INTRODUCTION

Smoking in Schizophrenia Population, it's Harmful Effects on Health, Finances, Influenced by Disease itself, Socio-Demography, and Mental Health Care System

The prevalence of smoking is exceptionally high (70% to 80%) within the schizophrenia population (Baker et al., 2006; Chapman et al., 2009; De Leon & Diaz, 2005; Dome et al., 2010; Leonard et al., 2001) compared to other psychiatric disorders (50%) and the general population (21%) (Fiore, 2008; "Quitting smoking among adults-United States, 2001-2010," 2011). The association of smoking with schizophrenia has been exhibited within the literature, including a meta-analysis by De Leon and Diaz 2005, which showed that individuals with schizophrenia are five times more likely to smoke than the general population and 1.9 times more likely than those suffering from other severe mental illnesses (De Leon & Diaz, 2005). Additionally, individuals with schizophrenia smoke heavily (Tidey, Rohsenow, Kaplan et al., 2005; Williams et al., 2010) extract higher nicotine than smokers in healthy individuals (C. Kelly & McCreadie, 1999; Olincy, Young, & Freedman, 1997; Williams et al., 2010) with high levels of nicotine dependence scores (De Leon & Diaz, 2005; D. Weinberger & Marenco, 2007).

The schizophrenic population has a substantially increased risk for a higher mortality (Brown, BARRACLOUGH, & INSKIP, 2000; Goff et al., 2005; Hannerz, Borgå, & Borritz, 2001; Kelly et al., 2011a) The mortality risk is higher than that of the general population (Saha, Chant, & McGrath, 2007) resulting in about a 20-25% reduction in average life span in people with schizophrenia (Colton & Manderscheid, 2006; Hennekens, 2007; Newman & Bland, 1991). A meta-analysis shows a linear increase in mortality over a period of three decades with an increased mortality gap (median SMRs for the 1970s, 1980s and 1990s were 1.84, 2.98 and 3.2) (Saha et al., 2007). Furthermore, the rates of death due to cardiac and pulmonary disease

is in women (C. Kelly & McCreadie, 1999). Besides this link for earlier onset smoking and the early onset of an illness, smoking is associated with higher severity of the disease, expressed as a higher PANSS total score (Schwartz, 2007). Additionally, this is supported by a recent study by Rajeev et al., which found that smoking could pre-date the onset of illness. However, the relationship between nicotine dependence and duration of prodromal period is yet to be known (Krishnadas, Jauhar, Telfer et al., 2012).

Smoking among schizophrenics puts a significant financial burden not only on patients but also on society in terms of taxes and frequent hospitalization. A study estimated that this population consumes 27% of the monthly income of those residing in a high tobacco tax state (Steinberg, Williams, & Ziedonis, 2004), which is higher than those of the general population only with 10% (Gilpin et al., 2001). Such high rates of smoking in individuals with schizophrenia places them as vulnerable targets for the tobacco industry (Els, 2007; Prochaska, Hall, & Bero, 2008).

WHY DO THEY SMOKE?

Several hypotheses have been suggested to explain the high rate of smoking and low rate of smoking cessation among schizophrenics. For example, smoking may improve the sensory gating (Adler et al., 1998), which is abnormal in these patients. Thus, resulting in cognitive impairment (Kumari & Postma, 2005) and perhaps as an attempt to correct such cognitive impairments.

Schizophrenic patients smoke; a habit which is better explained by the popular historical postulation entitled, "self medication hypothesis." Here it states that smoking may help these patients to manage their positive and negative symptoms by compensating for the underlying neurobiological deficits associated with the disorder (Adler et al., 1998; Dome et al., 2010; Leonard et al., 2001; Matthews, Wilson, & Mitchell, 2011; Olivier, Lubman, & Fraser, 2007; Patkar et al., 2002). Contrary to the hypothesis is that smoking improves cognitive functioning, where few studies have suggested that there are actual changes in some cognition-related brain processes and thus, increases concentration, alertness, and speed of performance (AhnAllen et al., 2008; Depatie et al., 2002; Jubelt et al., 2008; Larrison-Faucher, Matorin, & Sereno, 2004; Myers et al., 2004; Smith et al., 2005).

Social factors like unemployment, low educational attainment, peer influence and lack of smoking cessation treatment in mental health systems may also contribute to the increased risk of smoking in this population (Ziedonis et al., 2008). Similarly, it has been observed that smoking within this population helps these individuals cope with stress and boredom (Mann-Wrobel, Bennett, Weiner et al., 2011). In addition, it has been posited that nicotine may be used in this population to overcome side effects of variable anti-psychotic medications (Kelly & McCreadie, 2000; Levin et al., 1996; McEvoy et al. , 1995).

