

Association between alcohol consumption and skin prick test reactivity to aeroallergens

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Background: A few studies have indicated a positive association between consumption of alcohol and allergic sensitization in age and socioeconomically heterogeneous populations.

Objective: To investigate the association between consumption of alcohol and allergic sensitization in a young homogenous population of high social class (a group with a suspected high prevalence of sensitization).

Methods: A total of 1,668 students aged 18 to 35 years recruited from universities in Copenhagen, Denmark, underwent skin prick testing (SPT) in October or November 2002 and completed a questionnaire about respiratory disease and lifestyle habits, including alcohol consumption. SPT positivity was defined as a positive reaction (≥ 3 mm) against at least 1 of 10 common inhalant allergens.

Results: Before and after adjustment for sex, age, smoking, atopic predisposition, and pet keeping, no significant association was found between alcohol consumption (including type of beverage) and SPT positivity. Increasing alcohol consumption was significantly negatively associated with asthma symptoms and hay fever symptoms.

Conclusions: Alcohol consumption does not favor SPT positivity, but cumulated effects were not addressed in the present study. Individuals with asthma or hay fever symptoms seem to reduce alcohol intake (a healthy drinkers' effect).

Ann Allergy Asthma Immunol. 2007;98:70–74.

INTRODUCTION

Alcohol consumption has been linked to an increased prevalence of IgE sensitization.^{1–4} Increasing alcohol consumption is known to increase total IgE levels, the ethanol metabolite acetaldehyde has a direct histamine-releasing effect,⁵ and alcohol is a common trigger of exacerbations in asthmatic white patients⁶ and flushing syndrome in Asian individuals.⁵ Yet the impact of alcohol use on specific IgE synthesis is still controversial, because the available studies present contradictory data on the amount of alcohol needed for an increased risk of sensitization; furthermore, no study demonstrated an association with sensitization in both skin (skin prick testing [SPT]) and serum (specific IgE).^{1–4} The 4 available studies are based on 2 populations, which share heterogeneity concerning age and socioeconomic class, factors related to both prevalence and incidence of sensitization, and magnitude of daily and cumulated alcohol consumption.^{7–9} We aimed to investigate the impact of alcohol consumption on the prevalence of skin sensitization to common aeroallergens in young university students, a relatively homogeneous population at supposed high risk for IgE sensitization.¹⁰

METHODS

Participants

Students aged 18 to 35 years from the universities in the area of Copenhagen, Denmark, underwent SPT in October or

November 2002. On location, our SPT facility was strategically situated near lecture halls or large canteens. Passers-by were asked to participate and complete a questionnaire. All participants were informed that the aim of the survey was to study the pathogenesis of allergic disorders. The local ethics committee of Copenhagen approved the study.

Skin Prick Testing

Two technicians (K.A. and a study nurse) performed the SPT, using 1-mm lancets (AB Nordic Medifield Services, Täby, Sweden) and 10 standardized, commercially available aqueous aeroallergen solutions: pollens (birch, grass, mugwort), dander (horse, dog, cat), mites (*Dermatophagoides pteronyssinus* and *Dermatophagoides farinii*), and molds (*Alternaria alternaria*, *Cladosporium herbarum*) (Soluprick, ALK-Abellø, Hørsholm, Denmark).¹¹ According to international guidelines, SPT was performed in duplicate on the volar side of the antebrachium, and the results read after 15 minutes. Positivity was defined as a mean wheal diameter of 3 mm or larger. The results were transferred to data collection sheets using a fine-point felt-tip pen and translucent tape. Absent reaction to the positive control (histamine dihydrochloride, 10 mg/mL) and present reaction to the negative control (diluent solution) were considered abnormal. SPT positivity was defined as a positive SPT reaction to at least 1 allergen. Both SPT performers fulfilled the department's internal reproducibility standard of SPT with histamine dihydrochloride: a coefficient of variation less than 33%.¹¹

Symptoms

The questionnaire was a shortened version of a previously validated questionnaire.¹² Hay fever (asthma) symptoms were defined as an affirmative answer to the question, "Have you

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Received for publication June 23, 2006.

Accepted for publication in revised form September 19, 2006.

within this year or in previous years experienced red, itchy, or running eyes and/or itchy or running nose (wheezing, strenuous breathing, or dry cough) when near trees, grass, flowers, furry animals, or house dust (cleaning rooms, making beds, when in bed) or when in moist rooms?"

