Severe Acne Vulgaris and Tobacco Smoking in Young Men

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As the relationship between tobacco smoking and acne remains unclear, we examined the relationship between cigarette smoking and severe acne in a large cohort of young men. Trained nurses interviewed subjects upon discharge from compulsory military service, regarding family history, habits, and tobacco smoking habits. Data was correlated with severe acne status, as diagnosed and coded by board-certified dermatologists. In total, 27,083 male subjects participated in the study from 1983 to 2003, of which 237 (0.88%) had severe acne, 11,718 (43.27%) were active smokers, and 15,365 (56.73%) were nonsmokers at the time of interviews. Active smokers showed a significantly lower prevalence of severe acne (0.71%) than nonsmokers (1.01%) ($P=0.0078$). An inverse dose-dependent relationship between severe acne prevalence and daily cigarette consumption became significant from 21 cigarettes a day (χ^2 and trend test: $P<0.0001$), odds ratio: 0.2 (95% CI: 0.06–0.63). The study did not aim to establish a temporal correlation, and passive smoking and acne treatments were not measured. Previous *in vitro* and clinical studies strongly support an association with nicotine. We suggest a trial with topical nicotine treatment for acne to further investigate this association.

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INTRODUCTION

Acne vulgaris affects over 80% of all individuals during childhood and early adult life, with male subjects more commonly affected than female subjects. Prevalence of the severe form, characterized by multiple nodular and postular-cystic lesions (Kligman and Plewig, 1976; O'Brien *et al.*, 1998) that can leave permanent physical and psychological scars (Tan, 2004), ranges from 0.5% to 6% in males, depending on age and the clinical grading system used (Cunliffe and Gould, 1979; Rademaker *et al.*, 1989; Stern, 1992; Lello *et al.*, 1995; Bataille *et al.*, 2002). In view of the controversial association between acne and smoking (Mills *et al.*, 1993; Schafer *et al.*, 2001; Jemec *et al.*, 2002; Firooz *et al.*, 2005), we studied the relationship in a large group of young men being discharged from military service.

It is crucial to emphasize that any positive effects found must be traced to specific tobacco components that can be therapeutically used without smoking (e.g., nicotine patches or gums), to avoid any ''legitimatizing'' of smoking based on its beneficial effects on health.

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Abbreviation: IDF, Israel Defense Force

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RESULTS

A total of 27,083 males participated in the study during the years 1983–2003. Approximately 20 military nurses and over 30 board-certified dermatologists participated in the interview process and on the medical profile committees, respectively. There was severe acne in 237 (0.88%) subjects (Table 1). At the time of interview, 11,718 (43.27%) were active smokers and 15,365 (56.73%) were nonsmokers; 0.37% ($n=99$) subjects did not report their smoking status. Categories of the daily cigarette smoking of the 26,984 subjects were 0 cigarettes ($n=15,365$), 1–10 ($n=2,746$), 11–20 ($n=3,766$), 21–30 ($n=1,645$), 31–40 ($n=2,086$), and >41 ($n=1,475$). The prevalence of severe acne was significantly lower ($P=0.0078$) in active smokers (0.71%) than in nonsmokers (1.01%). There was an inverse, dose-dependent relationship between severe acne prevalence and daily cigarette consumption. The prevalence of acne in the aforementioned categories was 0.99, 1.27, 1.04, 0.18, 0.24, and 0.20%, respectively. The inverse relationship became statistically significant from 21 cigarettes a day (χ^2 and trend test: $P<0.0001$).

When the relationship between daily cigarette smoking and severe acne prevalence was controlled for father's origin and number of siblings, there was still a significant dose-dependent association between cigarette consumption and acne (see Table 2 and Figure 1).

DISCUSSION

The association between acne and smoking has been studied extensively with varying results. Mills *et al.* (1993) reported that 19.7% of 96 male acne vulgaris patients and 12.1% of 60

Table 1. Prevalence of severe acne and demographic data on subjects

Severe acne subgroup	No. of subjects (%) (*n*=27,073)	Age (years) ±s.d.	Origin of subjects (% of acne subgroup: no, yes)[a]			Average no. of siblings ±s.d.
			West	East	Israel	
No	26,846 (99.12%)	21.84±1.52	40.85%	52.65%	6.49%	4.12±2.29
Yes	237 (0.88%)	21.85±1.16	48.93%	43.78%	7.30%	3.52±1.70

[a]Descendants of West European and North and South American-born fathers were categorized as ''Western'', and descendants of fathers born in Eastern Europe, Africa, and Arab countries were categorized as ''Eastern''.

