A Review of Antipsychotic Medications on Hypercoagulability in Schizophrenia: Pathophysiology, Risks, and Management Strategies

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Abstract

Background: Schizophrenia is a severe psychiatric disorder with a global prevalence of 0.3-0.7%, characterized by symptoms like delusions, hallucinations, and cognitive deficits. Treatment typically involves antipsychotic medications, which are divided into typical (first-generation) and atypical (second-generation) categories. While effective for symptom control, these medications are associated with a range of adverse effects, including metabolic disturbances and hypercoagulability, which increase the risk of thromboembolic events. This review explores the mechanisms linking antipsychotic treatment to coagulation disorders and identifies strategies to mitigate these risks. Methods: A comprehensive review of existing literature was conducted, focusing on the pathophysiological mechanisms by which antipsychotics impact coagulation pathways. Data were drawn from clinical studies, case reports, and meta-analyses that evaluated the relationship between antipsychotic use and the occurrence of thromboembolic events. Mechanisms such as endothelial dysfunction, platelet activation, and chronic inflammation were explored. Results: Antipsychotic medications, particularly atypical antipsychotics like clozapine, olanzapine, and risperidone, are associated with significant metabolic disturbances, including weight gain, insulin resistance, and dyslipidemia, which predispose patients to a pro-thrombotic state. Elevated levels of inflammatory markers and endothelial dysfunction further exacerbate thromboembolic risks. Clinical evidence confirms an increased incidence of venous thromboembolism (VTE) and ischemic stroke among patients on antipsychotic medications, with SGAs showing a higher thromboembolic risk compared to FGAs. Conclusion: Schizophrenia patients treated with antipsychotic medications are at an elevated risk of coagulation disorders, particularly thromboembolic events. Clinicians should monitor metabolic and coagulation parameters and adopt a holistic approach to treatment that includes lifestyle interventions and pharmacological management of metabolic disturbances. Further research is needed to explore targeted therapies that can reduce thromboembolic risks associated with antipsychotic treatment.

Keywords: Antipsychotic Drug; Hypercoagulability; Schizophrenia; Venous Thromboembolism; Metabolic Syndrome

Significance | Understanding antipsychotic-induced hypercoagulability in schizophrenia is crucial for reducing thromboembolic risks and improving patient outcomes.

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Introduction

Schizophrenia is a chronic and severe mental disorder that profoundly impacts an individual's ability to think, feel, and behave.

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Its hallmark symptoms include delusions, hallucinations, and cognitive deficits, making it a significant public health issue worldwide. The global prevalence of schizophrenia is estimated to range between 0.3% and 0.7%, with onset typically occurring during late adolescence or early adulthood (World Health Organization, 2021). Antipsychotic medications represent the cornerstone of schizophrenia treatment and are classified into two main categories: typical antipsychotics (first-generation) and atypical antipsychotics (second-generation). Typical antipsychotics, such as haloperidol and chlorpromazine, primarily act by blocking dopamine D2 receptors, effectively alleviating positive symptoms like hallucinations and delusions. However, they are associated with considerable adverse effects, including extrapyramidal symptoms (EPS) and heightened cardiovascular risks (Kane & Correll, 2010). In contrast, atypical antipsychotics, such as clozapine, olanzapine, and risperidone, target both dopamine and serotonin receptors, providing a broader spectrum of efficacy. These agents exhibit reduced motor side effects but are linked to significant metabolic complications, including weight gain, dyslipidemia, and insulin resistance, all of which elevate the risk of cardiovascular and thromboembolic events (De Hert et al., 2012).

Hypercoagulability, characterized by an abnormal increase in blood clotting propensity, poses a serious clinical concern in individuals with schizophrenia. This condition can lead to adverse outcomes such as venous thromboembolism (VTE), stroke, and myocardial infarction. Several factors contribute to hypercoagulability in this population, including the intrinsic effects of schizophrenia, lifestyle factors like smoking and physical inactivity, and side effects of antipsychotic drugs (Mitchell et al., 2013). Additionally, schizophrenia has been linked to increased inflammatory markers, endothelial dysfunction, and a heightened risk of metabolic syndrome, further amplifying the pro-thrombotic state (Meyer & Stahl, 2009).