Alcohol Consumption

Participants answered the question, "How much beer (bottles per week), wine (glasses per week), and spirits (glasses per week) have you consumed within the last 12 months?" Alcohol consumption was defined as total number of drinks per week or as type of beverage (beer, wine, and spirits) on average during the last 12 months, presented as a categorical variable (Table 1).¹³

Other Variables

Participants reported the following explanatory variables (Table 1): sex, age, family history of atopy (at least one first-degree relative with symptoms of atopic dermatitis, hay fever, and/or asthma), smoking status (never, previous, or current smoker), and pet status (never, past, or currently pets in the home), all being previously associated with sensitization.¹⁴

Statistical Analyses

Only participants without abnormal SPT reactions to the positive or negative control and with complete questionnaires were included in the data analyses. These analyses were

performed with SPSS statistical software, version 11.0 (SPSS Inc, Chicago, IL) using the χ^2 test or Mann-Whitney *U* test for differences between groups. The independent effect of alcohol consumption on the prevalence of SPT positivity (dependent variable) was estimated by multivariable logistic regression analysis implementing the variables listed herein, and 95% confidence intervals were used. Statistical significance was reached at $P < .05$.

RESULTS

In total, 1,668 volunteering individuals (61% female) aged 18 to 35 years were enrolled in the study. Approximately 58,000 students (56% female) were attached to the universities in the Copenhagen area in 2002, but we have no relevant data on these nonattenders. Table 1 indicates that SPT positivity was positively associated with male sex, increasing age, atopic predisposition, and absent history of pet ownership (Table 1). Concerning alcohol consumption patterns, men consumed significantly more alcohol per week than women did (median, 9 vs 4 units; range, 0–53 units vs 0–30 units; $P < .001$; Mann-Whitney *U* test) and were more often high consumers (>10.6 units per week, the highest category; Table 1; 42% male vs 11% female; $P < .001$; χ^2 test).

Table 1 indicates that alcohol consumption was insignificantly associated with SPT positivity ($P = .18$). In additional

Table 1. The Relationship Between Skin Prick Test Reactivity and Demographic or Lifestyle Factors in 1,668 Danish University Students

Factor	Prevalence, % (No./total No.)	Crude odds ratio (95% CI)	P value	Adjusted odds ratio* (95% CI)	P value
Total	45.4 (758/1,668)				
Sex			.005		.006
Women	39.3 (398/1,013)	1.0		1.0	
Men	55.0 (360/655)	2.0 (1.6–2.4)		2.0 (1.6–2.5)	
Age, y			.009†		.008†
18–23	41.3 (286/692)	1.0		1.0	
24–29	47.9 (380/794)	1.3 (1.1–1.6)		1.38 (1.1–1.7)	
30–35	50.5 (92/182)	1.45 (1.1–2.0)		1.50 (1.1–2.1)	
Family history of atopy					.005
Not present	36.2 (311/860)	1.0	.005	1.0	
Present	55.3 (447/808)	2.19 (1.8–2.7)		2.23 (1.8–2.7)	
Alcohol consumption, units/wk			.62†		.18†
0.0–1.0	45.9 (112/244)	1.0		1.0	
1.1–4.5	44.4 (211/475)	0.94 (0.69–1.3)		0.98 (0.71–1.3)	
4.6–10.5	44.7 (250/559)	0.95 (0.71–1.3)		0.90 (0.65–1.3)	
10.6–60.0	47.4 (185/390)	1.07 (0.77–1.5)		0.80 (0.56–1.2)	
Smoking status			.86†		.81†
Never smoker	45.6 (533/1170)	1.0		1.0	
Past smoker	45.6 (88/193)	1.00 (0.74–1.4)		1.1 (0.77–1.5)	
Current smoker	44.9 (137/305)	0.98 (0.76–1.3)		0.97 (0.74–1.3)	
Furry animals in household			<.001†		<.001†
Never	59.5 (173/291)	1.0		1.0	
Past	45.7 (463/1,014)	0.57 (0.44–0.75)		0.64 (0.48–0.84)	
Current	33.6 (122/363)	0.35 (0.25–0.48)		0.42 (0.30–0.59)	

Abbreviation: CI, confidence interval.

* Adjusted for all other variables present.

† Test for trend.

subgroup analyses, type of beverage (beer, wine, spirits) was insignificantly associated with SPT positivity, as was alcohol consumption and SPT sensitization pattern (pollens, animal dander, house dust mites, molds) (data not shown). Table 2 indicates that increasing alcohol consumption was inversely related to reporting hay fever symptoms and asthma symptoms. Additionally, 705 individuals visited our mobile SPT facility but were excluded from data analyses; absent data on alcohol consumption habits (n = 453) was the most frequent cause (Table 3). Alcohol nonresponders differed from responders in several parameters (Table 3), most importantly in having a significantly lower prevalence of SPT positivity (38% vs 44%) and a lower atopic predisposition (older age, rarer family history of atopy, and more pet keeping).