Table 2. Multiple logistic regression model for acne prevalence and cigarette consumption

Variable	Odds ratio	95% confidence interval	
Daily cigarette smoking			
0 (reference)	1		
1–10	1.28	0.88	1.86
11–20	1.06	0.74	1.52
20–30	0.20	0.06	0.63
30–40	0.28	0.11	0.68
>40	0.25	0.08	0.78
Ethnic origin			
Western vs Israeli	1.13	0.67	1.89
Western vs Eastern	0.89	0.67	1.19
No. of siblings (ordinal variable)	0.90	0.84	0.98

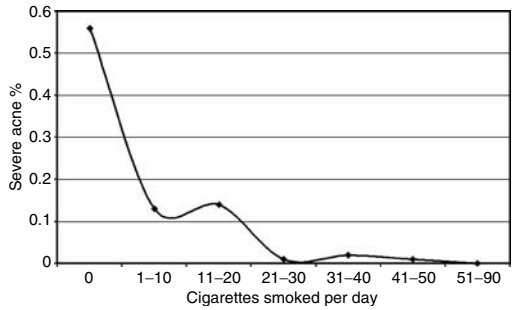

Figure 1. Relationship between prevalence of severe acne (*n*=237) and number of cigarettes smoked per day.

female ones were smokers, which was significantly less than national statistics (Mills *et al.*, 1993). Jemec *et al.* (2002) found that smoking was not significantly associated with acne in a random sample of 186 subjects (odds ratio: 0.54, 95% CI: 0.17–1.78). Schafer *et al.* (2001) found in 102 smokers compared with 184 nonsmokers that acne was significantly more prevalent in active smokers, but when only 15–40-year-olds were taken into account, there was no association between acne and smoking. Firooz *et al.* (2005) compared smoking status of 293 acne patients to 301 patients suffering from other dermatological conditions. After accounting for acne's higher prevalence and greater severity in men, no significant correlation was found.

Our study in which all subjects were diagnosed by board-certified dermatologists is the largest sample to date. Although different dermatologists had participated during the study years, all used the same diagnosis criteria, thereby compensating in part for possible inter-observer variability. Our cohort consisted only of males, which probably skewed the results in view of the known differences in prevalence and clinical grading between male and female subjects, most probably owing to hormonal differences (both androgenic and oral contraceptive related). In this respect, a study carried out only on males has the advantage of eliminating certain confounding gender-specific factors, but any generalizing of results must be performed with caution.

Although the prevalence of severe acne among smokers of 10–20 cigarettes per day was higher than the group of 0–10 per day, this finding was not statistically significant. The inverse relationship became significant from 21 cigarettes a day. A study measuring plasma cortisol levels in smokers found a similar effect (del Arbol *et al.*, 2000). The differences between light and heavy smokers may be related to the effect of nicotine on nicotinic cholinergic receptors. At low doses, nicotine stimulates acetylcholine receptors, whereas high doses of nicotine selectively block them (Seyler et al., 1986). The aspect of passive smoking was not included in this study owing to the difficulty of accurately estimating exposure in such a large subject population and long study duration.

All dermatologists were obliged to refer any patient with severe acne for official medical coding. Based on internal auditing, we estimate an under-diagnosis of up to 20% owing mostly to the large number of participating dermatologists, some of whom were civilian physicians less familiar with the military referral directives. The large sample size and the lack of any selective bias linked with smoking habits on the diagnosis or medical coding procedure probably compensated for this under-diagnosis. Another limitation of our study was the inclusion of only patients with severe acne, most of whom were referred to a dermatologist for retinoid treatment. However, as the clinico-pathological pathways of both moderate and severe acne involve inflammatory processes,

we assumed that the findings can be applied to a broad range of disease presentations, with possible exclusion of comedonic only grades.

Social factors may also have contributed to the findings of our study. Individuals with higher self-awareness of health status, hence less prone to smoking, may have sought diagnosis and treatment for acne more vigorously than the smoking population. However, an earlier study of the same population found similar rates of smoking among subjects diagnosed with asthma as compared to healthy individuals (Zimlichman *et al.*, 2004), supporting our assumption that health awareness was not a major reason for the present findings. Emotional stress is a known risk factor for smoking (Simantov *et al.*, 2000). More smokers due to stress are expected among the severe acne group. Our finding to the contrary might have significance, but this remains to be verified.

