Introduction

Smoking and depression

Cigarette smoking continues to be the most common cause of preventable morbidity and mortality in the US (US Department of Health and Human Services. ‘The health consequences of smoking: nicotine addiction’).

A substantial body of research suggests that smoking and depression co-occur more frequently than would be expected by chance.

This article reviews literature addressing several issues:

(1) Smokers are more likely to have a history of major depression than non-smokers

(1a) Depression and the dynamics of smoking. A National Perspective.

To obtain a national perspective on the role of depression in the dynamics of smoking, authors of this study analysed data from the first National Health and Nutrition Examination Survey (NHANES 1) and the National Health and Nutrition Examination Survey Epidemiologic follow-up study (NHEFS). They used the Center of Epidemiologic Studies Depression Scale (CES-D) to assess symptoms of depression and define persons as depressed (a score of 16 or more). NHANES 1, conducted by the National Center for Health statistics between 1971 and 1975, evaluated 2963 persons. Of these, 1167 (39%) were current smokers who were subsequently included in the NHEFS, conducted from 1982 to 1984. NHANES 1 showed that among both men and women, increases in the percentage of current smokers paralleled increased in CES-D score ($P < 0.0001$ for men and for women). The quit ratio decreased as the CES-D score increased ($P < 0.01$ for men and $P < 0.0001$ for women). After adjusting prevalence estimates for age and level of education there were no appreciable differences. Of the original cohort, of 1167 smokers eligible in the NHEFS, data from only 820 (70.3%) were available for analysis. The mean length of follow-up for the cohort of smokers was 8.2 years. Sixteen per cent of smokers (2.1 per 100 person years) quit during the follow-up period. Persons who were depressed had the lowest incidence of quitting of any subgroup. Heavier smokers, women, young persons and the less educated were also less likely to have quit during the follow-up period. The estimated cumulative incidence of quitting after 9 years of follow-up was 9.9% for depressed smokers and 17.7% for non-depressed smokers ($P < 0.05$). After adjusting for the amount of tobacco smoked, sex, age and educational attainment, it was found that depressed smokers were 40% less likely to have quit when compared with those who were not depressed (relative risk 0.6, $P < 0.05$).

Comment

These data suggest that depression plays an important role in the dynamics of smoking in the US. Cross-sectional data from NHANES 1 shows that the prevalence of smoking increased as the CES-D score increased. Furthermore, the likelihood of having quit smoking decreased as the CES-D score increased. Finally, prospective data from the NHEFS also indicated that smokers classified as depressed on the basis of the CES-D had a substantially lower likelihood of quitting during the follow-up period. As the NHEFS excluded persons who were adolescents at baseline, there were too few persons beginning smoking during the follow-up period available to enable assessment of the relationship between depression and smoking initiation. This issue is important because advertisements promising happiness and improved well-being encourage adolescents to use tobacco and may be particularly alluring for adolescents who are depressed.

Further studies on the influence of depression on smoking initiation are needed.
Between 1980 and 1983, the National Institute of Mental Health conducted a population-based survey in five different regional centres to establish the community prevalence of the more frequent and serious psychiatric illnesses. That study, known as the Epidemiologic Catchment Area (ECA) Program, was originally planned to assess smoking behaviour as well as psychiatric illness. However, all centres except St Louis, MO and Durham, NC opted to delete the smoking questions. The authors tested the association between a lifetime diagnosis of major depression and both the frequency of cigarette smoking and failure of smoking cessation efforts using the St Louis data set.

The catchment areas were selected to provide representation from inner-city areas, suburban areas and semi-rural areas on the distant outskirts of the city. Sampling was accomplished by randomly selecting census tracts, blocks within census tracts and households within blocks. Once a household has been selected, an interviewer personally contacted someone living within the household and enumerated all the household members by age. Only those who had smoked cigarettes daily for a month or more were asked questions on smoking (n = 3213); those who had smoked half a pack per day (0.5 p.p.d.) or less in the last year were considered successful quitters. Smoking behaviours of subjects who met the criteria of major depressive disorder (MDD) based on the DSM-III criteria were compared with those who did not meet criteria for any psychiatric diagnosis and with the total sample, excluding subjects with MDD.

