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Schizophrenia and coronary artery disease

Risk factors should be monitored to ensure the burden of cardiovascular comorbidities in schizophrenic patients does not continue to rise.

ABSTRACT: The prevalence of schizophrenia, a chronic and debilitating disease, is increasing nationally. Although suicide and high-risk behaviors contribute to the mortality of people with schizophrenia, the leading cause of death in this vulnerable patient population is coronary artery disease. Unfortunately, schizophrenic patients are not receiving adequate medical treatment to prevent risk factor progression to metabolic syndrome and CAD, and if they do develop CAD they are undertreated and receive poor follow-up care. Initiatives are needed to ensure that the burden of CAD in schizophrenic patients is controlled and does not continue to rise. These initiatives include ongoing monitoring for risk factors, improved communication between psychiatrists and physicians, and community outreach support. A current approach to CAD monitoring in a Canadian inpatient psychiatric ward involves obtaining baseline values for fasting blood glucose and other measurements when a patient is admitted, and then referring the patient to a physician if three of the measurements are outside normal limits.

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Schizophrenia is a debilitating disease affecting 1% of Canadians,[1] with prevalence rates climbing.[2] Compared with the general population, people with schizophrenia have a risk of premature death that is 2 to 3 times higher.[3,4] Although suicide and high-risk behaviors contribute to mortality, coronary artery disease (CAD) is the leading cause of death[5,6] and accounts for 50% of mortality. While cardiovascular mortality rates are decreasing globally, they are increasing in people with schizophrenia,[5] likely due to underrecognition of cardiovascular-related diseases and risk factors.[7] Recent studies confirm that schizophrenic patients are likely to have risk factors related to CAD and take medications that may increase CAD risk, yet they are consistently undertreated. A current approach to CAD monitoring in a Canadian inpatient psychiatric ward includes screening for risk factors and metabolic syndrome.

Risk factors

Lifestyle factors such as smoking and physical inactivity have long been known to predispose vulnerable patients to the development of CAD. Smoking is associated with increased risk of diabetes mellitus (DM) and CAD,[8] and is significantly more common in people with schizophrenia. Compared with 25% of people in the general population, 75% of people with schizophrenia smoke. Physical inactivity is over 3 times greater in schizophrenics, with poor cardiorespiratory fitness being 2 times higher than in the general population.[9] As well as increasing CAD risk, these poor lifestyle choices increase the risk of developing metabolic syndrome.

Metabolic syndrome includes abdominal obesity, elevated blood pressure, impaired fasting blood glucose

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levels, elevated cholesterol, and hypertension. Demographic analysis of the CATIE study, the largest US trial evaluating psychopharmacological agents in the schizophrenic population, revealed metabolic syndrome prevalence to be 41% using the Adult Treatment Panel III and 43% using the American Heart Association definitions. Metabolic syndrome prevalence was 36% in schizophrenic males and 52% in schizophrenic females. In comparison, metabolic syndrome prevalence in the general population is 20% in males and 25% in females.[10]

In a Canadian population-based study, Bresee and colleagues found the overall prevalence of CAD to be 27% in the schizophrenia cohort compared with 17% in the general population (OR 1.76, CI = 1.72-1.81).[11] DM has been found to be almost twice as common as in the general population (10% vs 6%), while hypertension and dyslipidemia are also significantly more prevalent in those with schizophrenia. The increased number of risk factors in those with schizophrenia may contribute to the higher prevalence of cardiac disease in this population. Prevalence of acute coronary syndromes, arrhythmia, heart failure, and stroke were greater in those with schizophrenia than those without by values ranging from 1.43 to 2.17.[11]

CAD and metabolic syndrome risk factors are a clear case of "less is more": studies have shown that the relative risk of CAD increases as the number of metabolic syndrome risk factors increases.[12] The odds ratio (OR) for each of these risk factors ranges from around 1.2 to 2.2. When more than one factor is present the ORs are increased by more than an additive rate so that all five metabolic syndrome risk factors lead to an approximately sevenfold increased risk. Unfortunately, people with schizophrenia are more likely to have multiple risk factors and a higher chance of developing three or more. The ORs for having one, two, or three cardiovascular risk factors are 1.23, 1.14, and 1.43, respectively, while the OR for having less than one is 0.78.[11]

lence of CAD morbidity and mortality with the increased popularity of second-generation atypical antipsychotics (SGA). Atypical antipsychotics have gained favor in the medical community because of their lower

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Role of medications

Integral to the discussion of risk factors in schizophrenia is the role of medications used for treatment. Mitchell and colleagues studied the causal effect of antipsychotics (as a group including first- and second-generation agents) to risk factor development. They found that in early schizophrenia (unmedicated and first episode) all risk factors and metabolic abnormalities were significantly less common. After finding an overall rate of metabolic syndrome of 9.8% in unmedicated schizophrenic patients and 9.9% in first-episode patients, they saw the rate of metabolic syndrome rise drastically to 53.5% in chronically medicated patients.[13] Multi-episode, chronically treated schizophrenics were at highest risk for developing multiple CAD risk factors, including obesity (OR 4.43), diabetes (OR 1.99), dyslipidemia (OR 2.73), low high-density-lipoprotein cholesterol (OR 2.35), and hypertension (OR 1.36).

