RESEARCH COMMUNICATION

A Pilot Study on Genotype Announcement to Induce Smoking Cessation by Japanese Smokers

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Abstract

Background: Genotype announcements related to susceptibility to hazardous effects of smoking may be effective to induce smoking cessation.

Methods: Subjects were municipal government employees, 63 young smokers employed in the previous year and 59 smokers with more than 45 pack-years, who were invited to educational sessions against smoking held in December 2003 and February 2004, respectively. In the session, those who wished genetic susceptibility tests (*GSTM1*, *GSTT1*, and *NQO1* C609T) were enrolled in the study. The smoking habit was ascertained three times: at the session, one month later, just before the genotype announcement, and at the follow-up three months after the announcement.

Results: Fifty eight (92.1%) and 49 (83.1%) smokers participated in the study, respectively. One out of 58 smokers was not a habitual smoker, so was not included in the analysis. The smoking cessation rates were 15.8% (9 participants) and 6.1% (3 participants) just before the genotype announcement, and 7.0% (4 participants) and 10.2% (5 participants) at the follow-up, respectively. All subjects were satisfied with the genotype testing except for two who rather regretted participating, but one of whom actually quit smoking.

Conclusion: The present pilot study without controls indicated that the effects of genotype announcements in this framework on smoking cessation were less than might have been expected. The temporary effect of the session on younger smokers may have been due to the participation per se. The potential effects of genotype announcements for heavy smokers should now be examined in studies with adequate controls.

Key Words: Smoking cessation – genetic polymorphisms – genotype announcements

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Introduction

Providing motivation for smokers to quit smoking is an essential step towards abstinence. Educational sessions on harmful effects of smoking have been held in various situations, such as at schools and worksites, and in community settings. We have learned that knowledge about harm is usually not effective to cause smoking cessation. "Support for smokers" is a useful concept, and actually beneficial influence has been documented in many studies (Fiore et al., 1994; Henningfield, 1995; Shiffman et al., 1997; Silagy et al., 2004; Molyneux, 2004). Now, nicotine gum and nicotine patches are available as useful tools of cessation support in many countries. Literally, support is to be provided for those who seek it, so that the application is not for the general smoking population. In this sense, "cessation inducement" may be a more appropriate concept, whose targets include smokers who have no intention of quitting the habit at the onset.

As approaches to induce cessation, uses of biomarkers indicating hazardous exposure derived from smoking, such as urinary cotinine and expired carbon monoxide, are considered to be effective (McClure, 2001). Announcement of genotype relating to disease susceptibility of smoking has also been examined in terms of cessation rate. However, one randomized study showed that *CYP2D6* (*cytochrome p450 2D6*) genotype announcement, added to consultation and exposure biomarker feedback, had no effect on the

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cessation rate, in comparison with consultation only and consultation plus exposure biomarker feedback. The depression score (CES-D score) for smokers who learned their genotype was temporarily elevated after two months, and reduced one year later to the same level as in the two control groups (Audrain et al., 1997). In contrast, another randomized study found that the cessation rate was higher among those announced to have specific *GSTM1* (*glutathione S-transferase M1*) genotypes (19% at 6 months and 15% at 12 months) than among those provided enhanced usual care (10% and 10%, respectively) (McBride et al., 2002).

The effects of genotype announcement on smoking cessation could vary among ethnic groups with different cultural or genetic traits. Some cultures may regard inherited genotypes as factors definitely related to destiny, while others may consider such information meaningless for daily life. The present pilot study without controls examined the short-term effects of genotype announcement on smoking cessation and responses to genotyping tests, for Japanese municipal government employees who attended a seminar against the smoking habit. Announced genotypes were for *glutathione S-transferase* (*GST*) *M1*, *GSTT1*, and *NAD*(*P*)*H:quinone oxidoreductase 1* (*NQO1*) C609T polymorphisms. The *GSTM1 null* type, *GSTT1 null* type, and *NQO1 609TT* have no enzyme activity to detoxify carcinogenic compounds in tobacco smoke, so that smokers with the genotypes are considered to be at a higher risk of cancer (Rebbeck, 1997; Siegel, et al., 1999; Hamajima et al., 2002).

