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Clinical characteristics of heavy and non-heavy smokers with schizophrenia

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ABSTRACT

Up to 50–90% of persons with schizophrenia smoke cigarettes. Limited data and theories suggest persons with schizophrenia may smoke for different reasons than persons without schizophrenia, making smoking cessation interventions particularly challenging in this population. Although health consequences of smoking are widely known, less information is available regarding characteristics of different amounts of smoking exposure in this population. This study was performed to investigate differences between heavy (≥1 pack per day) and non-heavy (<1 pack per day) smoking in patients with schizophrenia. Data from 745 patients, mean age 41.3 +/− 12.6 years, were drawn from a population of smokers admitted to State of Maryland inpatient mental health facilities (1994–2000). Records were reviewed to obtain demographic information, diagnosis, medication, smoking and substance use. 43% of patients were characterized as heavy smokers. Heavy and non-heavy groups did not differ in age, GAF, weight, or BMI. No differences were found in race, gender or antipsychotic treatments. However, patients smoking ≥1 packs per day were more likely to use other substances such as alcohol ($\chi^2 = 6.67$, df = 1, p = 0.01), cocaine ($\chi^2 = 6.66$, df = 1, p = 0.01), and other substances ($\chi^2 = 9.95$, df = 1, p = 0.003) compared to non-heavy smokers. No differences in cannabis or heroin use were found by smoking category. Controlling for age, race, sex and BMI, heavy smokers had higher total cholesterol (190.7(51.6) mg/dL) compared to non-heavy smokers (178.2 (43.0) mg/dL, p = 0.03), but no differences were found in glucose or blood pressure. Heavy smoking may be a particular health risk in schizophrenia and significant efforts for smoking cessation or reduction are needed.

1. Introduction

Cigarette smoking is common in persons with schizophrenia, with prevalence rates of 50%–90% across varying studies and an average prevalence of 62% in a recent meta-analysis of 42 studies (de Leon et al., 1995; Moeller-Saxone, 2008; Chapman et al., 2009) compared to approximately 20% of adults in the United States general population (MMWR, 2007). Data suggest that people with schizophrenia are three times more likely to initiate smoking and five times less likely to quit smoking than people in the general population (Diaz et al., 2006). In addition, persons with schizophrenia have an increased risk of initiation of daily smoking (Zhang et al., 2010). Smokers with schizophrenia are often highly nicotine dependent, and studies have reported greater carbon monoxide boost, puffs, puffs per cigarette, and increased saliva cotinine concentrations in smokers with schizophrenia as opposed to smokers without schizophrenia (Hitsman et al., 2005; Strand and Nybäck, 2005; Tidey et al., 2005; Williams et al., 2005).

There are multiple theories about the increased level of smoking in schizophrenia, including a theory of shared vulnerability between nicotine dependence and possibly related dysregulation or abnormalities in nicotinic receptors or other neurotransmitter systems (Wing et al., 2012). Other potential reasons include self-medication of negative/cognitive symptoms and neurophysiological abnormalities (Winterer, 2010), depressive symptoms (Lising-Enriquez and George, 2009), a means of activity or staving off boredom (Roick et al., 2007), or to decrease the extrapyramidal side effects of antipsychotics (Madden et al., 1997). Previous work from our group has found that people with schizophrenia report more frequently than controls that smoking improves the ease of social interaction and state enhancement (Kelly et al., 2012). However, a recent study (Levander et al., 2007) found no difference between nicotine users and non-users with schizophrenia spectrum disorders on symptoms, side effect, cognition, and outcome.