The metabolic abnormalities induced by atypical antipsychotics exacerbate these risks. Weight gain, insulin resistance, and hyperlipidemia collectively predispose patients to thromboembolic events (De Hert et al., 2012). Consequently, a comprehensive understanding of the relationship between antipsychotic treatment and hypercoagulability is essential for enhancing the safety and efficacy of schizophrenia management.

In this review, we investigate the mechanisms by which antipsychotic medications influence coagulation pathways, analyze clinical evidence linking these drugs to thromboembolic events, and identify strategies for mitigating associated risks. By synthesizing current knowledge, this review seeks to provide insights into optimizing treatment approaches and addressing gaps in research and clinical care.

2. Pathophysiology of Schizophrenia and Coagulation Disorders

Schizophrenia is a multifaceted psychiatric condition characterized by disruptions in thought processes, emotional regulation, and social functioning. While primarily recognized for its mental health manifestations, emerging evidence highlights its association with systemic physiological complications, particularly coagulation disorders and cardiovascular risks. These comorbidities significantly impact morbidity and mortality among individuals with schizophrenia, emphasizing the necessity for a broader understanding of its pathophysiology.

A pivotal mechanism linking schizophrenia to coagulation disorders is chronic low-grade inflammation, a hallmark of the disorder. Elevated levels of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and C-reactive protein (CRP) have been consistently observed in schizophrenia patients. These inflammatory markers disrupt endothelial function, promoting a pro-thrombotic state through increased tissue factor expression, platelet activation, and imbalances in coagulation pathways (Fernandes et al., 2016). Additionally, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, frequently observed in schizophrenia, results in hypercortisolemia. Elevated cortisol levels contribute to metabolic disturbances, including insulin resistance and visceral fat deposition, which are associated with endothelial dysfunction and heightened thromboembolic risks (Bremmer et al., 2008).

Neuroinflammation in schizophrenia extends beyond the central nervous system, affecting peripheral vascular health. Pro-inflammatory cytokines impair endothelial cells, reducing their anticoagulant properties. Dysfunctional endothelial cells express higher levels of von Willebrand factor (vWF) and tissue factor, key mediators of clot formation (von Känel & Dimsdale, 2002). Furthermore, elevated homocysteine levels, commonly linked to poor nutrition, smoking, and side effects of antipsychotic medications, exacerbate endothelial damage and hypercoagulability. Hyperhomocysteinemia significantly increases the risk of deep vein thrombosis and other thromboembolic events, presenting a notable concern for schizophrenia patients (Muntjewerff et al., 2006).

Metabolic syndrome—characterized by obesity, insulin resistance, dyslipidemia, and hypertension—is prevalent in schizophrenia, particularly among those treated with atypical antipsychotics. This syndrome independently and collectively amplifies thrombotic risks. Central adiposity is associated with elevated plasminogen activator inhibitor-1 (PAI-1), which hinders fibrinolysis and stabilizes clots (American Diabetes Association et al., 2004). Insulin resistance contributes to endothelial dysfunction and heightened platelet reactivity, compounding coagulation risks (McEvoy et al., 2005). Lifestyle factors such as physical inactivity, smoking, and poor dietary habits further exacerbate these risks, underscoring the

interplay between behavioral and biological factors in schizophrenia-related hypercoagulability.

Antipsychotic medications, both typical and atypical, also contribute to the heightened risk of coagulation disorders in schizophrenia patients. First-generation antipsychotics are associated with sedation and immobility, leading to venous stasis, a well-known risk factor for venous thromboembolism (VTE). Additionally, these medications have anticholinergic effects, which impair vascular tone and endothelial function (Ray et al., 2009). Second-generation antipsychotics, while often preferred for their improved psychiatric efficacy, are linked to metabolic disturbances such as obesity and insulin resistance. Medications like clozapine have been reported to increase platelet activation, further enhancing thrombosis risk (Parker et al., 2010).