Another hypothesis of "shared vulnerability" of nicotine and schizophrenia suggested that first-degree relatives of patients with schizophrenia are more likely to smoke (Esterberg, Jones, Compton et al., 2007) or an association between daily smoking and schizophrenia reflected a shared genetic vulnerability, in comparison to other addictions (De Leon & Diaz, 2012).

ROLE OF CAREGIVERS AND MENTAL HEALTH SYSTEM TO ADDRESS CIGARETTE ADDICTION

Several studies support the relatively less aggressive treatment of cigarette addiction in severely mentally ill patients. In a study to assess the rate of nicotine problems diagnosed by psychiatrists in routine clinical practice, it was found that only 9.1% of patients received treatment for nicotine dependence (Montoya, Herbeck, Svikis et al. , 2005). In spite of the well-known fact of high prevalence of smoking in patients of mental illness, psychiatric patients are often excluded from studies examining various strategies for smoking cessation (Gonzales et al., 2006).

In a study of community mental health centers, it was revealed that while the majority of psychiatrists ask the patients about their smoking habit, only 24% of them consider such information to be of major clinical value (Price, Ambrosetti, Sidani et al., 2007). Researchers and clinicians have come to expect lower rates of long-term cigarette abstinence subsequent to tobacco-dependence treatment, which is usually 25% or less at year 1, even with combination therapy (Fiore, 2008).

Moreover, many clinicians assume that their patients cannot tolerate cessation attempts due to the stress of withdrawal, which often leads to symptom exacerbation. However, various studies have provided enough evidence that patients can generally tolerate smoking cessation in the short-term without symptoms exacerbation (Dalack et al., 1999; Evins et al., 2001; George et al., 2002).

Kelly et al. suggested that patients with schizophrenia smoke heavily to overcome dopamine blockage produced by antipsychotics, an effect which could produce reward effects (Kelly & McCreadie, 2000). Schizophrenic patients smoke heavily once they begin treatment with typical antipsychotics (McEvoy et al., 1995). Others found typical antipsychotic medications can influence nicotine addiction and make smoking cessation difficult (McNeill & Owen, 2005). A single dose of Haloperidol in normal subjects could lead to significant increases in smoking with higher levels of nicotine in the following hour (Dawe, Gray, Russell et al., 1995). In accordance with these theories, chronic patients were advised by clinicians to smoke as a means of treating their illness and the side effects of antipsychotics (Kumari & Postma, 2005; Leonard et al., 2001; Sacco et al., 2004). Since it is now known fact that smoking is highly modifiable risk factor (Bobes, Arango, Garcia-Garcia et al., 2010) but its treatment often goes unaddressed by clinicians customarily in population of mental illnesses (Prochaska, 2010).

ARE THEY WILLING TO QUIT SMOKING?

Research suggests that an important factor in smoking cessation is motivation to quit. Motivation to change has been identified as an important construct in the smoking cessation process (Font-Mayolas, Planes, Gras et al., 2007). Little is known about motivation and isiog1 1 Tf0 Tw -1.575 -1.0520047004E004C0051004A0003>41.4005A03

given the high levels of smoking prevalence and tobacco dependence in these patients. Among those who had previously quit, the odds were 6 times higher in the general population than in the schizophrenia group, re f ecting that people with schizophrenia have a harder time quitting than those in the general population (Etter, Mohr, Garin et al. 2004).

schizophrenia populations, Bupropion emerged as a potent anti-addictive therapy for smoking cessation due to its antismoking effect (Slemmer, Martin, & Damaj, 2000; Warner & Shoaib, 2005). In 1997, bupropion was approved as the first non-nicotine medication for smoking cessation. In 2009, the FDA labeled a "black box" warning for Bupropion due to its possible adverse effects such as suicidal thoughts, hostility, depressed mood, agitation and suicide attempts (Food, 2010). Primarily, Bupropion posses an important and principal action upon the withdrawal symptoms following smoking cessation: it may attenuate multiple withdrawal symptoms, as well as prevent relapse after smoking cessation (Warner & Shoaib, 2005). Given the certain properties of Bupropion and its plan of action, it's being used and investigated for smoking cessation in general populations as well as in patients of various mental illnesses.

