Minimal Contact Treatment for Smoking Cessation

A Placebo Controlled Trial of Nicotine Polacrilex and Self-directed Relapse Prevention: Initial Results of the Stanford Stop Smoking Project

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To determine the effectiveness of nicotine polacrilex combined with self-administered relapse prevention materials in maintaining smoking cessation, we conducted a randomized, double-blind, placebo controlled trial. Volunteers aged 18 to 65 years responding to media announcements were required to quit smoking for 48 hours without assistance. Of 1844 potential participants, 136 were medically excluded, 535 declined to make a quit attempt, and 573 were unable to quit, leaving 600 participants (35%) who were randomized. Eight self-help relapse prevention modules were mailed weekly. Gum was used either ad lib for smoking urges or on a fixed, hourly schedule (12 pieces per day). Only 15% of the subjects in each gum group stopped using the gum altogether because of side effects, but only 20% of the ad lib groups and 40% of the fixed-dosage group used at least eight pieces of gum per day during the first week. The abstinence rates (for at least seven days) at the six-month follow-up were 31% in both active gum groups and 22% in the placebo and no gum groups. Relapse rates in the two active gum groups were about half those in the placebo and no gum groups. Nicotine polacrilex may be a useful adjunct to minimal contact smoking cessation formats, which have broad appeal. Also, minimal contact relapse prevention programs may assist physicians in helping patients to maintain smoking cessation using nicotine polacrilex.

(*JAMA* 1988;260:1575-1580)

CIGARETTE smoking is the single most important behavior contributing to illness, disability, and death in the United States.[1] Research designed to improve the applicability of cigarette smoking cessation procedures is in its infancy. Such research is important because survey data indicate that relatively few smokers will participate in formal smoking cessation clinics.[2] The large majority of smokers who desire to quit appear interested in self-administered, minimal contact treatment formats.[2] Such formats would be particularly useful to physicians with patients who need to quit smoking.

See also pp 1565, 1570, 1581, 1593, and 1614.

Although a number of "self-help" smoking cessation programs have appeared in the marketplace, most evaluations of self-help materials have been conducted under therapist-administered conditions.[3] Controlled evaluations of minimal contact cessation programs have appeared infrequently in the literature.[4-8] The findings from these studies do suggest that self-help programs may provide a reasonably cost-effective means of service delivery. However, more effective self-help programs would greatly enhance the potential impact of this type of treatment.

Nicotine polacrilex is a potentially useful pharmacologic aid for the elimination of cigarette smoking that could be used to enhance the effectiveness of minimal contact interventions. In 11 studies[8-18] comparing nicotine polacrilex with either placebo gum or no gum, combined with psychological therapy, six[8,9,11-14] showed significantly higher quit rates for active gum at six-month follow-up. Two studies[10,15] reported only one-year data, and the larger of the two reported a significant effect.[15]

When prescribed in a medical practice context with little additional intervention beyond physician advice, nicotine polacrilex has not proved as useful. Of seven studies examining nicotine polacrilex combined with medical advice,[19-25] only two reported a significant impact.[20,21] Both a standard review article[26] and a meta-analysis[27] covering most of these studies concluded that nicotine polacrilex is best used in conjunction with other smoking interventions.

The integration of pharmacologic and innovative psychological strategies within a minimal contact treatment format offers a challenging new area for smoking researchers. To date, only one uncontrolled trial has examined the effects of nicotine polacrilex combined with a minimal contact intervention, which produced a 41% abstinence rate at 12 months.[28] In this article we report two- and six-month smoking abstinence rates from an ongoing investigation of self-help treatment approaches combining nicotine polacrilex or placebo with self-administered smoking relapse prevention materials delivered through the mail. We predicted that abstinence rates for nicotine polacrilex conditions would be significantly greater than rates for placebo conditions at each assessment. If true, this would provide a practical means for intensifying the minimal contact approach, particularly for physicians.