DISCUSSION

Our study suggests that alcohol consumption is not positively related to either pollen or overall SPT positivity as previously suggested.^{2,3} The strengths of our study are the sample size and homogeneity. Of the comparable studies, ours presents the largest population with the narrowest span of age and social class: university students aged 18 to 35 years.¹ Half of the previous studies did not consider the impact of social differences in their conclusions^{1,2}; only Linneberg et al^{3,4} adjusted for social class. The relatively young age of the study participants makes it unlikely that any observed impact is a cumulated long-term effect. Furthermore, in the included population, we reproduced well-established risk factors for sensitization: male sex, atopic predisposition, and absence of pet keeping (healthy pet keeper's effect).^{3,14,15} Interestingly, we observed that age was positively and not inversely associated with sensitization, which could be due to the overall young age (<35 years) of our sample, all belonging to the cohort born after the early 1960s, a cohort characterized by an increased prevalence of allergy.¹⁶

A drawback of the study is the absence of objective measures for alcohol consumption (eg, γ -glutamyl-transferase or other alcoholism parameters), yet Gonzalez-Quintela et al² noted a correlation coefficient to self-reported data of only 0.44. We used a shortened form of the questionnaire devel-

oped and used by Linneberg et al^{3,4} and noted that the agreement between alcohol consumption reported in a dietary interview and by the traditional mean units per week was found satisfactory in other reports.^{13,17}

The existing evidence on the relationship between alcohol and IgE sensitization is based on 4 studies⁵: 3 cross-sectional studies (all with positive associations), one studied individuals with more than 7 units of alcohol per week and increased specific IgE to mite (but not grass pollen),¹ one studied individuals with more than 14 units of alcohol per week and increased SPT positivity to pollens (but not mite),² and one studied individuals with increasing alcohol (mainly wine) consumption and aeroallergen SPT positivity (but not specific IgE),³ and 1 follow-up study, which indicated a *trend* of increasing alcohol consumption and aeroallergen SPT positivity but not specific IgE.⁴ In our opinion, the heterogeneity of the conclusions suggests that alcohol's possible impact on the IgE sensitization pattern is of minor importance compared with that imposed by other variables (eg, atopic predisposition, sex, aeroallergen exposure, Table 1). Alcohol consumption increases serum total IgE and in a few reports also specific IgE, yet the functionality of the increased IgE levels has not been ascertained.⁵ Our cross-sectional study cannot provide any conclusion but suggests that no clear evidence exists for a positive relationship between alcohol consumption and respiratory symptoms in sensitized individuals (Table 2). Because alcohol is a well-established trigger of asthma in white individuals, one can speculate that the observed negative association is a healthy-drinker effect: having respiratory symptoms changes the behavior toward lower alcohol consumption to avoid alcohol-elicited symptoms.^{18,19} The ethanol metabolite acetaldehyde has a histamine-releasing effect on mast cells and could theoretically increase mast cell positivity to unspecific stimuli,^{5,20} but it remains to be shown that reduction in alcohol consumption reduces SPT positivity. It also remains to be elucidated whether the cumulated rather than the actual alcohol intake increases the risk of IgE sensitization; however, this theory was not supported in a cross-sectional study in patients with alcohol-induced hepatic cirrhosis²¹ or during 8 years of follow-up.⁴ Theoretically, the

Table 2. Relationship Between Alcohol Consumption and Prevalence of Asthma and Hay Fever Symptoms

Alcohol consumption	Asthma symptoms		Hay fever symptoms	
	Prevalence, % (No./total No.)	Odds ratio* (95% CI)	Prevalence, % (No./total No.)	Odds ratio* (95% CI)
Total	16.4 (274/1,668)		53.1 (885/1,668)	
Alcohol consumption, units/wk†				
0–1.0	15.7 (43/274)	1.0	15.7 (139/885)	1.0
1.1–4.5	31.4 (86/274)	1.10 (0.72–1.7)	28.8 (255/885)	0.93 (0.67–1.3)
4.6–10.5	34.3 (94/274)	0.95 (0.63–1.5)	34.1 (302/885)	0.90 (0.65–1.3)
10.6–60.0	18.6 (51/274)	0.64 (0.40–1.1)	21.4 (189/885)	0.63 (0.44–0.90)

Abbreviation: CI, confidence interval.

