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Cigarette Reduction: An Intervention for Adolescent Smokers

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Abstract

This observational study examined whether adolescents who weren't interested in quitting could reduce cigarette smoking and if cigarette reduction led to a corresponding and significant reduction in biomarkers of exposure. The study design was a randomized, open-label trial of nicotine patch and nicotine gum with an added placebo control. Participants (N=103) attended 4 treatment visits over 4 weeks and follow-up visits at 3- and 6-months. Participants were told to reduce their smoking by 25% of baseline smoking during the first week and by 50% of baseline smoking during the subsequent three weeks. Of consented participants, 91.3% (n=94/103) completed the study until the end-of-treatment, 85.1% (n=80/94) completed the three-month follow-up visit and 71.3% (n=67/94) completed the six-month follow-up visit. Participants had a very high prevalence of co-morbidity. With regard to the percentage of participants who achieved a 50% reduction of baseline smoking, there were no significant differences among treatment groups ($p=.89$). At the end-of-treatment, 49.4% of participants (n=41) had reduced smoking by at least 50%. Additionally, there was no significant group, visit or interaction effect of a biomarker measure for carcinogen exposure ($p>.05$). The results suggest that reduction may be a potential aid to engage adolescents who are unable or unwilling to quit, but should not be an end goal. The effect of treatment methods on outcome measures did not differ significantly.

Keywords

Adolescent; Cigarette Reduction; Smoking Cessation; Biomarkers; Nicotine Patch; Nicotine Gum

1. Introduction

There is a need to examine innovative interventions to enable adolescents to quit smoking (Mermelstein, 2003). Reduction in cigarette smoking may be one example of an intervention to engage adolescents who are not interested in quitting. Another intervention is to sustain reduction in adolescents who have not been successful in quitting. Both of these approaches may eventually lead to a successful quit attempt.

Research shows that a significant number of adolescents who enter smoking cessation treatment are able to reduce their level of smoking (see Sussman, 2002). To date, no studies apart from community interventions such as smoke-free policies and increasing cigarette costs

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have examined smoking reduction in adolescents who aren't trying to quit smoking (Fisher, Winickoff, Camargo, Colditz & Frazier, 2007; Institute of Medicine, 1994). In adults who are unwilling or unable to quit, intervention studies have shown that a reduction in cigarette smoking can be achieved and maintained at follow-up (Hughes and Carpenter, 2005).

Along with a reduction in smoking, a reduction in biomarkers of exposure has been observed in adults, although modest (Hecht et al., 2004; Hurt et al., 2000). Cigarette reduction is a viable intervention method if it significantly reduces exposure to tobacco toxicants or if it facilitates cessation.

The aims of this pilot and observational study are to determine if adolescents not interested in quitting can reduce cigarette smoking and if cigarette reduction leads to a corresponding and significant reduction in biomarkers of exposure.

2. Methods

Participants aged 13–19 years ($n=103$) were recruited from 14 traditional and alternative high schools located in suburbs of the Minneapolis-St. Paul area from 2002–2004. The eligibility criteria were as follows: (a) Smoking at least 5 cigarettes per day (CPD) for at least six months, (b) not using any other tobacco products more than once per week, (c) wanting to reduce smoking, but not having a quit date set within the next 2 months, (d) not using nicotine replacement therapy or bupropion, (e) not taking medication contraindicated for use with study medications, (f) not abusing alcohol or drugs, (g) not experiencing severe emotional problems within the past year, and (h) not taking psychoactive medications that were not stabilized or were likely to change during the course of the study. The intervention was expected to reach approximately 9.6% of high school students based on self-reported daily smoking rates in Minnesota in 2002 (Minnesota Department of Health Center for Health Statistics, 2005). The University of Minnesota Institutional Review Board granted approval to conduct the study. Participant and parental (for participants < 18-years-old) consent was obtained prior to study enrollment.

Participants met weekly for 6 weeks. Visits lasted about 20–30 minutes except for the screening visit, which was about 40 minutes. The first two weeks were baseline visits. During the next four weeks, participants began using study medications and reduced their smoking. Participants were told to reduce their cigarette smoking by 25% of mean baseline smoking during the first week and by 50% of average baseline smoking during the subsequent three weeks. During each treatment visit, participants received 10–15 minutes of cognitive-behavioral therapy (CBT) designed to reduce smoking.

At the end of four weeks of trying to reduce smoking, participants were asked if they wanted to set a quit date within one week. If they chose to set a quit date, they received four additional weeks of their choice of medication and CBT sessions designed to help them to quit. Follow-up visits were conducted at three- and six-months post-randomization.

