Transdermal Nicotine Therapy and Primary Care

Importance of Counseling, Demographic, and Participant Selection Factors on 1-Year Quit Rates

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Objective: To evaluate the smoking cessation efficacy of nicotine patch therapy as an adjunct to low-intensity, primary care intervention.

Design: Randomized, placebo-controlled, double-blind, multisite trial.

Settings: Twenty-one primary care sites in Nebraska.

Patients: A total of 369 smokers of 20 or more cigarettes per day.

Intervention: Two brief primary care visits for smoking intervention with 10 weeks of active or placebo patch therapy.

Main Outcome Measures: Confirmed self-reported abstinence 3, 6, and 12 months after the quit day.

Results: Compared with placebo control subjects, participants assigned nicotine patches had higher 3-month (23.4% vs 11.4%; P < .01) and 6-month (18.5% vs 10.3%; P < .05) abstinence rates. The 1-year abstinence rates for the active and placebo patch groups were 14.7% and 8.7%, respectively (P = .07). Of smokers aged 45 years and older, 9 (18.8%) of 48 using active patches compared with 0 of 31 using placebo patches achieved 12-month abstinence (χ² = 6.56; P < .05). Among those with high nicotine dependency scores (Fagerstrom score ≥ 7), 1-year abstinence rates were significantly higher in the nicotine patch group (19.1%) compared with the placebo group (5.0%) (χ² = 10.7; P = .001). However, there was no significant difference in 1-year quit rates for participants with low Fagerstrom scores (< 7).

Conclusions: Nicotine patch therapy enhanced 6-month quit rates as an adjunct to brief primary care intervention. The highest quit rates were achieved by participants who specifically contacted the site to enroll in the study or to obtain a prescription for nicotine patches. Differences in participant selection factors may account, in part, for the lower smoking cessation rates associated with primary care intervention. Duration of counseling, patient age, and Fagerstrom scores may be important factors related to the long-term smoking cessation success of nicotine patch therapy.

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TRANSDERMAL nicotine therapy repeatedly has been found to enhance smoking cessation rates when used as an adjunct to group or individual counseling programs.1-8 Most of these investigations, however, have been conducted in specialized smoking cessation settings. As a result, relatively limited information is available on the role of transdermal nicotine therapy in a primary care practice setting.

Results of five 1-year trials1-8 indicate that transdermal nicotine therapy is an effective smoking cessation aid as an adjunct to brief physician advice. Three of these studies,4-6 however, did not investigate patients seen in the course of routine practice but instead studied well-motivated smokers recruited through the news media. Two studies7,8 from Great Britain recruited patients from general practice settings. All 5 studies used multiple support and monitoring visits during the active treatment phase, which may have had a favorable impact on quit rates. Although these investigations clearly document that extensive group behavioral counseling is not needed to achieve efficacy with nicotine patch therapy, the intensive nature of the studies may not be truly representative of what most frequently takes place during intervention in a busy primary care practice.

Thus, the applicability of smoking cessation clinical trial findings to the primary care setting is not always clear. Clinical trials generally have recruited healthy smokers who are ready to quit smoking. Primary care physicians must address smokers in various stages of readiness to quit and wellness. Finally, the multiple support follow-up vis-
PARTICIPANTS AND METHODS

PARTICIPANTS

A total of 369 participants were enrolled at 21 family practice sites. Appropriateness of referral to the study was determined by a participating family physician. Only patients aged 19 to 65 years who smoked at least 20 cigarettes daily were eligible. Individuals with a generalized dermatologic disease; current use of psychotropic drugs; a recent history of drug or alcohol abuse (within 1 year of the study); or a history of angina pectoris, cardiac arrhythmias, or myocardial infarction within 4 years were excluded. Pregnant and nursing women and those believed reasonably likely to become pregnant during the 3 months of the treatment phase were also excluded. Stability of medical problems, however, was not required, and many participants had experienced a recent illness prior to their initial visit.

