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Research Article

The Impact of Smoking on Schizophrenia Relapses

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Abstract

Purpose: The authors studied the impact of smoking on relapses in schizophrenics.

Method: A lot of 134 schizophrenics diagnosed according to the ICD 10 was used. We looked into the number of cigarettes, association with other legal drugs, sex, psychiatric family history, comorbidities and the rate of relapse in time.

Results: As with psychoactive substances, the effect of smoking depends on dosage. Starting smoking after the onset of the disease, at a dosage of under 20 cigarettes a day is a positive prognostic factor for women. Starting smoking before the onset of the disease, regardless dosage, is a negative prognostic factor. Conclusions: Smoking has a differentiated psychoactive effect on schizophrenics, depending on the age of onset of smoking and of the illness, by sex, in relation to dosage, similar to psychotropic substances.

INTRODUCTION

It seems that "clinicians do not often address smoking during patient interviews" [1], although tobacco abuse is common in all psychiatric diseases, but especially in psychotic patients, both schizophrenics and affective [2]. Special attention must be given to the subject in the case of schizophrenics, because of the impact on disease evolution.

The dopaminergic neuro-transmission disorder is presently acknowledged as crucial in the occurrence and the evolution of the schizophrenic symptoms [3-8]. The frequent adherence of schizophrenics to smoking is considered to be connected to these effects [8-11].

Any smoker will claim that smoking is not just an addiction but a pleasure as well. In their biological explanations, addiction and pleasure are connected to the dopaminergic system [7]. Compared to the general population, where smokers represent 33%, the proportion of psychiatric patients who smoke is 45-70%, and in schizophrenia – 90% [12]. It is estimated that 200,000 psychiatric patients die annually from smoking [13]. The proposed models for the understanding of the relation between smoking and schizophrenia were the majority of neuro-receptor systems [12,14-17]. Although the burning of tobacco results in over 3 000 substances, nicotine remain incriminated in the general opinion. Some authors consider that most schizophrenic smoker cases are men and that nicotine influences particularly negative symptoms [18,19]. Some have concluded that it favors positive symptoms [13]. Many researchers believe that there are no differences between positive and negative symptoms and have assessed them together in order to better evaluate the impact on the illness [13, 20-22]. The precise location and action of nicotine is, for the present, based on models starting from laboratory accounts. The supporters of the relationship between smoking and schizophrenia, mediated by the dopaminergic system, consider either that the relation is direct, or it represents the final path [23-27]. Consistent research data links the relation between smoking and schizophrenia to the relation between nicotine and the α7 nicotinic acetylcholine receptors [28-33]. Nevertheless, smoking appears in the conclusions of all researchers as playing a major role in influencing the evolution of schizophrenia [24, 34]. Consequently, one may wonder what the impact of smoking on the evolution of schizophrenics is.

MATERIALS AND METHODS

A random lot of 134 schizophrenics (79M+55 W), diagnosed according to the ICD 10, were analyzed on the following: number of cigarettes smoked, association with other legal drugs, family psychiatric history, sex, comorbidities, and, naturally, the relapse rate in time.

RESULTS AND DISCUSSION

As it is clearly visible in Table (1), the majority of schizophrenics are smokers. The data is consistent with literature [12].

Table (2) shows that the average age of smokers is insignificantly lower than that of nonsmokers ($p>0.05$). It is noticed that the average age decreases as the number of cigarettes smoked/day increases. No data regarding this aspect has been found in literature.

Table 1: The distribution of cases in relation to the intensity of smoking
134 cases were studied, out of which:

	Number	%	% on sexes	
			M (79)	W(55)
Nonsmokers	62	46.26	36.7	60.0
Smokers	72	53.73	63.99	40.0
< 20cigarettes/day	20	14.92	16.45	12.72
20 cigarettes/day	39	29.10	35.44	20.0
>20 cigarettes/day	13	9.70	11.39	7.27

Table 2: Distribution of cases in relation to age.

