

Nicotine dependence and symptom severity in patients with schizophrenia in Morocco

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ABSTRACT

Background

The prevalence of smoking among patients suffering from schizophrenia is significantly higher than in the general population. Studies of the correlation between tobacco consumption and psychotic symptoms, as assessed by the PANSS test, have yielded different results. It is therefore interesting to examine how nicotine dependence levels impact symptom severity. **Objectives:** The aim of our study is to describe the degree of dependence in schizophrenic patients and to determine the correlation with the severity of clinical symptoms.

Method and Materials

172 patients hospitalized at the Ar-razi hospital in Salé. Sociodemographic data were collected using a questionnaire. Symptom severity was assessed using the Positive and Negative Syndromic Schizophrenia Scale (PANSS). And the degree of tobacco dependence was assessed using the Fagerström Test (FTND).

Result

Our main results show that the average age of our patients is 31.76 years. 80.2% use atypical antipsychotics, 79.1% use tobacco and 77.9% use cannabis. 43.6% showed a mild dependence on nicotine, while 25.6% had a high dependence, and 30.8% a very high dependence. The correlation test showed a significant association between the degree of nicotine dependence and PANSS score ($P < 0.002$), anxiety, cannabis use and use of atypical antipsychotics.

Conclusion

Tobacco addiction management must be integrated into disease management.

INTRODUCTION

Schizophrenia is a chronic mental illness with a lifetime prevalence of around 1% in the general population¹, and an average annual incidence of around 15 new cases per 100,000 people². In Morocco, more than 200,000 people aged 15 and over suffer from schizophrenia, and psychiatrists are often faced with the problem of comorbidity between schizophrenia and addiction³. The prevalence of smoking among patients with schizophrenia, estimated at between 64 and 79%⁴, is significantly higher than in the general population⁴. This prevalence is higher in men

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than in women (71% vs. 44%) De Leon et al , 2002 ⁵. Several studies have shown that schizophrenic patients have an extremely high prevalence of smoking, more so than other psychiatric disorders. Increased rates and intensity of smoking of almost 90% compared with only 33% in the general population and 45-70% in patients with other psychiatric diagnoses ⁶. However, in certain countries such as Japan, China, India, Turkey and Colombia, the prevalence of smoking among patients suffering from schizophrenia is lower than in the general population ⁷. Studies have shown that schizophrenic patients inhale smoke more intensely and deeply, taking more puffs per cigarette, which increases nicotine extraction per cigarette, resulting in higher blood and urine levels of cotinine (nicotine's main metabolite) than control subjects, free of any psychiatric pathology, for the same number of cigarettes smoked daily as controls (nicotine: 28 vs. 21 ng/ml, cotinine: 291 vs. 227 ng/ml) ⁸. Smoking schizophrenic patients have a significantly increased risk of early mortality due to the morbid consequences of their smoking and their difficulties in quitting. Many are under threat from cardiovascular pathologies because they accumulate risk factors (sedentary lifestyle, overweight, diabetes, dyslipidemia). Smoking also increases the risk of suicide ⁹. Ten to twenty times higher than in the general population ¹⁰. It diminishes the therapeutic effect of antipsychotics ¹¹. Tobacco consumption increases cardiovascular risk, which is aggravated in schizophrenic patients by other more frequent risk factors, in particular glycoregulation disorders, lipid metabolism disorders, obesity and sedentary lifestyle. Schizophrenic smokers have a higher frequency of hospitalization ¹². Indeed, the frequency of tobacco consumption among hospitalized subjects is higher than for other patient groups, notably patients with mood disorders ¹³, suggesting that institution-related factors, such as boredom, do not alone explain the high rates of tobacco consumption. Studies have shown that nicotine dependence is severe in this population, with an average score of six to seven depending on the study ¹⁴. Furthermore, studies have shown that tobacco consumption in schizophrenia patients, as in the general population, is associated with other addictions, principally cannabis ¹⁵. Thus, smoking individuals are more vulnerable to COVID-19. Smoking can exacerbate respiratory conditions, thereby

increasing the risk of severe complications in smokers. Additionally, it is crucial to consider the psychological impact that the disease can have on COVID-19 patients. Anxiety, fear, and stress associated with the illness can affect their mental and physical well-being. Therefore, providing adequate psychological support to patients during this challenging period is essential ¹⁶.