The average age of the sample was 42.5 (±18) years and the lifetime prevalence of MDD in the entire sample was 5.1%. Among individuals who had never smoked, the prevalence was 2.9%; among those who had ever smoked daily for at least 1 month it was 6.6%. The smoking behaviours of subjects with major depression are clearly different from those persons with either no depression or no diagnosis of other psychiatric illness (P < 0.001). Depressed subjects are more likely ever to have smoked, and less likely to have been successful in efforts to stop smoking.

Comment
The results of this study help confirm the hypothesis that major depression influences rates of cigarette smoking and smoking cessation. The study also verifies that this association exists, not only among patients presenting to a psychiatrist for treatment but also among those in the community with a lifetime diagnosis of major depression, whether or not they have ever sought treatment. Furthermore the study confirms the observation that a history of major depression adversely effects the outcome of smoking cessation efforts. Smokers without a psychiatric diagnosis were more successful in such efforts than smokers with a lifetime diagnosis of major depression (31% versus 14%, P < 0.001). These findings suggest a chronic and pernicious interrelationship between cigarette smoking and depression.

(2) Smokers with a history of depression have a lower likelihood of successfully quitting, and for those who quit, depression is more apt to be a prominent withdrawal symptom


This study examined data, based on 3-month follow-up information from 126 subjects, successfully treated with Clonidine for smoking cessation.

All subjects were heavy smokers (20 or more cigarettes daily) who had failed previous attempts to quit, did not have a current diagnosis of major depression or substance abuse or dependence, had not used psychotropic medication during the 6-week period prior to the study and did not have a lifetime diagnosis of a psychotic illness. The distribution of depressive disorders in those successfully treated was as follows: no history of MDD, 72%; single episode of MDD, 20%; and recurrent MDD, 8%. Comparative figures for treatment failures are 65, 16 and 20%, respectively (P < 0.005).

Major depression was defined as five or more of nine symptoms which lasted 2 weeks or more (DSM-III R criteria).

Within 3 months of ending the treatment, nine of 126 subjects experienced a new episode of major depression. The incidence of new major depression episodes following treatment for nicotine dependence was 2, 17 and 30%, respectively, among subjects without a history of MDD, those with a single major depression episode and those with recurrent major depression.

Comment
This study demonstrated that the incidence of a new major depression episode following smoking cessation treatment was higher among those with a past history of MDD, particularly the recurrent type, than that in those who had never been depressed. Furthermore, the study confirms other reports that smokers with a history of depression are less likely to quit smoking, but the authors did not study the incidence of post-treatment major depression among the group who did not maintain abstinence. Finally, this study shows the importance of obtaining information about history of depression in
smokers who are motivated to quit, and of remaining alert to the possible onset of depression, even weeks after smoking cessation treatment has ended.

(3) The utility of anti-depressant medication for smoking cessation is uncertain


This randomized, double-blind, placebo-controlled, dose–response study of Bupropion was performed at three sites (Mayo Clinic, Rochester, Minn.; The Palo Alto Center for Pulmonary Disease Prevention, Palo Alto, Calif.; and West Virginia University, Morgantown). A total of 742 volunteers were recruited, of whom 615 met the study criteria and underwent randomization.

Subjects were at least 18 years of age, had smoked an average of 15 cigarettes or more per day during the year prior to the study, were motivated to stop smoking and were in generally good health.

Exclusion criteria included the presence or a family history of a seizure disorder, a history of severe head trauma, predisposition to seizures, a history or current diagnosis of anorexia nervosa or bulimia, the presence of an unstable medical or psychiatric condition, pregnancy, lactation, a history of drug or alcohol dependence within the past year, current use of psychotropic medications, previous use of bupropion, current use of tobacco products other than cigarettes, and current use of any nicotine replacement therapy, fluoxetine, clonidine, buspirone or doxepin. Subjects with current depression were excluded, but those with history of major depression were not.