* Adjusted for variables listed in Table 1 except alcohol consumption.

† Test for trend *P* values are <.05 for asthma symptoms (SPT positive: .06; SPT negative: .71) and <.02 for hay fever symptoms (SPT positive: .84; SPT negative: .71).

Table 3. Differences in Explanatory Variables Between Included and Excluded University Students

Variable	Prevalence, % (No./total No.)		P value*
	Included (n = 1,668)	Excluded (n = 705)	
Causes of exclusion			
Palpable negative SPT result control	0	5.7 (40/705)	
Missing data, alcohol habits	0	64.3 (453/705)	
Missing data, other variables	0	30.0 (212/705)	
SPT reactivity	44.5 (805/1,668)	38.2 (173/453)	.008
Female	60.7 (1,013/1,668)	57.4 (260/453)	.19
Age, y			
18–23	41.5 (692/1,668)	36.6 (166/453)	.04†
24–29	47.6 (794/1,668)	48.5 (220/453)	
30–35	10.9 (182/1,668)	14.8 (67/453)	
Family history of atopy	48.4 (808/1,668)	39.1 (177/453)	<.001
Smoking status			
Never	70.1 (1170/1,668)	65.3 (296/453)	.10†
Past	11.6 (193/1,668)	12.6 (57/453)	
Current	18.3 (305/1,668)	22.1 (100/453)	
Furry animals in household			
Never	17.4 (291/1,668)	26.1 (118/453)	<.001†
Past	60.8 (1014/1,668)	57.4 (260/453)	
Current	21.8 (363/1,668)	16.6 (75/453)	
Alcohol consumption, units/wk			
0.0–1.0	14.6 (244/1,668)	NA	
1.1–4.5	28.5 (475/1,668)	NA	
4.6–10.5	33.5 (559/1,668)	NA	
10.6–60.0	23.4 (390/1,668)	NA	

Abbreviations: NA, not applicable (data missing); SPT, skin prick test.

* Comparisons (χ^2 test) between included participants and excluded alcohol noninformers.

† Test for trend.

observed association could be a co-phenomenon of other unmeasured lifestyle factors associated with alcohol consumption (eg, outdoor living, physical activity, nutrition^{7,22}); however, this awaits investigation.

We hardly know anything of most of the potential participants, a fate that our study shares with most other studies. However, the 453 alcohol noninformers were significantly less often skin sensitized (Table 3). This finding could be explained by a lower atopic burden (age, family history, pet keeping), but the most obvious cause for not reporting alcohol habits is extensive use or abuse (questionnaires were personal but rarely completed in solitude because of crowding at the SPT facility).^{17,23} Assuming a high alcohol consumption among alcohol noninformers does not change our conclusion because of the lower prevalence of SPT positivity in this group.

Our conclusion is affected by no or low alcohol consumption among alcohol nonresponders. Reluctance to report even a minor alcohol intake could theoretically be due to a cultural or religious alcohol ban, a rare scenario for inborn Danes. In Danish universities, the most dominant minority is second-generation Middle Eastern immigrants. However, an epidemiologic study has recently shown that this group has a higher prevalence of SPT positivity than inborn Northern

Europeans.²⁴ This assumption does not fit the observed lower prevalence of SPT positivity, but if accepted, our findings suggest that a possible impact of alcohol is counteracted extensively by well-known risk factors for sensitization.²²

In conclusion, our data suggest that alcohol consumption imposes a minor, if any, impact on skin sensitization in young, white university students. We plan to conduct a prospective study of individuals at supposed risk (ie, heavy drinkers with preserved hepatic and bone marrow and thus immunologic function) to ascertain the cumulated risk of alcohol consumption on IgE sensitization.

ACKNOWLEDGMENTS

We thank study nurses Anna Durst-Andersen, Birgit Sørensen, and Rita Beier for their exquisite assistance.

REFERENCES

1. Vidal C, Armisen M, Dominguez-Santalla MJ, et al. Influence of alcohol consumption on serum immunoglobulin E levels in atopic and nonatopic adults. *Alcohol Clin Exp Res*. 2002;26:59–64.
2. Gonzalez-Quintela A, Gude F, Boquete O, et al. Association of alcohol consumption with total serum immunoglobulin E levels and allergic sensitization in an adult population-based survey.

