Published in final edited form as:

J Stroke Cerebrovasc Dis. 2008 ; 17(6): 370–372. doi:10.1016/j.jstrokecerebrovasdis.2008.04.007.

The Effects of Study Participation in the Familial Intracranial Aneurysm Study on Cigarette Smoking

Laura Sauerbeck, MS¹, Richard Hornung, DrPH³, Charles J. Moomaw, PhD¹, Daniel Woo, MD, MS¹, Richard Curry, MD², Robert D Brown Jr., MD, MPH⁴, and Joseph Broderick, MD¹ for the Familial Intracranial Aneurysm (FIA) Investigators

¹ Department of Neurology, University of Cincinnati, Ohio

² College of Medicine, University of Cincinnati, Ohio

³ Center for Epidemiology and Biostatistics, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio

⁴ Department of Neurology, Mayo Clinic, Rochester, Minnesota

Background

Cigarette smoking has been identified as an important modifiable risk factor for aneurysm formation and rupture.^{1–5} Tobacco addiction has been found to be one of the most difficult to break, with intervention efforts having a less than 5% yearly rate of success.⁶ The danger of developing an IA, particularly in the setting of a family history, may have an effect on a person's willingness to quit smoking. The purpose of this paper is to determine whether participation in the FIA study has influenced participants' smoking habits.

Methods

Participants in this National Institute of Neurological Disorders and Stroke funded study were enrolled in the FIA protocol, which has been previously described.⁷ The study was approved by the Institutional Review Boards/Ethics Committees at each of the study sites. Enrollment into this study started in the fall of 2002.

Upon study entry, trained personnel used a standardized questionnaire to collect detailed histories. The interviewers queried whether the participants had ever smoked at least 100 cigarettes in their entire life and, if yes, the age at which they started and average daily amount smoked. Those previously diagnosed with an IA were asked if they were routinely smoking at the time of diagnosis. Unaffected participants were asked if they were routinely smoking at the time of the interview. If the respondent was a former smoker, the amount of time since the quitting was recorded.

Participants, or their proxies, were administered a follow-up questionnaire yearly on the anniversary of their study entry (± 30 days), which included current smoking status and average daily amount smoked. The study did not mandate risk reduction discussions, nor did it have

Correspondence to: Laura R. Sauerbeck, MS, Department of Neurology, University of Cincinnati, 260 Stetson Street, Suite 2300, Cincinnati, Ohio 45267-0525, E-mail: Laura.Sauerbeck@uc.edu, Fax: 513 558-2855, Phone: 513 558-1742.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

restrictions on giving information. The only consistent messages concerning the risks of cigarette smoking were those printed in the annual participant newsletters.⁸

Data Analysis

There were two outcome variables: a dichotomous variable for current smoking (yes/no) and a continuous variable for the number of cigarettes per day. The analysis was restricted to a maximum of 4 visits (baseline plus three yearly follow-ups) since only 2.2% of subjects had follow-ups beyond three years. A generalized estimating equation (GEE) version of multiple logistic regression was used, with smoking status as the binary outcome variable in order to account for correlation of outcomes within subjects over time.⁹ A repeated measures mixed effects linear model was used for analysis of smoking rates in cigarettes per day as a continuous outcome while treating subjects as a random effect.¹⁰ Both the GEE model and the mixed effects linear model permitted modeling of the correlation structure of repeated measurements. Bivariate associations between patient characteristics and smoking behaviors were analyzed via chi-square tests.

Results

Between August 2002 and June 2007, 2756 subjects were enrolled into the study, baseline characteristics are presented in Table 1. Of those enrolled, 2018 participants had completed at least one year of follow-up, with 1242 completing 2 years, and 611 completing 3 years. There were 913 subjects who reported being a current smoker at the time of diagnosis or study entry. Pre-study IA diagnoses occurred in 420 current smokers, and 56 additional smokers were diagnosed after entry.