METHODS

Design

The Stanford (Calif) Stop Smoking Project is a randomized clinical trial using a 4×3 fully crossed factorial design. The pharmacologic factor contains four levels: nicotine polacrilex (gum) delivered ad lib or on a fixed-dosage schedule, placebo gum, and no gum. The psychological treatment factor contains three levels: self-selected relapse pre-

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vention modules, randomly administered modules, and no modules. The full study calls for 100 subjects to be randomized into each of the 12 cells to provide sufficient power to compare pairs of cells. This design was chosen to allow early evaluation of the major intervention components by collapsing cells for analysis. In this article we compare the four gum conditions, ignoring module conditions, for the first 600 subjects (about 150 subjects per gum condition).

Recruitment and Exclusion Criteria

Participants aged 18 to 65 years were recruited through newspaper advertisements, radio public service announcements, and local television programs. The "self-help" nature of the study was emphasized in these announcements but no mention of nicotine gum was included. Interested smokers were instructed to telephone the project office and were then provided a brief overview of the study and administered a baseline survey. The study was then explained in detail, including the requirement that, to participate in the study, each person had to quit smoking for 48 hours and then come to a project office for additional interviews and biochemical confirmation of nonsmoking. Smokers who remained interested in participating set a quit date and were scheduled for a center visit 48 hours later. All other individuals were given the names of other smoking cessation resources in their area. Written informed consent was obtained during the postquit visit.

Potential participants were also asked a series of medical questions to assess their eligibility for nicotine polacrilex. Individuals who were pregnant, lactating, or receiving active treatment for cancer or peptic ulcer disease were excluded from the study. Individuals who reported temporomandibular joint disease or other difficulties with chewing gum were also excluded. Those who reported a history of heart disease, recent chest pain, diabetes, or thyroid disease were asked to obtain written permission to participate from their physicians. We provided a detailed letter to each physician explaining the nature of the study and the Food and Drug Administration cautions on the use of nicotine polacrilex.

The 48-hour abstinence requirement was included in the study for two reasons: (1) The intervention materials focus on relapse prevention, because this is the most important aspect of sustained smoking cessation (most smokers report previous quit attempts with abstinence periods as long as several months). (2) We wanted to exclude quitters who were likely to fail early so we could offer the intervention program to those most likely to benefit.

Evaluation

Questionnaires.—The baseline telephone questionnaire assessed demographic variables, smoking history, previous quit attempts, an index of nicotine dependence, and pertinent medical history. The dependence index was the Fagerstrom Tolerance Questionnaire[29] modified for telephone administration. During the first project center visit, 48 to 96 hours after quitting, additional information was collected by self-administered questionnaire, including the quit methods used, craving, urges, and withdrawal symptoms.

Follow-up questionnaires were administered by telephone 2, 6, 12, and 24 months after randomization. Self-reported smoking status was obtained for the past week, the past month, and since the previous assessment. Only participants who denied smoking even a single puff of a cigarette were considered nonsmokers (for the appropriate duration); they were asked to come to the project office for biochemical testing.

Biochemical Assessment. — Nonsmoking status was assessed by expired air carbon monoxide measurement and by saliva thiocyanate (two-month follow-up) or cotinine (6-, 12-, and 24-month follow-up) concentrations. Expired air carbon monoxide measurements were performed with the Ecolyzer (Energetics Science Inc, New York), and thiocyanate concentrations were measured using the automated method of Butts et al[30] slightly modified for saliva. Saliva samples were collected by having participants hold a dental roll in their mouths until it was saturated, as described by Luepker et al.[31] Thiocyanate measurements were used at two months because some subjects were still using active nicotine polacrilex and would therefore test positive for cotinine, a direct metabolite of nicotine (thiocyanate concentrations are elevated in the body fluids of smokers because of trace amounts of hydrogen cyanide in cigarette smoke). Cotinine is a better biochemical marker than thiocyanate because the latter has dietary sources and is therefore present in all individuals, whereas cotinine is undetectable in nonsmokers. Cotinine concentrations were measured for this study according to the method of Jacob et al.[32]

Nonsmokers were reclassified as smokers at the two-month visit if *both* the carbon monoxide concentration was greater than 8 ppm *and* the saliva thiocyanate concentration was greater than 100 mg/L.[33] At subsequent assessments, cotinine measurements alone were used, and reclassification occurred when the cotinine level exceeded 20 μg/L (this allows for some indirect cigarette smoke exposure).

