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Cardiovascular Considerations In Antipsychotic Use: An Editorial

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Introduction

Antipsychotic drugs are mainly used to treat schizophrenia and other psychotic disorders. There are three generations of these agents, with gradual improvement in clinical outcomes. However, adverse events are major obstacles and could lead to discontinuation of treatment [1]. These adverse reactions include, but are not limited to, mild sedation, parkinsonism, xerostomia, akathisia, oculogyric crisis, and life-threatening events (even sudden cardiac death) [2]. There is an increased risk of sudden cardiac death among those who receive antipsychotic agents. These rates are dose-related and, apart from that, are higher in those treated with second-generation antipsychotics compared to those treated with first-generation antipsychotics [3]. Antipsychotic cardiac toxicity is a term used for adverse cardiac events related to antipsychotic agents. Cardiac toxicity could present with different manifestations including heart rate changes, blood pressure alteration, electrocardiogram abnormalities, heart failure, myocarditis, ischemic heart diseases, ventricular hypertrophy, pulmonary thromboembolism, and sudden death [2].

Antipsychotic-related cardiac adverse events

Antipsychotic-related tachyarrhythmia has been attributed to the anticholinergic effects of these drugs. Tachycardia is more prevalent in patients receiving first-generation antipsychotics, especially chlorpromazine and thioridazine. Nonetheless, it has been reported that some second-generation antipsychotics accompany tachycardia (such as clozapine) [2, 4]. Bradycardia, on the other hand, is usually seen in treatment with second-generation

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antipsychotics and is more commonly seen in risperidone, quetiapine, and olanzapine [2]. Elderly patients are more susceptible to bradycardia and the symptoms tend to be more severe and even lead to arrest [5]. Likewise, elderly individuals are more susceptible to developing orthostatic hypotension when taking antipsychotic drugs [6]. The hypotensive properties of antipsychotic drugs are mainly attributed to α1-adrenergic inhibition potential [2]. This effect occurs more in first-generation antipsychotics and some of the second-generation agents (quetiapine, clozapine, and iloperidone) [2, 7]. Conversely, hypertension was reported in some patients; both in systolic and diastolic blood pressure [8].

Electrophysiological alterations due to antipsychotic treatment are relatively common side effects that could result in devastating outcomes. Antipsychotic-induced repolarization aberrancies present with QT prolongation and are principally related to potassium current imbalance across the cellular membrane [9]. Haloperidol, pimozide, sertindole, ziprasidone, amisulpride, chlorprothixene, clozapine, flupentixol, levomepromazine, paliperidone, quetiapine, risperidone, and sulpiride have an increased risk of QT prolongation. Torsades de pointes, left and right bundle-branch block, and atrioventricular branch block are other conduction disorders that are rare adverse events of antipsychotic drugs that could result in sudden cardiac death [2, 10].

Heart failure is another devastating consequence of antipsychotics, which could be caused by other side effects of these agents, including myocarditis and cardiomyopathy [2]. Clozapine is the main drug associated with myocarditis and cardiomyopathy. Acute myocarditis related to Clozapine has a death rate of around 25% [11]. The incidence of dilated cardiomyopathy is around 5:1 compared to the general population [11]. Additionally, antipsychotics have a high affinity for 5-HT2A receptors and, therefore, increase platelet aggravation. This makes these drugs (specifically chlorpromazine, thioridazine, and clozapine) risk factors for the development of pulmonary thromboembolism [2].

Ischemic heart diseases (IHD) are the main cause of death among patients with schizophrenia, with higher amounts in the female population. Clozapine, quetiapine, olanzapine, and thioridazine are antipsychotic agents with the highest IHD-related mortality rates [12]. Similar to the mechanism of pulmonary thromboembolism, antipsychotic-induced IHD is attributed to the inhibition of 5HT2A receptors [2].

There are limited numbers of studies assessing cardiac monitoring of patients who receive antipsychotic agents, with most of them having small sample sizes [2]. The measurement of creatine kinase, c-reactive protein, troponin, and brain natriuretic peptide (BNP), as well as electrocardiography and echocardiography (ECG), are the most common tools used to study cardiac injury in these subjects. Additionally, wrist-worn monitoring devices have been developed that can examine biometrics in real-time. Furthermore, implantable cardioverter defibrillators could be implemented in high-risk populations treated with antipsychotics [13].

Treatment and future direction

Drug discontinuation or replacement should be considered in some patients; however, it is not feasible in most cases. Medications to relieve symptoms are applicable management options for these patients. For example, beta-blockers are often used to decrease symptoms such as tachycardia. There are some reports on the role of cannabinoid receptors in antipsychotic-related cardiac adverse events, highlighting a potential therapeutic approach that needs to be investigated [14].

Third-generation antipsychotics have emerged as novel and efficacious medications that are safer than first- and second-generation antipsychotics [15]. Among the recently developed antipsychotics, roliperidone is noted for having the lowest incidence of cardiovascular adverse events, offering a potential therapeutic approach to mitigate the drawbacks of previous generations. However, further investigations are necessary to evaluate their effectiveness and safety profile.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this article.

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Conflict of Interests

The authors have no conflict of interest to declare.

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