



Prediabetes: An Alarming Epidemic in Schizophrenic Patients

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General Note

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ABSTRACT

Diabetes has reached pandemic proportions. The prevalence of diabetes is higher in patients with schizophrenia when compared to the general population. Besides the traditionally recognized risk factors, this population also suffers from higher BMI. They are more likely to be prescribed a second generation anti-psychotic drug. Poor living conditions and unhealthy life styles also play a role. The International Diabetes Federation estimates that over 300 million people suffer from prediabetes worldwide. The presence of prediabetes in patients with schizophrenia has not been well studied. Our data suggests that dysglycemia may be a hidden epidemic in this population.

1. INTRODUCTION

1.1. Diabetes Mellitus

The human population is experiencing an inexorable rise in diabetes. It is estimated that the prevalence of diabetes worldwide will increase from 285 million in 2010 to 438 million in the year 2030. (Diabetes Facts, 2012) Global projections for prediabetes indicate an increase from 344 million in 2010 to 472 millions in 2030. (Wild et al, 2004) This dysglycemic assault has important medical and economic relevance. In the United States, diabetes mellitus affects almost 30 million people, with over twenty five percent of these

patients remaining undiagnosed. (National Diabetes Fact Sheet, 2012) These numbers are estimated to increase to nearly 53 million by 2025. (Diabetes Data and Forecasts, 2012) Annual costs for the treatment of diabetes and its complications were \$174 billion in 2007 (ADA, 2008) and are expected to reach \$514 billion in 2025 (NDFS, 2012) Diabetes mellitus is a disproportionately expensive disease. In the United States in 2002, the per-capita cost of health care was \$13,243 for people with diabetes, while it was \$2560 for those without diabetes. (Hogan et al, 2002) The emergency department utilization rate by people with diabetes is twice that of the unaffected population. (Laditka et al, 2001) Diabetes mellitus is associated with significant morbidity and premature mortality. (Alain et al, 2002) It is associated with significant microvascular, and macrovascular complications. (Mokdad et al, 2001; Mokdad et al, 2000; Burke et al, 1999) These patients also suffer from several neuropathic complications. (Boulton et al, 1998; Zochodne et al, 2008)

1.2. Pre-diabetes

Prediabetes refers to dysglycemia that is not abnormal enough to be classified as diabetes. Prediabetes affects nearly 79 million Americans. (Diabetes.org, 2012) Prediabetes raises short-term absolute risk of type 2 diabetes by 3-to 10-fold, with some populations exhibiting greater risk than others (Haffner et al, 2000; Wilson et al, 2005). Prediabetes is also associated with a moderate increase in cardiovascular risk. (Earl et al, 2010) Most patients with prediabetes have all the cardiovascular risk factors as patients with type 2 diabetes. These include dysglycemia, dyslipidemia, hypertension, obesity, physical inactivity, insulin resistance, procoagulant state, endothelial dysfunction and inflammation. This places these patients at a high risk for macrovascular complications. Prediabetes is also associated with significantly increased all-cause mortality. It is estimated that prediabetes costs US almost 25 billion dollars a year (Zhang, 2009) Incidence of diabetes and prediabetes is however rising, and will further strain an already overburdened health care system.

1.3. Schizophrenia

People with schizophrenia suffer from high rates of physical comorbidity. (Jeste et al, 1996) These include pulmonary, cardiovascular and endocrine diseases. (Casey et al, 2011; Goff et al, 2005; Copeland et al, 2007) They also suffer from higher rates of smoking, alcoholism, malnutrition and lack of exercise. (Linde-Feucht, 2007) They are more likely to partake in substance abuse and have higher rates of accidents and suicide. (Dervaux et al, 2003; Wing et al, 2012; Jones et al, 2011) It is estimated that these behaviors and comorbidities account for the majority of premature deaths in this population. (Brown, 1997) Detection and management of these comorbidities is often poor in this population. (WFMH, 2010) One of the unrecognized medical comorbidity is prediabetes.