Cessation rates for smokers with schizophrenia are an increasing focus of study, and interventions should be further researched as well as a focus for inpatient (Olivier et al., 2007) and outpatient treatment planning (Ziedonis et al., 2008). Studies of cessation interventions in patients with schizophrenia have found varying rates of success, although positive results have been reported in the literature (Baker

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et al., 2006; George et al., 2008). Motivation for quitting may be lower in schizophrenia, as Kelly et al. (2012) found that motivation for quitting smoking in persons with schizophrenia is significantly lower than in controls. Baker et al. (2007) reported that, compared to general population samples, persons with psychotic disorders were more likely to indicate that stress reduction, stimulation, and addiction were reasons for smoking. Potential targets and challenges therefore exist for timing and type of smoking interventions in this population. Of additional concern, Kelly et al. (2012) also found that, compared to normal controls, people with schizophrenia demonstrated a significantly lower appreciation of the health risks that are a consequence of cigarette smoking, and rated health risks as less of a motivator for smoking cessation.

The health effects of cigarette smoking are well known, and increased morbidity and mortality in smokers both in the general population and in schizophrenia have been demonstrated (Kelly et al., 2011). Adults in the general population who smoke cigarettes die an average of 14 years earlier than nonsmokers (MMWR, 2002), and this is of even more concern in people with schizophrenia, as this population is more likely to have greater physical health issues and a decreased life expectancy as compared to the general population (Saha et al., 2007). Not surprisingly, smoking is considered to be a significant factor in the excess natural mortality of schizophrenia (Hennekens et al., 2005). Bobes et al. (2010), found that smokers with schizophrenia spectrum disorder showed a 10-year cardiovascular event risk excess verses non-smokers of 2.63. In addition, smokers with schizophrenia are more likely to be heavy smokers (at least a pack or pack and one half daily) compared to smokers in the general population (Kelly and McCreadie, 1999).

The amount of lighter smokers in the general (non-mentally ill) population appears to be increasing. The concept of "light smoking" or "non-heavy smoking", as it will be termed in this study, may be defined in different ways, as there is no consensus; including <1 pack per day (ppd), <15 cigarettes per day, <10 cigarettes per day, and 1–39 cigarettes per week (Husten, 2009; Schane et al., 2010). As many as 1/3 of adult smokers report smoking less than daily (2002 National Survey on Drug use and Health); some of these may be former heavier smokers or smokers trying to quit, and others may be smokers that maintain their current light smoking pattern (Levy et al., 2009; Schane et al., 2009).

Many have touted the benefits of smoking reduction as a means toward cessation, or as potentially associated with a decreased risk of health complications or mortality. However, the literature has been mixed regarding the benefits of smoking reduction or "light smoking" (Møller et al., 2002; Haustein et al., 2004; Hatsukami et al., 2005; Hughes and Carpenter, 2005; Song et al., 2008; Schane et al., 2010). Smoking reduction has been associated with a decreased risk of lung cancer (Godtfredsen et al., 2005; Song et al., 2008). Other studies have shown smoking reduction significantly decreases biochemical markers for cardiovascular disease risk, ischemic heart disease, relative risk for myocardial infarction and other major cardiac events, risk of GI cancers; and, respiratory tract infections, reproductive issues, poor bone mineral density, and cataracts (De Stefani et al., 1998; Coughlin et al., 2000; Haustein et al., 2004; Hatsukami et al., 2005; Hughes and Carpenter, 2005; Schane et al., 2009, 2010).

Data are also mixed on differences between outcomes and risks for heavy smokers compared to non-heavy smokers in the general population. Some studies suggest that risk for cardiovascular (CV) disease is similar among light/intermittent smokers and daily smokers (Bjartveit and Tverdal, 2005), and that male light smokers are still at increased risk of CV mortality and all cause mortality compared with male nonsmokers (Luoto et al., 2000; Schane et al., 2010). In the general population, some data does suggest that, compared to heavy smokers, non-heavy smokers are at reduced risk for postoperative complications, and may be at less risk for myocardial infarction and stroke than heavy smokers (Møller et al., 2002; Song and Cho, 2008).