The baseline smoking status point of time was the date of diagnosis for subjects with an IA prior to entry, or the date of study entry for individuals diagnosed with IA after entry. Of the 105 smokers diagnosed with IA completing 3 years of follow-up 38 (36.2%) had quit smoking, and of 91 unaffected smokers completing 3 years of follow-up, 14 (15.4%) reported smoking cessation. Overall, the percentage of current smokers decreased from 33.1% at baseline to 26.7% at three years.

For subjects who had continued smoking, there was a significant reduction in the daily amount of cigarettes smoked. Subjects who were current smokers at the time of IA diagnosis were significantly more likely to decrease their cigarette consumption (from 19.4 to 9.8 cigs per day $p<0.001$) than those who were not diagnosed with an IA (16.0 to 13.3 cigs per day, $p=0.002$). The other factor that was significantly associated with a change in cigarette usage was the subject's age at entry. Subjects 51 years of age or older had a greater reduction compared to those less than 51 years (2.3 cigs per day reduction vs. 1.5, $p=0.002$).

Odds ratios (ORs) comparing smoking status at study baseline to reported smoking status at yearly follow-ups one through three were estimated, with an OR <1.0 indicating that subjects decreased their current smoking. Odds ratios for all intervals showed highly significant decreases in smoking status, with the largest decrease occurring between baseline and the first yearly follow-up (Table 2). The ORs were adjusted for gender, age at initial interview, country entry, and diagnoses of IA. A test of interactions with these variables was significant for being diagnosed with an IA ($p<.001$) and for subjects age 51 years or greater ($p=0.002$).

Discussion

Changing addictive behavior such as smoking is challenging. It has been shown that high-risk individuals are willing to change their lifestyles in order to decrease their risk of developing a

serious condition.^{11–12} Studies have also described a “trial effect,” in which a subject’s behavior changes as a result of clinical trial participation.^{13–15}

Our data indicate that the diagnosis of a potentially life-threatening condition such as IA increases the likelihood of smoking cessation. However, 63.8% of baseline smokers who have been diagnosed with an IA remain smokers even though many had a significant family history of death and disability from a ruptured IA and all had received yearly newsletters describing the risk of IA rupture associated with smoking. The decrease in the rate and amount of smoking in FIA participants without a diagnosis of IA was much less, but still significant. Thus even in the face of a very strong family history of IA, FIA participants changed their behavior much less when they were not labeled as affected. Future identification of at-risk genes for IA is perhaps likely to change smoking behavior more than family history, but less likely than the clinical or imaging diagnosis of IA. If so, genetic testing for IA could have a major health impact, since smoking cessation is associated with a substantial reduction in risk of IA rupture, in addition to the other health benefits of smoking cessation.

In summary, participants in the FIA study had a decrease in smoking rates in both those with a diagnosis of IA and, to a lesser degree those without a current IA. More aggressive risk factor education and smoking cessation strategies are appropriate in this high-risk group. However, the most effective motivation to stop smoking is the imaging diagnosis of IA, and hopefully in the future, identification of these family members who have genes associated with a higher risk of IA formation and rupture.

Acknowledgements

This study was funded by grants from the National Institute of Neurological Diseases and Stroke (NINDS: R-01 NS39512)

