		
18–29 years ($n = 70$)	94.6 (42.0–266)	0.01
30–39 years ($n = 61$)	63.8 (25.1–135)	
40–49 years ($n = 74$)	49.0 (22.3–124)	
50–59 years ($n = 76$)	53.5 (22.9–100)	
60–69 years ($n = 70$)	67.0 (20.7–148)	
70–79 years ($n = 67$)	42.4 (14.9–138)	
> 80 years ($n = 47$)	39.9 (17.6–88.2)	
Allergic sensitization		
Present ($n = 120$)	168 (79.2–401)	< 0.001
Absent ($n = 345$)	40.6 (17.1–85.1)	
Smoking habits		
Non-smokers ($n = 365$)	51.0 (19.5–122)	0.001
1–9 cigarettes/day ($n = 21$)	52.4 (24.8–255)	
> 9 cigarettes/day ($n = 79$)	86.8 (43.0–251)	
Alcohol intake		
Abstainers ($n = 222$)	51.9 (21.2–125)	0.02
1–14 units/week ($n = 143$)	50.9 (19.4–126)	
> 14 units/week ($n = 100$)	81.8 (28.3–201)	

Figures are median and interquartile range (25th–75th percentiles), within parentheses. *Mann–Whitney test or Kruskal–Wallis test.

Table 3. Total serum IgE levels according to allergic sensitization in the different categories of alcohol consumption

Allergic sensitization	Total serum IgE (IU/mL)			P-value*
	Alcohol abstainers	Alcohol drinkers (1–14 units/week)	Alcohol drinkers (> 14 units/week)	
Present	154 (72.7–295) (n = 61)	165 (78.1–469) (n = 37)	230 (102–633) (n = 22)	0.15
Absent	38.2 (15.6–84.8) (n = 161)	34.9 (14.9–70.7) (n = 106)	54.5 (24.4–119) (n = 78)	0.006

Figures are median and interquartile range (25th–75th percentiles), within parentheses. *Kruskal–Wallis test.

Table 4. Analysis of variables associated with total serum IgE levels

Factor	Coefficient (B)	SE(B)	P-value
Male sex	0.16	0.12	0.18
Age (years)	0.0004	0.002	0.88
Allergic sensitization	1.49	0.11	< 0.001
Smoking habits			
Non-smokers	(reference)		
1–9 cigarettes/day	0.04	0.24	0.84
> 9 cigarettes/day	0.32	0.14	0.03
Alcohol intake			
Abstainers	(reference)		
1–14 units/week	– 0.006	0.12	0.95
> 14 units/week	0.37	0.16	0.02

Linear regression analysis. Logarithmic transformation of serum IgE values was performed for analysis. All variables entered the equation. B = slope of the regression model; SE = standard error.

allergic sensitization, smoking and alcohol intake were introduced in the linear regression model. In this model, allergic sensitization seemed the main determinant for total serum IgE levels. Age and gender were not significantly associated with serum IgE levels. Both smoking more than nine cigarettes/day and alcohol drinking of more than 14 units/week were significantly associated with an increase in serum IgE levels after adjusting for all the remaining variables (Table 4). Interaction terms between alcohol intake and smoking were not significant.

Allergic sensitization

A total of 121 cases (26%) had at least one positive SPT. Mites were the most common sensitizing aeroallergens in the sample studied (110 cases, 24%), followed by pollens (48 cases, 10%), moulds (11 cases, 2%) and animal danders (six cases, 1%). The median number of positive SPT in allergic sensitized subjects was two (range one to eight).

The relationship of allergic sensitization (overall sensitization, mite sensitization and pollen sensitization) with age, gender, smoking habit and alcohol consumption is represented in Table 5. Age was the main determinant for allergic sensitization. Ageing was negatively associated with overall sensitization, mite sensitization and pollen sensitization. This association between age and allergic sensitizations persisted after adjusting for gender, smoking habit and alcohol consumption.

Smoking more than nine cigarettes per day was positively associated with overall sensitization, mite sensitization and pollen sensitization, but the association became not significant after adjusting for age, gender and alcohol consumption.

Alcohol intake was not significantly associated with overall sensitization. However, an alcohol intake higher than 14 units/week was positively associated with pollen sensitization after adjusting for age, gender and smoking habit. In contrast, such alcohol intake tended to be negatively associated with mite sensitization. This association approached statistical significance in univariate analysis ($P=0.05$), but became not significant after adjusting for age, gender and smoking habit ($P=0.13$).