Previous work in individuals with schizophrenia and other serious mental illnesses has suggested an association between greater smoking severity and a current diagnosis of hypertension, oral/gum disease, greater perceived stress, and poorer subjective quality of life (Dixon et al., 2007), as well as increased positive symptoms, decreased negative symptoms, increased substance use, more frequent psychiatric hospitalizations, and fewer extrapyramidal side effects, (Goff et al., 1992; Ziedonis et al., 1994; Workgroup on Substance Use Disorders, 2006). However, these findings have been inconsistent, and the determination of clinical differences between heavy and non-heavy smokers with schizophrenia may contribute useful information for future smoking cessation programming and motivational factors for patients. In addition, recent data suggests African American patients with severe mental illnesses who smoke may do so to a lesser extent than their Caucasian counterparts (Dixon et al., 2009), a finding that deserves greater attention due to potential clinical implications.

The current study utilized a large administrative database to identify patients treated in inpatient mental health facilities in the State of Maryland who were smokers to explore the clinical, demographic, symptomatic, and substance use differences between heavy (≥1 ppd) and non-heavy (<1 ppd) smokers with schizophrenia.

2. Methods

Patients treated with antipsychotic medications in State of Maryland inpatient mental health facilities between 1994 and 2000 were identified through a State of Maryland Antipsychotic Database. Clinical data collection for the 3198 subjects who were treated at some point in State of Maryland inpatient facilities took place between 2003 and 2007. 1986 of 3198 (62%) subjects' clinical records were available for review, due to missing or incomplete medical records or record destruction.

Patients with a DSM-IV diagnosis of schizophrenia and a history of cigarette smoking were selected. Inpatient medical records from 7 hospitals were reviewed to obtain demographic information, diagnosis, and medication use as well as smoking and other substance use. A total of 745 unique patient records were identified meeting criteria for diagnosis and cigarette smoking. Medical records were reviewed to verify DSM-IV diagnoses, demographic information, comorbid diseases, smoking status, laboratory measures, weight, body mass index (BMI), and severity of illness (Global Assessment of Functioning, or GAF scores). Careful attention and verification were made for all diagnoses with computerized records and Axis I DSM-IV diagnosis on the most recent Individualized Treatment Plan (ITP). Only information from the first hospital admission during the period of study was collected if there were more than one. This study was approved by the University of Maryland Baltimore and Department of Health and Mental Hygiene Institutional Review Boards. The study was considered exempt, and the requirement for written informed consent was waived for use of administrative health records.

A total of 745 patients were identified either as heavy smokers (at least one pack of cigarettes per day, or ≥1 ppd) or as non-heavy (less than one pack of cigarettes per day, or <1 ppd) at their index admission. Approximately 62% of all schizophrenia records were considered smokers (Kelly et al., 2011). Only those with specific information on frequency or amount of use were included. Those listed with unknown smoking amounts were not included in the data analysis. Detailed information on smoking data and substance use was obtained using an a priori algorithm designed to locate information from the medical record, including admission records, hospital substance use questionnaires, and urine toxicology screens. Smokers were defined as subjects who reported current smoking at their index admission. Smokers were further categorized as subjects who smoked more than 1 pack daily (heavy smokers), less than 1 pack daily (non-heavy smokers) or unknown amount (not used for this analysis). Medical record reporting

of previous years of exposure was sporadic and reliable pack/year histories could not be extracted.

Substance use was defined as ever using any of the following substances identified by name or corresponding street name: alcohol, cocaine, cannabis, heroin, Lysergic acid diethylamide (LSD), Phencyclidine (PCP), 3,4-methylenedioxy-*N*-methylamphetamine (MDMA), inhalants, amphetamines and/or other hallucinogens. Data collection also included history of diabetes and cardiovascular disease as well as variables that could be associated with risk for cardiovascular disease, such as height and weight used to calculate BMI as well as systolic and diastolic blood pressure, blood glucose, cholesterol and triglyceride levels. These data was collected from the time of the index admission.