2. METHODS

We retrospectively reviewed the HbA1c results of 62 consecutive patients with schizophrenia seen in our office for medical reasons. All patients were diagnosed with schizophrenia by a psychiatrist and were under treatment with psychotropic drugs. According to the American Diabetic Association, (ADA, 2007) diabetes mellitus is diagnosed if symptoms of diabetes (polyuria, polydipsia, and unexplained weight loss) are associated with a casual plasma glucose concentration of 200 mg/dl (11.1 mmol) or more; a fasting glucose is more than 125 mg/dL, or 200 mg/dL or more at two hours after an oral 75-g glucose tolerance test, or hemoglobin A1c of 6.5% or higher. ADA's criteria for prediabetes is a fasting glucose of 100-125 mg/dL, or 140-199 mg/dL at two hours after an oral 75-g glucose tolerance test, or hemoglobin A1c of 5.7%-6.4%. In this study, diabetes mellitus was diagnosed if the HbA1c was 6.5% or higher. Known diabetics under dysglycemic treatment were labeled as diabetics. Prediabetes was diagnosed only if the HbA1c was 5.7% - 6.4% (39 - 46 mmol/mol).

3. RESULTS

Our patients ranged from the ages of 24 to 74 years. Of the 62 patients studied, there were 46 males and 16 females. 12 (8M; 4F) patients had HbA1c above 6.5 or were known diabetics. Of the remaining 50, 24(48%); (20M; 4F) had HbA1c in the prediabetic range, while 26 (52%); (18M; 8F) had HbA1c in the normal range. Of the total number of 62 patients, 24 (39%) were prediabetic.

4. DISCUSSION

4.1. Schizophrenia Statistics

Schizophrenia is a worldwide disease, with a prevalence of approximately 1%. It is the third leading cause of global disability in persons aged 15-44 years. It is responsible for 2.8 percent of the global burden of disability. (Health Organization, 2001) The clinical features and management of schizophrenia has been well studied. (APA, 2000; Sullivan et al, 2003; Woo et al, 2004) Patients with schizophrenia have a two to three fold higher mortality rate compared to the general population. (Laursen et al, 2007; Saha et al,

2007; Brown et al, 2010) Patients with schizophrenia have a higher rate of suicide and accidents. (Palmer et al, 2005) They also have unhealthy lifestyles. These include poor diet, lack of exercise and excessive smoking and alcohol intake. (Wildgust et al, 2010) They commonly have co-morbid substance abuse problems. (Foti et al, 2010) Schizophrenic patients also are more likely to be homeless or incarcerated, due to crimes, contributing to a further suboptimal lifestyle. (Fazel et al, 2009) Anti-psychotics also appear to contribute to this excess mortality due to adverse effects. (De et al, 2010) And finally, they appear to receive sub-optimal medical care. (Mitchell et al, 2010) Overall, patients with schizophrenia suffer from a 10-25 year reduction in life expectancy. They also account for approximately ten percent of America's totally and permanently disabled population. (Rupp et al, 1993)

4.2. Early Diagnosis

The high prevalence of prediabetes in the schizophrenia population is disturbing. Epidemiologic evidence suggests that the complications of diabetes begin early in the progression from normal glucose tolerance to frank diabetes. Early identification and treatment of persons with prediabetes have the potential to reduce or delay the progression to diabetes (Knowler et al, 2002; Dream, 2006; Li et al, 2008; Lindstrom et al, 2006; Gillies et al, 2007), and prevent or delay cardiovascular disease (Chiasson et al, 2003; Ratner et al, 2005) and microvascular disease (Dream, 2008)

4.3. Lifestyle Changes

Lifestyle changes are extremely important in preventing progression of prediabetes to overt diabetes mellitus. (Tuomilehto et al, 2001; Pan et al, 1997; Watanabe et al, 2003) The American Diabetic Association recommends that the treatment of choice for these patients should be lifestyle modification resulting in a 5-10% weight loss and incorporating physical activity of 30 min/day. The Diabetes Prevention Program study examined more than 3,200 overweight or obese adults with prediabetes and showed that lifestyle interventions, such as those taught in diabetes education programs, reduced the incidence of diabetes by 58% overall and by 71% in older adults. Lifestyle changes will also reduce other risk factors in this population, positively impacting mortality. (Wildgust et al, 2010) However, lifestyle changes may be difficult to enforce in a schizophrenia population.