With regard to the effect of tobacco consumption on psychotic symptomatology, studies of the correlation between tobacco consumption and psychotic symptoms, as assessed by the PANSS test, have produced different results.

In Morocco, few studies have shed light on the relationship between smoking and psychiatric disorders.

To better understand the impact of this dependence on psychiatric symptoms in patients, this study aims to examine how nicotine dependence levels, measured by the Fagerström Nicotine Dependence Test (FTND) score, are associated with symptoms assessed by the Positive and Negative Syndrome Scale (PANSS) in patients with schizophrenia hospitalized at the Ar-razi CHU Ibn Sina Hospital in Morocco.

METHODS

This cross-sectional study was conducted over two years in the psychiatric wards of the Ar-razi de Salé Hospital (HAS), part of the Ibn Sina University Hospital in Rabat. The study population consisted of 172 patients with schizophrenia hospitalized in the HAS psychiatric wards. Adult patients with confirmed schizophrenia according to the DSMV diagnostic criteria for schizophrenia, of both sexes, and willing to participate in the study were included. Patients with psychiatric or neurological comorbidity and those unable to answer the survey questions were excluded from the study.

Sociodemographic data were collected by means of a questionnaire administered to patients and/or their guardians, and the severity of mental disorders was assessed using the Positive and Negative Syndromic Scale of Schizophrenia (PANSS).

The PANSS is a 30-item scale, rated from 1 (absent) to 7 (extreme), which assesses psychopathological symptoms observed in patients with psychotic states, particularly schizophrenia. It calculates scores for three dimensions: positive symptoms (7 items), negative symptoms (7 items) and general psychopathology (16 items). In addition to this dimensional scoring,

it is also possible to evaluate the patient according to a categorical typology (subtype diagnoses), thus distinguishing between positive, negative and mixed forms of schizophrenia. Its use is particularly indicated for determining a psychopathological profile, looking for prognostic elements of progression and evaluating the efficacy of various therapeutic strategies.

The degree of nicotine dependence was measured by the Fagerström Test (FTND). The FTND is a standard self-administered six-item scale for assessing the intensity of physical dependence on nicotine. The test provides an ordinal measure of nicotine dependence related to smoking. The “yes/no” items are scored 0 or 1, and the multiple-choice items are scored from 0 to 3. Finally, the items are summed to give a total score from 0 to 10. The higher the Fagerström score, the more intense the degree of physical dependence on nicotine.

The approval of the Ethics Committee of the Faculty of Medicine and Pharmacy of Rabat, was obtained (n°956 of 31/10/2019) and the data were collected while respecting the anonymity and confidentiality of patient information.

The data collected were entered in Excel and, after filtration and coding, were transported on an SPSS medium. Qualitative variables were expressed as frequencies and quantitative variables as mean \pm standard error. A joint analysis was applied, that of chi2 at 5% error, and a Pearson correlation test was applied to look for possible links.

Ethical clearance: Not applicable

RESULTS:

Socio-demographic characteristics of schizophrenic patients

The table shows the socio-demographic characteristics of schizophrenic patients. It reveals a male predominance (86%) in the sample studied, with more than half the patients aged between 30 and 40, and a high proportion of single patients (84.9%). The majority of patients had no more than a secondary school education, and most of them had no stable occupation. The average age of schizophrenic patients was 31.76 years, with a standard deviation of 0.72, while the average age of the first episode of the illness was 22.25 years, with a standard deviation of 0.44. This result reflects the chronicity of the illness in these hospitalized patients. As for place of residence, the majority of our patients came from urban areas (93.6%).