3. Statistical analysis

Clinical information from medical records and administrative databases as described above were compared between heavy and non-heavy smokers using chi-square tests or Student's t. We hypothesized that heavy smokers may show indices of increased physical health problems, and more substance use, than non-heavy smokers. All statistical analyses were conducted using SAS version 9 (SAS institute Inc.). Tests were two-sided with alpha = 0.05. Logistic regression was used to compare risk of lifetime substance use (yes/no), and analysis of covariance to compare of levels of laboratory measures (continuous) in heavy versus non-heavy smokers, adjusting for age, race, BMI, and sex.

4. Results

4.1. Demographic and clinical characteristics

Of the 745 patients identified as smokers, 43% were classified as heavy smokers (at least 1 ppd) (n = 319) and 57% were non-heavy smokers (<1 ppd) (n = 426). Average age was 40.4 (11.4) years for heavy smokers, and 41.9 (13.4) years for non-heavy smokers (p = NS). There were no significant differences observed in gender or race. Heavy and non-heavy smoking groups were 67% and 64% male and 60% and 58% Caucasian, respectively. The average GAF for the heavy smoking group was 36.6 (11.0) and for the non-heavy smoking group was 38.2 (11.0) (p = n.s.). Patients were chronically ill, as the majority of the sample was derived from the longer-term inpatient psychiatric facility and had GAF scores in the mid 30s representing a population of severe symptomatology. Also, approximately 37% (n = 119) were treated with clozapine.

4.2. Laboratory measures and health history

No differences were found between heavy and non-heavy smokers in triglycerides, glucose, systolic or diastolic blood pressure, mean BMI, percentage obese or having reported diagnoses of existing cardiac disease or existing type I or II diabetes (see Table 1).

Total cholesterol was significantly higher at 190.7 mg/dL (51.6) in heavy smokers versus 178.2 mg/dL (43.0) in non-heavy smokers ($t = -2.23$, $df = 223$, $p = 0.02$). After adjusting for age, race, BMI and gender, heavy smokers continued to have higher total cholesterol than non-heavy smokers ($t = 2.26$, $df = 272$, $p = 0.03$). Other laboratory measures were not significantly different between the two smoking groups.

4.3. Substance use

Statistically significant differences were found between heavy and non-heavy smokers in the use of alcohol (68% vs 58%, 196/288 vs 204/351, $\chi^2 = 6.67$, $df = 1$, $p = 0.01$), cocaine (35% vs. 25%, 100/288 vs 89/351, $\chi^2 = 6.66$, $df = 1$, $p = 0.01$), and other substances of abuse (34% vs. 23%, 97/288 vs 81/351, $\chi^2 = 9.95$, $df = 1$, $p = 0.003$); however, no differences were found in cannabis (39% vs. 35%, 113/288 vs. 125/351, p = n.s.) or heroin (16% vs. 13%, 45/288 vs 41/351, p = n.s.). Adjustment differences in age, race, and sex continued to show significant associations between heavy smoking and lifetime alcohol (0.36 ± 0.18, $\chi^2 = 3.93$, $df = 1$, $p = 0.05$) and cocaine use history (0.54 ± 0.2, $\chi^2 = 7.2$, $p = 0.007$).

5. Discussion

In our sample of 745 heavy or non-heavy smokers with schizophrenia, approximately 43% were found to be heavy smokers. This number is concordant with rates of 50% to 68% found in previous studies, and also exceeds past estimates of the general population, where approximately 11% of smokers were found to smoke heavily (Ziedonis et al., 1994; Kelly and McCreadie, 1999; Lasser et al., 2000). We found few clinical or demographic differences between the heavy and non-heavy smoking samples. While the heavy smoking group had higher levels of total cholesterol, despite controlling for age, BMI, race and sex, we found no differences in weight, blood pressure, other lipids, glucose levels, or prevalence of obesity, cardiovascular disease or diabetes. We are not confident that all blood samples drawn were in the fasting state despite hospital protocols being listed as fasting for metabolic values. This may contribute to non-significant findings for glucose and triglycerides, since total cholesterol levels are less

Table 1
Demographics and clinical characteristics.

