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The Association between Self-Reported Glaucoma and *Ginkgo biloba* Use

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Abstract

Purpose—To assess the association between *Ginkgo biloba* extract (GBE) use and glaucoma.

Methods—Self-reported data on the past 12 months of GBE use and the presence of glaucoma were obtained from the 2002 National Health Interview Survey, a nationally-representative population-based sample. Crude and adjusted associations between GBE use and glaucoma were estimated.

Results—Those who reported having glaucoma were 26% less likely to report GBE use; however, this was not statistically significant. Following adjustment for potentially confounding demographic and medical characteristics, there was no difference in GBE use among those who did and did not report having glaucoma.

Conclusions—The results of this study fail to support a significant relationship between GBE use over the past 12 months and having glaucoma, though this finding requires replication in a prospective study. Moreover, whether GBE is efficacious in treating glaucoma patients remains an issue for future research.

Keywords

glaucoma; ginkgo biloba; herbal treatments; population-based sample

INTRODUCTION

Derived from leaves of the *G. biloba* tree, *Ginkgo biloba* extract (GBE) has been used as in traditional Chinese medicine for thousands of years, and has been one of the most prescribed drugs in Europe [1]. In part, due to its salubrious effects on blood circulation (e.g., potent inhibitor of platelet-activating factor, decreased viscosity, and vasoregulatory activity), it has been effectively used to treat diseases such as cerebral insufficiency and peripheral vascular disease [1]. Because glaucoma shares some etiological pathways with these disorders it has been hypothesized that GBE may be efficacious in treating glaucoma as well [2-4]. The few studies that have evaluated whether GBE may improve visual function have produced

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promising results [5-7]. For instance, in a rat model of chronic glaucoma, GBE was shown to be neuroprotective for the pre-treatment and early post-treatment phases of glaucoma [5]. Similarly, a hamster model demonstrated that GBE in combination with other herbal remedies, but not alone, resulted in neuroprotective outcomes such as improved retinal ganglion cell survival and regeneration [7]. In a small healthy human sample, GBE increased the ophthalmic artery's end diastolic velocity compared to a placebo, but there were no differences in IOP [8]. Finally, GBE significantly improved visual field sensitivities in a sample of 27 patients with normal tension glaucoma, but IOP did not change [6]. Taking advantage of rarely collected data on GBE use among a large, nationally representative sample, the objective of this study sought to evaluate the association between glaucoma and GBE use.

MATERIALS and METHODS

Data Source

The data for this study were drawn from the 2002 National Health Interview Survey (NHIS), which serves as the principal source of health information of the civilian, non-institutionalized, household population of the United States, and it represents a key data collection program of the National Center for Health Statistics and the Centers for Disease Control and Prevention [9]. Since its inception in 1957, the NHIS has used a repeated cross-section, multistage, stratified, cluster design to annually collect health information on tens of thousands of persons in the United States. Specifically, for the NHIS Sample Adult questionnaire, one adult member per family is randomly chosen to provide information on him/herself. When weighted, the data are nationally representative of the noninstitutionalized civilian U.S. population.

Supplemental questionnaires addressing current health topics play an increasingly important role in the NHIS with respect to enhancing topic coverage. In 2002, with co-sponsorship by the National Center for Complementary and Alternative Medicine, the Alternative Health/Complementary and Alternative Medicine Supplement (ALT) was administered. The ALT gathered information concerning the use of 17 non-conventional health care practices among the sample of adults, such as acupuncture, natural herbs, and relaxation techniques.

Study Population

Among the 31,044 persons (18 years of age and older) who were administered the Sample Adult questionnaire as well as the ALT, 30,964 responded to the question pertaining to glaucoma. The population for the present study was restricted to individuals 50 years of age and older to pertain to those at risk for glaucoma (N=12,376). Once weighted this study population represented a total of 75,699,243 individuals 50 years of age and older in the United States in 2002.