Table 1: Socio-demographic characteristics

Variable	Modality	Ni (%)
Type	Men	148 (86%)
	Women	24 (14)
Age groups	<30	45(26,2%)
	30<>40	88(51,2%)
	40<>50	33(19,2%)
	>50	6(3,5%)
Marital status	Single	146 (84,9%)
	Married	26 (15,1%)
Nivea instruction	<Secondary	135 (78, 5%)
	University	37 (21, 5%)
Profession	Without	151 (87, 8%)
	With	21(12, 2%)
Place of residence	Rural	11 (6, 4%)
	Urban	161 (93, 6%)
Current age	mean \pm SD	31.76 \pm 0.72 years
Age of 1 ^{er} episode	mean \pm SD	22.25 \pm 0.44 years

Clinical characteristics of patients

The table shows the results of the patients' clinical characteristics. Paranoid schizophrenia is the most common, with a prevalence of 69.8%. However, almost 30% of patients had attempted suicide. On the other hand, 77.9% claimed to use cannabis, the majority of them on a daily basis, and 79.1% used tobacco. As for treatment, 80.2% used atypical antipsychotics, while 30% turned to conventional antipsychotics. In addition, over 94% of hospitalized patients suffered from symptoms of depression and anxiety. Symptom severity, as assessed by the PANSS scale, showed a mean score of 85.50, with a standard deviation of 1.67. The positive PANSS subscale had a mean score of 26.63 \pm 0.62, the negative subscale a mean of 22.56 \pm 0.6, and the psychopathological subscale a mean score of 36.32 \pm 0.79.

Table 2: Clinical characteristics of patients

Variable	Modality	ni (%)
Type of schizophrenia	Paranoid	111 (69,8%)
	Disorganized	12(7,5%)
	Other	36(22,6%)
Number of suicide attempts	0 times	120 (70,6%)
	1 time	27 (15,9%)
	2 times	15 (8,8%)
	More than 2 times	8 (4,8%)

Variable	Modality	ni (%)
Case history	Yes	52 (31,5%)
Cannabis consumption	Yes	134 (77,9%)
Tobacco consumption	Yes	136 (79,1%)
Medication	Classic antipsychotics (yes)	56 (32,4%)
	Atypical antipsychotics (yes)	138 (80,2%)
Hospitalization	Yes	163 (94,8%)
Fagerström test	mean±SD	5,27±0,26
PANSS symptoms Positive	mean±SD	26,63±0,62
PANSS negativesymptoms	mean±SD	22,56±0,6
PANSS psychopathologicalsymptoms	mean±SD	36,32±0,79
PANSS total	mean±SD	85,50±1,67
Frequency of cannabis use	Daily	102 (59,6%)
	Periodical	31 (18,1%)
Anxiety	mean±SD	1,89 ±0,09
Depression	mean±SD	1,47±0,72

FTND test study

The results of the study revealed that the distribution of patients according to their FTND score showed an average of 5.27 ± 0.27 , with a minimum score of 0 and a maximum score of 7. On the basis of these scores, patients were divided into three nicotine dependence groups. Those with an FTND score of 0 to 5 were classified as having mild dependence, those with an FTND score of 6 to 7 were classified as having high dependence, and those with an FTND score above 7 were classified as having very high dependence.

In the sample of 172 participants, 43.6% (n=75) showed signs of mild nicotine dependence, while 25.6% (n=44) were classified as having high dependence, and 30.8% (n=53) were considered very attached to nicotine consumption. These results highlight the diversity of nicotine dependence levels among the patients in the study.

Analyzing the relationship between levels of nicotine dependence and symptoms measured by the PANSS scale, the study revealed a very highly significant difference with the PANSS total score ($P<0.002$), a significant correlation with positive PANSS ($P<0.010$) and with negative PANSS ($P<0.024$) and also with the psychopathological scale ($P<0.013$). This suggests that patients with higher levels of nicotine dependence also have more pronounced psychiatric symptoms in our

patient sample. A significant association was found with anxiety ($p<0.05$) and treatment with atypical antipsychotics ($p<0.05$). The comorbidity of tobacco and cannabis was confirmed in our study, with a highly significant association ($P<0.000$). Cannabis-dependent patients are more likely to have physical dependencies on tobacco.