Characteristic	≥1 Pack per day (N = 319)	<1 Pack per day (N = 426)	Statistical values
Age (years)	40.4 (11.4)	41.9 (13.4)	$t = 1.59$, $df = 742$, $p = 0.11$
Sex (male)	67% (213)	64% (274)	$\chi^2 = 0.57$, $df = 1$, $p = 0.45$
Race (white)	60% (171)	58% (218)	$\chi^2 = 2.8$, $df = 2$, $p = 0.25$
Treatment = clozapine	37% (119)	38% (160)	$\chi^2 = 0.005$, $df = 1$, $p = 0.94$ OR = 1.0 CI = 0.7–1.3
GAF	36.6 (11.0)	38.2 (11.0)	$t = 1.83$, $df = 618$, $p = 0.068$
BMI (kg/m^2)	26.9 (5.9)	27.1 (5.4)	$t = 0.38$, $df = 477$, $p = 0.70$
Obese	26% (52/201)	24% (67/278)	$\chi^2 = 0.20$, $df = 1$, $p = 0.66$ OR = 1.1 CI = 0.7–1.7
Total cholesterol (mg/dL)	190.7 (51.6)	178.2 (43.0)	$t = -2.31$, $df = 307$, $p = 0.02$
Triglycerides (mg/dL)	159.4 (93.2)	151.8 (109.4)	$t = -0.63$, $df = 303$, $p = 0.53$
Glucose (mg/dL)	98.1 (36.4)	99.3 (46.7)	$t = 0.25$, $df = 327$, $p = 0.80$
Systolic BP (mm Hg)	117.6 (14.5)	118.6 (14.7)	$t = 0.74$, $df = 490$, $p = 0.46$
Alcohol use	68% (196/288)	58% (204/351)	$\chi^2 = 6.67$, $df = 1$, $p = 0.01$ OR = 1.5, 95% CI = 1.1–2.1
Marijuana use	39% (113/288)	35% (124/351)	$\chi^2 = 1.04$, $df = 1$, $p = 0.31$ OR = 1.2, 95% CI = 0.9–1.6
Cocaine use	35% (100/288)	25% (89/351)	$\chi^2 = 6.63$, $df = 1$, $p = 0.01$ OR = 1.6, 95% CI = 1.1–2.2
Heroin use	16% (45/288)	12% (41/351)	$\chi^2 = 2.11$, $df = 1$, $p = 0.15$ OR = 1.4, 95% CI = 0.9–2.2
Other substances use	34% (97/288)	23% (81/351)	$\chi^2 = 8.85$, $df = 1$, $p = 0.003$ OR = 1.7, 95% CI = 1.2–2.4)

OR = odds ratio, CI = 95% confidence interval.

affected by fasting status. Elevated cholesterol is an important risk factor for coronary heart disease (Kannel et al., 1971). Cigarette/tobacco smoke and high cholesterol are two of the six main modifiable risk factors for cardiovascular disease, and smoking is known to increase LDL and decrease HDL, as well as slightly increase triglycerides (Criqui et al., 1980; Craig et al., 1989). Unfortunately, the lack of HDL and other lipid measurements limits our ability to further analyze the results in this population.

In the general population, current tobacco use has been associated with the use of other substances (alcohol, cannabis, etc.) (Degenhardt and Hall, 2001). In our sample, the finding that heavy smokers with schizophrenia were more likely to have used substances of abuse such as cocaine and alcohol as compared to non-heavy smokers suggests that this population may be at higher risk for morbidities and mortality from smoking and health risks but also inherent risks from added abuse and dependence on illegal drugs and alcohol. Others have also found many associations of cigarette use and drug use, however few have examined the increased drug use we found in smokers who are considered heavier smokers with schizophrenia. Baker et al. (2007) reported that heavy smokers with schizophrenia who currently use drugs and alcohol generally report the onset of smoking earlier in their teens. Vanable et al. (2003) report elevated risk for substance use disorders with smoking status. Interestingly, in a recent report in 90 patients with substance use, the authors find that people who used recreational drugs smoke less, however this was a small sample Meszaros et al. (2011).

