CIGARETTE SMOKING IN SCHIZOPHRENIC PATIENTS THAT ARE CURRENTLY TREATED IN A MEXICAN HOSPITAL

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Abstract

Objective: tobacco smoking is the most commonly substance abused in psychiatric patients; among them, patients with schizophrenia are the highest abusers. Smoking is related to a decrease in the quality life and life expectancy, as well as interacting with psychotropic drugs. In Mexico, there is not basic descriptive knowledge about the main variables related to cigarette smoking in psychiatric population. The aim of this study was to know the relation among variables (beginning and course of the disease, use of other drugs and times of hospitalization among others) and cigarette smoking in a Mexican population of hospitalized schizophrenic patients.

Method: The relation between the main variables and smoking were evaluated in a Mexican population of schizophrenic patients while hospitalized. A casuistic sampling was performed in 96 patients diagnosed with schizophrenia and they were divided into three groups: 1) non-smokers, 2) ex-smokers and 3) smokers; according to their score on the Fagerström Test for Nicotine Dependence.

Results: The results showed that hospitalized schizophrenic patients smoke 2.7 times more than the general population. Most of these patients showed moderate to high dependence of nicotine, as well as a higher risk for other drugs abuse (marihuana mainly). Most patients started smoking before the first positive symptoms of schizophrenia appeared, and their symptoms started at an earlier age than in patients without a smoking background.

Conclusions: Similar studies will allow deepening into specific aspects that modify and or improve the prescribed treatments for each psychiatric patient in hospital settings.

Key words: smoke, Mexican population, schizophrenia, hospital

Declaration of interest: Dr. Nicolini has received research funds from Pherin Pharmaceuticals, Transcept Pharmaceuticals, and Forum Pharmaceuticals Inc., and speaking honoraria from MSD and Landsteiner Mexico. The other authors have nothing to disclose.

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Introduction

Worldwide, cigarette smoking is among the top five causes of risk mortality and is the single largest preventable cause of death; it promotes more than 5 million of annual deaths, causing 11% of ischemic heart deaths and more than 70% of lung, bronchus and trachea cancer (WHO 2014).

Varied studies explain that approximately 600,000 of the above mentioned deaths are among passive smokers (also called second-hand smokers). A third of the adult population is exposed to active smokers, which represents a high smoking rate. Even though cigarette smoking is decreasing among the general population, in United States of America only, was estimated that 46 million adults continued smoking in 2008, and this action could cause more than 1 billion deaths throughout this century (CDC 2009).

In the Mexican population, cigarette smoking is an important public health problem, as described on the National Addiction Survey (ENA for Encuesta Nacional de Adicciones) (Reynales-Shigematsu et al. 2012). The ENA 2011 reported an active smoking prevalence of 21.7% which means that 17.3 million adults in Mexico smoke. Active smoking among males was 31.4% and among females 12.6%. Of all the smokers, 8.9% reported to smoke every day (7.1 million), 26.4% (21 million) reported to be ex-smokers and 20.1% were occasional

Submitted January 2015, accepted April 2015

smokers (16 million). In contrast, 51.9% of the Mexican population (41.3 million) had never smoked (Reynales-Shigematsu et al. 2012).

Daily smokers in Mexico (between 12 and 65 years old), start on average at 20.4 years old (men at 20 years and women at 21.7 years of age); the usual number of cigarettes smoked was 6.5 per day (Reynales-Shigematsu et al. 2012).

Cigarettes contain at least 4000 chemical compounds and about 250 of these chemicals are considered harmful; additionally, at least 50 of those are known to cause cancer (Shields 2002). Nicotine is the main tobacco alkaloid and produces important physiological and pharmacological effects in humans; it has been described that nicotine is the major compound responsible for the development and maintenance of cigarette (nicotine) addiction (Improgo et al. 2010).

Cigarette smoking in a psychiatric population

Cigarette (nicotine in particular) is considered as the drug with a higher prevalence of abuse among adults with a psychiatric diagnose; this population smokes one of every two cigarettes sold in the United States of America (Grant et al. 2004, Lasser et al. 2000).

The mental disorder most associated with cigarette smoking is schizophrenia, and its prevalence is directly proportional to the patients' financial income, which spend about 30% on cigarettes.

Smoking is the main risk cause of heart disease in schizophrenic patients, contributing to 20% decrease of their life expectancy; therefore, it is a major negative-factor in the quality life of these patients (Colton and Manderscheid 2006). Among other substances (drugs) abused by schizophrenic patients in Mexico and Latin-American are alcohol, marihuana, solvents and cocaine, all related to comorbidity of other mental disorders as depression and bipolar disorder (Jiménez-Castro et al. 2010).