Discussion

The present study in an adult general population confirms that habitual alcohol consumption above a certain threshold (14 drinking units per week, approximately equivalent to 140 g of ethanol per week) is associated with an increase in total serum IgE levels. Previous studies demonstrated that alcoholics admitted to the hospital have increased total serum IgE levels [19–24]. Fewer studies have focused on the influence of lower quantities of alcohol consumption on total serum IgE levels, and all of them were performed in selected populations. In a previous study, the authors observed that an alcohol consumption greater than seven units per week is associated with an increase in total serum IgE in patients studied in an allergy clinic [30]. Similarly, Criqui et al. found an association between alcohol consumption and elevated total serum IgE in patients studied in a lipid research clinic [33]. As previously reported, the association between alcohol consumption and total serum IgE is more significant in patients without allergic sensitization [30]. The predisposition to allergic sensitization (or atopy) is likely to be the major determinant for IgE increase, overshadowing the possible influence of additional factors. In addition, the number of subjects with allergic sensitization and high alcohol consumption was too small to demonstrate statistical significance.

The association of alcohol intake with an increase in IgE levels was maintained after adjusting for potential confounding factors such as gender, age and smoking. The possible interacting or confounding effect of smoking and alcohol consumption on IgE was specifically investigated because both factors are correlated in the population [17]. The effects of cigarette smoking on IgE levels have been extensively studied, but without adjusting for alcohol consumption [2–10]. In the present study, both alcohol consumption (of more than 14 units/week) and smoking (more than nine cigarettes per day) were independently associated with an increase in IgE levels after adjusting for age, gender and allergic sensitization. However, part of the

Table 5. Analysis of variables associated with allergic sensitization

	Overall sensitization†		Mite sensitization‡		Pollen sensitization§	
	Crude OR	Adjusted OR	Crude OR	Adjusted OR	Crude OR	Adjusted OR
Age (years)	0.96 (0.95–0.97)*	0.96 (0.95–0.97)*	0.96 (0.95–0.97)*	0.96 (0.95–0.97)*	0.96 (0.94–0.98)*	0.96 (0.94–0.98)*
Gender (male)	1.03 (0.68–1.58)	1.13 (0.69–1.87)	1.05 (0.68–1.62)	1.27 (0.76–2.13)	1.05 (0.57–1.94)	0.66 (0.30–1.47)
Smoking habits						
Non-smokers	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
1–9 cigarettes/day	1.63 (0.63–4.23)	0.85 (0.32–2.25)	1.86 (0.71–4.84)	0.96 (0.36–2.56)	1.75 (0.48–6.33)	1.04 (0.26–4.08)
> 9 cigarettes/day	1.88 (1.11–3.18)**	1.04 (0.58–1.87)	1.92 (1.12–3.28)**	1.10 (0.61–2.01)	2.40 (1.19–4.81)**	1.33 (0.65–2.68)
Alcohol intake						
Abstainers	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)	1 (reference)
1–14 units/week	0.93 (0.57–1.51)	1.08 (0.66–1.78)	0.99 (0.61–1.62)	1.15 (0.69–1.91)	1.20 (0.57–2.52)	1.51 (0.70–3.25)
> 14 units/week	0.70 (0.40–1.23)	0.79 (0.40–1.56)	0.54 (0.29–1.00)****	0.56 (0.27–1.18)	1.91 (0.92–3.94)	3.15 (1.19–8.34)***

Logistic regression analysis. Figures are odds ratios (OR) and 95% confidence intervals (within parentheses). For adjusted odds ratios, every variable was adjusted for all other listed variables. †Positive skin prick test against any of 13 allergens tested; ‡Positive skin prick test against any of the three mites tested; §Positive skin prick test against any of the four pollens tested; * $P < 0.001$; ** $P = 0.01$; *** $P = 0.02$; **** $P = 0.05$.

effects on serum IgE levels attributed to smoking may be due to concomitant alcohol consumption, which could act as a confounder.