Variable Definitions

As part of the ALT, all study participants were asked whether they had ever used a natural herb for health or treatment. Those who responded affirmatively were subsequently asked whether they used a natural herb in the *past 12 months* for health or treatment, and if so to subsequently name the natural herb(s) taken. In addition, study participants were asked whether a physician or other health care professional had ever told them they have glaucoma (type not specified), and if so, whether they had glaucoma in the *past 12 months*. Thus, for the present study, this self-reported information was used to create variables for GBE use and the presence of glaucoma, both over the past 12 months.

Data on demographic characteristics (i.e., age, gender, and race), and self-reported information on medical characteristics and chronic conditions based on physician diagnosis (i.e., hypertension, coronary heart disease (CHD), angina, stroke, myocardial infarction, diabetes, cataract, diabetic retinopathy, and macular degeneration) that may confound the association between GBE and glaucoma were also obtained. In addition, cigarette smoking status, height, and weight were ascertained from respondents; the latter variables were used to calculate body mass index.

Statistical Analysis

Respondents with and without glaucoma were compared with respect to GBE use and demographic and medical characteristics using chi-square and t-tests for categorical and continuous variables, respectively. Logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the association between GBE and glaucoma with and without adjustment for demographic and other covariates. To account for the stratified clustered design of the survey, the PROC SURVEY procedures in SAS (SAS Institute; Cary, NC) were used for all analyses. P-values of ≤ 0.05 (two-sided) were considered statistically significant. This study was approved by the University of Alabama at Birmingham Institutional Review Board for Human Use.

RESULTS

Table 1 presents demographic, smoking, GBE use, and health characteristics according to glaucoma status. The average age is significantly higher for those who reported having glaucoma compared to those who did not. There was no difference between the groups with respect to gender, though racial differences indicated that blacks were disproportionately represented among those who reported glaucoma compared to those who did not. There were more former smokers and fewer current smokers among those who reported glaucoma. Of principal interest in this study, among those who reported having glaucoma, 2.7% reported using GBE compared to 3.7% of those who did not have glaucoma, though this difference was not statistically significant. The prevalence of hypertension, CHD, angina, stroke, myocardial infarction, diabetes, diabetic retinopathy, cataract, and macular degeneration were all significantly higher among those who reported having glaucoma. There was no association between body mass index and glaucoma.

Table 2 presents crude and adjusted logistic regression models estimating the association between GBE use and glaucoma. Results for the crude model indicates that there is not a statistically significant association between GBE use over the past 12 months and glaucoma (OR 0.74; 95% CI 0.38-1.42). The adjusted models sequentially control for first, demographic characteristics and smoking status; second, all variables in Table 1; and third, age and cataracts, which were significant confounding variables. The effects of GBE use on glaucoma remained statistically non-significant in each of the adjusted models (ORs 1.02, 1.09, and 0.94, respectively).

DISCUSSION

Using a nationally-representative, population-based sample, this cross-sectional study investigated the relationship between GBE use over the past 12 months and self-reported glaucoma. Although past animal and human studies have shown promising results with regard to the effects of GBE use on visual function [4-8], the results of this study suggest that there is not a significant association with glaucoma.

However, several limitations need to be addressed to draw firmer conclusions. One possible explanation for the lack of a significant association relates to the cross-sectional nature of

the study design. The NHIS does not collect information regarding the duration of GBE use nor glaucoma, and thus it was not possible to address the issue of temporality. Even with such data, while it would be possible to limit GBE use to that which occurred prior to glaucoma diagnosis, the etiologically relevant duration and amount of use remains unknown and could only be investigated in an exploratory manner. Another possible explanation relates to the self-reported nature of the NHIS data. If misclassification exists with respect to GBE use and/or glaucoma then a truly protective association may be obscured. However, while non-differential misclassification may bias associations towards the null it should have little effect on the relative strength of the associated risk factors to the disease. Thus, given that other known risk factors such as age, race, smoking status, hypertension, CHD, angina, stroke, myocardial infarction, diabetes, cataracts, diabetic retinopathy, and macular degeneration did show significant associations with glaucoma as defined in this study, the finding that GBE use was not associated indicates that it is a relatively small association compared with other known risk factors.