Participants were randomly assigned to receive one of the three following treatment conditions during the reduction phase: nicotine patch, nicotine gum or a placebo medication. The recommended amount of nicotine gum to use was based on participants' baseline level of smoking. One piece of 2 mg nicotine gum was substituted for one cigarette. Dosing of the nicotine patch was as follows: those smoking ≥ 15 CPD used a 14 mg nicotine patch during the first week and increased to 21 mg during the last 3 weeks; those smoking 10–14 CPD, used a 7 mg nicotine patch during the first week and increased to 14 mg during the last 3 weeks; and those smoking 5–9 CPD used a 7 mg nicotine patch for the entire 4 weeks. Participants assigned to the placebo condition took a 400 mg folic acid pill daily.

2.1. Dependent measures

For biochemical verification, participants provided expired-air carbon monoxide (CO) samples using the Bedfont Micro Smokerlyzer device at each visit. Urine samples were collected to assess the following biomarkers for carcinogen uptake and metabolic activation: (a) 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL) and its glucuronides (NNAL-Gluc) (total NNAL), urinary metabolites of the tobacco-specific lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK), and (b) nicotine metabolites including cotinine (total cotinine). They were collected at seven visits; but analyzed for biomarkers of exposure only at baseline and end-of-treatment (only cotinine was analyzed at follow-up).

2.2. Statistical methodology

Analysis-of-Variance (ANOVA) was applied to test the overall equality of means of continuous variable among three treatment groups, while Chi-square test was used to test the difference of distribution of categorical variables.

For repeated measurement outcomes, a linear mixed model with random subject effect to evaluate treatment group and time effects was used (means reported are least square means). Interaction term was introduced in the initial model and removed if it was insignificant. Time (visit) was treated as a discrete variable. Akaike Information Criterion (AIC) was applied in model selection. Adjustment of p-values for multiple comparisons was preformed by Bonferroni method. SAS 9.1 (SAS Institute, Cary) was used for statistical analysis. Significance level was set at 5%.

3. Results

3.1. Treatment completion and follow-up rates

Of participants, 91.3% (n=94/103) completed the study until the end-of-treatment, 85.1% (n=80/94) completed the three-month follow-up visit and 71.3% (n=67/94) completed the six-month follow-up visit.

3.2. Demographics

There were no significant differences (defined as $p < .05$) between randomization groups with regard to demographic variables (Table 1). However, the nicotine patch group showed some substantial, but no significant differences in baseline variables (e.g., duration of prior abstinence, fewer females).

3.3. Reduction in cigarettes smoked, carbon monoxide levels, cotinine levels and total NNAL levels

Table 2 describes summary statistics for smoking variables across treatment groups. No treatment or medication effects were found by visit in most of these variables ($p > .05$). Only visit effects will be reported unless otherwise noted.

Using a linear mixed model with random subject effect, participants reduced the mean cigarettes smoked per day significantly at the end-of-treatment and at the follow-up visits compared to baseline (all adjusted p-values are < 0.0001). At the end-of-treatment, 49.4% of participants (n=41/83) had reduced smoking by at least 50%.

Overall, CO levels decreased significantly at the end-of-treatment. However, at the follow-up visits, CO levels increased. There was a significant interaction between group and visit for CO levels. The mean CO level was significantly higher in nicotine gum group than in nicotine patch group at the third visit, $t(472)=2.42$, $p=.05$.

Cotinine levels did not decrease significantly at the end-of-treatment or at the follow-up visits. Mean cotinine levels decreased at the three-month follow-up visit, but increased significantly at the six-month follow-up visit, $t(220)=2.47$, $p=.04$. There was also no significant reduction in mean total NNAL at the end-of-treatment compared to baseline, $t(83)=1.34$, $p=.18$.

There was a significant interaction between group and visit for CO per cigarette (CO/cigarette). Overall mean CO/cigarette increased during the treatment period. It increased from 0.58 ppm/cigarette at baseline to 1.36 ppm/cigarette at the end-of-treatment (34.5% increase). It increased to 5.31 ppm/cigarette at three-month follow-up visit, but decreased to 1.65 ppm/cigarette at the six-month follow-up visit. The CO/cigarette was significantly higher in the placebo group than in the nicotine patch and nicotine gum group at the three-month follow-up visit, $t(428)=4.64$, $p<.0001$ and $t(428)=4.28$, $p<.0001$, respectively.

The mean level of cotinine per cigarette increased significantly across visits. It was significantly higher in the placebo group (1391.2 ng/ml/cigarette) than in the nicotine gum (506.3 ng/ml/cigarette) or nicotine patch (788.7 ng/ml/cigarette) groups at the three-month follow-up visit, $t(182)=4.37$, $p<.0001$ and $t(182)=4.32$, $p<.0001$, respectively.

