Depressive, anxious, withdrawal symptoms, and craving as possible predictors of abstinence maintenance in smokers attending a 12-week quitting program

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BACKGROUND INFORMATION: Depressive, anxious, withdrawal symptoms, and craving might affect differently the probability to maintain abstinence after quitting smoking.
OBJECTIVE: The objective of this study was to assess depressive, anxious, nicotine withdrawal symptoms, and craving in a sample of smokers attending a smoking cessation program over a period of 12 weeks.
METHODS: A naturalistic study was conducted in which 78 smokers were consecutively recruited for a 12 week evaluation program. Socio-demographic data and clinical information were collected, rating scales were used to assess anxious and depressive symptoms, nicotine dependence, withdrawal symptoms, and craving.
RESULTS: Of the 78 recruited smokers, 17 remained abstinent and 61 reverted to smoking during the period of 12 weeks. The probability of maintaining abstinence was increased when low depressive symptoms or low craving occurred during the cessation program.
CONCLUSION: The present results strengthen the importance of assessing depressive symptoms and craving over the follow-up of a physician-assisted smoking cessation program to detect abstaining smokers at risk to relapse.

KEYWORDS: Smoking cessation, Anxious symptom, Depressive symptom, Tobacco withdrawal, Craving.

■ INTRODUCTION

Relapse in smoking cessation during treatment continues to be a compelling problem. Relapse researchers have long been interested in withdrawal syndrome and negative affectivity (i.e., depressive/anxious symptoms under the diagnostic threshold of affective disorders) showing that they might contribute to maintain smoking.[1,2] Withdrawal symptoms and craving have been mainly studied as a whole as well as depressive and anxious symptoms have been mainly studied as a single variable, that is negative affectivity. However, withdrawal symptoms are important instigators of relapse,[3] although early clinical investigations found little evidence of it.[4] However, craving does not seem to be a valid withdrawal symptom since some moderators may influence its relationship with cessation outcome.[5] Similarly, odds of relapse have been shown when depressive symptoms occur both in men and women[4] while the results on anxious symptoms are mixed. According to some authors anxiety is predictive of relapse in women but not in men;[6,7] according to others anxiety significantly predicts subsequent quitting in females.[8]

In this framework, we studied depressive, anxious, tobacco withdrawal symptoms, and craving as separate possible predictors of maintaining abstinence in smokers following a smoking cessation program.

■ MATERIALS AND METHODS

A longitudinal study on smokers attending a 12-week smoking cessation program at the University

Hospital of Pisa was conducted. Smokers were consecutively enrolled from March 2010 to January 2012 and assisted by pulmonologists according to a standardized protocol including an individualized pharmacological therapy (i.e., nicotine replacement therapy, bupropion, or varenicline). Exclusion criteria were: a. age < 18 years; b. smoking < 1 cigarette/day; c. drinking daily > 6 cups of coffee or 4 standard alcohol units; d. daily use of psychotropic medications or substances; e. self-reported chronic medical conditions or lifetime psychiatric disorders; f. current psychiatric disorder. Approval of the study was granted by the Medical Ethics Review Board of the University Hospital of Pisa.

In order to exclude subjects with a current personal history of psychiatric disorders, the Hospital Anxiety Depression Scale (HADS)[9] was administered at first contact. In case the score on one of the two HADS subscales was higher than 7, the Mini International Neuropsychiatric Interview[10] was administered. Thus, subjects satisfying at least one psychiatric disorder diagnosis were excluded according to a previously described procedure.[11]

Subjects eligible for the study underwent the following routine: (i) screening; (ii) baseline visit; (iii) 2-3 weeks later was quit day (QD); (iv) follow-up visits were made 1, 3, 6, 9, and 12 weeks after the QD. During the screening session, socio-demographic information and smoking history were collected through standardized questions. The expired carbon monoxide (CO) was assessed as an objective measure of smoking exposure. The severity of tobacco dependence was assessed by the Fagerström Test for nicotine dependence.[12] At baseline and at each follow-up visit a psychological evaluation including the Montgomery Asberg Depression Rating Scale,[13] the Anxiety Status Inventory,[14] and the Profile of Mood State[15] was performed in order to assess mood and anxiety. At each follow-up visit, CO was measured to verify the smoking status; tobacco withdrawal symptoms and craving were assessed via the Smoker Compliant Scale.[16]

Abstainers were those who maintained abstinence from week 1 to week 12 (i.e., "not a puff" in the 7 days before and a CO level < 5 parts per million at each follow-up visit). Smokers were those who relapsed during the 12 weeks.