LOGISTICS AND STAFF TRAINING

To help ensure that an approximately equal number of participants could be assigned to the 2 treatment regimens at each site, a random code was generated so that an equal number of active and placebo patches would be contained in each block of 10 participants. Thus, study charts and patches were taken to the sites in groups of 10. An approximately 1-hour orientation visit was arranged to coincide with the initial delivery of the study materials. At this visit, the site physician and participating staff members were given information about the recommended techniques required to complete the case report forms and to obtain informed consent. Family practice sites were encouraged to complete enrollment of their initial 10 participants within 2 months, but in some cases the enrollment period exceeded 6 months. Site physicians could request an additional block of 10 participants only after they had enrolled 10 participants. Each physician, however, was limited to enrolling a maximum of 20 participants. In practices with multiple physicians, a maximum of 30 participants could be recruited. After the study charts were checked during a monitoring visit at the site, the charts were collected and taken to a central site (University of Nebraska Medical Center, Omaha), where the 3-, 6-, and 12-month follow-up visits were performed.

STUDY DESIGN: FAMILY PRACTICE SITES

This was a double-blind, placebo-controlled, parallel group study conducted at 21 family practice sites in a 3-county area of Nebraska that included a major urban center, Omaha. The protocol was approved by the University of Nebraska Medical Center Institutional Review Board, and all participants gave informed consent. Study-eligible patients completed a brief questionnaire that included the 8-question Fagerstrom Tobacco Dependency Questionnaire. In the Fagerstrom scoring system, higher point totals are awarded for heavier cigarette use (≥26 cigarettes per day = 2 points), always inhaling (2 points), smoking within 30 minutes of awakening (1 point), and persistent cigarette use as exemplified by self-reported difficulty with smoke-free environments or smoking during an illness that required extended bed rest. Patients were also asked to rate their motivation to quit smoking on an 11-point scale ranging from 0 (unsure of desire to quit) to 10 (extremely high desire to quit). The study questions were designed to be completed within 10 minutes. Participants were asked to set a quit day within 2 weeks of the visit. No screening tests were required. No stipulations were given regarding the nature of the counseling required other than the need to establish a quit day within 2 weeks of the initial visit.

As a result of the randomization, the demographic and smoking history data for the 369 participants were similar for both treatment regimens. However, there was a small, but significantly higher Fagerstrom score and number of cigarettes smoked per day in the placebo group (Table). One hundred eighty-four participants were assigned nicotine patches and 19 participants (10.3%) as compared with 21 participants using placebo patches (8.7%) in the placebo group ($P = .07$). In an earlier study, the Transdermal Nicotine Study Group (TNSG) reported 6-month quit rates using the identical study patch regimen. Figure 2 shows a comparison of 6-month quit rates between the more intensive TNSG study and the present primary care investigation.

Participant selection factors seemed to play an important role. At the 3-month follow-up visit, 148 participants (40.1%) were categorized as self-referrals. These individuals specifically contacted the site to enroll in the study or to obtain a prescription for nicotine patches. Among these participants, abstinence rates were similar to the 6-month quit rates reported in the TNSG study. Twenty-two (29%) of 75 self-referral participants using active patches achieved 6-month abstinence (Figure 2).
Participants were assigned randomly, in a double-blind fashion, to receive a 2-week supply of either nicotine (Nicoderm, Alza Corp, Palo Alto, Calif) or placebo patches. They were directed to start using the patches on the morning of their designated quit day; were given the Nicoderm support booklet, “The 6-2-2 Committed Quitter's Program”; and were asked to return within 1 week of their designated quit day. At the 1-week follow-up visit, performed at the family practice sites, patients provided a rating of overall tobacco withdrawal symptoms on a 0 (very comfortable) to 10 (extremely uncomfortable) scale. Unless the family practice physician decided otherwise, study participants, regardless of smoking status, received their remaining 8-week supply of patches. For those assigned active patches, the total 10-week regimen included 6 weeks of 21-mg, 2 weeks of 14-mg, and, finally, 2 weeks of 7-mg patches.