The adverse effects of tobacco on the skin are well known (Misery, 2004). Several studies suggest a possible protective action of nicotine against the development of inflammatory skin disorders. The nicotine constituent might even be beneficial to certain diseases. Positive effects were found in pemphigus, ulcerative colitis, pyoderma gangrenosum, aphthous stomatitis, and herpes simplex (Wolf *et al.*, 2004). Nicotine enhanced keratinocyte adhesion, differentiation, and apoptosis and inhibited keratinocyte migration (Grando *et al.*, 1995). Nicotine also inhibited inflammation through effects on the central and peripheral nervous systems (Sopori *et al.*, 1998). Nicotine altered immune responses by directly interacting with T cells. Transdermal application of nicotine (patches) was followed by a decrease in response to sodium lauryl sulfate as well as the erythema response to UVB (Mills, 1998). Paradoxically, nicotine worsened buccal inflammation, in contrast to ameliorating small bowel and colonic inflammation (Eliakim and Karmeli, 2003).

Using current acne status at the time of discharge from service time excluded subjects previously diagnosed with severe acne whose diagnosis changed owing to clinical improvement. However, owing to the cross-sectional nature of the study, it was not possible to delineate the time sequence of severe acne development and smoking. Some subjects may have started smoking after the onset, or even as a consequence, of acne, or *vice versa*. The dose-dependent relationship might indicate that smoking more than 20 cigarettes a day contributed somewhat in improving preexisting acne. Future prospective studies are needed to establish time sequence and therefore cause and effect.

The following limitations of this large-scale study must be noted: the inclusion of only males and only severe acne; and the exclusion from the study protocol of acne therapy, data on the temporal relationship between smoking and development of acne, and the effect of passive smoking.

The underlying causal mechanisms of the relationship between severe acne and smoking need further clarification, but previous *in vitro* and clinical studies strongly support an association with nicotine. We suggest a randomized controlled trial with topical nicotine treatment for acne to further investigate the significant inverse correlation between cigarette smoking and severe acne vulgaris observed in our study.

MATERIALS AND METHODS

The prospectively established database of the Israel Defense Forces (IDFs) Medical Corps during the years 1983–2003 served as the basis for this cross-sectional study.

Subjects

The study population came from a large-scale ongoing prospective survey of health behavior and attitudes, conducted among randomly selected soldiers of the IDFs. The survey systematically collected a representative sample of IDFs men at discharge from compulsory 3-year military service, ranging 21–22 years of age, as previously described (Kark and Laor, 1992). The IDFs Medical Corps Review Board approved the survey as well as the manner in which informed consent was obtained from the subjects.

Each IDFs recruit went through medical tests at intake and in the event of a change in health status during service. Board-certified dermatologists made the diagnosis of severe acne according to the military criteria based on the Kligman and Plewig grading (1976) and the Leeds acne grading system (O'Brien *et al.*, 1998); severe acne is defined as the presence of nodular and postular-cystic lesions. The diagnosing dermatologist then referred the soldiers to a military medical profiling committee for a review of the required clinical evidence and an official numerical encoding of the diagnosis. The data referred to the committee did not include the soldier's smoking status. We used this code, called the medical military profile, to classify subjects with and without severe acne vulgaris.

Data collection

Subjects were asked to participate in the study on the day of discharge from military service. Trained nurses from the IDF Public Health Branch interviewed them about smoking status (current smoker, past smoker, or never smoked), average number of cigarettes smoked a day (0–10, 10–20, 20–30, 30–40, >40), father's country of origin, found to correlate with smoking habits by Zimlichman *et al.* (2004), and number of siblings, found to be reversely associated with adult social class by Blane *et al.* (1999). Nurses did not know the current acne coding status of the soldier. Current acne status at discharge time as reflected by the medical profile was collected separately for all participants and analyzed against the above parameters.

Statistical analysis

Data were analyzed by the Statistical Analysis System version 9.2. (SAS Institute Inc., Cary, NC, USA). Proportions of smoking, family origin, and number of siblings were compared between subjects with severe acne and those without, using χ^2 test. Mean number of cigarettes smoked per day was compared using analysis of variance. Trend tests were performed in $2 \times N$ tables when appropriate. Multiple logistic and linear regression analyses were carried out taking severe acne prevalence as the dependent variable. All models included ethnic origin, number of siblings, and quantitative parameter of smoking status. The LOGISTIC and GLM procedures were used. Results were expressed as mean $\pm$ s.d., or n (%); $P<0.05$ was considered significant.

CONFLICT OF INTEREST

The authors state no conflict of interest.

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