Intervention

Individuals who quit for 48 hours (carbon monoxide concentration ≤8 ppm) were randomized into one of the 12 intervention cells. Assignment to gum condition was double-blind; since the placebo gum was given only ad lib, neither the project staff nor the participants were told the details of the design during the study. Unblinding occurs at the 24-month follow-up.

Active (2 mg) and placebo gum were supplied to the participants in identical packaging along with appropriate instructions and warnings (both active and placebo gum were supplied by the Merrell Dow Research Institute, a division of Merrell Dow Pharmaceuticals Inc, Cincinnati). Participants in the *ad lib* and *placebo* groups were instructed to chew a piece of gum whenever they felt a strong need to smoke a cigarette. Starting in week 4, these participants were asked to cut back on their gum use as quickly or as slowly as they chose, with the goal of chewing no gum by week 9. An upper limit of 30 pieces of gum per day was set. Participants in the *fixed-dosage* group (all using active gum) were instructed to chew one piece of gum per hour at least 12 hours per day. This could be doubled to two pieces per hour if smoking urges continued. Beginning in week 4, a fixed tapering schedule was provided to gradually eliminate gum use by week 9. Gum use could be extended to three months, but we provided no additional gum, active or placebo, beyond that time. All instructions were provided by trained research assistants who were not physicians.

Sixteen written modules were designed by the investigators to provide self-instruction on how to avoid smoking in specific high-risk situations (eg, while drinking alcohol, while driving, after eating). Using the modules, participants identified specific triggers in the context of the situation and made cognitive and behavioral plans for avoiding relapse when confronted by the triggers. The modules emphasized performance-based experience by encouraging participants to place themselves in high-risk situations and to use their plans to overcome urges to smoke.

All participants in the relapse prevention module conditions were given the first module, "How to Cope With the Urge to Smoke Without Smoking." Individuals in the self-selecting condition then chose another seven modules to receive weekly by mail based on their

Table 1.—Baseline Characteristics of Subjects by Experimental Condition*

Variable	Experimental Condition			
	Ad Lib	Fixed Dosage	Placebo	No Gum
No. of subjects	152	147	148	153
Sex, % male†	48.7±4.1	45.6±4.1	52.0±4.1	44.4±4.0
Married, %†	49.3±4.1	46.9±4.1	47.3±4.1	54.9±4.0
Employed, %†	72.4±3.6	72.1±3.6	79.0±3.3	71.0±3.7
12 y of education, %†	17.8±3.1	22.4±3.4	19.6±3.3	22.9±3.4
Race, % White non-Hispanic†	80.9±3.2	83.0±3.1	91.2±2.3	87.6±2.7
Cigarettes per day‡	24.0±12.3	23.4±11.5	26.0±11.5	25.5±13.2
Duration of smoking, y‡	25.5±11.4	25.0±10.0	25.5±10.4	25.3±11.4
Nicotine level, mg‡	0.8±0.3	0.7±0.3	0.8±0.3	0.8±0.3
No. of previous quit attempts‡	3.4±1.9	3.2±1.9	3.5±2.0	3.4±1.9
Dependence index‡	14.7±3.7	14.6±3.9	14.8±3.0	14.8±3.6

*No differences are statistically significant ($P<.05$) by χ^2 analysis or analysis of variance.
†±SE.
‡Mean±SD.