- Clin Exp Allergy*. 2003;33:199–205.
3. Linneberg A, Nielsen NH, Madsen F, et al. Factors related to allergic sensitization to aeroallergens in a cross-sectional study in adults: The Copenhagen Allergy Study. *Clin Exp Allergy*. 2001;31:1409–1417.
 4. Linneberg A, Petersen J, Nielsen NH, et al. The relationship of alcohol consumption to total immunoglobulin E and the development of immunoglobulin E sensitization: the Copenhagen Allergy Study. *Clin Exp Allergy*. 2003;33:192–198.
 5. Gonzalez-Quintela A, Vidal C, Gude F. Alcohol, IgE and allergy. *Addict Biol*. 2004;9:195–204.
 6. Vally H, de Klerk N, Thompson PJ. Alcoholic drinks: important triggers for asthma. *J Allergy Clin Immunol*. 2000;105:462–467.
 7. Suter PM. Alcohol, nutrition and health maintenance: selected aspects. *Proc Nutr Soc*. 2004;63:81–88.
 8. Schafer T, Ruhdorfer S, Weigl L, et al. School education and allergic sensitization in adults. *Allergy*. 2001;56:1206–1210.
 9. Osler M, Jorgensen T, Davidsen M, et al. Socioeconomic status and trends in alcohol drinking in the Danish MONICA population, 1982–92. *Scand J Public Health*. 2001;29:40–43.
 10. Bergmann RL, Edenharter G, Bergmann KE, et al. Socioeconomic status is a risk factor for allergy in parents but not in their children. *Clin Exp Allergy*. 2000;30:1740–1745.
 11. Bodtger U, Jacobsen CR, Poulsen LK, et al. Long-term repeatability of the skin prick test is high when supported by history or allergen-sensitivity tests: a prospective clinical study. *Allergy*. 2003;58:1180–1186.
 12. Linneberg A, Jorgensen T, Nielsen NH, et al. The prevalence of skin-test-positive allergic rhinitis in Danish adults: two cross-sectional surveys 8 years apart: The Copenhagen Allergy Study. *Allergy*. 2000;55:767–772.
 13. Gronbaek M, Heitmann BL. Validity of self-reported intakes of wine, beer and spirits in population studies. *Eur J Clin Nutr*. 1996;50:487–490.
 14. Bornehag CG, Sundell J, Hagerhed L, et al. Pet-keeping in early childhood and airway, nose and skin symptoms later in life. *Allergy*. 2003;58:939–944.
 15. Boulet LP, Turcotte H, Laprise C, et al. Comparative degree and type of sensitization to common indoor and outdoor allergens in subjects with allergic rhinitis and/or asthma. *Clin Exp Allergy*. 1997;27:52–59.
 16. Linneberg A, Nielsen NH, Madsen F, et al. Is the increase in allergic respiratory disease caused by a cohort effect? *Clin Exp Allergy*. 2002;32:1702–1705.
 17. Rockett IR, Putnam SL, Jia H, et al. Declared and undeclared substance use among emergency department patients: a population-based study. *Addiction*. 2006;101:706–712.
 18. Vally H, Thompson PJ. Alcoholic drink consumption: a role in the development of allergic disease? *Clin Exp Allergy*. 2003;33:156–158.
 19. Druce HM. Allergic and non-allergic rhinitis. In: Middleton E JR, Reed CE, Ellis EF, Adkinson NF Jr, Yunginger JW, Busse WW, eds. *Allergy: Principles & Practice*. St Louis, MO: Mosby-Year Book Inc; 1998:1005–1016.
 20. Shimoda T, Kohno S, Takao A, et al. Investigation of the mechanism of alcohol-induced bronchial asthma. *J Allergy Clin Immunol*. 1996;97:74–84.
 21. Vidal C, Quintela AG, Millan I, et al. Serum IgE levels in liver cirrhosis: contrasting results in alcoholic and non-alcoholic patients. *Clin Exp Allergy*. 1994;24:540–548.
 22. O'Connell EJ. Pediatric allergy: a brief review of risk factors associated with developing allergic disease in childhood. *Ann Allergy Asthma Immunol*. 2003;90:53–58.
 23. Stockwell T, Donath S, Cooper-Stanbury M, et al. Under-reporting of alcohol consumption in household surveys: a comparison of quantity-frequency, graduated-frequency and recent recall. *Addiction*. 2004;99:1024–1033.
 24. van Amsterdam JG, Bischoff EW, Hady M, et al. The prevalence of allergic sensitisation in immigrant children in The Netherlands. *Int Arch Allergy Immunol*. 2004;133:248–254.
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