Given these multifactorial risks, clinicians must adopt a comprehensive approach to managing schizophrenia patients. Routine monitoring of inflammatory markers, metabolic parameters, and coagulation profiles is critical. Preventive strategies, including lifestyle modifications and early interventions for metabolic disturbances, can mitigate risks and improve overall outcomes. Balancing the psychiatric benefits of antipsychotics with their systemic effects remains a cornerstone of optimal care.

Schizophrenia's association with coagulation disorders underscores the importance of viewing the condition through a holistic lens. Addressing both psychiatric and systemic health challenges is essential for reducing the substantial burden of morbidity and mortality. Further research into the interplay between schizophrenia and coagulation pathways can pave the way for targeted therapies, enhancing the quality of life for affected individuals.

3. Mechanism of Action of Antipsychotics and Their Effects on Coagulation

Typical antipsychotics, also known as first-generation antipsychotics (FGAs), have long been used as the cornerstone of schizophrenia treatment. These medications, such as haloperidol, chlorpromazine, and fluphenazine, primarily work by blocking dopamine D2 receptors in the brain. This mechanism effectively reduces positive symptoms like hallucinations and delusions but often causes significant side effects, including extrapyramidal symptoms (EPS) and cardiovascular complications (De Hert et al., 2012).

The impact of FGAs on coagulation, while indirect, is clinically relevant. Sedation and immobilization, common side effects, lead to venous stasis, a critical factor for venous thromboembolism (VTE). Reduced mobility diminishes blood flow in veins, increasing the risk of clot formation, particularly in the lower extremities. Patients on high doses of FGAs are at an increased risk of developing deep vein thrombosis (DVT) and pulmonary embolism (PE) (Parker et al., 2010). Additionally, FGAs' anticholinergic properties can impair vascular tone and contribute to endothelial dysfunction, reducing the body's natural anticoagulant efficiency. Although FGAs do not directly alter coagulation pathways, their combined effects significantly elevate thromboembolic risks in long-term use (Mitchell et al., 2013).

In contrast, atypical antipsychotics or second-generation antipsychotics (SGAs) include medications like olanzapine, risperidone, quetiapine, and clozapine. SGAs target both dopamine D2 and serotonin 5-HT2A receptors, which broadens their efficacy and minimizes motor side effects. They are effective in treating both positive and negative symptoms of schizophrenia. However, SGAs are linked to metabolic side effects that increase pro-thrombotic risks (Meyer & Stahl, 2009).

SGAs, particularly olanzapine and clozapine, are associated with weight gain, insulin resistance, and dyslipidemia, which directly contribute to endothelial dysfunction and hypercoagulability. Central obesity exacerbates this risk by promoting the release of pro-inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which enhance platelet aggregation and activate the coagulation cascade (De Hert et al., 2012). Clozapine, in particular, is linked to higher incidences of VTE compared to other SGAs, possibly due to its effects on platelet activation and elevated prothrombin fragment levels (Hagg et al., 2000). Additionally, clozapine has been associated with myocarditis, further complicating cardiovascular health (Haas et al., 2007).

3.1 The metabolic side effects of SGAs include:

Weight Gain and Obesity: SGAs like olanzapine and clozapine frequently cause significant weight gain, particularly visceral fat accumulation. This type of obesity is linked to increased levels of plasminogen activator inhibitor-1 (PAI-1), which inhibits fibrinolysis and promotes clot formation. Chronic low-grade inflammation caused by obesity further increases thrombosis risks (Goff et al., 2005).

Insulin Resistance and Hyperglycemia: SGAs often induce insulin resistance, which leads to hyperglycemia and sometimes type 2 diabetes mellitus (T2DM). Insulin resistance and hyperglycemia cause endothelial dysfunction and increased platelet reactivity, which are significant thromboembolic risk factors. Hyperglycemia also facilitates advanced glycation end-product (AGE) formation, which damages the endothelium and encourages coagulation (Kessing et al., 2010).

Dyslipidemia: Dyslipidemia, marked by elevated triglycerides and reduced high-density lipoprotein (HDL) cholesterol, is another common side effect of SGAs. It contributes to atherosclerosis, raising the risk of arterial thrombosis, including ischemic stroke and myocardial infarction (Solomon & Majumdar, 2009).