Most of the schizophrenic-smokers (90%) start their history of cigarette smoking before their first psychotic break (Kelly and McCreadie 1999, Ma et al. 2010); furthermore, 60% of schizophrenic-smokers are intense smokers, which mean they smoke more than 25 cigarettes per day (Prochaska 2010). Some studies indicate that around 30-76% of schizophrenics are active smokers, while only 17% of the general population has a cigarette addiction; which strongly suggests a high susceptibility to develop drugs (licit or illicit) addiction (Cantwell et al. 1999).

Harmful to human health

The impact of smoking among schizophrenic patients, not only increases metabolic and vascular risks (McCreadie 2003), it also increases the suicide risk (Malone et al. 2003) and decreases the antipsychotic therapeutic effects as smoking induces the medication metabolism in the liver reducing up to 48% the active metabolites in serum (Rostami-Hodjegan 2004). Schizophrenic-smokers show more hospitalization frequency (than schizophrenic non-smokers) and also require more depot medication (Kelly and McCreadie 1999), having less adherence to treatment. There is a direct relation between the smoking intensity and a reduced response to pharmacologic treatment, apart from the pathologies associated to smoking as cancer, lung emphysema and erectile dysfunction among others (McCreadie 2003).

Neurobiology

Various studies, including some that have studied evoked potentials (P50 auditory evoked potential for example) have found that nicotine is used to compensate cognitive deficits (essentially attention deficit) (Olincy et al. 2003). Attention deficits are present in the majority of schizophrenics during prodromal and psychotic stages, as well as in 50% of the first degree relatives (Adler et al. 1998, Smith et al. 2006). Some studies suggest that this attention deficit is related to stimulus discrimination and could be a consequence of a modification of the nicotine receptor in the hippocampus; and the deficit could be temporally improved by the cigarette nicotine (Leonard and Bertrand 2001). The attention deficit is noticeable before the clear manifestation of schizophrenia (Olincy et al. 2003).

Besides improving attention, cigarette smoking can enhance working-memory (closely interwoven and crucial to functional attention) in schizophrenic patients (Timofeeva and Levin 2011).

In normal subjects it has been found that cigarette smoking leads to dopamine release in the reward cerebral area, as well as into a ligand-binder in the nicotine receptor (McClernon, 2009). In that regard, it has been proposed that the high affinity antagonism to nicotine and acetylcholine receptors in schizophrenic smokers could induce a more intense cigarette smoking. Nevertheless, the metabolic deficit in brain neurons associated to schizophrenia (insufficient expression and/or low transport/receptors efficacy) results in a higher smoking behavior; this suggests that even when the nicotine exposure augments, the need for smoking does not decrease (McKee et al. 2009, Mexal et al. 2010). The number of alpha-7 neuronal nicotine receptor in the brain of schizophrenic smokers (post mortem analysis) is low; nevertheless, when comparing schizophrenic smokers versus schizophrenic non-smokers, an increase of alpha-7 neuronal nicotine receptor is observed among the smokers, suggesting that smoking induces genetic changes (Mexal et al. 2010).

Various studies have found an increase of the cerebral response to motivational clues or signs (images of cigarettes or people smoking), where the individuals that presented higher points on the Fagerström scale show higher activity of the ventromedial prefrontal cortex, the anterior cingulate cortex, the insular cortex and the medium are of the gyrus temporal superior (Goudriaan et al. 2010).

In cigarette smokers without any psychosis, it has been proposed that one of the main mechanisms that encourage smoking is the dopaminergic hypofunction of the frontal-subcortical circuits, in which nicotine administration has positive effects (Timofeeva and Levin 2011). Nicotine inhalation also has a low-term improvement on functional attention, cognitive effort and decision making (Warburton 2001).

Besides the biochemical changes that nicotine produces on cigarette-addicted individuals, other changes have been observed on their brain (anatomical and functional changes) such as a lower concentration of the prefrontal cortex white-matter and higher concentrations of nicotine receptors (McClernon 2009). Furthermore, other studies have found that schizophrenic patients with a chronic smoking addiction that have not been benefited by stop-smoking therapies, show cognitive deficits that involve a poor prefrontal cortex function (Moss et al. 2009).

Some studies have suggested that nicotine could benefit the positive and negative symptoms, cognitive deficits and the neuroleptic side effects (for example,

extrapiyramidal symptoms), may be due to a decrease of the antipsychotic blood levels (Kumari and Postma 2005).

