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Assessment of Nicotine Dependence in a Large Cohort of Smokers – Social and Medical Aspects

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Abstract

Chronic smoking is a disease associated with long-time daily consumption of tobacco products and is synonymous with nicotine dependence. Nicotine is the major determinant of tobacco addiction, causing psychoactive pharmacological effects, which together with the genetic, social and environmental factors, learned or conditioned, are the substrate of smoking status. We conducted a retrospective study on a cohort of 535 smokers presenting to the Smoking Cessation Counseling Medical Office of the Iasi Clinical Rehabilitation Hospital between January 2009-December 2012 aimed at studying the psychosocial and medical parameters associated with the vulnerability to nicotine addiction. The analyzed psychosocial factors were age, sex, marital status, absence or presence of other smokers in home and motivation to quit smoking. The measurable parameters of tobacco dependence were the number of previous attempts to quit smoking, the amount of cigarettes smoked (pack years), the carbon monoxide breath test, and score of Fagerström test for nicotine dependence. The results showed that the profile of the smokers with nicotine addiction who attempts to quit smoking is middle-aged men, married, with smoking partner, and severe chronic smoking expressed in a large number of pack years and elevated breath CO levels, and concern with his own health status. The severity of nicotine dependence is best reflected by the objective medical parameters, but its psychological components are still undervalued in practice, the professionals involved in the fight against tobacco addiction being deprived of major levers for action.

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Keywords: nicotine dependence; tobacco addiction; smoking behavior; smoking cessation; Fagerström test.

Introduction

Smoking, a true global epidemic, is one of the greatest threats to public health. This reality is reflected in the existence of more than one billion of smokers, nearly 80% being found in low-and middle-income countries. Of these, nearly five million people a year die as a direct result of tobacco use, and at least other 600,000 non-smokers die from exposure to tobacco smoke („Tobacco. Fact sheet N°339”, 2013).

For Romania, according to WHO statistics, in 2010 the smoking prevalence among adults was of 40.3% in men and 25.1% in women, while among youth the prevalence of cigarette smokers was of 17.6% among boys and 9.5% among girls, 52.8% of young people being exposed to tobacco smoke in the home environment and 59.1% outside home. In these circumstances, the Romanian government became involved in tobacco control policies, the 2008 allocated budget being 7,940,100 USD („Tobacco control”, 2013).

Chronic smoking is the disease associated with long-term daily use of tobacco products (cigarettes, pipe, cigar, hookah, chewing tobacco, etc.) and is synonymous with tobacco or nicotine dependence. Initiation and perpetuation of smoking behavior is due to psychosocial and genetic factors and development of nicotine dependence (Societatea Română de Pneumologie [SRP], 2008).

Psychosocial factors are represented by the social acceptance of this vice, association of smoking with a symbol of emancipation, the relatively low price, and aggressive tobacco advertising, promotion, and sponsorship, to which long time underestimated risk to health and absence of health education programs on smoking were added (Mokdad, Marks, Stroup, & Gerberding, 2004; SRP, 2008). The genetic factors have been identified in the last decade by twin studies (Li, Cheng, Ma, & Swan, 2003) and genome-wide association (GWA) studies which identified the genes responsible for the susceptibility to addictive behaviors, nicotine dependence included (Li & Burmeister, 2009). Nicotine, readily absorbed through the skin and mucous membranes, is the main determinant of tobacco addiction, producing psychoactive pharmacological effects, which together with genetic, social, and environmental factors, learned or conditioned, is the substrate for smoking status (Benowitz, 2010).

In the brain, nicotine binds to cholinergic nicotinic receptors, opening ion channels for sodium and calcium; increased intracellular calcium concentration triggers the release of neurotransmitters. Of these, dopamine is associated with a pleasant experience and is very important in promoting readministration and in

reinforcing this behavior (Dajas-Bailador & Wonnacott, 2004). Other mediators with increased release are glutamate, which stimulates the release of dopamine, and gamma-aminobutyric acid (GABA), which inhibits it; as nicotine exposure prolongs, a process of desensitization of some brain cholinergic receptors takes place resulting in increased excitation of dopamine neurons, decreased GABA-mediated inhibitory tone, and finally, increased responsiveness to nicotine (Mansvelder & McGehee, 2002). Additionally, the condensation products of acetaldehyde from cigarette smoke and biogenic amines inhibit monoamine oxidases type A and B, thereby reducing dopamine metabolism and contributing to tobacco addiction (Lewis, Miller, & Lea, 2007).