Recent publications from Canada,[14] the US,[15] and Denmark[16] have noted greater incidence and prevarisk for causing extrapyramidal motor control disabilities, such as parkinsonian-type disorders, rigidity, dystonia, and involuntary tremors.[17] In a Canadian population-based study, SGA drugs were used in the treatment of 80% of diagnosed schizophrenics in 2006 compared with only 50% in 2002.[18] Compared with first-generation antipsychotics, SGAs are associated with a 3 times higher incidence of developing metabolic syndrome.[19]

The question of which antipsychotic drug should be preferred for treatment of schizophrenia is controversial. Newcomer showed that among the SGAs, clozapine and olanzapine are associated with the highest risk of substantial weight gain (a risk similar to that of low-potency first-generation antipsychotics such as thioridazine or chlorpromazine), and an increased risk of diabetes and dyslipidemia.[20] Patel and colleagues showed that risperidone was associated with the smallest elevations in triglyceride and total cholesterol levels.[21] Importantly, patients receiving antipsychotic polytherapy rather than monotherapy have even higher

rates of metabolic syndrome and lipid markers of insulin resistance.[22] Studies show that comparing typical and atypical antipysychotics for risk of metabolic syndrome oversimplifies[23] the problem and that clinical judgment and informed patient preference are of utmost importance.

Along with medications, genetics may play a part. In 2013, Andreassen and colleagues identified 10 overlapping single nucleotide polymorphisms associated with schizophrenia and increased BMI, increased waist-to-hip ratio, increased systolic blood pressure, and abnormal lipids, which implies plausible causal genetics and shared mechanisms between schizophrenia and CAD risk factors. The majority of the identified loci were involved in lipid pathways, suggesting a strong relationship between schizophrenia and lipid levels.[24]

Barriers to care

Despite data regarding CAD risk, patients with schizophrenia are consistently undertreated. In one study, schizophrenic patients were 40% less likely to receive treatment for their comorbidities.[25] Undiagnosed comorbidities had nontreatment rates of 30% for DM, 62% for hypertension, and 88% for hyperlipidemia.[26] Even with an established CAD diagnosis, the revascularization rate was 47% less than in the general population. In a British schizophrenic population, 82% were prescribed beta-blockers, 51% given a statin,[27] and only 53% received follow-up with a cardiologist within 30 days of discharge. Not surprisingly, the risk of death within 30 days following discharge from hospital after admission for an acute coronary syndrome was 1.56 times higher in the schizophrenic population.[28] In the late 1990s, a Canadian database study found that patients with dyslipidemia and chronic psychiatric disease had poorer control of lipid levels than patients who did not have psychiatric disease.[25] Kurdyak and colleagues found recently that Canadian schizophrenic patients were more likely to die after an acute myocardial infarction, possibly due to less invasive management and inadequate follow-up with a cardiologist.[28]

Overcoming barriers

Obstacles to adequate treatment of CAD-related comorbidities in schizophrenia may include patient noncompliance and unwillingness to seek help, physician discomfort when treating patients with mental illness, and difficult-to-access health networks. At the very least, a schizophrenia diagnosis and treatment with second-generation antipsychotics should signal the need for attentive assessment of cardiovascular risk factors by way of metabolic monitoring.[29] Studies have shown that education can prevent the development and sequelae of metabolic syndrome even in the schizophrenic population. DM education in patients with schizophrenia, especially when it incorporates diet and exercise advice, can have a positive impact on weight reduction and a significant decrease in blood glucose levels.[30]

The Department of Psychiatry at St. Paul's Hospital has developed a screening program for CAD risk factors and metabolic syndrome. Upon admission, all new psychiatry patients undergo laboratory testing to obtain baseline values (fasting blood glucose, LDL-C, HDL-C, triglycerides), and nursing staff obtain blood pressure and waist circumference measurements. If three or more of the measurements obtained fall outside normal limits, a referral is made to the consulting family practice physician, who then determines how best to address these risk factors.

Summary

Schizophrenia is a chronic and debilitating disease that predisposes patients to coronary artery disease. The natural progression of schizophrenia, genetics, and the sequelae of treatment all increase the development of CAD risk factors. Unfortunately, schizophrenic patients are not receiving adequate medical treatment to prevent risk factor progression to metabolic syndrome and CAD, and if they do develop CAD they are undertreated and receive poor follow-up care. CAD is the leading cause of death in this vulnerable patient population.

Initiatives are needed to ensure that the burden of CAD in schizophrenic patients is controlled and does not continue to rise. These initiatives include ongoing monitoring for CAD risk factors, improved communication between psychiatrists and consulting or family physicians, and community outreach support. As well, further research is needed to identify the cardiometabolic effects of various antipsychotic medications.

Primary care practitioners and assertive community treatment teams are particularly well placed to ensure that CAD risk factors and CAD treatment are not overlooked. Clinicians should consider prescribing antipsychotics associated with a lower risk of metabolic side effects. They should also consider routine monitoring of metabolic parameters and begin patient education and behavioral and pharmacological interventions early. Weight gain begins soon after patients start antipsychotic therapy, so BMI should be included in a baseline risk profile. CAD risk in this vulnerable group of mentally ill patients needs to be taken seriously by patients and physicians alike.

Competing interests

None declared.

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