Age	Nonsmokers		Smokers							
			Total		Smokers < 20 cigarettes		Smokers 20 cigarettes/ day		Smokers >20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%	Number	%
<20 years	-	-	2	2.8	-	-	-	-	2	15.4
21-30 years	14	22.6	7	9.7	2	10.0	5	12.8	-	-
31-40 years	17	27.4	35	48.6	8	40.0	20	51.3	7	53.8
41-50 years	17	27.4	15	20.8	5	25.0	7	17.9	3	23.1
>50 years	14	22.6	13	18.1	5	25.0	7	17.9	1	7.7
Limits	24-67 years		19-64 years		28-62 years		22-64 years		19-54 years	
Average	41.7±5.3 years		39.8±6.7 years		41.4±7.5 years		39.5±6.2 years		37.5±5.1 years	

The presence of family history is significantly higher for nonsmoking patients than for smokers (p<0.05) (Table 3). No data about this aspect has been found in literature.

Table (4) reveals that somatic diseases are significantly more frequent in smoking patients compared to nonsmokers (p<0.05). This data is relevant with other data found in literature about general health.

The use of legal toxic substances (Table 5) is significantly more frequent in smokers compared to nonsmokers (p<0.01), especially coffee, data that is consistent with literature [35].

In what compliance is concerned (Table 6), it can be noticed that smokers are more compliant to treatment than nonsmokers (59.7% versus 44.4%) (p<0.05). 80% of the patients that smoke less than 20 cigarettes a day are compliant to treatment compared to 51-54% of the rest of the smokers (p<0.04). This data corroborates data about nicotinic receptors regulation in schizophrenics [33], in which nicotine, in doses up to a point improves cognitive processes and, through this mechanism, it controlls reaction and behaviour.

Table 7 demonstrates that there are no significant differences between the average age of the disease's onset in smoking or nonsmoking patients (p>0.05). Under 30 years of age, the disease's onset was recorded on 71.0% nonsmokers and 77.8% smokers (p>0.05). We notice that while with nonsmokers the ratio between patients with onset between 21-30 years and those under 20 years of age is almost 1 (1.1:1), with smokers, this ratio is over 2 (2,1:1) (p<0.01). There has not been found any data in literature regarding this aspect of the research, so no comparison coud be made.

There are no significant differences in what the age of the disease is concerned in smokers and nonsmokers, regardless the quantity of cigarettes (p>0.05) (Table 8).

Table (9) displays that the youngest smoking age is recorded in patients with more than 20 cigarettes/day (11.4), significantly lower than in the patients with less than 20 cigarettes a day (14.2) (p<0.02), in correlation to the average age (the lowest average age is recorded in aptients who smoke more than 20 cigarettes a day).

In smokers with less than 20 cigarettes a day the average number of relapse/ year is significantly lower than in the case of smokers of 20 cigarettes/day (p=0.221) or more (p=0.124) and slightly less significant in nonsmoking patients (p<0.05) (Table 10). Data becomes apprehensible through general psychopharmacological data, attesting the fact that the majority of psychoses have a certain effect up to a specific dosage, and another effect after that dose.

The number of relapses in patients who smoked before the onset of the disease is significantly higher (Table 11) than in patients who started smoking after the onset of the disease (p=0.021). The number of relapses in smokers after the onset of the disease is not significantly different from that of nonsmokers (p>0.05). This might signify that the cognitive effects of nicotinic receptor disorder is experienced, in some cases, long before the onset of the disease and that, those patients have fortuitously discovered the beneficial effect of smoking.

Table (12) shows that, for smoking men, the number of relapses/year is significantly higher than in nonsmoking men (p=0.045). For smoking women, the number of relapses is significantly smaller than for nonsmoking women (p=0.046), the opposite form the situation of men. For nonsmoking men the

Table 3: The distribution of cigarettes in relation to family history.