The use of other substances of abuse such as cannabis and heroin were not found to be greater in our comparison of heavy and light smokers with schizophrenia. This may warrant future attention to distinguish if use and abuse patterns may differ between various substances. However, the increased use of alcohol and cocaine in the heavy smoking sample is of note for future research and clinical intervention, as use of other substances may also add to the challenge of tobacco cessation interventions for this population. This is evidenced by the fact that de Leon et al. (2005) find that predictors of successful smoking cessation include lack of lifetime drug abuse.

Our study is limited to its retrospective nature, including information regarding smoking status, other substance use, metabolic measures and GAF. Lipid and glucose data were only sparsely available, and were not available for every patient. These measurements may also have been collected more frequently and commonly in persons considered to be at risk for abnormal findings (i.e., obesity, history of heart disease, history of high cholesterol, etc.), which would have limited the ability to detect differences linked solely to smoking status. In addition, years of smoking history were only intermittently available, which may be of great importance when studying long-term health consequences of cigarette use. We were able to categorize heavy smoking as greater than one pack per day similarly to other reports (Anda et al., 1990; de Leon et al., 1995; Vanable et al., 2003). We are aware that there are a range of cutoffs used to categorize heavy smoking and others have used higher values such as 25 or 30 cigarettes daily (de Leon and Diaz, 2005). We were limited by the retrospective data collection and were able to accurately identify less than and greater than one pack per day. More precise information on length of illness, population of non-smoking inpatients, level of education, medication dose and duration, and concomitant medications would also have been useful parameters. In addition, this information was derived from a predominantly inpatient sample, which limits generalizability. Missing data points limit the extent to which our analyses can be used to derive definitive conclusions.

In conclusion, our study suggests that people with schizophrenia who are heavy smokers have elevated rates of co-occurring or past substance use compared to non-heavy smokers. In addition, heavy smokers may have additional health risks such as higher total cholesterol levels compared to schizophrenia patients who smoke less frequently. Other recent work from our group has shown that all cause mortality is 2 fold higher in smokers compared to nonsmokers and this risk is almost 3 fold higher in those who smoke more than a pack per day (Kelly et al., 2011). It is clear that smoking and elevated cholesterol contribute to a higher risk than smoking alone. Due to these combined effects, every effort to decrease cigarette intake or stop smoking should be made for smokers with schizophrenia as part of a multifaceted treatment plan for the mental and physical health of this patient population.

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The funding source for this manuscript had no role in the analysis of data nor in the preparation of this manuscript.

Contributors

Heidi Wehring assisted in data collection, assimilation, and presented this in abstract form at the Society for Research on Nicotine and Tobacco meeting February 2010 and the College of Psychiatric and Neurologic Pharmacists meeting in April 2010, and coordinated the preparation of manuscript for publication. Fang Liu performed statistical analyses and assisted in manuscript preparation. Robert P. McMahon provided oversight for statistical analyses and assisted in manuscript preparation. Kristen Mackowick assisted in data collection, assimilation, and manuscript preparation. Raymond C. Love coordinates the CAMP and atypical antipsychotic databases and provides oversight for state hospital coordination of data. He also assisted in manuscript preparation. Lisa Dixon assisted in manuscript preparation. Deanna L. Kelly designed this study and data analysis, organized autopsy information and assimilation, wrote the protocol, and assisted in manuscript preparation.

Conflict of interest

The authors report no conflicts of interest for this manuscript.

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