A bivariate comparison between abstainers and smokers was performed using: the t-test for independent samples for normally distributed continuous variables; the Mann-Whitney test for independent samples for non-normally distributed continuous variables; the chi-square test for dichotomous variables. Multivariate logistic regression analyses, adjusted for age, gender, for the Fagerström Test for Nicotine Dependence, and for treatment received, were performed to identify independent predictors of persevering in smoking abstinence among the clinical variables measured at baseline. At three-month abstinence status was the dependent variable. The probability of remaining in abstinence during the follow-up period was analyzed via the random-effects Generalized Estimating Equation (GEE) model. The influence of depressive symptoms (as measured through the Montgomery Asberg Depression Rating Scale and the Profile Of Mood State) was studied adjusting for the treatment received and the Smoker Complaint Scale total score. The influence of anxious symptoms (measured through the Anxiety Status Inventory) was studied adjusting for gender, treatment, and Smoker Complaint Scale total score. The influences of withdrawal symptoms and craving (measured through Smoker Complaint Scale subscale scores) were studied adjusting for treatment, Montgomery Asberg Depression Rating Scale, and Anxiety Status Inventory total scores.

Significance levels were set at p ≤ 0.05 (two-tailed). All of the analyses were performed using SPSS, version 19.0.

■ RESULTS

Seventy-eight current smokers, out of 378 applying for the smoking cessation program, satisfied the inclusion criteria (51 males, 27 females; mean age: 47.0 ± 13.9 years). Seventeen subjects (abstainers) maintained abstinence from week 1 to week 12; 61 subjects (smokers) relapsed during the follow-up period. Compared to abstainers, relapsing smokers had statistically significant higher Fagerström Test for Nicotine Dependence (5.69 ± 2.18 vs. 3.87 ± 2.30; p = 0.008), HADS anxiety subscale score (5.67 ± 3.31 vs 3.12 ± 2.42; p = 0.001), and baseline Profile Of Mood State confusion subscale score (5.57 ± 3.21 vs. 3.29 ± 2.05; p = 0.007). No differences were found with regard to the clinical variables measured at each follow-up visit (data not shown). According to the multivariate logistic regression analyses, the probability of maintaining abstinence versus continuing smoking was influenced by the level of fatigue and confusion assessed at baseline (Table 1).

Table 2 reports the probability of maintaining abstinence versus continuing/going back to smoking from baseline to week 12 associated with exposure to depressive/anxious symptoms or with exposure to withdrawal symptoms/craving. Statistically significant relationship was found between the probability of maintaining abstinence and a decrease of the Montgomery Asberg Depression Rating Scale and the Smoker Complaint Scale craving score.

■ DISCUSSION

Experiencing low confusion or high fatigue at baseline as well as low depressive symptoms or low craving during the 12-week smoking cessation program increased the probability of maintaining abstinence. The results of confusion and fatigue cannot be compared with the literature since there are no reports about them.

Table 1 - Multivariate logistic regression analysis adjusted for nicotine dependence (FTND), age, gender, and treatment received. The odds ratio expresses the probability of maintaining abstinence versus continuing smoking. The clinical variables were measured at baseline

Model information	Baseline		
	OR	95% CI	p
MADRS	1.002	0.837 - 1.200	0.981
ASI	1.068	0.916 - 1.247	0.400
POMS - tension	0.965	0.711 - 1.311	0.820
POMS – depression	0.899	0.669 – 1.208	0.479
POMS – hostility	1.011	0.819 – 1.247	0.921
POMS – vigor	0.929	0.783 – 1.103	0.400
POMS - fatigue	1.569	1.102 – 2.235	0.012
POMS - confusion	0.551	0.355 – 0.855	0.007

MADRS: Montgomery Asberg Depression Rating Scale; ASI: Anxiety Status Inventory; POMS: Profile of Mood State

Table 2. Probability of maintaining abstinence versus continuing smoking with exposure to depressive/anxious symptoms or with exposure to withdrawal symptoms/craving over the follow-up period (i.e., from baseline to week 12). Generalized estimating equation model

Influence of depressive/anxious symptoms		
Measure	β (95% CI)	p
MADRS	-0.114 (-2.187 - -0.042)	0.042
MADRS Dysphoria	-0.663 (-0.177 - 1.502)	0.122
MADRS Retardation	-0.390 (-1.123 - 0.344)	0.297
MADRS Vegetative Symptoms	-0.564 (-0.409 - 1.537)	0.256
ASI	0.663 (-0.326 - 1.653)	0.189
POMS	2.128 (-7.120 - 11.376)	0.652
POMS Tension/Anxiety	-0.005 (-1.270 - 1.259)	0.994
POMS Depression/Discouragement	-0.028 (-1.600 - 1.544)	0.972
POMS Aggressiveness/Rage	1.425 (-0.622 - 3.472)	0.173
POMS Vigor/Activity	0.694 (-1.343 - 2.731)	0.504
POMS Tiredness/Indolence	0.891 (-0.292 - 2.074)	0.140
POMS Confusion/Bewilderment	0.310 (-0.595 - 1.216)	0.502
Influence of withdrawal symptoms/craving		
Measure	β (95% CI)	p
SCS Withdrawal Symptoms	-1.333 (-4.461 - 1.796)	0.404
SCS Craving	-2.340 (-4.069 - -0.611)	0.008

MDRS: Montgomery Asberg Depression Rating Scale; ASI: Anxiety Status Inventory; POMS: Profile of Mood State; SCS: Smoker Compliant Scale