HCH	Nonsmokers		Smokers							
			Total		Smokers < 20 cigarettes		Smokers 20 cigarettes		Smokers > 20 cigarettes	
	Number	%	Number	%	Number	%	Number	%	Number	%
With HCH	19	30.6	15	20.8	4	20.0	11	28.2	-	-
Schizofrenia	7	11.3	10	13.9	4	20.0	6	15.4	-	-
Depression	12	19.4	6	8.3	1	5.0	5	12.8	-	-

Table 4: The distribution of cases in relation to somatic diseases.

Somatic diseases	Nonsmokers		Smokers							
			Total		Smokers<20 cigarettes/ day		Smokers-20 cigarettes/ day		Smokers>20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%	Number	%
	5	8.1	9	12.5	2	10.0	7	17.9	-	-

Table 5: Distribution of cases in realtion to use of toxic substances.

Toxics	Nonsmokers		Smokers							
			Total		Smokers<20 cigarettes/ day		Smokers-20 cigarettes/ day		Smokers>20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%	Number	%
Use of toxic substances in general, excluding stupefiants	11	17.7	51	70.8	15	75.0	29	74.4	7	53.8
Alcohol	4	6.5	7	9.7	1	5.0	6	15.4	-	-
Coffee	9	14.5	49	68.1	14	70.0	28	71.8	7	53.8

Table 6: The distribution of cases in relation to compliance.

Compliance	Nonsmokers		Smokers							
			Total		Smokers<20 cigarettes/ day		Smokers 20 cigarettes/ day		Smokers>20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%	Number	%
Yes	16	44.4	43	59.7	16	80.0	20	51.3	7	53.8
Incomplete	8	22.2	-	-	-	-	-	-	-	-
No	12	33.3	29	40.3	4	20.0	19	48.7	6	46.2

Table 7: The distribution of cases in relation to the disease's onset age.

The disease's onset age	Nonsmokers		Smokers							
			Total		Smokers<20 cigarettes/ day		Smokers 20 cigarettes/ day		Smokers>20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%	Number	%
<20 years	21	33.9	18	25.0	4	20.0	10	25.6	4	30.8
21-30 years	23	37.1	38	52.8	10	50.0	23	59.0	5	38.5
31-40 years	13	21.0	15	20.8	6	30.0	6	15.4	3	23.1
41-50 years	4	6.5	1	1.4	-	-	-	-	1	7.7
>50 years	1	1.6	-	-	-	-	-	-	-	-
Limits	15-56 years		16-43 years		16-40 years		16-38 years		17-43 years	
Average	26.0±8.3 years		26.0±7.2 years		27.3±8.1 years		24.9±7.0 years		25.9±6.9 years	

Table 8: The distribution of cases in relation to the age of the disease.

The age of the disease	Nonsmokers		Smokers							
			Total		Smokers<20 cigarettes/ day		Smokers 20 cigarettes/ day		Smokers>20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%	Number	%
<5 years	15	24.2	11	15.3	4	20.0	5	12.8	2	15.4
6-10 years	14	22.6	21	29.2	5	25.0	10	25.6	6	46.2
11-15 years	7	11.3	13	18.1	4	20.0	8	20.5	1	7.7
16-20 years	6	9.7	7	9.7	2	10.0	4	10.3	1	7.7
>20 years	20	32.3	20	27.8	5	25.0	12	30.8	3	23.1
Limits	1-39 years		1-47 years		1-39 years		1-47 years		1-47 years	
Average	15.1±6.8 years		14.4±7.3 years		15.1±6.8 years		14.4±7.3 years		14.4±7.3 years	

There are no significant differences in what the age of the disease is concerned in smokers and nonsmokers, regardless the quantity of cigarettes ($p>0.05$) (Table VIII).

Table 9: Distribution of cases in relation to the age smoking habit.