**FOLLOW-UP VISITS AT UNIVERSITY OF NEBRASKA MEDICAL CENTER**

Participants were contacted by telephone for follow-up visits at 3, 6, and 12 months after their quit day. At the 3-month telephone contact, all participants, regardless of smoking status, were informed that they were eligible for a $75 honorarium if they came to the university site to relate their experiences with the patch. They were also reminded to return all of their unused patches. At the 3-month visit, smoking status was assessed and participants who were reportedly smoke free were asked to record the date since no cigarettes. The incidence of delayed quitting and the 2-week grace period were determined by computing the interval between the date since no cigarettes and the patient's target quit day. Also, at the 3-month visit, participants were asked how they initially heard about the study and were categorized accordingly. Participants were asked about the total duration of counseling they received at the family practice sites, excluding the time involved in completing study forms and informed consent documents. Adverse events that occurred during the treatment phase were also recorded. All self-reported quitters were asked to perform an exhaled carbon monoxide measurement and to provide a sample of saliva. Cotinine levels were measured in frozen saliva samples by radioimmunoassay (American Health Foundation, Valhalla, NY).

**Efficacy**

To permit comparison with a previous smoking cessation investigation that used an identical patch regimen, an analysis of efficacy was performed using continuous self-reported abstinence from 2 weeks from the quit day and an exhaled carbon monoxide measurement of 8 ppm or less. In addition, 1-year abstinence was also confirmed by a salivary cotinine level less than 20 mg/mL.10

**Statistics**

Continuous measures were analyzed using analysis of variance, and categorical measures were analyzed using Cochran-Mantel-Haenszel techniques. The relationship between duration of counseling and study quit days was assessed by the Pearson product moment correlation. Sample size calculations were based on a treatment effect of active patches of 13% compared with placebo at 3 months using a type I error of .05 and an 80% power. Withdrawal symptoms were analyzed by analysis of variance, with treatment as a factor to test equality between treatments. The efficacy data were analyzed based on intent-to-treat, with participants who were unavailable for or lost to follow-up categorized as smokers.

Two hundred seventeen participants (58.8%) reported that they were first informed about the study by primary care practice personnel. As a group, site-referred participants had significantly lower quit rates than did participants who specifically requested smoking cessation therapy ($\chi^2 = 16.7; P<.001$). Of these site-referred participants, 36 (16.6%) indicated that they were first told about the study during a sick visit, whereas 181 (83.4%) noted that they were first told about the study during a nonsick contact such as a routine physical examination or a flu shot. Site-referred participants who enrolled in the study during a sick visit had significantly higher 6-month quit rates whether they were assigned to active or placebo patches ($\chi^2 = 15.8; P<.001$) than did site-referred nonsick participants. With 6 (32%) of 19 sick participants who were assigned active treatment achieving 6-month abstinence, this group had quit rates similar to those of self-referral participants who were assigned active treatment.

**Early Quitting and Long-Term Abstinence**

Approximately an equal percentage of active (63.0%) and placebo (62.2%) group members reported that they succeeded in remaining smoke free on their target quit day. Of those who indicated quit day abstinence, 68 (58.6%) of 116 participants assigned nicotine patches and 45 (39.1%) of 115 participants assigned placebo patches reportedly quit for 30 days or longer ($\chi^2 = 8.8; P<.05$). Twenty-three (92%) of 25 verified 1-year quitters using nicotine patches and 15 (94%) of 16 of those assigned placebo reported successful abstinence on their target quit day. Of those who failed to quit smoking after 2 weeks of patch therapy, only 1 additional person succeeded in achieving continuous, self-reported, verified abstinence longer than 10 months.

