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Antipsychotics in Treatment of Schizophrenic Patients with Past Medical History of Coronary Artery Disease

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ABSTRACT

Antipsychotic use in schizophrenia has been linked with a myriad of negative cardiovascular outcomes including the recurrence of coronary artery disease. This article evaluates the pathological mechanisms that correlate the relationship between antipsychotic use in schizophrenia and coronary artery disease in a patient predisposed to the condition. The study hypothesizes that certain atypical antipsychotics can increase the risk of recurrence of CAD accompanied by the development of metabolic syndrome, diabetes mellitus, and lipid disorders in a chronic schizophrenia patient. Additionally, it is essential to address the problem of the knowledge gap due to insufficient data and limitations of the undertaken study group. Extending the research on specific disorders such as metabolic syndrome and exploring the topic of medication compliance with patients is vital. Lifestyle management and pharmacological intervention significantly reduce mortality and morbidity due to CAD in schizophrenia patients.

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Introduction

Schizophrenia is a chronic illness leading to profound functional and cognitive impairment. Schizophrenia affects approximately about 24 million people worldwide (32% of the population worldwide). In the US population alone, the prevalence is between 0.6%-1.9%. Multiple studies have shown that the prevalence of schizophrenia is equal in both males and females, but males in their early twenties tend to experience symptoms, whereas women experience in their late twenties or thirties. Schizophrenia is mainly thought of being a genetic disorder, but in reality there are studies that support the idea that the pathophysiology behind schizophrenia is a combination of genetic, environmental, and social factors. There are multiple theories that base the pathophysiology of schizophrenia with various either excess or deficiencies of neurotransmitters including dopamine, serotonin, glutamate, and gamma-aminobutyric acid (GABA). Symptoms of schizophrenia can be divided into positive symptoms, which include hallucinations, delusions, unusual thought process, disorganized speech, and bizarre behavior. Cognitive dysfunctions include reduced ability to comprehend, understand, and make plans and inattention. Negative symptoms include flat affect, apathy, anhedonia, and most commonly social withdrawal. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) the criteria for diagnosis requires ≥ 2 or more of the following active symptoms, including ≥ 1 from symptoms such as delusions, hallucinations which are often auditory, disorganized speech, catatonic behavior and negative symptoms. The active symptoms must be present for >6 month.

The treatment for schizophrenia is complex and can be divided into 2 categories: antipsychotics for the positive symptoms, which are more responsive, and nonpharmacological therapy such as

psychotherapy for negative symptoms. Negative symptoms often persist after treatment, despite resolution of positive symptoms. Antipsychotics are the first line of treatment in patients with schizophrenia and include typical, and atypical psychotics. The typical antipsychotics such as Haloperidol, fluphenazine, thioridazine, chlorpromazine, and pimozide are the high potency drugs and have more neurological side effect such as extrapyramidal symptoms (EPS) [1]. Of these, chlorpromazine, and thioridazine have a more potent antimuscarinic blockade and can lead to the side effect of muscarinic blockade such as dry mouth, constipation, and sedation. The most feared outcome with the use of typical antipsychotics is EPS. Acute dystonia, which occurs hours to days, is characterized by muscle spasms and pain, with stiffness. Days to months, akathisia or the compelling urge to move/inability to sit or stand still, follow by parkinsonism which is characterized by cogwheel rigidity, stiff gait, bradykinesia, and tremor. The most feared complication is Tardive dyskinesia, which presents months or years after being on a typical antipsychotic. Clinical features include involuntary movements of mouth, tongue, limbs, face, chorea movements, and repetitive chewing and lip smacking. For these reasons, treatment of schizophrenia has shifted towards atypical antipsychotic such as olanzapine, quetiapine, aripiprazole, lurasidone, ziprasidone, and risperidone. Most of the atypical antipsychotics have fewer EPS symptoms than typical antipsychotics, but all prolong the QT interval, cause metabolic syndrome and lead to increased risk of cardiovascular mortality, and hyperprolactinemia with risperidone. Clozapine is not recommended as the first line due to the adverse effect of agranulocytosis [2]. Clozapine is used for treatment-resistant schizophrenia, which decreases the rate of suicide. The treatment for negative symptoms has more effect with psychotherapy, which include supportive/counseling, personal and family therapy sessions, social skills, and possibly rehabilitation therapies for patients who fail trails. Studies have shown that group therapies may help patients improve their social functioning. Coronary artery disease also known as ischemic heart disease or coronary heart disease is a term for the buildup of plaque in the walls of the arteries leading to failure of the coronary blood supply to the cardiac muscle and surrounding tissue resulting in myocardial infarction. Risk factors for coronary artery disease include dyslipidemia, diabetes, arterial hypertension, obesity, smoking, and a sedentary lifestyle, as well as stress, older age, male gender, and a family history of CHD. Cardiovascular diseases (CVDs) are the leading cause of death in almost every region of the world. 1-4 According to the World Health Organization 2015 statistics, CVDs account for 17.7 million or 31% of all deaths worldwide.