With time, smokers develop a phenomenon called neuroadaptation or tolerance consisting in increased number of binding sites for nicotine on the brain cholinergic neurons as a result of their nicotine-mediated desensitization (Govind, Vezina, & Green, 2009) and in the activation of corticotropin-releasing factor (CRF) - corticotropin-releasing factor receptor 1 (CRF1) system that mediates stress response. CRF causes anxiety and CRF1 receptor blockade contributes to inhibiting the anxiety-like effects during nicotine withdrawal. These adaptive changes favor withdrawal symptoms when the number of smoked cigarettes is reduced or cessation of smoking is attempted (George et al., 2007).

Nicotine has many psychoactive effects: improves concentration and task performance, decreases reaction time, and reduces anxiety and stress. From a behavioral standpoint, with time smokers develop a conditioned type of behavior by associating the anticipated pleasurable effects of nicotine with specific situations and moods or with some environmental factors, called *smoking-related cues*. Animal model studies have shown that the substrate of this conditioning generated by repeated exposure to nicotine is the change in the expression of some neuronal proteins and synaptic changes, process called neural plasticity (Kauer & Malenka, 2007).

Individual vulnerability to nicotine addiction development varies and depends on many factors. Age at starting smoking is important, the addiction risk being higher in smokers who started smoking at a young age, studies in teenager-rats showing even the presence of permanent brain changes generating addiction (Placzek, Zhang, & Dani, 2009). There are also gender differences in terms of nicotine addiction: women are more vulnerable to conditioning through smoking-related cues, metabolize nicotine faster and thus addiction develops faster, smoking cessation being also more difficult for women (Perkins & Scott, 2008).

Another explanation for the different behavior in the smoker population is the differences in the rate at which nicotine is metabolized to cotinine by the liver enzyme CYP2A6; smokers with the variant *CYP2A6* genes associated with slower enzyme activity develop low degree dependence, smoke fewer cigarettes daily and can easily cease smoking (Malaiyandi, Sellers, & Tyndale, 2005). Also, the

co-existence of a psychiatric illness or other substance-abuse disorders predisposes to nicotine addiction through mechanisms involving relief of some symptoms and inhibitory effect of nicotine on monoamine oxidase (Ziedonis et al., 2008).

In clinical practice and research, nicotine addiction is most often assessed by the Fagerström Tolerance Questionnaire (FTQ) (Fagerström, 1978) and its shorter and more refined version - Fagerström Test for Nicotine Dependence (FTND) (Heatherton, Kozlowski, Frecker, & Fagerström, 1991). The 8-items of the original questionnaire were derived from information on nicotine dependence, with statistically significant correlations between some items and biochemical markers, while other items, as those related to inhalation and nicotine ratings seem to add error variance to the final score and were abandoned in the FTND version. Thus, FTND corrects some of the psychometric and conceptual problems of the initial questionnaire (Heatherton et al., 1991). The limitations of this test are that it rather evaluates physical dependence than its particularly important psychological aspects, such as cravings, behavioral automaticity and saliency, compulsion to smoke, which are core constructs of dependence (Shadel, Shiffman, Niaura, Nichter, & Abrams, 2000).

Other methods for assessing nicotine addiction are Tobacco Dependence Screener (TDS) (10-item questionnaire), Wisconsin Inventory of Smoking Dependence Motives (WISDM-68), a multidimensional measure of dependence (68 items consisting of 13 domains), Cigarettes Dependence Scale - 12 (CDS-12) or -5 (CDS-5) and Nicotine Dependence Syndrome Scale (NDSS), a multidimensional questionnaire based on Edward's syndromal conceptualization of dependence (Sato, Sato, Nozawa, & Sugimura, 2012).

In this context, we conducted a retrospective study on a large cohort of smokers who presented to the Smoking Cessation Counseling Medical Office of the Iasi Clinical Rehabilitation Hospital aimed at studying the psychosocial and medical parameters associated with the vulnerability to nicotine addiction.

Method

Participants

In this retrospective study were included 535 smokers of both sexes, who presented consecutively to the Smoking Cessation Counseling Medical Office of the Iasi Clinical Rehabilitation Hospital between January 2009-December 2012. The subjects were included in the national „Smoking Cessation” program in order to gain professional care and the medication necessary for the treatment of nicotine addiction.