Several authors have explained drug-abuse in psychotic disorders as an adjuvant therapy to reduce anhedonia, depression or the discomfort caused by the first positive symptoms, and it increases the relation with suicide attempt (Gut-Fayand et al. 2001). Therefore, it is likely that psychotic patients start smoking as a self-medication action before the premorbid neuropsychological cognitive deficits fully appear (Beratis et al. 2001, Weiser et al. 2004). Consequently, there is a possibility that smoking increases vulnerability to schizophrenia.

Specific treatments and mental health policies

As mentioned before, about 50% of the sold cigarettes in USA are smoked by people with a psychiatric disorder (Prochaska 2010) and there is not enough information of the impact that smoking causes to this patients. Williams (2008) mentioned that the programs for treating depressive and schizophrenic patients that smoke, have systematically failed to help them to stop smoking, as most of the programs do not consider smoking as an addiction. Even though smoking has an immediate benefit to severely ill psychiatric patients, it does not overcome the negative health consequences produced over medium and long term.

In Mexico, cigarette smoking is widely accepted by mental health personnel (mainly in psychiatric hospitals), which has lead to develop places and times for patients to smoke while they are hospitalized, using smoking to reinforce behavior changes. These places do not have smoking desintoxication and cessation programs, leaving patients to suffer nicotine withdrawal symptoms without any help.

There are a few places in USA and England trying to have psychiatric hospitals and health centers free of smoking. This task is not simple; nevertheless, all smokers should have access to a safe and comfortable nicotine-desintoxication similar what is done to treat other substances addictions and avoid withdrawal symptoms; for that reason, a multidisciplinary team is required to treat smoker-psychiatric patients, using medication as well as a nicotine replacement therapy as part of the treatment (Williams 2008).

Public policies to decrease cigarette smoking in the general population have had great success and they have also created cigarette-cessation health centers; however, there are no programs targeting serious psychiatric conditions even though these patients deserve the same protection against cigarette smoking than the general public (Williams 2008).

Justification

The main variables related to cigarette smoking in psychiatric patients are unknown in Mexican hospitals settings, representing an important factor to a low quality of life. Cigarette smoking is the main cause associated with an increase in morbidity and mortality in schizophrenia; it has also been reported as a risk factor for the disease onset, abusing other substances and a decrease of the pharmacological treatment efficiency (psychophysiological effects).

Methods

An exploratory research was performed on a casuistic sample of 96 individuals with schizophrenic diagnose, comparing the ones that abuse drugs and the ones who do not. The study was executed in the hospitalization area of the "Fray Bernardino Alvarez Psychiatric Hospital" during 3 months.

The patients that participated had been diagnosed with schizophreniform disorder and/or schizophrenia, in accordance to the American Psychiatric Association criteria and reconfirmed using the "MINI" structured interview (Mini International Neuropsychiatric Interview) (Sheehan et al. 1998). The participants were between 18 and 55 years old (mean=33.36 years; standard deviation=8.77). Women represented 41.66% of the sample (n=40), while men represented 58.34% (n=56); all the individuals accepted to participate and signed an informed consent form.

Exclusion criteria: Background on other medical or neurological disorders found on laboratory and/or imaging studies, doubtful diagnoses and lack of cooperation to accomplish the interview. Patients that did not have all the information needed for this study were excluded, as well as the ones that gave unreliable information (consequence of their mental state).

The operational definitions used to perform the analyses were:

- Smoker: Individuals who mentioned they have smoked at some point in their lives and had been continually smoking during the last year.
- Ex-smoker: Individuals who had smoked continuously for at least a year in their lives, and had stop smoking over a year ago.
- No smoking history (non-smokers): Individuals that mentioned had never smoked continuously.

The statistical analyses included the Pearson correlation coefficient and the Student's T test.

Results

The participants in the study were 42.33% smokers (n=41), 36.45% ex-smokers (n=20) and 36.45% had no smoking history (n=35). The **table 1** shows the main characteristics of the studied population.

Table 2 shows the levels of nicotine dependency of the participants with smoking history (smokers and ex-smokers) in accordance to the Fagerström Test for Nicotine Dependence (Heatherton et al. 1991).

It can be observed (on table 2) that 34.14% of patients had a low nicotine dependency, 19.51% had a moderate dependency and 46.34% showed a severe nicotine dependency.