These metabolic disturbances create a pro-thrombotic state, making patients more susceptible to coagulation disorders. Therefore, managing these risks through regular monitoring, lifestyle changes, and pharmacological interventions is critical for reducing thromboembolic risks in patients with schizophrenia.

4. Evidence from Clinical Studies

Several studies have investigated the connection between antipsychotic medications and the risk of hypercoagulability or thromboembolic events in schizophrenia patients. Research consistently shows that antipsychotic use, especially second-generation antipsychotics (SGAs), increases the likelihood of developing coagulation disorders like venous thromboembolism (VTE) and stroke. One meta-analysis of observational studies found a significant association between antipsychotic use and thromboembolic risk, showing that patients using these drugs had a 1.5 to 2-fold higher risk of developing VTE compared to non-users. This risk was particularly pronounced during the first three months of treatment, suggesting an acute pro-thrombotic effect early in therapy (Sandhu et al., 2009).

Markers of hypercoagulability, such as elevated levels of D-dimer, fibrinogen, and prothrombin fragments, have been observed in schizophrenia patients on long-term antipsychotic treatment. These markers, which reflect active clot formation and breakdown, are significantly elevated in patients taking SGAs, pointing to a heightened risk of thromboembolic events (Desai & Grossberg, 2005). Comparative studies between first-generation (typical) and second-generation (atypical) antipsychotics suggest that SGAs are more strongly linked to metabolic disturbances, contributing to higher thromboembolic risk. For instance, a large cohort study comparing haloperidol (a typical antipsychotic) and olanzapine (an atypical antipsychotic) revealed that olanzapine-treated patients had a higher incidence of VTE and ischemic stroke. The authors attributed this to olanzapine-induced weight gain, insulin resistance, and dyslipidemia, which promote a pro-thrombotic state (Haas et al., 2007).

Similarly, a case-control study evaluating thromboembolic risks with clozapine (an atypical antipsychotic) and haloperidol found clozapine to be associated with a higher rate of VTE, including deep vein thrombosis (DVT) and pulmonary embolism (PE). Clozapine's effects on platelet activation and inflammatory processes were identified as contributing factors to this heightened risk (Hagg et al., 2000).

Population-based studies have provided additional evidence of the thromboembolic risks linked to antipsychotic medications. A large-scale retrospective cohort study conducted in the United Kingdom examined electronic health records of over 100,000 patients on antipsychotics. This study found that both typical and atypical antipsychotics increased VTE risk, with atypical agents like quetiapine and risperidone showing a higher incidence of thromboembolic events. Additionally, the study highlighted a dose-dependent relationship, with higher doses correlating with greater VTE risk (De Hert et al., 2011).

Case reports further support these findings, documenting stroke and other coagulation-related disorders in patients on specific antipsychotic medications. A notable case series reported multiple ischemic strokes in elderly patients receiving risperidone, leading to increased scrutiny of antipsychotic use in this population (Manu et al., 2013). Regulatory agencies, including the U.S. Food and Drug Administration (FDA), have issued warnings about the increased risk of stroke and mortality in elderly patients with dementia-related psychosis treated with antipsychotics. Similarly, case reports have highlighted clozapine-induced thromboembolism, including rare but fatal cases of pulmonary embolism. Although the mechanism remains unclear, clozapine has been linked to platelet activation and elevated pro-inflammatory cytokines, contributing to its thromboembolic potential (Millar et al., 2010).

Despite strong evidence linking antipsychotics to thromboembolic events, significant gaps remain in the literature. Most data come from retrospective or observational studies, limiting the ability to establish causation. Few studies have prospectively monitored the long-term effects of antipsychotics on coagulation markers, and the direct effects of these drugs on coagulation pathways are underexplored. Future research should focus on prospective cohort studies monitoring markers like D-dimer, fibrinogen, and plasminogen activator inhibitor-1 (PAI-1) in patients treated with different classes of antipsychotics. Randomized controlled trials (RCTs) are also needed to determine whether interventions such as antithrombotic prophylaxis or metabolic management can reduce thromboembolic risks associated with antipsychotic therapy.