References

1. Kissela BM, Sauerbeck L, Woo D, et al. Subarachnoid hemorrhage: A preventable disease with a heritable component. *Stroke* 2002;33:1321–1326. [PubMed: 11988610]
2. Broderick JP, Viscoli CM, Brott T, et al. Major risk factors for aneurysmal subarachnoid hemorrhage in the young are modifiable. *Stroke* 2003;34:1375–1381. [PubMed: 12764233]
3. Anderson CS, Feigin V, Bennett D, et al. Active and passive smoking and the risk of subarachnoid hemorrhage: An international population-based case-control study. *Stroke* 2004;35:633–637. [PubMed: 14752125]
4. Connolly ES Jr, Choudhri TF, Mack WJ, et al. Influence of smoking, hypertension, and sex on the phenotypic expression of familial intracranial aneurysms in siblings. *Neurosurgery* 2001;48:64–8. [PubMed: 11152362]discussion 68-9.
5. Juvela S, Porras M, Poussa K. Natural history of unruptured intracranial aneurysms: Probability of and risk factors for aneurysm rupture. *J Neurosurg* 2000;93:379–387. [PubMed: 10969934]
6. CDC. Cigarette smoking among adults—United States, 2000. *MMWR* 2002;51:642. [PubMed: 12186222]
7. Broderick JP, Sauerbeck LR, Foroud T, et al. Familial intracranial aneurysm (FIA) study protocol. *BMC Med Genet* 2005;6:17. [PubMed: 15854227]
8. The Familial Intracranial Aneurysm Study. Available at: www.FIAStudy.org
9. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. *Biometrics* 1986;42:121–130. [PubMed: 3719049]
10. Diggle PJ. An approach to the analysis of repeated measurements. *Biometrics* 1988;44:959–971. [PubMed: 3233259]
11. Sauerbeck LR, Khoury JC, Woo D, Kissela BM, Moomaw CJ, Broderick JP. Smoking cessation after stroke: Education and its effect on behavior. *J Neurosci Nurs* 2005;37:316–9. 325. [PubMed: 16396084]

12. Miller ET, Spilker J. Readiness to change and brief educational interventions: Successful strategies to reduce stroke risk. *J Neurosci Nurs* 2003;35:215–222. [PubMed: 12942656]
13. Hebert-Croteau N, Brisson J, Lemaire J, Latreille J. The benefit of participating to clinical research. *Breast Cancer Res Treat* 2005;91:279–281. [PubMed: 15952061]
14. Brauholtz DA, Edwards SJ, Lilford RJ. Are randomized clinical trials good for us (in the short term)? Evidence for a “trial effect”. *J Clin Epidemiol* 2001;54:217–224. [PubMed: 11223318]
15. Meineche-Schmidt V, Hvenegaard A, Juhl HH. Participation in a clinical trial influences the future management of patients with gastro-oesophageal reflux disease in general practice. *Aliment Pharmacol Ther* 2006;24:1117–1125. [PubMed: 16984506]

Table 1

FIA Participants' baseline characteristics (n=2756)

Characteristic	All Subjects (N=2756)	%	Non-smokers * (n=931)	%	Former Smokers * (n=912)	%	Current Smokers * (n=913)	%
Gender								
Male	946	34.3	306	32.9	335	36.7	305	33.4
Female	1810	65.7	625	67.1	577	63.3	608	66.6
Age (years)								
< 51 years	1318	47.8	499	53.6	332	36.5	487	53.3
≥ 51 years	1438	52.2	432	46.4	580	63.5	426	46.7
Race								
White	2498	90.6	831	89.3	851	93.3	816	89.4
Other	258	9.4	100	10.7	61	6.7	97	10.6
Country of Enrollment								
Australia	336	12.2	92	9.9	121	13.4	123	13.4
Canada	493	17.9	156	16.8	158	17.3	179	19.6
New Zealand	80	2.9	24	2.6	20	2.2	36	4.0
United States	1847	67.0	659	70.8	613	67.1	575	63.0
Diagnosed 1A								
Yes	1026	37.2	214	23.0	336	36.9	476	52.1
No	1730	62.8	717	77.0	576	63.1	437	47.9

* Cigarette smoking.

Table 2

Adjusted Odds Ratio for Smoking Status (current to non-smoker) at each follow-up compared with baseline

Study Visit	Current Cigarette Smoker (%)	Odds Ratio	Confidence Interval (95%)	p-value
Baseline	33.1			
First annual follow-up	30.0	0.83	0.78–0.89	<.001
Second annual follow-up	27.6	0.74	0.68–0.80	<.001
Third annual follow-up	26.7	0.71	0.64–0.78	<.001