The age of the smoking habit	Smokers							
	Total		Smokers<20 cigarettes/ day		Smokers 20 cigarettes/ day		Smokers>20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%
<5 years	14	19.4	6	30.0	5	12.8	3	23.1
6-10 years	23	31.9	6	30.0	13	33.3	4	30.8
11-15 years	11	15.3	2	10.0	7	18.0	2	15.4
16-20 years	11	15.3	3	15.0	5	12.8	3	23.1
>20 years	13	18.1	3	15.0	9	23.1	1	7.7
Limits	<1 – 39 years		<1 – 38 years		<1 – 39 years		<1 – 34 years	
Average	14.4±7.3 years		12.5±6.3 years		15.0±7.7 years		11.4±6.7 years	

Table 10: The number of relapses/ year comparatively for smokers and nonsmokers.

Number Relapses/ year	Nonsmokers		Smokers							
			Total		Smokers<20 cigarettes/ day		Smokers 20 cigarettes/ day		Smokers>20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%	Number	%
Limits	0.16-3.00/year		0.09-3.50/year		0.09-1.90/year		0.13-2.50/year		0.24-3.50/year	
Average	0.99±0.34 years		1.01±0.42 year		0.82±0.32/year		1.06±0.40/year		1.11±0.48/ years	

Table 11: Number of relapses in relation to the moment when smoking was taken up.

	Nonsmokers	Smokers prior to the onset of the disease	Smokers after the onset of the disease
Relapses/year			
Limits	0,16-3,00/ year	0,14-2,67/year	0,09-3,50/year
Average	0,99±0,34/year	1,13±0,44/year	0,90±0,28/ year

Table 12: Number of relapses/ year in relation to sex.

Sex	Number of relapses/year	
	Nonsmokers	Smokers
Men		
Limits	0.16-2.50/year	0.09-2.67/year
Average	0.88±0.27/year	1.04±0.33/year
Women		
Limits	0.16-3.00/year	0.14-3.50/year
Average	1.03±0.31/year	0.90±0.30/year

number of relapses /year is significantly lower than the one for nonsmoking women (p=0.045). For smoking men, the number of relapses/year is significantly higher than the one for smoking women (p=0.047). No data regarding this aspect has been found in literature.

A decrease of the number of relapses/year with ageing is noticed. For nonsmokers the number of relapses/year is significantly higher for ages<40 compared to those over 40 years of age (p=0.0324), and for smokers at ages <30 compared to those over 30years of age (p=0.0256). Both for smokers and for nonsmokers, the smallest number of relapses/year is recorded at ages >50 years of age, without significant differences between the two lots (p=0.255), as Table 13 demonstrates.

Table (14) shows that in patients with an age of the disease<5 years the number of relapses/year is significantly higher than in those with >5 years of disease, both for smokers and for nonsmokers (p=0.0221, p=0.0287). Also, in patients with a disease of 6-15 years, the number of relapses is significantly higher than in those with a disease > 16 years (p=0.0445, p=0.0462). There are no significant differences between smokers and nonsmokers in what the number of relapses/year is concerned in relation to the age of the disease.

The number of relapses has a decreasing trend in relation to the age of smoking (Table 15). This information, corroborated with data from (Table 16) leads to the conclusion that the tendency in lower relapse rates with age depends on schziophrenia evolution per se, and is not influenced by smoking.

The number of relapses per year is significantly higher in noncompliant patients compared to compliant ones, both in smokers (p=0.022) and in nonsmokers (p=0.046). This means that there is a ration between the positive evolutionary factor (treatment) and the negative evolutionary factor (smoking), which could be controlled by increasing doses of antipsychotics depending strictly on symptomatology, because nicotine

Table 13: The number of relapses/year in relation to age.

Age	Number ofrelapses/year		Significance (p)
	Nonsmokers	Smokers	
<30 years			
Limits	0.43-2.75/year	0.50-3.50/year	
Average	1.25±0.47/year	1.54±0.53/year	0.043
31-40 years			
Limits	0.30-3.00/year	0.14-2.50/year	
Average	1.18±0.38/year	0.98±0.35/year	0.064
41-50 years			
Limits	0.27-1.88/year	0.55-1.90/year	
Average	0.82±0.24/year	1.04±0.37/year	0.051
>50 years			
Limits	0.16-1.50/year	0.09-1.48/year	
Average	0.61±0.20/year	0.57±0.57/year	0.255

Table 14: Number of relapses/year in relation to the age of the disease.