Our model does not indicate a significant interaction between group and visit in total NNAL per cigarette. The mean level of total NNAL per cigarette increased significantly from .06 pmol/mg/cigarette at baseline to .20 pmol/mg/cigarette at end-of treatment, $t(72)=2.91$, $p=.005$.

3.4. Abstinence rates

Of the 103 participants, 53 entered smoking cessation treatment (nicotine patch group, $n=21$; placebo group, $n=19$; and nicotine gum group, $n=13$). Few participants achieved a 7-day point prevalence rate of abstinence at the end-of-treatment (1.9%, $n=2$), three-month (12.6%, $n=13$) or six-month follow-up visits (6.8%, $n=7$). No participants attained a 30-day period of abstinence at the end-of-treatment. At the three-month and six-month follow-up visits, 6.8% ($n=7$) and 4.9% ($n=5$) participants achieved a 30-day period of abstinence, respectively. There were no significant differences among treatment groups with regard to 7- or 30-day abstinence rates (all adjusted p -values are $>.05$).

4. Discussion

There are three main conclusions that can be drawn from this study. First, reducing smoking among adolescents is achievable, although whether this reduction has beneficial effects is uncertain and debatable. The results of this study showed that nearly half of the participants (49.4%, $n=41$) reduced their smoking by at least 50%. However, participants' level of reduction waned by the six-month follow-up visit to a reduction of only 27.1% of their baseline smoking rate.

Second, there were no important differences in treatment groups with regard to reducing smoking or the related outcomes. Interestingly, nicotine replacement seems to reduce compensatory smoking as measured by CO/cigarette and cotinine/cigarette, but only at the 3-month follow-up.

Third, reducing smoking led to only a modest reduction in some biomarkers (CO), but not others (total NNAL). Unless smoking reduction is sustained and perhaps reduced further, decreasing smoking may not lead to substantial reductions in toxicant uptake (see Hecht et al., 2004).

As a cautionary note, although participants reduced their smoking level at the six-month follow-up visit, their CO and cotinine levels increased. In some participants ($n=11$), although the mean of the baseline cotinine levels was lower than the level observed at follow-up, one of the baseline cotinine values was in fact higher. We cannot totally rule out the effect of cigarette reduction on increased smoke exposure after treatment in our smokers. A subset of smokers may have learned to smoke their cigarettes more efficiently (e.g., puffing harder on a cigarette). The increase in CO and cotinine levels could be due to inaccurate reporting of smoking rate by the participants (e.g., social desirability influences) or measurements made at times when there were no restrictions on smoking (summer months or holidays). After looking at the data, independent investigators believed observed results were most likely a function of greater free time, variability in smoking patterns and the trajectory towards increased smoking behavior.

There are several limitations of this study. First, there was no placebo for the nicotine patch or the nicotine gum, nor was the study double-blinded. This study also had limited power to detect inter-group differences due to being an observational and safety study. Second, feasibility of the replicating this study in the community may be limited in terms of the cost of providing medication, CBT and participant compensation. Third, this sample may be unrepresentative of adolescent smokers. There was a very high level of co-morbidity among participants. This may be because 3 of the 14 schools where the study was conducted were for students who have recently completed alcohol or drug treatment. A final consideration is whether advertising a smoking reduction program at schools could influence adolescents to think that smoking at a reduced level poses no health issues or that quitting isn't necessary.

In summary, reduction in smoking may be a potential method to aid adolescents who are unable or unwilling to quit, but should not be an end goal. Furthermore, some caution should be exercised because adolescents may learn to smoke more efficiently when reducing smoking and the health benefits from reduction are unknown. Future research is necessary to determine if reduction could facilitate an abstinence attempt in adolescent smokers not immediately interested in quitting.

