

CONTROLLED TRIAL OF THE 24-HOUR TRANSDERMAL NICOTINE PATCH IN CONJUNCTION WITH COGNITIVE-BEHAVIOURAL THERAPY

6-Months' Results

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INTRODUCTION

The transdermal nicotine system is an adhesive patch that slowly and continuously delivers nicotine into the bloodstream by percutaneous absorption. The transdermal nicotine system has been shown to be effective as an aid to smoking cessation (1). Concurrent behavioural intervention including a relapse prevention component enhances the maintenance of abstinence following smoking cessation (2).

OBJECTIVES

The objectives of the study were:

- To assess the effectiveness of the 24-hour transdermal nicotine patch when it is used as an adjunct to a cognitive behavioural intervention.
- To assess the extent to which the nicotine transdermal patch assists in the amelioration of nicotine withdrawal symptoms.
- To assess subjects' physical reactions (local and systemic) to the patch over time.

Table 1. Subject characteristics on entry to study

Characteristic	Nicotine (n=156)	Placebo (n=157)
Male	48%	48%
Tertiary Education	50%	55%
Mean age in years	42 (11.5)*	41 (10.5)
Mean expired CO (ppm)	16.7 (8.6)*	17 (10.8)
Mean number of cigs per day	28.5 (11.4)*	30.3 (14.3)
Mean duration of smoking (years)	24.3 (11.1)*	23.6 (10.4)
Smoking within 5 minutes of waking	34%	41%
Mean Fagerström score	6.0 (2.2)*	6.3 (2.3)
At least 1 serious attempt to quit	91	88
Quit for more than 3 months	30	28

*Standard deviation

- To assess whether the patch is more successful for smokers with a high or low level of nicotine dependence.

METHOD

The study employed a double-blind, randomised, placebo-controlled research design in which subjects were randomly assigned to either the active transdermal nicotine patch condition or the placebo control condition, and they were assessed at three and six months to determine cessation rates.

Study Sample

Subjects were recruited from the local community in response to media coverage about the nicotine patch. The study took place at the Lifestyle Unit, Prince of Wales Hospital, Sydney. Three hundred and fifteen subjects were randomly assigned to receive either the active patch (n=158) or the placebo patch (n=157). The sample size was based on an 80% chance of detecting an effect size of 13% at follow up between experimental and control group. All subjects took part in the Smokescreen Program conducted at Lifestyle Unit and were asked to sign a consent form following clearance from their general practitioners that they could join the study and use the patch. The exclusion criteria consisted of: those aged less than 17 or more than 70 years; those with a history of cardiovascular disease; pregnancy/breast feeding; those with chronic dermatological disorder; those with severe renal impairment; those with history of peptic ulcer disease; those with history of hyperthyroidism, pheochromocytoma, IDDM. The inclusion criteria consisted of all other smokers including people who had psychiatric disorders, including depression, were excessive users of alcohol. Table 1 shows the pretreatment characteristics of subjects in the active and placebo groups.

Nicotine Replacement Treatment

Subjects in the active nicotine patch condition had nicotine administered transdermally, at three different levels of dosage across a ten-week treatment period: they received

patches each containing 21mg of nicotine in the first six weeks; patches containing 14mg of nicotine in the following two weeks, and patches containing 7mg of nicotine in the final two weeks of treatment. Each patch was changed daily and delivered the specified dosage level of nicotine over the course of 24 hours.

Subjects in the placebo patch condition received patches identical in appearance, packaging and labelling to the active patches with the exception that they only contained 1mg of nicotine in the drug reservoir in order to mimic the odour of the active patches.

Cognitive Behavioural Intervention

The Smokescreen Program is a multicomponent smoking cessation program consisting of five two-hourly sessions held once a week for five consecutive weeks. The components of the program are as follows: Session 1 is aimed at preparing participants to stop smoking; Participants are required to undergo self-monitoring of cigarette intake in order to identify the habit pattern; carbon monoxide and lung function tests are taken. Session 2 is quit day; Participants discuss their strategies and coping skills for giving up smoking. Session 3 is aimed at sharpening the coping skills and progress is evaluated. Session 4 is devoted to stress management and relapse prevention. Session 5 is devoted to lifestyle factors that will promote long term abstinence, such as diet and exercise.

Determination of Outcome

At three and six months following treatment, point prevalence abstinence (not smoking at a particular follow up point) and continuous abstinence (not smoking continuously across all follow up points) were taken to assess rates of smoking cessation. Abstinence was verified using expired carbon monoxide.

RESULTS

Cessation Rates

The point prevalence abstinence rates at three months were 48% for the active and 21% for the placebo group ($\chi^2=28.4$; $p<0.001$) and at six month were 33% for the active and 14% for the placebo group ($\chi^2=14.5$; $p<0.001$), a difference of 19% (95% CI, 0.12-0.32).

The three months continuous abstinence rates were 33% for subjects in the active and 13% for the placebo group ($\chi^2=16.9$; $p<0.001$). At six months, 25% of subjects in the active group had maintained complete abstinence compared with 12% in the placebo group ($\chi^2=8.9$; $P<0.01$).

The dropout rate at six months was 18% of subjects in the active group and 50% of those in the placebo ($p<0.001$). All subjects lost to follow-up were classified as continuing smokers.

Compliance

Eighty per cent of the active group and 83% of the placebo group complied perfectly to the treatment protocol.

Withdrawal Symptoms

Ratings of craving were lower for the active group compared to the placebo group throughout the nicotine replacement therapy (t values were between 3.8 [$p<0.001$] and 1.9

[$p < 0.05$]). Ratings of mood-related withdrawal symptoms (anger, restlessness, frustration, irritability, anxiety and difficulty concentrating) were also significantly lower in the active than in the placebo group (t between 5.0 [$p < 0.001$] and 2.3 [$p < 0.05$]).

Adverse Events

The most common adverse event was sleep disturbance: 30% of the active group reported vivid dreams compared to 6% in the placebo group ($p < 0.001$). Insomnia was reported by 26% of the active group compared to 16% of the placebo group ($p < 0.05$). Local skin irritation was reported by 23% of the active group and 12% of the placebo group ($p < 0.01$). Nausea was reported by 6% of the active group compared to 1% of the placebo group ($p < 0.05$).

Pretreatment Predictors of Abstinence

At three months the predictors of continuous abstinence were: being concerned about weight gain ($p < 0.05$); level of nicotine dependence ($p < 0.001$) with those in the low to moderate category being more likely to be abstinent than those who were highly dependent.

At six months we found that: younger subjects were more likely to relapse than older subjects ($p < 0.05$); early starters had more chance of relapsing than late starters ($p < 0.05$); and low to moderately nicotine dependent subjects were more likely to be successful than those in the highly dependent group.

DISCUSSION

The nicotine patch has been shown to be an effective smoking cessation aid when used in conjunction with a cognitive behavioural program. Cessation rates for the active patch group were double those in the placebo group throughout the study, and ratings of cravings and mood-related withdrawal symptoms were significantly lower for the active patch group. The adverse events reported by the subjects in the trial were relatively minor and improved without treatment.

Low to moderately dependent smokers were more likely to be successful which indicates that 21 mg patch may not have been adequate for heavier smokers. Further research is needed to determine nicotine dose requirements for highly dependent smokers.

The present study also highlights the importance of specialist smoking cessation clinics in providing a venue for research and development of new therapies, as well as offering help to those who need assistance in smoking cessation (3,4).

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