Table 3 displays the range of cigarettes smoked per day among the smokers and ex-smokers; it shows that

Table 1. *Main characteristics of the sample (n=96)*

Characteristic	*Mean*	*Standard Deviation*
Age of onset of smoking	18.66	3.99
Age of onset of schizophrenia (or schizophreniform disorder)	20.89	5.88
Number of psychiatric hospitalizations	4.21	5.22

Table 2. *Total score on the Fagerström Test for Nicotine Dependence (FTND) (smokers and ex smokers)*

FTND	*N*	*%*
Mild (1-3)	14	34.14
Moderate (4-6)	8	19.51
Severe (7-10)	19	46.34

Table 3. *Smoked cigarettes per day*

Cigarettes per day range	*Smokers*		*Ex smokers*	
	N	*%*	*N*	*%*
1 to 10	23	56.09	10	50
11 to 20	11	26.82	10	50
21 to 30	5	12.19	0	0
More than 30	2	4.87	0	0

56.09% of smokers have 1-10 cigarettes, 26.82% have 11-20 cigarettes, 12.19% have 21-30 cigarettes and 4.87% have more than 30 cigarettes per day. Among the ex-smokers, 50% have 1-10 cigarettes and 50% have 11-20 cigarettes per day.

A significant correlation was found between the disease onset and the age of starting smoking (R= -0.347; p= 0.006), this correlation was higher in the smokers group (R= -0.434; p= 0.005). Nevertheless, the ex-smokers group does not show that association. Although non significant, there is a trend to associate cigarette smoking with the times of hospitalization in ex-smokers (mean = 4.81 ±5.21) and in smokers (mean = 6.75 ±7.73). No correlation was found among other variables.

Using the Student's t test (means difference test) we found a statistical significance between the disease onset and the smoking behavior, versus the non-smokers (p=0.020; F=24.93, t=2.40; mean dif=3.47). Smokers' age of onset of schizophrenia was 19.7 years old (±3.7), while non smokers' was 23.2 years (±7.8). We also found a significant difference among gender and the beginning of smoking (p= 0.033; F=2.37; t=-2.19; mean dif=-2.37), being men (17.9 ±3.5) who start smoking earlier than women (20.3 ±4.8).

Table 4 shows the patients that have used other psychoactive substances by group. Among the smokers, 65.85% were marihuana users (n=27), 31.7% were cocaine users (n=13), 21.95% solvent users (n=9) and 21.95% were alcohol consumers (n=9). Finally, on the non-smokers 20% declared to consume alcohol (n=7).

Table 4. *Number of subjects that use other substances*

Other substances	*Smokers*		*Ex smokers*		*Non smokers*	
	N	*%*	*N*	*%*	*N*	*%*
Marijuana	27	65.85	9	45	0	0
Cocaine	13	31.70	4	20	0	0
Solvents	9	21.95	2	10	0	0
Alcohol	9	21.95	8	40	7	20

These data analyses can be observed on **figure 1**.

The antipsychotics used on the patients' treatment were: haloperidol 32%, risperidone 21.8%, olanzapine 16.6% and clozapine 10.41%. Because the use of clozapine is an indicator of disease severity (most patients are treated with clozapine have more severe symptoms), when we divided the drugs into two groups 1) clozapine and 2) other antipsychotics, we found that the ones treated with clozapine (n=10) presented a disease onset at 16.9 years of age (±3.66), while the other patients presented the onset at 21.46 years old (±5.72).

Figure 2 illustrates the proportions of patients that have used different antipsychotics per group. Smokers were mainly treated with haloperidol (39%), followed by olanzapine (24%), risperidone (15%), clozapine (12%)