**Demographic Factors**

Several demographic factors were associated with 1-year abstinence rates. Fagerstrom scores at baseline were highly associated with treatment success at 1 year. Because of the slight difference in the Fagerstrom score at baseline, an analysis of quit rates stratified by Fagerstrom score was performed. Among those with high Fagerstrom scores (≥7), 1-year abstinence rates were significantly higher in the nicotine patch group (19.1%) compared with the placebo patch group (5.0%) ($\chi^2 = 10.7; P = .001$). There was no significant difference in 1-year quit rates among patients with low Fagerstrom scores (<7), but abstinence rates were higher among those assigned the placebo regimen, 15.2% vs 8.9% ($\chi^2 = 1.4; P = .24$; [Figure 3](#)). Most sustained quitters smoked
between 20 and 30 cigarettes daily. Of 88 participants who smoked more than 30 cigarettes per day, only 6 achieved 12-month abstinence, 3 per regimen ($\chi^2 = 0.12; P = .73$). Because of slight baseline differences in cigarette consumption, a stratified analysis was also performed using 28 cigarettes per day as a cut off point. Among the heavier smokers ($\geq 28$ cigarettes per day), the 1-year abstinence rates tended to be lower in the placebo patch group (6.9%) compared with the nicotine patch group (14.5%) ($\chi^2 = 2.87; P = .09$). Among the lighter smokers (<28 cigarettes per day), the 1-year quit rates were nonsignificantly higher in the nicotine patch group (14.9% vs 10.8%) ($\chi^2 = 0.65; P = .42$). Participant age also affected abstinence rates. A comparison of 1-year abstinence rates in participants younger than 45 years showed no significant treatment effect (13.2% vs 10.4%, $\chi^2 = 0.57; P = .45$). In contrast, of those smokers aged 45 years and older assigned to the nicotine patch group, 9 (18.8%) of 48 achieved 1-year abstinence compared with a 0% success rate in 31 smokers using placebo patches ($\chi^2 = 6.56; P < .05$) (Figure 4). Finally, participants who resided with smokers compared with those who did not were significantly less likely to achieve 1-year abstinence ($\chi^2 = 8.5; P < .01$).

Of the baseline characteristics, only motivation to quit distinguished the self-referred from the site-referred participants. The mean ± SD motivation to quit score for the self-referred group was 8.51 ± 1.37 compared with 7.90 ± 1.77 ($P < .01$) for the site-referred group.

**Duration of Counseling**

At the 3-month visit, patients were asked to recall the amount of time spent in counseling at their respective family practice sites. The mean ± SD counseling time provided for the 2 office visits combined was 17 ± 6 minutes. The 8.5 minutes per visit allotted for counseling time suggests that brief intervention was achieved. The time spent with individual patients, however, was variable. Quit rates showed a clear relationship, increasing with intervention time (Figure 5). There was a significant correlation between length of counseling time and self-reported duration of cigarette abstinence during the study ($r = 0.28; P < .01$).

**Patch Use**

An estimate of patch use was obtained by counting the unused patches that were returned. Eighty-five participants (46.0%) assigned placebo patches and 54 participants (29.3%) assigned active patches used fewer than
half of their allotted supply of patches ($\chi^2 = 10.8; P < .01$). Nearly half (48%) of all participants returned 14 or more unused patches. Of these, 102 (57.6%) were assigned inactive patches and 75 (42.4%) were assigned nicotine patches ($\chi^2 = 8.96; P < .01$). Of the 1-year abstainers, 20 (80%) of 25 participants assigned nicotine patches and 8 (50%) of 16 participants in the placebo group used all of their patches ($\chi^2 = 4.06; P < .05$).

Nicotine patch therapy produces a favorable quit rate when used in conjunction with brief intervention in a primary care setting. Several demographic factors seem to affect quit rates. In particular, the mechanism by which a participant was referred, which in turn reflected participants’ motivation to quit, seems to affect quit rates. Patients who contacted their primary care physician to enroll in the study or to obtain a prescription for nicotine patches had the highest 6-month abstinence rates and the highest overall motivation to quit scores. Patients referred by site personnel had lower quit rates as a whole, but those referred during sick visits had high quit rates comparable with those of self-referred patients.

Results of previous studies10 show increased smoking cessation rates among patients who recently suffered a myocardial infarction. Hospitalization also has been suggested as an opportunity to intervene successfully to achieve smoking cessation.11 The elevated quit rate observed in a subset of patients enrolled in the study during a sick visit suggests that there may be a “window of opportunity” favorable for cessation in the outpatient setting as well.

The overall quit rates in the present study were lower than those reported in several other studies, including 1 by the TNSG study7 that used an identical nicotine patch regimen. The present study differs from the TNSG study, however, in 2 fundamental ways. First is the nature of the behavioral support program and follow-up visits and second is the nature of participant accrual. The TNSG study used intensive group counseling and multiple follow-up visits in specialized centers, whereas the present study used brief intervention at 1 or 2 visits in a primary care setting. Participants in the TNSG study, moreover, were recruited either from smoking cessation clinics or from advertisements specifically designed to recruit smokers for the smoking cessation study.