Table 2.—Adherence to Treatment Program Elements by Experimental Condition

Program Element	Experimental Condition				P*
	Ad Lib	Fixed Dosage	Placebo	No Gum	
Returned weekly reports, %†‡	86.2±2.8	88.4±2.6	77.0±3.5	81.0±3.2	.039
Recorded trigger, %†‡	62.6±3.9	74.0±3.6	47.0±4.1	53.8±4.0	.001
Used strategy, %†‡	40.4±4.0	50.0±4.1	22.6±3.4	29.8±3.8	<.001
Used gum, %†§	21.0±3.3	43.5±4.1	20.3±3.3	...	<.001
Week 1 gum use, pieces per day‖	5.4±4.5	9.5±6.5	5.6±4.9	...	<.001
Week 2 gum use, pieces per day‖	5.0±5.1	8.9±5.9	4.0±4.8	...	<.001
No. of weeks used gum‖	4.8±3.0	5.8±2.7	3.6±2.9	...	<.001

*By χ^2 analysis or analysis of variance.
†±SE.
‡Proportion of subjects who returned at least five of eight weekly report forms.
§Proportion of subjects who used eight pieces or more of gum per day in the ad lib group and ten pieces or more per day in the fixed dosage group.
‖Mean±SD.

perceived efficacy at coping with different high-risk situations. The random group received seven modules selected at random from the 15 remaining modules.

The entire study center visit required between 45 and 75 minutes, most of which was spent in data collection. Instructions on gum and module use lasted ten to 20 minutes. No specific relapse prevention advice was offered by the research assistants, who were not acting as therapists. Contact during the eight-week intervention period was limited to data collection inquiries and responses to problems with the gum, both by telephone, and averaged one to two contacts per participant.

Adherence to the treatment program was monitored through weekly progress reports mailed by participants to the project offices. These reports included the number of cigarettes smoked each day, degree of craving, a 16-item self-efficacy scale, and, where appropriate, the number of pieces of gum used, gum side effects, and questions about use of the modules. Each participant left a $40 deposit, which was returned if all assessment materials were returned and the two-month visit was completed. In addition, subjects returned all unused gum at the two-month visit.

Analysis

Analyses were limited to the first 600 participants in the study and compared the results by gum condition, ignoring module condition. This analysis was planned at the beginning of the study because the final sample size is required for individual cell pair comparisons; the effectiveness of nicotine polacrilex can therefore be evaluated at this time. This analysis can be repeated in the second 600 subjects later as a replication study; this will be a more powerful test of the effectiveness of nicotine polacrilex than evaluating the gum once in all 1200 subjects.

The smoking status after two and six months was available for all 600 participants. The principal outcome variable was the proportion of each group that reported not smoking even a puff for the past week (seven-day abstinence rate). We also compared the proportion who reported not smoking for the past month (one-month abstinence rate).

A χ^2 analysis was done to test the hypothesis that the different gum conditions were statistically the same. Individual gum groups were compared in pairs using the Bonferroni adjustment for multiple comparisons (alpha, 0.05; confidence, 0.95). Standard statistical software packages were used.

In addition to comparing abstinence rates at two specific time points, we also compared relapse rates during the entire follow-up. Relapse was defined as self-reported smoking of at least one puff on seven consecutive days. All subjects were abstinent when randomized, and the time to relapse was obtained at follow-up. The proportion of each experimental group that remained abstinent over time can thus be plotted using standard survival analysis methods.[34]

RESULTS

Recruitment

During the first year of recruitment, nearly 2500 telephone inquiries were received, evenly distributed among the three program offices (Oakland, Calif, 29%; San Jose, Calif, 35%; and Stanford, 37%). Baseline interviews were completed for 75% of these inquiries; about half of the 25% of the callers who were not interviewed were ineligible (out of the age range or calling for someone else), and the other half of these callers could not be reached or were no longer interested when telephoned. Of the 1844 individuals who completed baseline surveys, 136 were ineligible, mostly on medical grounds. Sixty-nine percent of those eligible to participate (1173) scheduled a postquit visit, and 600 were successfully randomized (51% of those scheduled, or 35% of those eligible). Eligible subjects who did not schedule a postquit visit (535 subjects [31%]) were not interested in participating in the study after it was fully explained at the end of the baseline interview. The 573 scheduled participants who were not randomized were unable to quit for the required 48 hours.