Materials and Methods

The subjects were municipal government employees including managers, officials, technicians, manual workers, and nurses, who stated they were smokers at annual health checkup questioning. The section of health management made a list from newly employed smokers and smokers with a history more than 45 pack-years. Listed were 145 smokers aged less than 40 years and 124 smokers aged more than 40 years, respectively (Table 1). Sessions were conducted on two occasions (December 8 and 25, 2003) for newly employed smokers and one occasion (February 25, 2004) for heavy smokers. In total, 122 smokers attended. Each was for 3-hours, with education to explain the hazardous effects of smoking and related genetic susceptibility. A color pamphlet with 8 pages on polymorphism genotypes, as well as sheets of the study description and questionnaire on smoking habits, were handed to all participants. Fifty-eight newly employed smokers and 49 heavy smokers agreed to participate in the study. After a signature was received on an informed consent form, blood was drawn at the session room. The blood samples were anonymized with numbers to link to the participants and genotyped at the Department of Preventive Medicine / Biostatistics and Medical Decision Making, Nagoya University Graduate School of Medicine.

Table 1. Sex and Age Distribution of Newly Employed Smokers and Heavy Smokers with 45 Pack-years

	Newly employed	Heavy smokers	Total
Listed	145	124	269
Attended	63	59	122
Males	51	57	108
Females	12	2	14
Participated	58	49	107
Males	49	47	96
Females	9	2	11
Age 23-29	42	0	42
30-39	16	0	16
40-49	0	6	6
50-60	0	43	43

One month after each session, the results sealed in an envelope were sent to the section of health management, and handed to the participants. A questionnaire to be completed before opening the envelope was attached. The staff did not have any chance to learn the genotype of individual participants. Three months after the genotype announcement, a follow-up questionnaire was distributed and collected. Anonymized questionnaires at enrollment, one month later just before genotype announcement, and at the follow-up three months after genotype announcement were sent to the study office at Nagoya University. The questionnaires were linked with the subject number put on each.

Stage of smokers concerning smoking cessation was classified into four categories; no concern, feel concern but have no intention to quit smoking, have an intention to quit smoking but not in one month, and have an intention to quit smoking within one month (Prochaska, 1994). The latter two categories were combined into "wish to quit" in the analysis. At the follow-up, the genotype announcement was evaluated by two questions. One was "How did you feel when your genotypes were announced ?" Answers were: 1) Relieved; 2) nothing; 3) became slightly anxious; 4) became very anxious; 5) became anxious enough to be disturbed in daily life ("seriously anxious" in Table 4); and 6) cannot remember the genotypes or forgot how I felt ("not remember" in Table 4). The other was concerning satisfaction/regret for genotype testing, as shown in Table 4.

GSTM1, *GSTT1*, and *NQO1* C609T were genotyped by polymerase chain reaction with confronting two-pair primers (Kawase et al., 2003). This study was approved by the Ethical Committee of Nagoya University Graduate School of Medicine (Approval number: 98, issued on November 17, 2003)

Results

The participants were 58 (92.1%) out of 63 newly employed attendants and 49 (83.1%) out of 59 heavy smoker attendants. By the questionnaire before genotype

Table 2. Stage of Smokers at Enrolment, One Month Later Just before Genotype Announcement, and at Three Months after Genotype Announcement

	Newly employed N=57*	Heavy smokers N=49	Total N=106
At enrolment			
No concern	10 (17.5)	8 (16.3)	18 (17.0)
No intention	39 (68.4)	33 (67.3)	72 (67.9)
Wish to quit	8 (14.0)	8 (16.3)	16 (15.1)
Just before the genotype announcement			
Quit	9 (15.8)	3 (6.1)	12 (11.3)
Not quit	48 (84.2)	46 (93.9)	94 (88.7)
No concern	5 (8.8)	5 (10.2)	10 (9.4)
No intention	28 (49.1)	28 (57.1)	56 (52.8)
Wish to quit	14 (24.6)	11 (22.4)	25 (23.6)
No answer	1 (1.8)	2 (4.1)	3 (2.8)
Three months after the announcement			
Quit	4 (7.0)	5 (10.2)	9 (8.5)
Not quit	52 (91.2)	43 (87.8)	95 (89.6)
No concern	4 (7.0)	5 (10.2)	9 (8.5)
No intention	31 (54.4)	32 (65.3)	63 (59.4)
Wish to quit	15 (26.3)	6 (12.2)	21 (19.8)
No answer	2 (3.5)	0 (0.0)	2 (1.9)
No response	1 (1.8)	1 (2.0)	2 (1.9)