5. Potential Mechanisms Underlying Hypercoagulability in Antipsychotic Use

Antipsychotic medications, particularly second-generation antipsychotics (SGAs) like olanzapine and clozapine, are associated with hypercoagulability, which increases the risk of blood clot formation (Figure 1). This condition involves endothelial dysfunction, platelet activation, and systemic inflammation, all of which contribute to heightened thrombotic risks.

Endothelial cells lining blood vessels play a critical role in maintaining vascular health by regulating blood flow and preventing clot formation. When these cells become dysfunctional, the balance between pro-thrombotic and anticoagulant factors shifts, favoring clot formation. Antipsychotics can induce endothelial dysfunction through oxidative stress, which generates reactive oxygen species (ROS) harmful to endothelial cells. This oxidative damage impairs nitric oxide (NO) production, a molecule essential for vasodilation and inhibition of platelet aggregation.

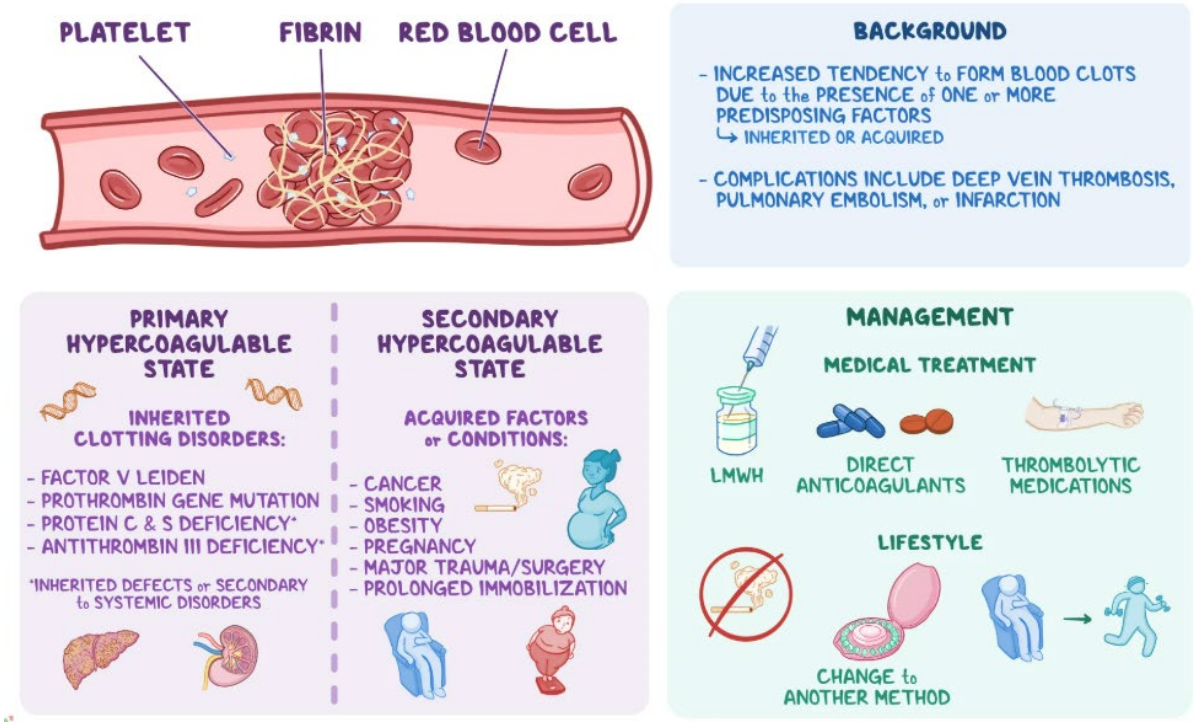

Figure 1. Hypercoagulable states, or thrombophilias, increase the risk of abnormal blood clot formation due to inherited or acquired factors. This infographic illustrates the causes, mechanisms, symptoms, and treatment strategies, highlighting primary disorders like factor V Leiden and secondary factors such as cancer, pregnancy, and autoimmune conditions like antiphospholipid syndrome.

Reduced NO availability leads to vasoconstriction and increased platelet adherence, promoting a pro-thrombotic state (Stubbs et al., 2015).