Baseline Comparisons

Table 1 compares the four gum groups at baseline on selected personal and smoking characteristics. Approximately equal numbers of men and women were randomized to each group; most were employed, and most were white. The average smoking level was 25±12 cigarettes per day (mean±SD). None of the groups differed significantly on these or other variables.

Adherence

Table 2 compares the various experimental groups for adherence to differ-

Table 3.—Subjects Reporting Gum Side Effects by Experimental Condition

Side Effect	Experimental Condition, % of Subjects: Ad Lib	Fixed Dosage	Placebo	P*
Oral soreness or burning	42.9	54.7	39.4	.030
Excessive salivation	24.8	24.1	18.9	.459
Hiccups	20.7	29.9	7.8	<.001
Nausea	24.1	35.0	15.8	.001
Lightheadedness	19.3	17.5	21.3	.744
Oral sores or ulcers	27.0	33.6	23.4	.170
Gastrointestinal distress	24.8	34.3	20.5	.033
Jaw soreness	19.3	34.3	35.9	.004
Anorexia	12.8	18.2	7.9	.044
Headache	22.1	24.1	22.8	.927
Discontinued gum use due to side effects	13.7	12.5	14.2	.920

*By χ^2 analysis.

Table 4.—Abstinence Rates Corrected for Biochemical Measures by Experimental Condition

	Abstinence Rates by Experimental Condition, % of Subjects: Ad Lib		Fixed Dosage		Placebo		No Gum		
Follow-up	Rate	95% Confidence Interval	Rate	95% Confidence Interval	Rate	95% Confidence Interval	Rate	95% Confidence Interval	P*
2 mo									
7-d	38	31-46	40	32-49	24	17-31	28	21-36	.005
1-mo	36	28-44	34	27-42	18	12-25	22	16-30	.001
6 mo									
7-d	30	23-38	30	23-38	22	16-30	22	16-30	.156
1-mo	24	17-31	29	23-37	19	13-26	17	12-24	.072

*By χ^2 analysis.

ent elements of the treatment program. Over 80% of the subjects returned at least five of the eight weekly reports, while lower proportions of each group recorded a personal relapse trigger or that they had used a strategy to deal with the trigger without smoking. The groups receiving active gum were the most compliant, and the placebo group was the least compliant; the no gum group fell between the active and placebo groups. A minority of the patients met the adherence criteria, but twice as many met these criteria in the fixed-dosage group. The amount and duration of gum use also varied significantly among the three groups receiving gum. Pairwise comparisons of these three groups using a Bonferroni correction for multiple comparisons showed that the fixed-dosage group used significantly more gum than either the ad lib or placebo groups during both the first and second weeks; the ad lib and placebo groups did not differ from one another. However, all three pairwise comparisons of the duration of gum use (mean number of weeks) were significant. In summary, treatment program adherence was generally better in the groups that received active gum; the fixed-dosage group showed the best adherence and had significantly greater exposure to the gum.

Side Effects

Overall, about 75% of the subjects who received gum reported at least one side effect during the first four weeks; this fell to 35% in the last four weeks. Table 3 shows the proportion of each gum group that reported the ten most common side effects ascribed to nicotine gum. Only hiccups and nausea were clearly more prevalent in the active gum groups, although there were trends for anorexia, oral soreness, gastrointestinal distress, and jaw soreness. Not surprisingly, considering the adherence data presented above, the fixed-dosage group tended to have a higher prevalence of side effects than the ad lib group. However, the three groups did not differ in the proportion of participants who actually stopped using the gum because of side effects.