* Since one male participant stated in the questionnaire before genotype announcement that he was not a habitual smoker, but an occasional smoker, so he was removed from the analysis.

announcement, one newly employed male was found not to be a habitual, but rather only an occasional smoker. He was removed from the analysis, though he completely quit smoking after the enrollment. The questionnaire before genotype announcement found that the great majority understood the genotype testing with the lecture and pamphlet completely (57.9% and 59.2%, respectively) or partly (40.4% and 24.5%, respectively). As shown in Table 2, 9 newly employed smokers and 3 heavy smokers had quit smoking before the genotype announcement. Among the newly employed, 6 out of 9 quitters resumed smoking, and one quit after the genotype announcement, resulting in 4 quitters at the follow-up three months after the announcement. Among heavy smokers, one of 3 quitters before genotype announcement continued abstinence, but the other two resumed smoking. Another 4 heavy smokers quit after the announcement. Out of 9 quitters as a whole at the follow-up, six had no intention to quit smoking at enrollment (8.3% of 72), and the other three wished to quit smoking (18.8% of 16). All quitters were males.

Table 3 shows data for the final quitters according to genotypes. There were no marked differences in the cessation

Table 3. Quitters at the Follow-up Three Months after Genotype Announcement according to Genotype

	Newly employed N=57	Heavy smokers N=49	Total N=106
GSTM1			
Present	4/43 (9.3)	2/26 (7.7)	6/69 (8.7)
Null	0/14 (0.0)	3/23 (13.0)	3/37 (8.1)
GSTT1			
Present	2/31 (6.5)	3/23 (13.0)	5/54 (9.3)
Null	2/26 (7.7)	2/26 (7.7)	4/52 (7.7)
NQO1			
609CC	0/19 (0.0)	1/20 (5.0)	1/39 (2.6)
609CT	3/28 (10.7)	4/25 (16.0)	7/53 (13.2)
609TT	1/10 (10.0)	0/4 (0.0)	1/14 (7.1)
Number of null genotypes*			
0	2/16 (12.5)	1/9 (11.1)	3/25 (12.0)
1	1/33 (3.0)	3/28 (10.7)	4/61 (6.6)
2	1/7 (14.3)	1/11 (9.1)	2/18 (11.1)
3	0/1 (0.0)	0/1 (0.0)	0/2 (0.0)

* *GSTM1 null*, *GSTT1 null*, and *NQO1 T/T* were counted as null genotypes with no enzyme activity.

Table 4. Quitters at the Follow-up Three Months after Genotype Announcement according to Anxiety and Regret for Attending Genotype Testing

	Newly employed N=56*		Heavy smokers N=48*		Total N=104*	
How did you feel when your genotypes were announced ?						
Relieved	1/9	(11.1)	0/9	(0.0)	1/18	(5.6)
Nothing	0/19	(0.0)	2/21	(9.5)	2/40	(5.0)
Slightly anxious	2/22	(9.1)	2/15	(13.3)	4/37	(10.8)
Very anxious	0/2**	(0.0)	0/0	(-)	0/2	(0.0)
Seriously anxious	0/0	(-)	0/0	(-)	0/0	(-)
Not remember	0/3	(0.0)	1/2	(50.0)	1/5	(20.0)
No answer	1/1	(100.0)	0/1	(0.0)	1/2	(50.0)
Are you satisfied with or do you regret the genotype testing ?						
Satisfied	2/39	(5.1)	2/28	(7.1)	4/67	(6.0)
Rather satisfied	2/17	(11.8)	1/17	(5.9)	3/34	(8.8)
Rather regret	0/0	(-)	1/2***	(50.0)	1/2	(50.0)
Regret	0/0	(-)	0/0	(-)	0/0	(-)
No answer	0/0	(-)	1/1	(100.0)	1/1	(100.0)

