BRIEF REPORT

Nicotine use in patients with schizophrenia evaluated by the Fagerström Tolerance Questionnaire: a descriptive analysis from a Brazilian sample

O uso de nicotina em pacientes com esquizofrenia avaliado pelo Questionário de Tolerância de Fagerström: uma análise descritiva em uma amostra brasileira

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Abstract

Objective: *This is a descriptive study to determine smoking prevalence rates in a convenience sample of patients with schizophrenia and to describe clinical/demographic variables for nicotine use in this population.* ***Method:*** *Patients with schizophrenia were consecutively invited to answer a standard clinical/demographic questionnaire and a questionnaire on smoking habits (Fagerstrom Tolerance Questionnaire).* ***Results:*** *Eighty-three patients were interviewed. The smoking rate was 57.8% (n = 48). Male (68.8%) patients smoked more than females did (31.3%; p = 0.081). Compared to patients who smoked at the time of disease onset, those who only started smoking after disease onset had a lower mean age at the time of disease onset [24 years old (SD = ± 6.8) vs.19 years old (SD = ± 3.9; p = 0.041)]. Patients who preferred high-nicotine content cigarettes (p < 0.01) had higher frequency of smoking inhalation (p < 0.05) and had more urgency to smoke the first cigarette in the morning (p < 0.05). Twenty-seven (56.3%) of smoking patients were heavy smokers (FTQ ≥ 8).* ***Conclusions:*** *Patients with schizophrenia in our convenience sample smoked in a higher rate compared to the general population in Brazil. Smoking patients were heavy smokers evaluated by the Fagerstrom Tolerance Questionnaire.*

Descriptors: *Nicotine; Smoking; Schizophrenia; Statistical analysis; Data display*

Resumo

Objetivo: *Este é um estudo descritivo para determinar os índices de prevalência de tabagismo em uma amostra de conveniência de pacientes com esquizofrenia e para descrever variáveis clínicas/demográficas para o uso de nicotina nesta população.* ***Método:*** *Pacientes com esquizofrenia foram convidados de forma consecutiva a responder a um questionário clínico/demográfico padrão e a um questionário sobre tabagismo (Questionário de Tolerância de Fagerstrom).* ***Resultados:*** *Oitenta e três pacientes foram entrevistados. O índice de tabagismo foi de 57,8% (n = 48). Pacientes masculinos (68,8%) fumaram mais do que os femininos (31,3%; p = 0,081). Em comparação com pacientes que fumavam no momento do início da doença, aqueles que somente começaram a fumar após o início da doença tiveram uma idade média de início da doença menor [24 anos de idade (DP = ± 6,8) vs.19 anos de idade (DP = ± 3,9; p = 0,041)]. Pacientes que preferiam cigarros com alto conteúdo de nicotina (p < 0,01) tinham freqüência mais alta de inalação de tabaco (p < 0,05) e tinham maior urgência pelo primeiro cigarro da manhã (p < 0,05). Vinte e sete (56,3%) dos pacientes fumantes eram fumadores pesados (FTQ ≥ 8).* ***Conclusões:*** *Os pacientes com esquizofrenia em nossa amostra de conveniência tiveram índices mais elevados de tabagismo em comparação com a população geral do Brasil. Pacientes tabagistas eram tabagistas pesados segundo a avaliação do Questionário de Tolerância de Fagerstrom.*

Descritores: *Nicotina; Tabagismo; Esquizofrenia; Análise estatística; Apresentação de dados*

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Introduction

Nicotine dependence is the most common comorbidity among patients with schizophrenia, occurring in 50 to 90% of the patients.[1] Many factors should be considered in the management of these patients including nicotine stimulating effects in neurotransmission, reduction of circulating levels of antipsychotic medications; improvement in cognitive functioning, and withdrawal symptoms that could worsen in psychiatry symptoms.

Previously published reports indicate that first-episode schizophrenia patients smoke in the same intensity as those who are chronic patients.[2] Adler et al. suggested that cognitive deficits could be responsible for nicotine intake among patients with schizophrenia.[3] Patients would self-medicate with nicotine to alleviate both positive and negative symptoms.[4]

Chronic nicotine use could increase dopaminergic neurotransmission, especially in the prefrontal cortex.[5] Reducing prefrontal activity could lead to negative symptoms and cognitive deficits;[6] therefore, improvement in dopaminergic activity in this region by nicotine could alleviate these symptoms. The resulting symptom relief could motivate patients with schizophrenia to continue smoking.

Morphological examinations found alterations in nicotinic receptors in postmortem tissue of individuals with schizophrenia compared to controls, especially in the α-7 and α-4b2 subtypes. In nicotinic receptor stimulation studies of patients with schizophrenia, improvement in sensory inhibition and cognitive deficits were observed following treatment, although the effects were transient.[7] Alfa -7-type nAChRs have been suggested to be potential therapeutic targets for Alzheimer's disease, schizophrenia and possibly other pathologies. Acetylcholine receptors containing alfa-6 subunits have been suggested to have a role in nicotine-evoked dopamine release.[8] In our study we investigated the smoking prevalence and smoking habits among patients with schizophrenia.