Follow-up

At the two-month follow-up, we were unable to locate five subjects (0.8%), who were counted as smokers. Biochemical test results were obtained for 535 subjects (89.2%), while 11 had moved out of the area, and 49 refused to visit the survey center (only eight of these 49 denied smoking). Of the 535 who returned to the survey center, 212 denied smoking in the past seven days; nine of these nonsmokers (4%) were reclassified as smokers based on their carbon monoxide and thiocyanate results. Eight more nonsmokers were reclassified because they were missing both biochemical measures, leaving 195 nonsmokers at the two-month follow-up for analysis.

At the six-month follow-up, we were unable to obtain telephone histories from 20 subjects, and 419 reported that they had had at least a puff of a cigarette in the past seven days. The remaining 161 subjects were self-reported nonsmokers, but 49 (30%) failed to come to the survey center for testing (we have since instituted home visits to reduce this proportion). Of the other 112 subjects, only five (4%) had elevated saliva cotinine levels (12 others were using nicotine gum or had inadequate saliva samples but had low expired air carbon monoxide levels and were classified as nonsmokers). Since visiting a study center requires a significant effort, we did not reclassify the 49 unconfirmed nonsmokers. In fact, nine of these 49 nonsmokers had moved out of the area, and 26 continued to report abstinence at one year (15 had low cotinine levels, often at a home visit), leaving only 14 who could well have been smoking at the six-month follow-up. Considering the very low rate of reclassification in those who did provide saliva, however, some were probably truly abstinent. The outcome results reported below count 156 participants as seven-day nonsmokers at six months. The 49 unconfirmed nonsmokers were equally distributed among the four gum groups ($\chi^2 = 1.17$, $P = .76$).

Outcome

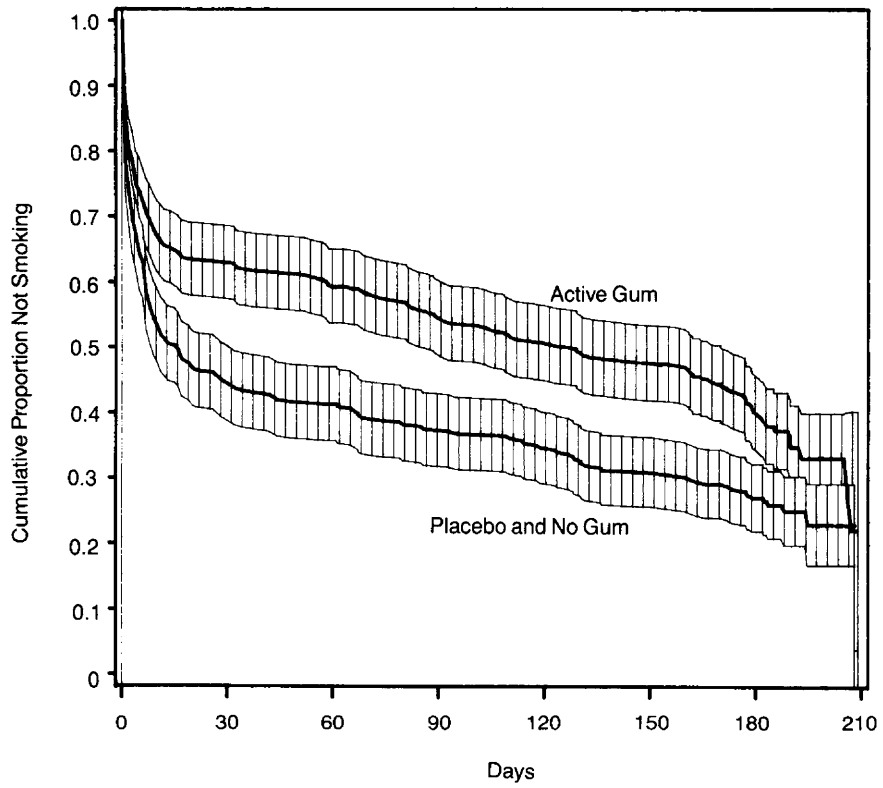
Table 4 displays the two- and six-month abstinence rates for each experimental condition. These rates are based on self-reports corrected for biochemical measures as described above (195 nonsmokers at two months and 156 at six months). The seven-day abstinence rates are comparable with those of other studies and clearly show a significant treatment effect, with both active gum groups outperforming the other two groups. A similar pattern is seen for the one-month abstinence rate. Both abstinence rates show a similar pattern at six months, although the χ^2 test no longer shows a statistically significant difference in rates (at the .05 level).