An estimated 7.4 million of these deaths are due to coronary heart disease (CHD) [3]. Unhealthy diet and physical inactivity appear to be increased among schizophrenia patients and contribute to the high prevalence of obesity and diabetes mellitus. Antipsychotic medications also predispose to changes in weight, lipid abnormalities and glucose intolerance in schizophrenic patients. It is crucial to evaluate the risks and benefits of antipsychotic treatment in schizophrenia and its close link in mechanisms involved with progression of coronary artery disease. Hence, the objective of the study is to assess the effect of antipsychotics in schizophrenia patients with history of coronary artery disease [3].

Results

In total, we analyzed 12 studies examining the use of antipsychotics in patients with Schizophrenia and Coronary Artery Disease. We found that schizophrenia patients are more likely to smoke, be obese, have diabetes, and develop metabolic syndrome; at the same time, many first-generation (FGA) and second-generation antipsychotics (SGA) can cause excessive weight gain, dyslipidemia, metabolic syndrome, diabetes mellitus, and cardiovascular disorders together contributing to the high prevalence of coronary artery disease (CAD) among patients with chronic schizophrenia [4]. Even though some evidence showed no significant relationship between antipsychotics and CAD current research also indicates that CAD is under-diagnosed in this group, reason why this review supports a hypothesis suggesting that antipsychotics, specifically certain atypical antipsychotics such as olanzapine and quetiapine, may increase the risk of CAD recurrence in patients who have previously had CAD.

For this very reason, schizophrenic patients with a history of CAD or cardiovascular risk factors such as smoking, obesity, hypertension, or diabetes should be offered pharmaceutical intervention to reduce their risk and undergo ECG before starting any antipsychotics, as these have proven to be effective in these cases Also, more research should be conducted to explore the effects of antipsychotics in patients with CAD. Existing data is not enough to come to any strong conclusion [4].

Discussion

To avoid reiterating what has already been established in our results, we shall mainly touch upon the fact that there may, in fact be a correlation between CAD and schizophrenic patients using antipsychotics.

Moreover, if our established correlation does carry implications, they will have far-reaching effects in the daily practice of general physicians, psychiatrists as well as cardiologists. All three of these specialties will need to be aware of their patient's preexisting health conditions. For Psychiatrists, they will have to screen their patients for CAD before prescribing antipsychotics in order to reduce the chance of worsening the CAD [4]. If screening is not possible, the least they should do is properly study their medical records and establish whether CAD preexists in such patients. Special care should be taken to prescribe males as well as middle aged patients and beyond, since CAD tends to begin in this age group. Males usually have a later onset, and it is a well-established fact that they have a much higher risk of developing CAD compared to females; therefore, care should be taken when prescribing them. Patients with extreme cases of CAD should not be prescribed antipsychotics and should be put mainly on supportive treatment. But if treatment is necessary then they shall undergo concomitant treatment for their CAD, for which invasive and noninvasive procedures can both be considered. Also, care should be taken to prescribe only the antipsychotic with the least risk of metabolic syndrome. All the specialty doctors should also note the compliance of their patients regarding drug treatment for both schizophrenia and CAD.

A few suggestions also come to mind from this study. Since CAD is a specific part of metabolic syndrome, we can extrapolate and research on the correlation between antipsychotics and other features of metabolic syndrome, such as prevalence of diabetes, prevalence of blood disorders and so on [4]. Such specific data will help us establish a strong pattern. And from there on, a broader study could also be done where subjects can be tested mainly for metabolic syndrome, rather than its specific parts. However, data as of now would be academically inconclusive since 12 articles over 3 decades are not enough. New hypotheses need to be formed and fresh research should be conducted since there is a significant gap in knowledge here.

Some alternative explanations can also be considered for the results: It should be noted how there can be some compliance issues in people with preexisting CAD who later develop schizophrenia, owing to the flat affect and apathy associated with the disease. So what if the results could be better explained by patients simply not taking medication for their CAD, rather than it being the effect of their antipsychotic drug?

A limitation of this study is that in certain countries such as the USA, prevalence of obesity and diabetes is already very high in the population before the typical onset age of schizophrenia. Therefore, it cannot be said for sure whether the drugs merely exacerbate the preexisting condition or whether they induce it in the first place [5-10].

Conclusion

In conclusion, it is imperative to address the knowledge gap on this research otherwise, we're potentially putting significant part of population (geriatric as well as middle aged) at risk. If antipsychotics are necessary patients, lifestyle adjustments and accommodations will have to be prescribed by the psychiatrist, otherwise there could be a significant effect on mortality.

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