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Table 1

Demographics of study participants

Measure (mean, SD)	Nicotine patch n=34	Nicotine Gum n=33	Placebo n=36	Overall n=103	P value
Cigarettes per day	11.1 (5.2)	12.7 (4.9)	11.6 (6.7)	11.8 (5.6)	0.52
Age (years)	16.7 (1.10)	16.7 (1.10)	16.3 (1.3)	16.6 (1.2)	0.25
CO (PPM)	7.1 (4.1)	6.9 (3.4)	5.7 (3.2)	6.6 (3.6)	0.22
Weight (lb)	157.7 (43.3)	148.5 (35.3)	151.4 (36.8)	152.5 (38.4)	0.61
SBP (mmHg)	115.2 (8.5)	113.9 (9.7)	113.1 (8.4)	114.0 (8.9)	0.62
Age first cigarette (years)	12.1 (2.2)	11.1 (2.4)	11.2 (2.4)	11.5 (2.4)	0.21
Age daily smoker (years)	13.7 (2.0)	12.9 (2.0)	13.1 (2.0)	13.3 (2.0)	0.30
Number of quit attempts	7.6 (12.8)	3.5 (2.4)	3.6 (2.4)	4.9 (7.8)	0.09
Longest period of abstinence from smoking (days)	42.5 (98.2)	29.3 (44.8)	14.4 (15.3)	28.7 (62.7)	0.29
Alcoholic drinks/occasion	4.9 (2.7)	4.6 (1.9)	4.7 (3.3)	4.7 (2.7)	0.95
Most alcoholic drinks/occasion	5.7 (4.9)	6.9 (5.2)	6.0 (5.0)	6.1 (5.0)	0.80
Measure (%)	Nicotine Patch	Nicotine Gum	Placebo	Overall	P value
Females	48.5	57.6	66.7	57.8	0.31
Caucasian	90.9	84.9	83.3	86.3	0.75
African American	0	0	0	0	
SE Asian/Pac. Is.	0	6.1	8.3	4.9	
Native American	3.0	3.0	0	2.0	
More than one race	6.1	3.0	5.6	4.9	
How many of 3 closest friends smoke					
0	0	0	0	0	0.45
1	0	3.1	8.6	4.1	
2	19.4	21.9	14.3	18.4	
3	80.6	75.0	77.1	77.5	
Past Nicotine Replacement Therapy use					
Gum	26.5	21.9	27.8	26.5	0.91
Patch	20.6	25.0	19.4	22.5	
Smoked cigars	28.1	37.5	36.1	34.0	0.18
Smokeless tobacco use	6.1	15.2	8.33	9.8	0.57
Brand smoked					
Marlboro	61.3	58.6	41.2	53.2	0.29
Camel	12.9	10.3	20.6	14.9	
Newport	9.7	20.7	29.4	20.2	
Parliament	6.4	6.9	8.8	7.4	
Other	9.7	3.5	0	4.3	
Psychiatric treatment	54.3	51.6	77.1	61.4	0.06

Measure (mean, SD)	Nicotine patch n=34	Nicotine Gum n=33	Placebo n=36	Overall n=103	P value
Psychiatric medication use	29.4	41.9	54.8	41.7	0.12
Alcohol use	57.6	43.8	48.6	50.0	0.53
Marijuana or other drug use	32.4	18.8	15.2	22.2	0.20
Alcohol/drug treatment	51.6	51.6	50.0	51.0	0.99
Caffeine use	90.9	87.9	88.6	89.1	0.92

Table 2
Summary statistics for smoking variables across treatment groups

Visit	Measure (mean, S.D.)	Nicotine Patch n=34	Nicotine Gum n=33	Placebo n=36	Overall n=103
Baseline					
Cigarettes Per Day		11.1 (5.2)	12.7 (4.9)	11.6 (6.7)	11.8 (5.6)
CO ^a		7.1 (4.1)	6.9 (3.4)	5.7 (3.2)	6.6 (3.6)
Cotinine ^b		3476.4 (2025.3)	3759.4 (2652.2)	3071.6 (2099.7)	3425.1 (2266.7)
Total NNAL ^{c,d}		0.66 (0.72)	0.79 (0.71)	0.54 (0.54)	0.66 (0.66)
End-of-treatment					
Cigarettes Per Day		5.0 (4.5)	6.0 (2.5)	5.4 (2.3)	5.4 (3.3)
CO		5.2 (4.0)	6.7 (3.9)	5.1 (3.6)	5.6 (3.8)
Cotinine		3464.4 (2763.1)	3946.0 (2671.1)	2505.0 (2486.8)	3284.4 (2681.1)
Total NNAL		0.65 (0.71)	0.87 (0.86)	0.76 (1.48)	0.75 (1.07)
3-Month Follow-up					
Cigarettes Per Day		6.1 (6.5)	7.6 (5.5)	4.6 (4.8)	6.0 (5.7)
CO		7.6 (7.2)	7.9 (5.0)	5.4 (4.4)	6.9 (5.7)
Cotinine		3263.5 (3401.5)	2718.5 (2019.4)	2733.8 (3007.1)	2912.8 (2858.4)
6-Month Follow-up					
Cigarettes Per Day		8.9 (7.8)	9.3 (7.2)	7.8 (6.5)	8.6 (7.0)
CO		8.7 (5.0)	9.1 (5.9)	6.0 (4.9)	7.6 (5.4)
Cotinine		4659.8 (2967.4)	4346.3 (3631.0)	3949.1 (3762.5)	4264.4 (3484.5)

^a (ppm)

^b (ng/ml)

^c (pmol/mg)

^d NNAL was not analyzed at 3- or 6-month follow-up visits

No treatment effects were found across these visits ($p > .05$). These inferences are based on a linear mixed model.