Materials and Procedure

Studied parameters. For this study we used data from the initial assessment of smokers recorded in their medical record, aimed at a more thorough evaluation in view of establishing the therapeutic indications. These data were used to study two categories of parameters: psychosocial factors possibly related to the development and maintenance of nicotine dependence and medical parameters of tobacco use. The psychosocial parameters are represented by age, sex, marital status (married, single, divorced), absence or presence of other smokers in home, usually family members (partner, parents, children, siblings, other persons), motivation to attempt smoking cessation, which may be related to health, peer pressure, financial reasons, desire of not being dependent, religious and esthetic reasons, reaching the saturation point („I've had enough!"), or other strictly private reasons. Medical parameters of nicotine dependence are the severity of smoking quantified by pack years, the number of attempts to stop smoking (lasting more than one day), measurement of carbon monoxide (CO) by breath test, and assessment of the degree of nicotine dependence by Fagerström Test for Nicotine Dependence (FTND).

Quantifying the severity of tobacco use. To determine the degree of tobacco exposure, often correlated with the risk for nicotine dependence, number of pack years is calculated according to the following formula: Number of pack years = (number of cigarettes smoked per day × number of years smoked)/ 20 (1 pack has 20 cigarettes).

Measurement of carbon monoxide (CO) by breath test. This was done by using The Micro⁺ Smokerlyzer®, a breath carbon monoxide monitor intended for multi-patient use by healthcare professionals in smoking cessation programs, research, and as an indicator of carbon monoxide poisoning (Bedfont Scientific, 2008). The cut-off point between smoker and nonsmoker has been found to be 6 ppm CO; 0-6 ppm means *nonsmoker*, 7-15 ppm is a *low dependence smoker* and above 15 ppm are *strongly addicted smokers*.

Assessment of the severity of nicotine dependence. All study subjects filled in the Fagerström Test for Nicotine Dependence; based on their responses to the 8-items, a score between 1 and 10 was calculated for each subject, and according to this score the smokers were classified in one of the dependence categories: *mild* (0-3 points), *moderate* (4-6 points) and *severe* (7-10 points).

Procedure and ethical considerations

The data used in the study were collected and analyzed retrospectively, respecting the confidentiality. Mention should be made that at the time of initial assessment information were obtained from smokers by individual physician-patient discussion, and the details on the motivation for smoking cessation were obtained by motivational interview.

Data analysis

The data were processed using SPSS 14.0 for Windows (SPSS Inc., Chicago, IL). For the studied variables the descriptive statistics parameters and their frequencies were determined and the statistical significance of differences between groups was assessed by Student T-test for parametric variables and Kruskal-Wallis H or Chi-square tests for ordinal and nominal variables.

Results

During this 4-year study, there were 535 smoking subjects, of which 37.4% (N=200) women and 62.6% (N=335) men with an overall mean age of 39.13 ± 12.75 years, 39.9 ± 13.33 years for females and 38.67 ± 12.38 years for males (*p* = .291). In terms of marital status, 62.1% of the smokers were married, 30.7% unmarried, and 7.3% divorced, their gender distribution being presented in *Table 1*.

Table 1. *Gender and marital status distribution of smokers*

		MARITAL STATUS		
		MARRIED	UNMARRIED	DIVORCED
SEX	FEMALE	N=126 (38%)	N=56 (34.1%)	N=18 (46.2%)
	MALE	N=206 (62%)	N=108 (65.85%)	N=21 (53.8%)
Total		332	164	39

The absence of other smokers in home was reported by 46.2% of the smokers included in this study, while other smokers in the entourage were mainly close relatives: spouse (27.7%), parents (12.3%), children (4.3%), siblings (5.8%), others (3.7%) as it is seen in *Figure 1*. The most common motivation for subjects presentation to the Smoking Cessation Counseling Medical Office was health related (38.9%), followed by the economic burden of smoking (21.9%), the desire to end the state of dependence (16.3%), or peer pressure (13.3%) (see *Figure 2*).