The "American Journal of Psychiatry Clinical Guidelines" and the updated treatment recommendations from 2009 from the "Schizophrenia Patient Outcomes Research Team" (PORT) both recommend that people with schizophrenia who want to quit smoking should be offered Bupropion SR with group support and education (Dixon et al., 2010; Kreyenbuhl et al., 2010). Several studies on combination therapy have been done on BUP SR, NRT and support group for smoking cessation or reduction in this population (Addington et al., 1998; Chou et al., 2004; Evins et al., 2001; Fatemi et al., 2005; George et al., 2002; Weiner et al., 2001). Yet aside from applying various interventions and different combinations, this population continues to smoke (Montoya & Vocci, 2007).

In 1999, Evins et al. reported the first case of Bupropion used f T b

that the Bupropion group had a higher 4-week continuous abstinence rate 16% versus 0% and maintained abstinence until the end of the intervention with longer duration of abstinence in Bupropion group versus placebo group.

After various studies on bupropion versus placebo, this drug was also studied with various combinations and showed more promising results than having it alone. In consideration of combination therapy, Evins et al. looked at the same components (Bupropion versus placebo), but it was reported on the basis of short-and long-term

smokers where Varenicline produced significant improvements in cognitive test scores. This was primarily associated with verbal learning and memory, but not in scores on visual-spatial learning or memory, nor on attention. Concurrently, it has a beneficial effect on smoking abstinence with no significant increases in psychopathology scores or clinical depression and suicidal ideation (Smith et al., 2009). Considering the effect of Varenicline on cognition, a double-blind study by Shim JC et al. (Shim et al., 2011) in which the author studied cognitive impairments amongst 120 stable patients with schizophrenia were treated with an adjunctive Varenicline . After the dropping of 3 patients, 117 were examined with the figure of 59 on Varenicline and 58 on placebo. Compared to the placebo, patients of Varenicline demonstrated significant improvements in the digit symbol substitution test (P=0.013) and Wisconsin card sorting test (non-preservative error, P=0.043). Similarly to Smith's 2009 study, none of the patients reported symptoms of depression or suicidal ideation. Though, both studies didn't identify significant improvement in overall cognition with the use of Varenicline. Thus, this important action of the drug has yet to be studied and sufficient data should be at place in order to understand its role in cognition.

Regarding efficacy and safety of Varenicline, a recent study (Williams, 2012) by Williams JM et al. had a 12-week, randomized, double-blind study, in which 84 participants received Varenicline and 43 received the placebo. They concluded that 19.0% met the criteria of smoking cessation for those on Varenicline versus 4.7% for placebo. William et al. found Varenicline was well tolerated without exacerbation of symptoms and had significantly higher smoking cessation rates versus the placebo. As for side-effects, few reported nausea, which was not that frequent due to the antiemetic property of antipsychotics, and irritability, anxiety and abnormal dreams which may be associated with the process of nicotine withdrawal (Williams, 2012).

Pachas et al. conducted a larger study (Pachas et al., 2012) with 112 stable individuals in an open labeled trial for outpatient smokers with schizophrenia and nicotine dependencies. These individuals participated for a 12 week smoking cessation trial of Varenicline and had weekly group cognitive behavioral therapy sessions. Participants had47%. Thed p mos.1receith evinaupa0.8h(Cerimel]TJ-0.0242ia021 Tw & DuTDigo1.278 TdJ-0 a278 TDormal 0.8(3s1 1 TfT*[00.ntip)0.20.6(abstinen

which has encouraging results and thus calls for further research to be done on larger scales .

Early deaths, short life span due to cardiovascular components or any other metabolic factor, should alert clinicians to increase the frequency of follow-up for these patients. Also, there should be a focus on preventing initial cardio-metabolic risks because subsequent reduction in this risk is more difficult to achieve, either through behavioral or pharmacologic interventions. Considering these facts and ignorance at the level of primary care health physicians, this issue should be addressed at the primary care level by regular assessments of the following factors: fasting glucose, body mass index, fasting triglycerides, fasting cholesterol, waist, high-density lipoprotein/low-density lipoprotein, blood pressure and symptoms of diabetes. In terms of interventions, most guidelines recommended advice on physical activity, diet, psycho-education of the patient, treatment of lipid abnormalities, treatment of diabetes, referral for advice and treatments, psycho-education of the family and smoking cessation advice.

Steinberg ML et al. did the first study, which examined the relationship between task persistence and smoking cessation outcome in smokers with schizophrenia. Task persistence may make important contributions to smoking cessation successful. This will be exhibited by indicating that the contribution of task persistence to smoking cessation is similar for smokers with schizophrenia and non-psychiatric smokers, which too, warrants more in-depth consideration on larger scales (Steinberg et al., 2012).

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