Method

Eighty-three patients were interviewed from April to May of the year 2002 in two psychiatry care units. None of the patients we approached declined participation in the interview. Inclusion criteria comprised aging from 18 to 65 years and meeting CID-10 criteria for schizophrenia (F20 to F25). The exclusion criterion was inability to answer the interview due to disorganized speech or thought content. The study was reviewed and approved by the Ethics Committee Board at Hospital São Paulo under the number – CEP 0353/02.

All patients answered a standard clinical/demographic questionnaire. Smoking patients responded to the Fagerström Tolerance Questionnaire (FTQ). FTQ evaluates smoking dependence from zero to eleven points (mild = zero to 4; moderate = 6 and 7; severe = 8 to 11).

An Ethics Committee Board (ECB) approved the study. Patients were included in the study after signing the approved informed consent form.

Clinical and demographic variables were evaluated using the chi-square test. Smoking dependence was determined through the FTQ. FTQ total score distribution was evaluated by clinical and demographic categorized variables using the t-student test for age in years of treatment onset, and chi-square test for all other variables.

Results

The overall rate of smoking was 57.8%. Forty-eight (57.8%) were males and 35 (42.2%) were females. Male (68.8%) patients smoked more than female patients (31.3%; $p = 0.081$). Among smokers, those who already smoked at the time of disease onset had a mean age at disease onset of 24 years old (SD = $\pm$ 6.8). Those who only started smoking after schizophrenia onset had an earlier disease onset, around 19 years old (SD = $\pm$ 3.9). This comparison was statistically significant ($p = 0.041$).

Twenty-seven (56.3%) of the patients who were smokers were heavy smokers (FTQ $\geq$ 8). FTQ showed statistically significant differences in 3 of the 8 variables: high-nicotine content cigarettes ($p < 0.01$), smoking inhalation frequency ($p < 0.05$) and urgency for the first cigarette in the morning ($p < 0.05$).

Discussion

The rate of 57.8% we found in our convenience sample was similar to studies that assessed samples of younger patients but with a higher frequency of males.[9] To our knowledge, this is the first Brazilian study to describe factors associated with nicotine use in schizophrenia.

Kelly et al. found a rate of 58% of nicotine consumption prevalence.[4] Male patients (68.8%) smoked more than female did (31.3%; $p = 0.018$). Compared to patients who smoked at the time of disease onset, those who only started smoking after the disease onset had a lower mean age at the onset of schizophrenia [24 years old (SD = $\pm$ 6.8) vs.19 years old (SD = $\pm$ 3.9; $p = 0.041$)]. Kelly et al. observed that individuals with schizophrenia started to smoke at least 4 years earlier before disease onset, but this difference was not statistically significant.[4]

Freedman et al. suggested that vulnerability to schizophrenia was associated with smoking.[10] Patients with schizophrenia would have more difficulty in discriminating stimuli, a deficit also found in family members. Nicotine use would normalize these deficits through stimulation of specific receptors with low affinity to nicotine, therefore family members who are not affected by schizophrenia would smoke more than the non-affected general population.

Freedman et al. suggested variations in the regulation of α-7 nicotinergic gene subunits in chromosome 15 could be a marker of schizophrenia.[11] Adler et al. observed a brief and temporary normalization of P50 wave in evoked potential when nicotine was administered acutely in schizophrenic family members and in patients.[12] They conclude this brief normalization could improve cognitive symptoms, making patients would seek for nicotine by brain reward and reinforcement mechanisms.

The FTQ scores showed statistically significant differences in 3 individual items of the FTQ: nicotine content cigarettes (high-nicotine cigarette content), frequency of smoking inhalation (always inhale smoke) and urgency to smoke (smoke up to 30 minutes) - Table 1. These patients prefer high-nicotine content cigarettes and most frequently smoke the cigarette until the very end where nicotine concentration is higher.[13]

It seems that studies investigating neurobiological relations between smoking and schizophrenia provide us with more robust evidence that could be replicated in similar studies.

The main limitation of our study is the sample size. However, it points that nicotine use is high among patients with schizophrenia. It raises the discussion whether smoking could be a marker for the neurodevelopmental form of the illness or it could play a protective role in vulnerable individuals with schizophrenia. Larger comparative studies are warranted in determining nicotine's role in our population with schizophrenia.