4.4. Therapeutic Interventions

Therapeutic interventions have also been studied in this population to help preserve or restore normal glucose tolerance and insulin sensitivity. (Buchanan et al, 2002; Chiasson et al, 2002, DPPRG, 2002) Prediabetic subjects when treated with metformin, benefit from a 31% reduction in the development of diabetes mellitus. (Knowler et al, 2002) The American Association of Clinical Endocrinologists recommends that blood pressure be maintained at 130 systolic and 80 diastolic or below, with an ARB or an ACE as the first treatment choice. They also recommend low dose aspirin provided there are no GI contraindications. Lipid profile is also important in this population. It is recommended that LDL cholesterol levels of less than 100 mg/dl or non-HDL cholesterol of less than 130 mg/dl are targeted and achieved. (Alan et al, 2008) Prediabetics have abnormal apoA-1 and apolipoprotein B-100 metabolism, contributing to the acceleration of atherosclerosis (Watts et al, 2003) Therapeutic modulation of the lipid profile may therefore benefit patients with prediabetes. Impaired glucose tolerance patients may benefit more from fibrate treatment, whereas impaired fasting glucose patients may be better candidates for statin therapy (Krysiak et al, 2010).

4.5. Selection of Antipsychotic Medications

Antipsychotic medications are used in schizophrenics to treat the most severe psychiatric symptoms, such as hallucinations, paranoid thoughts, and delusions. Research shows that some of these medications may put patients at a higher risk of metabolic derangements, such as obesity and insulin resistance. (ADA, 2004; Spoelstra et al, 2004; Nasrallah et al, 2004) They may thus cause or worsen prediabetes. Newer antipsychotics, like clozapine and olanzapine, are associated with a higher risk of metabolic side effects than others, like aripiprazole and ziprasidone. (Lamberti et al, 2005; de Leon et al, 2005; Evans et al, 2005; Lamberti et al, 2006) The former drugs should be avoided in African-Americans as they have a higher propensity to develop weight gain and metabolic abnormalities. (Krakowski et al, 2009) The patients on clozapine and olanzapine should have their metabolic parameters closely monitored and if needed, switched to antipsychotic drugs with lower risk profiles. (Buckley et al, 2008; Morrato et al, 2009)

5. CONCLUSION

The findings of this study are alarming. Our study found that nearly one of every three patients with schizophrenia suffers from prediabetes. These findings are similar to those recently reported in a hospitalized schizophrenia population (Manu et al, 2011) Presence of prediabetes in almost 39% of the antipsychotic-treated schizophrenic patients suggests a huge and hidden metabolic epidemic in this population. The adverse contribution of antipsychotic drugs to this phenomenon needs to be studied further.

Lifestyle changes are important and strategies to incorporate these in this population need to be developed. Finally, guidelines for the initiation of metformin and lipid lowering medications are needed for the prediabetic schizophrenia population.

SUMMARY OF RESEARCH

- Schizophrenia patients experience poor lifestyles. They have higher rates of smoking, alcoholism, malnutrition and lack of exercise. They suffer from high rates of physical co-morbidity. These include hypertension, diabetes, lung disease and many others common ailments. As a result, they experience premature mortality.
- Our research shows that prediabetes is much more common in patients with schizophrenia when compared to the general population. This may be partly due to poor lifestyle, newer antipsychotic drugs and yet unknown factors specific to this population
- Prediabetics have an increased risk of progressing to type 2 diabetes. Prediabetic patients have a higher risk of developing cardiovascular and diabetes-related complications. Prediabetes is also associated with higher all-cause mortality..
- Interventions should include an improved diet, smoking cessation and regular exercise in these patients. Proper selection of anti-psychotic drugs may also help. The role of prophylactic initiation of metformin and/or fibrate or statin therapy needs to be considered in select patients.

DISCLOSURE STATEMENT

The author has no conflicts of interest to disclose.

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