DISCUSSION

The mean age of our study population was 31.7 years, with a standard deviation of 0.72. This result is similar to that of Bipul Sharma et al¹⁷, while the age of the 1^{er} episode was 22.2 years with a standard deviation of 0.44. This result reflects the chronicity of the disease in our study population. The high unmarried rate among patients (84.9%) may have implications for their social and family support network, and could play a role in disease progression and prognosis. What's more, schizophrenia patients' limited educational level may impact on their access to care and their ability to understand and follow prescribed treatments. It is therefore essential to offer treatment adapted to their level of understanding, and to promote mental health awareness and education. Lastly, the high proportion of patients without stable employment raises the question of the professional integration of people with schizophrenia. Analysis of socio-demographic characteristics underlines the importance of taking into account not only the symptoms of schizophrenia, but also the social and demographic context of patients in their care.

In terms of tobacco consumption, the majority of participants in our sample were smokers (79.1%). This rate is in line with the results of several studies whose smoking rates exceed 70% (18-19) and are three times higher than in the total population. The degree of nicotine dependence assessed via the Fagastrom test revealed that the majority of our patients have a high to very high level of dependence (56.4%). Our results are similar to those of a Turkish study which found that 51.7% of schizophrenic patients had a high dependence²⁰, and to a Brazilian study whose rate was 57,8%²¹.

The correlation between degree of dependence and the PANSS positive and negative schizophrenia symptom scale showed an association between higher Fagerström scores and PANSS total scores ($P<0.002$). This shows an increase in the degree of nicotine dependence with symptom severity. The same was true of the PANSS

Table 3: Description of variables in schizophrenic patients, according to their nicotine dependence status (Fagerström scores) :

Variable	Nicotine dependence			Test	P- value
	Slight (n=75)	High (n=44)	Very high (n=53)		
FTND score	1,96 ±2,06	6,59±0,49	8,85±0,79	F=371,99	P<0,000***
Hospitalization	68 (41,72%)	42 (25,77%)	53 (32,52%)	Chi2=7.83	P<0,02*
Suicide attempts	0,47±0,12	0,55±0,16	0,52±0,10	F=0,087	P<0,92
Classic antipsychotics	24(42,86%)	14 (25%)	18 (32,14%)	Chi2=0.065	P<0,97
Atypical antipsychotics	55 (39,86%)	40(28,99%)	43 (31,16%)	Chi2=5.89	P<0,05*
Age 1 st episode Mean±SD	22,82±0,93	22,18±0,60	21,66±0,56	F=0,64	P<0,53
Con. Cannabis	41 (30,60%)	41(30,60%)	52 (38,81%)	Chi2=42.07	P<0,000
D.C. cannabis Mean±SD	5,50±1,35	10,53±2,06	13,13±1,18	F=5,92	P<0,005**
Tobacco consumption	39(28,68%)	44(32,35%)	53 (38,97%)	Chi2=58.88	P<0,000***
Anxiety mean±SD	1,64±0,13	2,23±0,24	1,92±0,18	F=2,85	P<0,05*
Depression mean±SD	1,58±0,14	1,23±0,065	1,52±0,15	F=1,69	P<0,18
PANSS total score	79,73±2,49	85,95±2,96	93,30±2,98	F=6,42	P<0,002**
Positive PANSS	24,6±1,02	27,37±1,18	28,89±0,93	F=4,71	P<0,010*
PANSS negative	21,01±0,88	22,44±1,22	24,85±1,04	F=3,82	P<0,024*
PANSS psychopathological	34,12±1,06	36,14±1,40	39,57 (1,65)	F=4,45	P<0,013*

positive, negative and psychopathological subscale scores. This result differs from that of Yee et al (2015)²² whose patients with a high degree of dependence present negative symptoms with low rates. Similarly, a positive correlation was found between the degree of nicotine dependence and anxiety ($p<0.05$). Our results corroborate those of an Egyptian study which found a positive correlation between nicotine dependence and symptoms of anxiety/ depression²³. These results suggest that the study of the association of dependence with each symptom of the disease could yield more interesting results for explanations of the phenomenon.