Subjects were randomly assigned to receive either a sustained release form of bupropion at a dose of 100 mg per day (50 mg BID), 150 mg per day (150 mg each morning and placebo each evening) or 300 mg per day (150 mg per day for 3 days followed by 150 mg BID) or placebo (twice a day). The course of treatment was 7 weeks. Subjects set a ‘target quit date’, usually the eighth day of medication, and were followed for 11 months. Brief individual counseling (approximately 10–15 minutes) was provided by a study assistant at each visit.

Self-reported abstinence was validated by a carbon monoxide level in expired air of 100 p.p.m. or below. A total of 219 subjects did not complete the 12-month study.

At the end of 7 weeks of treatment, rates of smoking cessation were 19.0% in the placebo group, 28.8% in the 100 mg group, 38.6% in the 150 mg group and 44.2% in the 300 mg group (*P* < 0.001). At 1 year the respective rates were 12.4, 19.6, 22.9 and 23.9%. Rates for the 150 mg group (*P* = 0.02) and the 300 mg group (*P* = 0.01) but not the 100 mg group (*P* = 0.09) were significantly better than those for the placebo group.

Among the subjects who were continuously abstinent throughout the treatment, the mean absolute weight gain was inversely associated with the dose (a gain of 2.9 kg). In the placebo group, this was 2.3 kg in the 100 mg and 50 mg groups, and 1.5 kg in the 300 mg group (*P* = 0.02). No effects of treatment were observed on depression scores as measured serially by the Beck Depression Inventory. Thirty-seven subjects stopped treatment prematurely because of adverse events; the frequency was similar among all groups.

Comments
Nicotine may act as an antidepressant in some smokers, and development of a depressed effect or depression after smoking cessation may lead to relapse. Medications that do not contain nicotine, such as antidepressants, might play a crucial role in smoking cessation.

This study concluded that a sustained release form of bupropion was effective for smoking cessation and was accompanied by reduced weight gain and minimal side effects. There were significant numbers of failures at 1 year in all groups.

The 300 mg dose was the only one to show effectiveness throughout the treatment.

Conclusion
The Surgeon General’s (1988) report on the health consequences of tobacco use concluded that (a) cigarettes and other forms of tobacco use are addictive; (b) nicotine is the drug in tobacco that causes addiction and (c) the processes that determine nicotine addiction are similar to those that determine addiction to drugs such as heroin and cocaine.

Unfortunately, despite recent advances in treatment, relapse continues to be frequent. In published cessation studies, most smokers relapse within 1 year of treatment termination (Shiffman, 1993).

Nicotine activates central nervous system pathways to release norepinephrine, dopamine, and other neurotransmitters and elevates dopamine levels in areas of the brain associated with the reinforcement of the effects of amphetamines, cocaine and opiates.

Although the link between smoking and depression is well established, its mechanism is uncertain and the action of antidepressant drugs for smoking cessation is unclear.

Results of clinical trials of antidepressant therapy for smoking cessation have been mixed. The initial experience with doxepin was promising; however, no large trials have been reported. A study using a serotonin uptake inhibitor failed to demonstrate reduction of smoking rates in heavy smokers.
In a recent study of about 200 smokers, nortriptyline, a tricyclic antidepressant, doubled the rates of smoking cessation, and the benefit was seen equally in smokers with and those without a history of depression.

Bupropion appears to work primarily by inhibiting neuronal uptake of norepinephrine and dopamine. Tricyclic antidepressants block the re-uptake of norepinephrine as well as serotonin. Both bupropion and tricyclic antidepressants reduce the firing rates of noradrenergic neurons in the locus ceruleus. These effects are shared with clonidine, which also appears to have some benefit in smoking cessation.

Because depression appears to reduce a smoker’s ability to quit, it is likely that in the future, the prevalence of depression will be highest among smokers. Antidepressants are commonly used for several months to treat depression or chronic pain and have little potential for abuse. Additional research is needed to determine both whether smoking cessation is facilitated by treatment of depression, and the optimal duration of treatment.