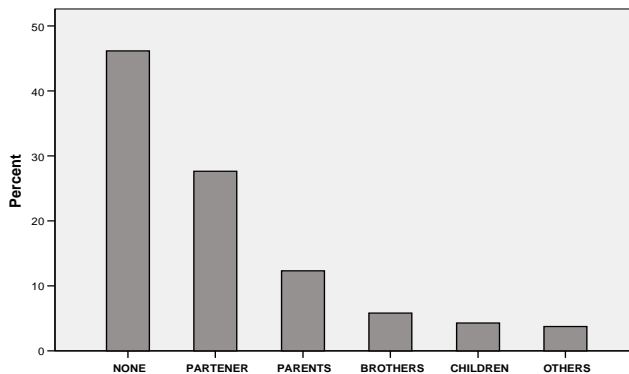


Figure 1. *Other smokers in the entourage*

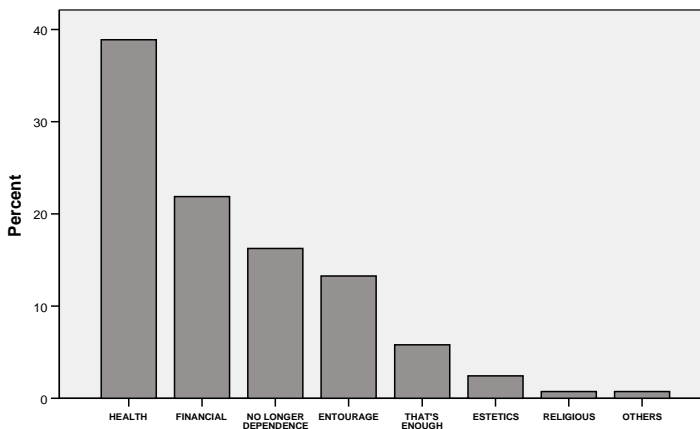


Figure 2. *Motivation for smoking cessation attempt*

Quantification of the severity of tobacco use showed pathological mean values for all analyzed parameters: pack-years (26.42 ± 18.01), baseline CO (31.24 ± 7.60 ppm), and number of attempts to quit smoking, longer than one day (0.66 ± 0.865). The analysis by gender and marital status revealed statistically significant differences in pack years and baseline CO, but no difference in the number of attempts to quit smoking (see *Table 2*).

Also, when comparing the marital status-based groups of smokers, the results showed a significant difference between groups in terms of baseline CO ($p = .000$) and pack years ($p = .000$), but no difference in the number of attempts to quit smoking ($p = .977$) (onewayAnova).

Table 2. Evaluation of the statistical significance of sex and marital status-related differences in some parameters of nicotine dependence

Variable	Mean difference	Std Error Difference	95% Confidence Interval		p
			Lower	Upper	
Initial CO (ppm) Female vs. Male	-2.730	.642	-3.992	-1.468	.000
Pack years (Log) Female vs. Male	-.071	.029	-.129	-.013	.017
Smoking cessation attempts (Log) Female vs. Male	-.044	.040	-.123	.035	.275
Initial CO (ppm) Married vs. unmarried	3.575	.701	2.196	4.953	.000
Initial CO (ppm) Married vs. divorced	.610	1.267	-1.938	3.159	.632
Initial CO (ppm) Unmarried vs. divorced	-2.964	1.325	-5.619	-.310	.029
Pack years (Log) Married vs unmarried	.296	.030	.237	.355	.000
Pack years (Log) Married vs. divorced	-.079	.044	-.168	.009	.080
Pack years (Log) Unmarried vs. divorced	-.375	.049	-.473	-.277	.000
Smoking cessation attempts (Log) Married vs. unmarried	-.0005	.044	-.088	.087	.991
Smoking cessation attempts (Log) Married vs. divorced	.016	.078	-.141	.174	.838
Smoking cessation attempts (Log) Unmarried vs. divorced	.016	.083	-.150	.183	.842

The distribution of nicotine dependence scores obtained by FTND in the study group was significantly in favor of severe dependence (76.6%), followed by moderate dependence (23%), and mild dependence in a minority of cases (0.4%); gender distribution is seen in *Table 3*.

Table 3. Gender distribution of nicotine dependence severity (Fagerström score)

		FAGERSTROM SCORE		
		mild	moderate	severe
SEX	FEMALE	2	50	148
	MALE	0	72	263
Total		N=2 .4%	N=122 23.0%	N=411 76.6%

No significant differences in dependence score in relation with gender ($\chi^2 = 1.564, p = .211$) or marital status (married, single, divorced) ($\chi^2 = .774, p = .679$) were found. Also, there was no significant association between the presence of other smokers in home, usually family members, and Fagerström dependence score ($\chi^2 = 7.969, p = .158$) or between a certain motivation to quit smoking and this score ($\chi^2 = 7.117, p = .417$).