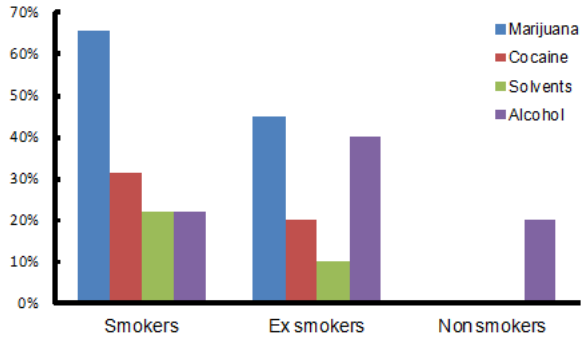

Figure 1. *Percentage of patients taking other psychoactive substances*

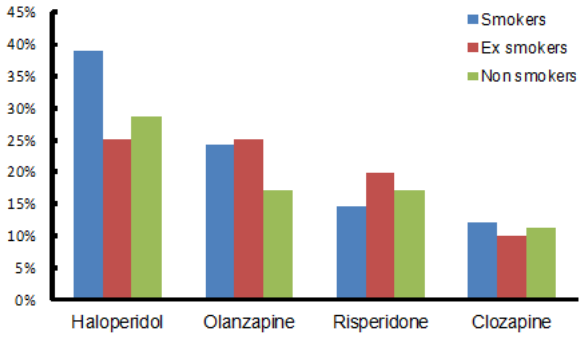

Figure 2. *Percentage of antipsychotic drugs consumed per group*

and other less common antipsychotics (10%). The ex-smokers group were treated on equal proportion with haloperidol and olanzapine (25% each), followed by other antipsychotics (20%) and olanzapine (10%). The non-smokers on the other hand, were treated with haloperidol (29%), olanzapine and risperidone (17% each), clozapine (11%) and other less common antipsychotics (20%).

Discussion

Among the Mexican population, the cigarette smoking proportion is similar to the world wide population (Grant et al. 2004), while the schizophrenic population smokes 2 to 3 times more in comparison to the general population. Cigarette abuse in psychiatric patients represents 50% of the total cigarette smokers (Grant et al. 2004, Lasser et al. 2000) being the schizophrenic patients the smoking majority, this information suggests they are a high risk population to develop a cigarette addiction. The 2008 National Addiction Survey in Mexico reported it is likely that the intense smokers (3%) have a psychiatric disorder apart from the cigarette addiction, as cigarette smoking is strongly associated with other mental illnesses.

We found that the proportion of schizophrenic patients that smoke cigarettes regularly is similar to what has been reported before (Prochaska 2010). Other studies have found that 60% of schizophrenic patients are intense smokers (>25 cigarettes per day) (Colton and Manderscheid 2006); however, the patients in our study smoked less that 21 cigarettes per day, which could be associated to the socioeconomic level and work functioning of each patient; therefore, this possibility should be evaluated in the future. A limitation in our study was that the severity of cigarette smoking was evaluated in a captive population (therefore, they patients were not as free to smoked as they are when they are not hospitalized) as well as using a self reporting questionnaire. Future studies should evaluate psychiatric patients from the external consultation, using other more objective measurements; for instance, carbon monoxide exhalation levels and/or blood cotinine (nicotine active metabolite) levels.

Contradictory to what Kelly (1999) reported, we did not find significant differences of the frequency that patients have to be hospitalized and the amount of antipsychotics use as treatment, among smokers, ex-smokers and without cigarette smoking history (non-smokers).

We found that most of the patients treated with olanzapine, have a cigarette smoking history, which could indicate that this patients present a drug resistance to other antipsychotics; therefore, they become patients difficult to manage. The above mentioned suggests a schizophrenic-endophenotype worth to be explored in future studies.

Patients with a history of cigarette smoking (smokers and ex-smokers) presented a younger-age disease onset when compared to the ones without a smoking history; similar to what Ma (2010) [11] reported. Ma found a significant difference on the age of disease onset, earlier for the patients with a smoking history than the non-smokers; this might be related to the prodromal stages of the illness and as a way of self medication when the first symptoms appear (attention deficit, stimuli discrimination and visual-spatial memory) (Kelly and McCreadie 1999, Ma et al. 2010, Olincy et al. 2003, Adler et al. 1998, Smith et al. 2006, Beratis et al. 2001, Weiser et al. 2004).

Contrary to Jiménez-Castro et al. (2010), our study only evaluated a hospitalized population and found that smoker patients showed a higher risk for other substances abuse; furthermore, we found a high difference when compared the 3 groups of schizophrenic patients: smokers and ex-smokers used marihuana in large proportions, followed by cocaine, solvents and alcohol; this could be explained by Morrison (2009) report, as he suggests there is a close relation between the endocannabinoid receptors and the psychotic break. There is no great difference between our results and what has been previously reported about cigarette and other substances abuse.

Is necessary a better understanding of the main characteristics and variables that intervene in smoking behavior and nicotine addiction of hospitalized psychiatric population and considering the smoking addiction as a dual pathology, that help to deepen the knowledge of specific aspects that could change and improve existing protocol treatments prescribed for each type of patient.

Up to today, there are just a few places where an integrated treatment for seriously ill psychiatric patients with a smoking addiction has been implemented (Williams 2008). This study reveals the necessity to create spaces and programs for the integrated treatment of cigarette smoking in severe psychiatric patients (outpatients and hospitalized) in Mexico.

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