However, we might hypothesize that low confusion is a favorable trait to face challenges, and thus to enhance the chance of quitting smoking. We may also suggest that a high level of fatigue might motivate the subjects to maintain abstinence in order to improve their general level of health status, similarly to what happens when the diagnosis of an organic disease is formulated.[17] Our results on depressive symptoms are consistent with previous reports[2,7] and allow us to propose the following hypotheses: according to the principles of allostatic load, smokers following a quitting program and suffering from depressive symptoms might give up because they are exposed to a challenge that is

extremely taxing or that exceeds their coping skills.[18] We found statistically significant results for the Montgomery Asberg Depression Rating Scale but not for the Profile of Mood State. This disagreement is apparently due to the different characteristics of the scales: the Montgomery Asberg Depression Rating Scale was constructed to be sensitive and accurate to changes in depressive symptoms due to pharmacological treatment; the Profile of Mood State test was constructed to detect mood changes due to psychotherapy. Anxious symptoms did not influence the probability of maintaining abstinence when experienced during the 12-week period. This result is consistent with

what has been observed in men.[6,7] Unfortunately, we did not stratify the analyses for gender since the female subsample was too small to run a powerful statistical analysis. However, we adjusted by gender those GEE analyses that evaluated the influence of anxious symptoms.

The role of craving in affecting smoking cessation is widely known.[1] The lack of effects due to withdrawal symptoms experienced during the follow-up period finds support in early clinical investigations.[4] According to Piasecki,[3] the experience of withdrawal symptoms is a reliable predictor of relapse when one takes into account that withdrawal symptoms can be chaotic, prolonged, or increasing over an 8-week period. Thus, it could be claimed that the Smoker Complaint Scale, assessing withdrawal symptoms at each follow-up visit, is inadequate to catch a chaotic profile. Notwithstanding this, not being retrospective, it has the advantage of not introducing selective recall biases.

Some limitations must be acknowledged. The naturalistic nature of the design might reduce the internal validity of the research but to the benefit of its external validity.

The observed rates of failures in quitting may seem high. According to the conservative approach used in intention-to-treat analyses, subjects who dropped out were defined as smokers (http://www.cochrane-net.org/openlearning/html/mod14-4.htm); this increases the relative number of failures to the detriment of the number of abstainers.

In conclusion, experiencing low confusion or high fatigue at baseline as well as experiencing low depressive symptoms or low craving while quitting resulted in an increase of the probability of maintaining abstinence. Overall, the present study offers insights into the emerging evidence which tends to consider depressive symptoms separately from anxious symptoms as well as to consider withdrawal symptoms separately from craving. Future replications are needed.

■ SUMMARY

Experiencing low confusion or high fatigue at baseline as well as low depressive symptoms or low craving during a 12-week smoking cessation program increased the probability of maintaining abstinence.

■ AUTHOR CONTRIBUTION

Cosci F, Pistelli F, Carrozzi L conceived the study. Bertoli G, Pistelli F, Carrozzi L were involved in the collection of data. Cosci F, Bertoli G ran the statistical analyses. Fiammetta Cosci F wrote the manuscript. Cosci F, Bertoli G, Pistelli F, Carrozzi L approved the final version of the manuscript.

■ CONFLICT OF INTEREST

All authors declare no conflicts of interest relative to this project.

SINTOMAS DE DEPRESSÃO, ANSIEDADE, E DE ABSTINÊNCIA COMO POSSÍVEIS PREDITORES DE MANUTENÇÃO DE ABSTINÊNCIA EM FUMANTES DURANTE UM PERÍODO DE 12 SEMANAS

INFORMAÇÕES: Sintomas de depressão, de abstinência e ânsia podem afetar de forma diferente a probabilidade de manter a abstinência depois de parar de fumar.

OBJETIVO: O objetivo deste estudo foi avaliar depressão, ansiedade, ânsia e sintomas de abstinência de nicotina numa amostra de fumantes atendidos num programa de cessação do tabagismo durante um período de 12 semanas.

MÉTODOS: Um estudo naturalístico foi conduzido, incluindo 78 fumantes recrutados durante um período de 12 semanas. Dados sócio-demográficos e as informações clínicas foram coletadas; escalas de avaliação foram utilizadas para avaliar sintomas ansiosos e depressivos, a dependência da nicotina e os sintomas de abstinência.

RESULTADOS: Dentre os 78 fumantes, 17 permaneceram abstinentes e 61 racaíram. A probabilidade de manutenção da abstinência foi aumentada quando sintomas depressivos ou desejo ocorreram de forma pouco intensa durante o programa de cessação.

CONCLUSÃO: Os resultados reforçam a importância de avaliar os sintomas depressivos e a ânsia de fumar sobre o acompanhamento de um programa de cessação do tabagismo assistido por médico para detectar fumantes em abstenção que apresentem risco de recaída.

PALAVRAS-CHAVE: cessação do tabagismo, sintomas ansiosos, sintomas depressivos, de abstinência de tabaco, ânsia.

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