* Participants who did not respond the follow-up were removed.
** A male in his 20s with two null genotypes, and a male in his 30s with two null genotypes. Both stated they quit smoking temporarily.
*** A male in his 50s with no null genotypes, and a male in his 50s with one null and two non-null genotypes.

rate among participants with different genotypes. The number of null genotypes with no enzyme activity was not associated with smoking cessation.

Table 4 demonstrates the responses to the genotype testing, as well as the cessation rate according to the response. Two males with two null genotypes at 20s and at 30s "became very anxious", but were "satisfied with the genotype testing". They quit smoking temporarily, and were smokers at the follow-up with a wish to quit within one month. Another two males in their 50s rather regretted the genotype testing. One with one null and two non-null genotypes became slightly anxious and quit smoking, while the other with no null genotypes felt nothing and had no intention to quit.

Discussion

The cessation rate observed in follow-up studies is usually low; for example, a 3% two-month rate was achieved for 2,207 health checkup examinees (Hamajima et al., 2001). Intervention studies have indicated that the effectiveness of educational sessions are marginal in comparison with the controls; 8% vs 4% for a six-month rate for health checkup examinees (Shimizu et al., 1985), 20% vs 9% for five-month rates for outpatients (Ogawa et a., 1993), and 10% vs 4% for one-year rates for 839 health checkup male examinees (Higashi et al., 1997). Generally, the cessation rate is higher among patients than among health checkup examinees.

The present pilot study also found that the genotype announcement had a usual size of intervention effect on smoking cessation (8.5%) in this framework, where the genotypes were sent to the participants, without individual explanation using their genotypes. For newly employed younger smokers, the impact of participation per se seemed larger than that of the announcement of their genotypes. The cessation rate was thus reduced after three months , as observed in many cessation programs. However, for the middle-aged heavy smokers, the announcement could have been more effective; four smokers quit smoking after the genotype announcement. Genotypes may be more influential for middle-aged smokers, who can realize the importance of health. Age is a common factor for smoking cessation, as well as other factors such as being males and suffering disease onset (Ockene et al., 1992; Hamajima et al., 1999). Of interest is that smokers with no null genotypes had a similar cessation rate to that of smokers with one or more null genotypes. Therefore simple awareness of genetic traits may induce cessation behavior.

Two male participants at 20s and 30s who answered that they became very anxious but were satisfied with the genotype testing, and another two male participants who answered that they rather regreted the genotype testing, were interviewed a half year later from the follow-up. The participant in his 30s quit one week before the interview, stating that the announcement became the motivation to quit smoking. The male in his 20s also stated that the announcement provided motivation, but still was a smoker. One who rather regretted the genotype testing remained a quitter because he was anxious at having a high risk of cancer. The other rather regretted the genotype testing without being anxious, simply because the explanation was too difficult for him to understand. The interview found all four participants suffered no substantial stress due to the genotype announcement.

Studies in the United States to evaluate the effects of genotype announcement have shown inconsistent results. One was not effective for smokers recruited with newspaper advertisements, while the other was effective for African-

Americans with low income recruited at a community health clinic. Differences in the subject characteristics and mode of genotype explanation may have been causes of the inconsistency. We have observed an elevated cessation rate for genotype-announced outpatients at a cancer hospital, which will be reported elsewhere. However, the cessation rate was not marked for the present subjects. Targeting the subjects and the instruction mode of genotype interpretation thus appear to be important for effective genotype announcement.

In conclusion, the present pilot study without controls indicated that the effect of genotype announcement in this framework on smoking cessation was less than expected. The temporary effects on younger smokers may be due to the participation per se. The potential effects of genotype announcement on heavy smokers should now be examined in larger studies with controls. Although no serious problems due to genotype announcement were observed in this study, we have to pay attention to the response of smokers after genotype announcement.

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