Studies performed in primary care settings, in general, found lower quit rates than those performed in specialized centers. Results of the present study suggest that a selection effect may account for some of the differences between controlled clinical trials at specialized centers and studies in primary care practices. Specifically, the mechanism of recruitment seems to be associated with motivation to quit.

Results of previous studies2,3,12-14 show an inconsistent relationship between age and Fagerstrom score with successful abstinence. Although results of a recent study12 suggest that age-related differences may affect smoking behavior, the complete absence of successful 1-year abstainers among participants aged 45 years and older treated with placebo was unexpected. Age may represent a subtle measure of cigarette addiction, with older smokers needing to break a more persistent, higher pack-per-year habit. Prospective studies, however, are required to confirm this finding. The association of smoking cessation with the Fagerstrom score, a well-established measure of cigarette dependence, also supports a relationship between dependency and benefit from nicotine replacement. The randomization procedure resulted in a small but significant difference between baseline Fagerstrom scores. The benefits of nicotine replacement, however, were not related to the slightly lower Fagerstrom scores. Specifically, of those with high Fagerstrom scores ($\geq 7$), 1-year quit rates were significantly higher among participants assigned nicotine patches. Conversely, no benefit was shown for nicotine replacement in participants with low Fagerstrom scores in part because of high placebo quit rates.

Counseling was provided by physicians, nurses, and other office staff personnel according to the practice at each site. Primary care practices varied greatly in their practice patterns, but a variety of professionals were effective in the counseling roles. The counseling data were

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**Figure 4.** Categorization of 1-year smoking abstinence rates by age and treatment. Asterisk indicates significance at $P < .05$.

**Figure 5.** Quit rates related to counseling time. Time spent in counseling was recorded retrospectively at the 3-month evaluation. Self-reported quit rates at 1 year were confirmed by exhaled carbon monoxide and salivary cotinine levels. Self-reported counseling time for the 2 visits combined was recorded at the 3-month evaluation.
dependent on retrospective recall of counseling time and may have had an assessment bias in favor of the benefits of counseling. Patients who did not return for the second visit because they failed to quit smoking would not have recorded any counseling time for that particular visit. Nevertheless, duration of counseling was noted to be significantly related to length of self-reported abstinence.

The data clearly indicate that counseling seems to maximize smoking cessation rates with the nicotine patch. This is of particular relevance because nicotine patches are approved for over-the-counter use. Results of the present study suggest that limited physician support, including setting a quit day and providing brief counseling and a follow-up visit, aids smoking cessation efforts.

It generally has been asserted that the best cessation strategy is rapid, complete termination of smoking. Similar to findings in previous studies,6,8,14 the most successful 1-year quitters were abstinent 2 weeks after the target quit day. This supports the concept that participants who use patches to aid with smoking cessation should make an all-out effort to achieve total abstinence. Continued patch use should be discouraged in individuals who smoke beyond 2 weeks of the target quit day because it is unlikely that they will succeed in their smoking cessation attempt. Instead, it seems more reasonable to reassess reasons for lack of success and to plan a second quit attempt. Many smokers will quit only on subsequent attempts.

In summary, results of the present study demonstrate that nicotine replacement therapy using transdermal nicotine patches can significantly increase quit rates among smokers in a primary care practice setting. Although some counseling seems to be beneficial, the amount of counseling does not seem to exceed the time constraints of a routine visit. Some individuals, moreover, seem to be better candidates for nicotine replacement treatment, particularly older individuals and those with higher Fagerstrom scores, consistent with the concept that nicotine replacement is more important in individuals with higher levels of nicotine dependence. Results of the present study also suggest that the relatively poorer quit rates observed in primary care practice settings compared with specialized center–based smoking cessation clinical trials may be because of participant selection factors. Effective cessation, however, can clearly be achieved in a primary care setting, and nicotine replacement treatment using the transdermal patch can augment quit rates, particularly in selected patient groups. Use of such interventions should help many individuals who smoke achieve abstinence.

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