Testing for possible correlations between Fagerström dependence score and the objective parameters of smoking severity showed only a tendency to a weak positive correlation with baseline CO ($r = .272, p = .000$) and pack years ($r = .223, p = .000$) but also the absence of any relationship with the number of attempts to quit smoking ($r = -.020, p = .648$) or smokers' age ($r = .065, p = .132$).

Discussion

Smokers develop nicotine dependence differently depending on a large number of factors, the most extensively studied being the objective, measurable ones. Beyond this, there is great interindividual variability, involving especially psychosocial factors that are more difficult to measure. Our analysis was performed on a cohort of smokers who became aware of the risks and, to some extent, of the addictive behavior, thus the structure of our study population being somewhat different from the general population smokers. Also, the mean age of smokers was relatively low (39.13 ± 12.75 years), implying that most of those seeking smoking cessation counseling started smoking at a young age and were thus more likely to develop early nicotine addiction. These findings emphasize the importance of developing a nation-wide strategy for parenting education as a form of support and consolidation of children's rights, widely supported by sociologists (Cojocaru, Cojocaru, & Ciuchi, 2011), including early education for health maintenance. In addition, the filled in Fagerström questionnaire proved that 76.6% of the subjects seeking professional counseling were severely dependent smokers.

The proportion of female smokers seeking counseling at our smoking cessation medical office was lower than that of men (37.4% vs 62.6%). Also, the objective data in our study showed significantly lower average pack years and baseline CO levels in age-matched women smokers compared to male smokers, but the number

of attempts to quit smoking longer than one day was similar. This means that at a lower tobacco use severity, women have greater difficulty in attempting tobacco withdrawal, conclusion supported by the literature on the existence of a stronger addiction and a lower success rate of smoking cessation in women smokers.

Maintenance and reinforcement of smoking behavior are supported by the family environment of smokers, by the presence in home of a majority of other close family members who smoke (50.1%), the smoking partner ranking first (27.7%). This true „familial aggregation” of smokers emphasizes the need and importance of behavioral counseling both of the smoker who attempts to quit smoking, and of his/her partner and/or other smoking family members (parents, children, siblings, etc.). The opposite is also true in some families, 13.3% of our subjects admitting that the main motivation for the attempt to quit smoking was family pressure and in 21.9% economic reasons, among which the reduction of family income. The objective parameters of smoking severity showed significantly higher pack years and baseline breath CO levels in the married or divorced smokers as compared to the unmarried ones, which could mean that unmarried persons take better care of themselves, but the number of attempts to quit smoking, were relatively similar among these three smoker categories.

Motivational interviewing revealed that the most important stimulus for smoking cessation is health impairment (38.9%) in the form of smoking-related or potentially smoking-related diseases. This finding emphasizes that the health care provided to smokers should focus on smoking related health issues by acting in several directions: smokers should become aware that smoking itself is a long-term chronic disease with cycles of remission or relapse, to inform the smokers who seek counseling on smoking-associated risks, and to explain the treatment options and the advantages and disadvantages of each method.

A weak positive correlation was found only between the severity of nicotine dependence, measured by the Fagerström test, and pack years and baseline breath CO level, but without significant differences between smokers in relation to gender, marital status, existence of other smokers in home, or the motivation of the attempt to quit smoking, suggesting that there are many other variables, especially psychological, and thus difficult to measure, that contribute to the severity of nicotine dependence and which are not currently assessed. In this regard, an interesting and unexplored area in tobacco-addicted subjects approach could be the assessment of trait-emotional intelligence and the two „candidate” variables that connect with life satisfaction - self-esteem and social support (Runcan & Iovu, 2013).

In conclusion, the profile of the smokers with nicotine dependence seeking counseling for smoking cessation is middle-aged men, married, with smoking partner, severe chronic smoking expressed by elevated breath CO levels and a large number of pack years smoked, and concerned with his own health status.

Also, the severity of nicotine dependence is best reflected by the objective medical parameters, but its psychological components are still undervalued in practice, the professionals involved in the fight against tobacco addiction being deprived of major levers for action.

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