Age of the disease	Number of relapses/year		Significance (p)
	Nonsmokers	Smokers	
<5 years			
Limits	0.75-3.00/year	0.50-3.50/year	
Average	1.65±0.54/year	1.54±0.53/year	p>0.05
6-10 years			
Limits	0.30-2.50/year	0.14-2.50/year	
Average	0.98±0.32/year	0.98±0.35/year	p>0.05
11-15 years			
Limits	0.20-1.79/year	0.55-1.90/year	
Average	0.97±0.34/year	1.04±0.37/year	p>0.05
16-20 years			
Limits	0.16-1.00/year	0.55-1.90/year	
Average	0.57±0.22/year	0.64±0.37/year	p>0.05
>20 years			
Limits	0.16-1.11/year	0.09-1.48/year	
Average	0.59±0.23/year	0.57±0.57/year	p>0.05

Table 15: The number of relapses/year in relation to the age of smoking.

Age of smoking	Number of relapses/year
<5 year	
Limits	0.13-3.50/year
Average	1.71±0.63/year
6-10 years	
Limits	0.09-2.67/year
Average	1.06±0.43/year
11-15 years	
Limits	0.33-2.22/year
Average	1.34±0.48/year
16-20 years	
Limits	0.24-2.17/year
Average	1.03±0.47/year
>20 years	
Limits	0.14-1.50/year
Average	0.73±0.56/year

Table 16: The number of relapses/year in relation to compliance.

Compliance	Number of relapses/year									
	Nonsmokers		Smokers							
			Total		Smokers<20 cigarettes/ day		Smokers20 cigarettes/ day		Smokers>20 cigarettes/ day	
	Number	%	Number	%	Number	%	Number	%	Number	%
Compliant										
Limits	0.26-2.33/year		0.09-1.78/year		0.09-1.67/year		0.33-1.78/year		0.24-1.33/year	
Average	0.99±0.42/year		0.89±0.32/year		0.80±0.35/year		0.51±0.31/year		0.75±0.42/year	
Noncompliant										
Limits	0.16-3.00/year		0.13-3.50/year		0.13-1.90/year		0.13-2.50/year		0.47-3.50/year	
Average	1.06±0.33/year		1.25±0.44/year		0.89±0.34/year		1.14±0.50/year		1.66±0.54/year	
	p=0.046		p=0.022		p>0.05		p=0.001		p=0.001	

accelerates the drug's metabolism [36]. A comparative study of optimal therapeutic maintenance dose in schizophrenics that are smokers as opposed to nonsmokers is necessary.

CONCLUSION

The natural tendency to relapse in schizophrenics is influenced differently by smoking in relation to some biological parameters.

The habit of smoking prior to the onset of the disease is a negative prognosis factor.

As with all psycho-active substances, the effect of smoking depends on dose: with less than 20 cigarettes/day getting one result and with more than 20 cigarettes/day getting another result.

There is a difference in the impact of smoking in relation to sex, as it is more harmful for men, with a higher number of cigarettes, compared to women who smoke less than 20 cigarettes/day and have a positive effect. Those who smoke more than 20 cigarettes/day have experienced a harmful effect directly related to dosage, yet less harmful than in men.

Smoking less than 20 cigarettes a day, with the habit of smoking taken up after the onset of the disease, especially in women, is a positive prognosis factor.

These tendencies are valid for both a compliant and a non-compliant lot.

It is possible that these differences are due to hormonal differences. It is speculative to launch hypotheses at this point. Nevertheless, whether it is by the direct action on the α7 nicotinic receptors or by the indirect action on the dopaminergic receptors, or a metabolic effect, smoking influences the evolution of schizophrenia, fact which may suggest new ways of psycho-pharmacological research.

The research of the relationship between smoking and relapse in schizophrenia is well worth closer consideration, both from the point of view of understanding the disease, as well as for treating it.

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