Table 1 – Fagerström Tolerance Questionnaire

		Total		Chi square test
		n	%	X^2
Nicotine content	Low nicotine	4	8.3%	11.187 *
	Medium	5	10.4%	
	High	39	81.3%	
Do you inhale smoke?	No	3	6.3%	7.631 **
	Sometimes	7	14.6%	
	Always	38	79.2%	
Do you smoke more in the mornings?	No	17	35.4%	0.200
	Yes	31	64.6%	
Time of the day that is harder for you to NOT smoke	All the other cigarettes	12	25.0%	0.032
	The first in the morning	36	75.0%	
Can you refrain from smoking in forbidden places?	No	23	47.9%	3.074
	Yes	25	52.1%	
Do you smoke even when sick?	No	23	47.9%	0.548
	Yes	25	52.1%	
How many cigarettes a day?	0-15	23	47.9%	2.674
	16-25	14	29.2%	
	≥ 26	11	22.9%	
How many minutes after you wake do you smoke	After 30'	9	18.8%	5.035 **
	Up to 30'	39	81.3%	
Total		48	100%	

*$p < 0.01$; **$p < 0.05$

Disclosures

Writting group member	Employment	Research grant[1]	Other research grant or medical continuous education[2]	Spekear's honoraria	Ownership interest	Consultant/ Advisory board	Other[3]
Leonardo Passos Chaves	Abbott Laboratórios do Brasil	—	—	—	—	—	—
Itiro Shirakawa	PROESQ - UNIFESP	—	—	—	—	—	—

** Modest*
*** Significant*
**** Significant. Amounts given to the author's institution or to a colleague for research in which the author has participation, not directly to the author.*
Note: PROESQ = Programa da Esquizofrenia; UNIFESP = Universidade Federal de São Paulo.
For more information, see Instructions to Authors.

References

1. Ziedonis DM, George TP. Schizophrenia and nicotine use: report of a pilot smoking cessation program and review of neurobiological and clinical issues. *Schizophr Bull*. 1997;23(2):247-54.
2. McEvoy JP, Freudenreich O, Wilson WH. Smoking and therapeutic response to clozapine in patients with schizophrenia. *Biol Psychiatry*. 1999;46(1):125-9.
3. Adler LE, Olincy A, Waldo M, Harris JG, Griffith J, Stevens K, Flach K, Nagamoto H, Bickford P, Leonard S, Freedman R. Schizophrenia, sensory gating, and nicotinic receptors. *Schizophr Bull*. 1998;24(2):189-202.
4. Kelly C, McCreadie RG. Smoking habits, current symptoms and premorbid characteristics of schizophrenic patients in Nithsdale, Scotland. *Am J Psychiatry*. 1999;156(11):1751-7.
5. Vezina P, Blanc G, Glowinski J, Tassin JP. Nicotine and morphine differentially activate brain dopamine in prefrontalcortical and subcortical terminal fields: effects of acute and repeated injections. *J Pharmcol Exp Ther*. 1992;261(2):484-90.
6. Svensson TH. Effect of nicotine on dynamic functions of brain catecholamine neurons. In: Bock G, editor. *The Biology of Nicotine Dependence*. New York: Wiley; 1990. p. 69-80.
7. Adams CE, Stevens KE. Evidence for a role of nicotinic acetylcholine receptors in schizophrenia. *Front Biosci*. 2007;12:4755-72.
8. Papke RL, Dwoskin LP, Crookls PA. The pharmacological activity of nicotine and nornicotine on nAChRs subtypes: relevance to nicotine dependence and drug discovery. *J Neurochem*. 2007;101(1):160-7.
9. Goff DC, Henderson DC, Amico E. Cigarette smoking in schizophrenia: relationship to psychopathology and medication side effects. *Am J Psychiatry*. 1992;149(9):1189-94.
10. Freedman R, Adler LE, Bickford P, Freedman R, Adler LE, Bickford P, Byerley W, Coon H, Cullum CM, Griffith JM, Harris JG, Leonard S, Miller C, et al. Schizophrenia and nicotinic receptors. *Har Rev Psychiatry*. 1994;2(4):179-92.
11. Freedman R, Coon H, Myles-Worsley M, Orr-Urtreger A, Olincy A, Davis A, Polymeropoulos M, Holik J, Hopkins J, Hoff M, Rosenthal J, Waldo MC, Reimherr F, Wender P, Yaw J, Young DA, Breese CR, Adams C, Patterson D, Adler LE, Kruglyak L, Leonard S, Byerley W. Linkage of a neurophysiological deficit in schizophrenia to a chromosome 15 locus. *Proc Natl Acad Sci U S A*. 1997;94(2):587-92.
12. Adler LE, Hoffer LD, Wiser A, Freedman R. Normalization of auditory physiology by cigarette smoking schizophrenic patients. *Am J Psychiatry*. 1993;150(12):1856-61.
13. Masterson E, O'Shea B. Smoking and malignancy in schizophrenia. *Br J Psychiatry*. 1984;145:429-32.