Because the outcomes in the active gum groups resemble one another and the outcomes in the placebo and no gum groups also appear similar, we combined these pairs and compared the outcome using active gum with the outcome using no active gum (Table 5). This analysis demonstrates a significant effect of

Table 5.—Abstinence Rates for Active Gum Conditions Combined (n = 299) and No Active Gum Conditions Combined (n = 301)

	Abstinence Rates by Combined Experimental Condition, % of Subjects						
	Active Gum		Placebo or No Gum		Difference Between Groups		
Follow-up	Rate	95% Confidence Interval	Rate	95% Confidence Interval	Rate	95% Confidence Interval	P*
2 mo							
7-d	39	34-45	26	21-31	13	6-20	.001
1-mo	35	30-41	20	16-25	15	8-22	<.001
6 mo							
7-d	30	25-36	22	18-27	8	1-15	.022
1-mo	26	22-32	18	14-23	8	2-15	.016

*By χ^2 analysis.



Proportion of participants without smoking relapse (defined as smoking at least one puff on each of seven consecutive days) in two active gum groups combined and in placebo gum and no gum groups combined.

nicotine polacrilex at both the two- and six-month follow-up. Both the seven-day and one-month abstinence rates are about 1.5 times higher in the nicotine polacrilex groups.

As noted above, biochemical test results are unavailable for 49 of the 156 nonsmokers at the six-month follow-up. Although most of these subjects were probably truly abstinent, we repeated the analysis in Table 5 with these 49 subjects reclassified as smokers. The abstinence rates were lower, of course (21% in the active gum users and 14% in nonusers), but the comparison remains significant ($\chi^2 = 5.30$, $P = .02$).

The "survival" (nonsmoking) analysis is shown in the Figure. The proportion of each group that did not have a relapse declined rapidly in the first month and then leveled off, although relapses continue to occur steadily. The active gum groups relapsed at about 40% of the rate of the other two groups over the entire period, and the benefit is present from an early point. The average curve for the two active gum groups is significantly different than the one for the placebo and no gum groups (log-rank $\chi^2 = 13.8$, $P = .0002$).

COMMENT

This study is among the first controlled investigations of nicotine polacrilex combined with a minimal contact psychological intervention. The combined treatment produced higher abstinence rates after six months than either placebo gum or no gum. While those receiving a fixed dosage of gum received a higher dose overall and tended to do better at two months, by six months they were indistinguishable from the ad lib dosage group. Quit rates in the active gum conditions were about 1.5 times higher than in the other two groups, which is clinically significant and consistent with the findings of previous studies on nicotine polacrilex.[8-28] The adequate sample size and experimental design of this trial plus the absence of a placebo effect (compared with no gum) all support the inference that the treatment differences were due to the active agent, nicotine polacrilex.

Side effects from the gum were common but generally manageable. About 15% of the subjects stopped using the gum because of the side effects regardless of whether it was active or placebo. Several of the side effects are probably related to chewing and not to nicotine. Indeed, despite the efforts of the research team, overall use of the gum (placebo or active) was rather low (20% of participants in the ad lib groups and 40% of those on the fixed-dosage schedule). These results indicate that some other route of administration of nicotine (eg, transnasal) may be preferable.