The present study does not show a significant relationship between alcohol consumption and overall allergic sensitization as revealed by SPT. However, some association of alcohol consumption with allergic sensitization was present when subgroups of sensitization were analysed. This association was dual, with a trend towards a lower prevalence of mite sensitization in alcohol consumers of more than 14 units/week, and a significantly higher prevalence of pollen sensitization in such alcohol consumers, even after adjusting for age, gender and smoking. Interestingly, a similar (but inverse) dual association has been observed with smoking. In European studies, smoking was found to be associated with an increased risk of sensitization to mites [9, 16], but with a decreased risk of sensitization to pollens [9, 13, 16] and animal dander [9, 16]. To our knowledge, only one previous study investigated the relationship between alcohol consumption and allergic sensitization [15]. In a cross-sectional study in Copenhagen, Linneberg et al. reported an association between alcohol consumption and overall SPT positivity against a battery of allergens. In that report, the rates of specific sensitizations were not given, but the 'symptom group' of patients (which included the vast majority of cases with positive SPT) was obtained from subjects who reported nasal or bronchial symptoms upon exposure to either pollen or furry animals [15]. If the prevalence of pollen sensitization in the Copenhagen study was high, as expected, their findings would be in keeping with the increased prevalence of pollen sensitization in alcohol consumers observed by the authors.

The mechanisms for the alcohol effect on IgE responses are not entirely known. The IgE system is very sensitive to environmental immunomodulatory factors. It is therefore not surprising that IgE responses can be influenced by the consumption of alcohol, a drug with significant immunomodulatory actions [18]. Alcohol consumption induces profound changes in the production of cytokines involved in IgE synthesis [23, 24, 28, 34]. In addition, alcohol intake promotes lipopolysaccharide (endotoxin) absorption from the gut [35]. Lipopolysaccharide is responsible for most immunological alterations after

alcohol abuse [34] and can, under some circumstances, increase IgE synthesis [36].

Methodological issues of the present study should be taken into account. Some of them are inherent in study design. In cross-sectional studies, exposure to relevant factors may have occurred years beforehand. This may be more important for allergic sensitization than for total serum IgE levels, given the short half-life of this immunoglobulin. A low participation rate may be a limitation in this kind of study, but in this case it was satisfactory (67%). The presence of allergic disease could favour the participation of affected subjects, but the observed overall rate of SPT positivity was similar to that reported in other Spanish studies [37]. The presence of disease may also lead to changes in lifestyle, so that a negative association with an environmental factor may be a consequence rather than a protective factor for the disease. It is unlikely, however, that this had occurred with alcohol consumption and it would not explain the positive relationship observed between alcohol consumption and either allergic sensitization or total serum IgE increase. SPT were employed for assessment of allergic sensitization following the recommendations for epidemiological studies [31]. It is unlikely that the association between alcohol intake and allergic sensitization was due to an unspecific effect of alcohol on skin reactivity, as alcohol intake was found to be associated with either an increased or decreased rate of SPT positivity depending on the group of allergens considered. Seasonal IgE variability in patients with pollen allergy [38] could not be considered because the sensitization profile was unknown prior to blood extraction for IgE assay according to the study design. Finally, it should be noted that the study was performed in a predominantly rural environment, a factor that can protect from adulthood allergy [39].

Additional issues are related to the difficulties in the assessment of alcohol consumption. The proportion of habitual alcohol consumers was entirely similar to that of the general Spanish population [40]. The system of self-reported standard drinking units is widely applied to quantify alcohol consumption and to provide comparable data [41, 42]. The type of drink consumed was not analysed separately in the present study. In societies such as Spain, where wine is the most common alcoholic beverage, the system of standard drinking units can underestimate

the alcohol content in units of spirits [42]. Serum GGT, a surrogate marker of alcohol consumption, showed a significant correlation with the number of standard drinking units consumed per week, confirming a degree of validity in the method. In order to minimize variation (both interviewer-variation and individual daily variation) alcohol intake was stratified in categories.

In conclusion, habitual consumption of alcoholic beverages is associated with significant immunomodulation affecting the IgE system. The increase in serum IgE levels in consumers of more than 14 units of alcoholic beverages per week is consistent with previous reports. The association of such alcohol consumption with allergic sensitization should be interpreted with caution, however, due to the paucity of similar previous reports, and the risk of mass significance in analyses of subgroups. The effects of alcohol consumption on IgE responses are probably small, but they acquire significance when the high prevalence of alcohol consumption in many societies is considered. Analyses of the influence of environmental factors on IgE levels or allergic sensitization should be adjusted for alcohol intake. Longitudinal studies that aim to evaluate the risk of allergic sensitization after alcohol consumption are warranted. Further studies are also needed to ascertain the molecular mechanisms of the influence of alcohol consumption in this aspect of the immune response.

Acknowledgement

The study was supported by a grant from the Fondo de Investigaciones Sanitarias of the Spanish Ministry of Health (number 1306/99).