There is strong evidence of a pathophysiological link between nicotine exposure through smoking and schizophrenia. Nicotine plays an important role in smokers, modulating the transmission of dopamine and glutamate in the central nervous system. Nicotine receptors are located in dopaminergic neurons in the ventral tegmental area, and nicotine stimulates dopamine release in this region. Nicotine-induced dopamine release in the mesocortical dopamine system enhances

cognitive function and reduces negative symptoms²⁴. These findings support the self-medication hypothesis.

In schizophrenia, the dopaminergic system appears to be characterized by an imbalance between cortical and subcortical dopaminergic projections. Meso-limbic dopaminergic projections appear to be hyperactive, resulting in hyperstimulation of D2 receptors and the onset of positive symptoms, whereas meso-cortical dopaminergic projections to the prefrontal cortex appear to be hypoactive, resulting in hypostimulation of D1 receptors and the onset of negative symptoms and cognitive deficits. Nicotine affects dopamine release and metabolism differently, as well as the electrophysiological properties of dopaminergic neurons in these two functional systems. Animal studies indicate that acute nicotine treatment increases dopamine synthesis and catabolism in the nucleus accumbens but not in the dorsal striatum²⁵.

What's more, the mesocortico-limbic dopaminergic system, which is most often associated with psychotic symptoms, appears to be much more sensitive to the

effects of nicotine than the extrapyramidal motor system, supporting the hypothesis of self-medication of psychotic symptoms for nicotine use.

What's more, chronic nicotine use and dependence leads to desensitization of nicotinic receptors, and consequently to the disappearance of the effect of tobacco on the cognitive symptoms of schizophrenia²⁶. Some authors have suggested the influence of genetic vulnerability factors common to both tobacco dependence and schizophrenia.

Finally, it should be noted that the management of addiction leads to a reduction in the severity of psychiatric symptoms, whereas simply managing the symptoms of schizophrenia has no impact on addiction²⁷.

Linked to tobacco consumption, cannabis use was found to be very frequent in our patients (77.9%). Our results are similar to several studies, notably that of Ouanouche et al²⁸ conducted in Morocco, in the same context as ours, where the frequency of cannabis use was 72.63%. It has been reported that early cannabis use considerably increases the risk of schizophrenia. The risk is four times higher when consumption begins before the age of 15²⁹. Cannabis use has been shown to cause weakness in self-control in schizophrenic patients. It is suggested that cannabis use is one of the main explanatory factors for poor compliance with treatment during first psychotic episodes³⁰. It can also constitute a major obstacle to treatment and influence the prognosis of the disease.

Our study also revealed a highly significant association between the degree of tobacco dependence and cannabis use ($p < 0,000$). Similar results were found in the study of Anne-Laure ($p = 0.043$)³¹. Rabin et al (32) stipulate that 70% of patients with severe psychiatric pathology who take drugs smoke tobacco. In schizophrenia, tobacco consumption predisposes to cannabis use. Clearly, in schizophrenia, tobacco use potentiates cannabis use, and vice versa.

In practice, our results suggest that managing tobacco and cannabis addiction could reduce the severity of psychiatric symptoms. It is crucial to integrate prevention and withdrawal programs to reduce the use of these substances and improve the overall health of patients with schizophrenia, as well as other diseases such as tuberculosis³³. This explains the significant association of atypical antipsychotics with smoking in schizophrenia. Antipsychotics induce fewer extrapyramidal effects, and improve the negative symptoms and cognitive disorders of schizophrenia, which are themselves improved by smoking. The predominant use of atypical antipsychotics raises questions about the efficacy and appropriateness of the treatments prescribed.

CONCLUSION

In our context, subjects with schizophrenia are vulnerable to developing severe nicotine dependence. This study sheds light on the problem of tobacco consumption and its relationship with the severity of psychiatric symptoms in schizophrenia. As a result, the management of tobacco addiction must be integrated into the management of the disease, and could reduce the severity of symptoms.

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