A third possible explanation is that information regarding suspected risk factors for glaucoma (e.g., IOP, family history) was not available thus introducing the possibility that the observed results are subject to residual confounding. Finally, it is possible that the observed effects of GBE use in human crossover trials and animal studies, if true, are not sufficient to reduce the risk of glaucoma.

In summary, despite research suggesting its use is associated with improvements in certain glaucoma-related physiologic parameters, the results of the current study provide no evidence for a strong association between GBE use and glaucoma compared to the effects of known risk factors (e.g., age, race, smoking status, hypertension, CHD, angina, stroke, myocardial infarction, diabetes, cataracts, diabetic retinopathy, and macular degeneration). However, the cross-sectional design and the possibility of misclassification limits the ability to accurately measure the true association between GBE use and glaucoma other than its effect relative to other known risk factors. Thus, additional research is warranted that is able to address these methodological limitations.

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Table 1
Demographic, GBE Use, and Health Differences between Those With and Without Glaucoma

	Self-Reported Glaucoma				p-value
	Yes (N=2,944,975)		No (N=72,754,268)		
	N / Mean	% / SD	N / Mean	% / SD	
Demographic Characteristics					
Age	70.9	0.5	63.6	0.1	<0.0001
Gender	1,261,967	42.9	33,517,336	46.1	0.2017
Race					< 0.0001
White	2,381,956	80.9	62,835,953	86.4	
Black	461,291	15.7	6,441,452	8.9	
Other	101,728	3.5	3,476,863	4.8	
Smoking Status					0.0030
Non-smoker	1,417,505	49.0	34,774,774	48.3	
Former smoker	1,179,231	40.8	25,586,749	35.5	
Current smoker	297,155	10.3	11,708,975	16.3	
Ginkgo biloba					
GBE use in past 12 months	73,227	2.7	2,419,991	3.7	0.2900
Health Characteristics					
Hypertension	1,899,490	64.6	31,518,700	43.5	<0.0001
CHD	473,689	16.2	6,746,626	9.3	<0.0001
Angina	291,343	10.0	4,285,809	5.9	0.0066
Stroke	317,065	10.9	3,729,136	5.1	0.0005
Myocardial infarction	398,048	13.6	5,345,369	7.4	<0.0001
Diabetes	730,930	25.3	9,197,500	12.8	<0.0001
Cataracts	1,655,754	56.4	14,525,659	20.0	<0.0001
Diabetic retinopathy	177,922	6.1	986,575	1.4	0.0012
Macular degeneration	295,597	10.2	1,751,590	2.4	<0.0001
Body mass index					
Under / normal weight	941,698	33.6	24,934,940	35.9	0.3535
Overweight	1,085,318	38.7	26,989,048	38.9	0.9326

	Self-Reported Glaucoma						p-value
	Yes (N=2,944,975)			No (N=72,754,268)			
	N / Mean	% / SD		N / Mean	% / SD		
Obese	779,967	27.8		17,479,583	25.2		0.2374

Table 2

Crude and Adjusted Logistic Regression Models Estimating GBE Use on Glaucoma

	Crude OR (95% CI)	Adjusted* OR (95% CI)	Adjusted [†] OR (95% CI)	Adjusted [‡] OR (95% CI)
GBE use in past 12 months	0.74 (0.38-1.42)	1.02 (0.52-1.98)	1.09 (0.55-2.17)	0.94 (0.49-1.83)

* Adjusted for age, race, gender and smoking status.

[†] Adjusted for all variables in Table 1.

[‡] Adjusted for age, cataracts