References

- Freijen M, Gerritsen J, Postma DS. Genetics of allergic disease. *Br Med Bull* 2000; 56:894–907.
- Gerrard JW, Heiner DC, Ko CG, Mink J, Meyers A, Dosman JA. Immunoglobulin levels in smokers and non-smokers. *Ann Allergy* 1980; 44:261–2.
- Burrows AB, Halonen M, Barbee RA, Lebonitz M. The relationship of serum immunoglobulin E to cigarette smoking. *Am Rev Res Dis* 1981; 123:523–5.
- Zetterström O, Osterman K, Machado L, Johansson SGO. Another smoking hazard: raised serum IgE concentration and increased risk of occupational allergy. *Br Med J* 1981; 283:1215–7.
- Warren CPW, Holford-Strevens V, Wong C, Manfreda J. The relationship between smoking and total immunoglobulin E levels. *J Allergy Clin Immunol* 1982; 69:370–5.
- Bahna SL, Heiner DC, Myhre BA. Immunoglobulin E pattern in cigarette smokers. *Allergy* 1983; 38:57–64.
- Wuthrich B, Schindler C, Medici TC, Zellweger JP, Leuenberger P. IgE levels, atopy markers and hay fever in relation to age, sex and smoking status in a normal adult Swiss population. SAPALDIA (Swiss Study on Air Pollution and Lung Diseases in Adults) team. *Int Arch Allergy Immunol* 1996; 111:396–402.
- Sapigni T, Biavati P, Simoni M et al. The Po River Delta respiratory epidemiological survey: an analysis of factors related to level of total serum IgE. *Eur Respir J* 1998; 11:278–83.
- Jarvis D, Chinn S, Luczynska C, Burney P. The association of smoking with sensitisation to common environmental allergens: results from the European Community Respiratory Health Survey. *J Allergy Clin Immunol* 1999; 104:934–40.
- Court CS, Cook DG, Strachan DP. The descriptive epidemiology of house dust mite-specific and total immunoglobulin E in England using a nationally representative sample. *Clin Exp Allergy* 2002; 32:1033–41.
- Barbee RA, Kaltenborn W, Lebowitz MD, Burrows B. Longitudinal changes in allergen skin test reactivity in a community population sample. *J Allergy Clin Immunol* 1987; 79:16–24.
- Linneberg A, Nielsen NH, Madsen F, Frolund L, Dirksen A, Jorgensen T. Smoking and the development of allergic sensitization to aeroallergens in adults: a prospective population-based study. The Copenhagen Allergy Study. *Allergy* 2001; 56:328–32.
- Omenaas E, Bakke P, Elsayed S, Hanoa R, Gulsvik A. Total and specific IgE levels in adults: relationship to sex, age, and environmental factors. *Clin Exp Allergy* 1994; 24:530–9.
- Baldacci S, Modena P, Carrozzi L et al. Skin prick test reactivity to common aeroallergens in relation to total IgE, respiratory symptoms, and smoking in a general population sample of northern Italy. *Allergy* 1996; 51:149–56.
- Linneberg A, Nielsen NH, Madsen F, Frolund L, Dirksen A, Jorgensen T. Factors related to allergic sensitisation to aeroallergens in a cross-sectional study in adults. The Copenhagen Allergy Study. *Clin Exp Allergy* 2001; 31:1409–17.
- Jarvis D, Luczynska C, Chinn S, Burney P. The association of age, gender and smoking with total IgE and specific IgE. *Clin Exp Allergy* 1995; 25:1083–91.
- Zacny JP. Behavioral aspects of alcohol–tobacco interactions. *Recent Dev Alcohol* 1990; 8:205–19.
- Szabo G. Consequences of alcohol consumption on host defence. *Alcohol* 1999; 34:830–41.
- Smith WI, van Thiel DH, Whiteside T et al. Altered immunity in male patients with alcoholic liver disease: evidence for defective immune regulation. *Alcohol Clin Exp Res* 1980; 4:199–206.
- Hällgren R, Lundin L. Increased total serum IgE in alcoholics. *Acta Med Scand* 1983; 213:99–103.
- Vidal C, González-Quintela A, Millan I, Gude F, Cuervas-Mons V. Serum IgE in liver cirrhosis: contrasting results in alcoholic and non-alcoholic patients. *Clin Exp Allergy* 1994; 24:540–8.
- González-Quintela A, Vidal C, Gude F et al. Increased serum IgE in alcohol abusers. *Clin Exp Allergy* 1995; 25:756–64.
- González-Quintela A, Vidal C, Lojo S et al. Serum cytokines and increased total serum IgE in alcoholics. *Ann Allergy Asthma Immunol* 1999; 83:61–7.
- Domínguez-Santalla MJ, Vidal C, Viñuela J, Pérez LF, González-Quintela A. Increased serum IgE in alcoholics: relationship with Th1/Th2 cytokine production by stimulated blood mononuclear cells. *Alcohol Clin Exp Res* 2001; 25:1198–205.
- González-Quintela A, Domínguez-Santalla MJ, Pérez LF, Lojo S, Vidal C. Serum levels of soluble CD30 and total IgE in alcoholics. *Allergol Int* 2002; 51:33–7.
- Minuk GY, Boyd ND, Matheson DS, Fritzler MJ, Green BJ. Serum immunoglobulin E levels in patients with primary biliary cirrhosis. *J Allergy Clin Immunol* 1989; 83:462–6.
- González-Quintela A, Alende MR, Lojo S et al. Total serum IgE in chronic hepatitis C. Influence of interferon-alpha therapy. *Int Arch Allergy Immunol* 2001; 125:176–81.
- Starkenburger S, Munroe ME, Waltenbaugh C. Early alteration in leukocyte populations, and Th1/Th2 function in ethanol-consuming mice. *Alcohol Clin Exp Res* 2001; 25:1221–30.
- Bjerke T, Hedegaard M, Henriksen TB, Nielsen BW, Schiotz PO. Several genetic and environmental factors influence cord blood IgE concentration. *Pediatr Allergy Immunol* 1994; 5:88–94.
- Vidal C, Armisen M, Domínguez-Santalla MJ, Lojo S, González-Quintela A. Influence of alcohol consumption on total and specific serum IgE levels in atopic and non-atopic adults. *Alcohol Clin Exp Res* 2002; 26:59–64.