Bias is an unlikely explanation of the results presented here. Baseline covariables were equally distributed among the groups, and the double-blind design minimized the potential for cointervention. However, the gum groups did receive, on average, one additional telephone contact to discuss side effects. It is unlikely that these contacts account for the treatment effect, since they also occurred in the placebo group. The active gum groups did show better adherence to the written materials, especially compared with the placebo group. However, since the materials were self-administered, this is best viewed as a desirable cointervention, perhaps due to the perceived usefulness of the gum or to decreased withdrawal symptoms. Indeed, since the placebo group had the lowest adherence, it may be that a lack of perceived gum effect led to "resentful demoralization" in this group.[35] Biased self-reporting of smoking status could not explain the results, because biochemical testing was done for most participants, because those who were not tested were equally distributed among the four experimental groups, and be-

cause the results were not changed by restricting the analysis to only those with available biochemical markers.

Some features of the study design may have limited the impact of nicotine polacrilex. Smokers volunteered for a self-help program, not for nicotine gum, and individuals who specifically request nicotine replacement might benefit more than those who do not. The 48-hour quit requirement may have eliminated some highly dependent smokers who would have benefited more from nicotine polacrilex. We discouraged gum use beyond three months, and a longer intervention period might have resulted in more differences at six months.

This trial may be more generalizable than many smoking cessation studies. Subjects were recruited from a wide geographic area and included equal numbers of men and women. Randomized subjects constituted 35% of people who were eligible for the trial, and most of those eligible who were not randomized were unable to quit initially. The results should be generalizable to the large number of smokers who are sufficiently motivated to make a quit attempt. The intervention involves minimal contact, which has wide appeal to both smokers and health care providers. The results are particularly relevant to practicing physicians, who are asked to prescribe nicotine polacrilex but are rarely able to provide additional behavioral counseling. For patients who are not interested in group programs, physicians can prescribe self-help programs along with nicotine polacrilex.

Some caution is appropriate in comparing the results of this study with those of other smoking cessation studies. The abstinence rates in Tables 4 and 5 are based on the 600 randomized participants who were able to quit smoking for 48 hours without assistance from the investigators. An approximately equal number of individuals tried to quit for 48 hours but were unsuccessful. The abstinence rates can be halved to assess the impact of the program on all the smokers who were at least interested in trying to quit. It is probable, however, that some proportion of these unsuccessful "attempters" would also have dropped out of a structured group program at an early stage and would not have been included in the final analyses. It is therefore difficult to compare directly the results of this study with those of other smoking cessation studies.

In summary, this study supports the use of nicotine polacrilex to enhance the effectiveness of a self-directed behavior change program in assisting motivated individuals to maintain abstinence from cigarette smoking. Prescribing the gum in a fixed dosage does not appear to improve its efficacy but does significantly increase the amount and duration of gum use. Such a fixed-dosage schedule may be useful, therefore, in selected individuals with high physical dependency or persistent withdrawal symptoms with ad lib use. Physicians interested in assisting those smoking patients who are uninterested in group programs could incorporate self-help materials, such as those available from the American Lung Association, New York, and the American Academy of Family Physicians, Kansas City, Mo, into a comprehensive approach that includes nicotine polacrilex. Requiring a 48-hour quit time before continuing treatment may also help focus a physician's efforts on those most likely to benefit.

This study was supported by US Public Health Service grant 5 RO1 CA38303 from the National Cancer Institute and by the Merrell Dow Research Institute, Cincinnati.

The authors thank Nathan Maccoby, PhD, Abby C. King, PhD, David P. L. Sachs, MD, and Marilyn Winkleby, PhD, for commenting on earlier drafts of the manuscript, Paul T. Williams, PhD, for statistical advice, Ann Varady, MS, for statistical programming, and Cathy Nevin for typing the manuscript.

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