- 31 Haahtela T. Skin tests used for epidemiological studies. *Allergy* 1993; 48 (Suppl.):76–80.
- 32 Levy PS, Lemeshow S. *Sampling of Populations: methods and Applications*, 3rd edn. New York: John Wiley & Sons, 1999.
- 33 Criqui M, Seibles JA, Hamburger RN, Coughlin SS, Gabriel S. Epidemiology of immunoglobulin E levels in a defined population. *Ann Allergy* 1990; 64:308–13.
- 34 McClain CJ, Barve S, Deaciuc I, Kugelmas M, Hill D. Cytokines and alcoholic liver disease. *Semin Liver Dis* 1999; 19:205–19.
- 35 Bode C, Kugler V, Bode JC. Endotoxemia in patients with alcoholic and non-alcoholic cirrhosis and in subjects with no evidence of chronic liver disease following acute alcohol excess. *J Hepatol* 1987; 4:8–14.
- 36 Vercelli D, Baldini M, Martinez F. The monocyte/IgE connection: may polymorphisms in the CD14 gene teach us about IgE regulation? *Int Arch Allergy Immunol* 2001; 124:20–4.
- 37 Cortés X, Soriano JB, Sanchez-Ramos JL, Azofra J, Almar E, Ramos J. European study of asthma. Prevalence of atopy in young adults of 5 areas in Spain. *Med Clin (Barc)* 1998; 111:573–7.
- 38 Moller C, Elsayed S. Seasonal variation of the conjunctival provocation test, total and specific IgE in children with birch pollen allergy. *Int Arch Allergy Appl Immunol* 1990; 92:306–8.
- 39 Kauffmann F, Oryszczyn MP, Maccario J. The protective role of country living on skin prick tests, immunoglobulin E and asthma in adults from the Epidemiological Study on the Genetics and Environment of Asthma, Bronchial Hyper-responsiveness and Atopy. *Clin Exp Allergy* 2002; 32:379–86.
- 40 Ministerio de Sanidad y Consumo. *Encuesta Nacional de Salud de España*. Madrid: Centro de Publicaciones del Ministerio de Sanidad y Consumo, 1997.
- 41 Lemmens PH. The alcohol content of self-report and 'standard' drinks. *Addiction* 1994; 89:593–601.
- 42 Gual A, Martos AR, Lligona A, Llopis JJ. Does the concept of a standard drink apply to viticultural societies? *Alcohol* 1999; 34:153–60.