Metabolic disturbances caused by antipsychotics exacerbate endothelial dysfunction. Conditions such as insulin resistance and dyslipidemia increase the formation of advanced glycation end-products (AGEs) and the accumulation of low-density lipoprotein (LDL) in blood vessels, damaging the endothelium. This damage promotes the expression of adhesion molecules like P-selectin and E-selectin, facilitating platelet-endothelial interactions and clot formation (Leucht et al., 2013).

Platelet activation also plays a significant role in hypercoagulability. While platelets are essential for hemostasis, their hyperactivity can lead to pathological clot formation and increased risks of venous thromboembolism (VTE) and stroke. Antipsychotics, particularly clozapine, elevate levels of soluble P-selectin, a marker of platelet activation, and platelet-derived microparticles, which promote coagulation. Clozapine's effects on platelet activation may occur directly or via inflammatory pathways (Saha et al., 2007).

Metabolic conditions like obesity and insulin resistance, frequently induced by antipsychotics, further heighten platelet reactivity. Visceral fat releases pro-inflammatory cytokines such as interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α), which enhance platelet aggregation. Insulin resistance also increases plasminogen activator inhibitor-1 (PAI-1) levels, impairing the body's ability to dissolve clots and sustaining a pro-thrombotic environment (Tiihonen et al., 2017).

Systemic inflammation is another central contributor to hypercoagulability. Inflammatory responses activate endothelial cells, platelets, and the coagulation system, driving clot formation. Cytokines such as IL-6, TNF-α, and C-reactive protein (CRP) stimulate tissue factor expression on endothelial cells and monocytes, triggering the coagulation cascade. Antipsychotics, especially SGAs, are linked to increased levels of these pro-inflammatory cytokines, reflecting chronic low-grade inflammation. This inflammation not only promotes coagulation but also exacerbates endothelial dysfunction and platelet activation, creating a feedback loop that heightens thrombotic risk (Howes et al., 2017).

The interplay between metabolic syndrome and inflammation further underscores the pro-thrombotic risks of antipsychotics. Obesity, dyslipidemia, and insulin resistance—common side effects of these medications—are associated with increased adipokine release from adipose tissue, perpetuating systemic inflammation. This chronic inflammatory state contributes to both venous and arterial thrombosis, complicating the management of schizophrenia patients on long-term antipsychotic therapy (Haddad & Sharma, 2007).

Understanding the mechanisms linking antipsychotics to hypercoagulability is crucial for mitigating thrombotic risks in patients with schizophrenia. Clinicians should monitor metabolic and inflammatory markers carefully and implement preventive strategies such as lifestyle interventions and adjunctive therapies. Future research should focus on identifying targeted interventions to address the multifactorial pathways contributing to antipsychotic-induced hypercoagulability.

6. Management of Hypercoagulability in Schizophrenia Patients

The management of hypercoagulability in schizophrenia patients receiving antipsychotic treatment requires a comprehensive and individualized approach. These patients face elevated risks of thromboembolic events, including venous thromboembolism (VTE), deep vein thrombosis (DVT), and stroke. This necessitates integrating pharmacologic and non-pharmacologic strategies to mitigate complications. The association between antipsychotic medications and pro-thrombotic states is well-documented, with factors such as metabolic disturbances, endothelial dysfunction, platelet activation, and systemic inflammation contributing to this risk (De Hert et al., 2012; Mitchell et al., 2013). Tailored interventions based on patient-specific risk factors and clinical presentations are essential.

Currently, schizophrenia-specific guidelines for managing hypercoagulability in patients on antipsychotic therapy are lacking. General thrombosis management frameworks from cardiology and hematology, such as the American College of Chest Physicians (ACCP) guidelines, can be adapted to this population (ACCP, 2012). Clinical strategies should focus on risk stratification, coagulation marker monitoring, and antithrombotic prophylaxis for high-risk patients.

6.1 Risk Stratification

Effective risk stratification is critical for identifying patients at high risk of thromboembolic events. Factors such as older age, obesity, smoking, physical inactivity, and metabolic syndrome must be evaluated (De Hert et al., 2012). Second-generation antipsychotics (SGAs), particularly olanzapine and clozapine, are associated with increased metabolic disturbances, necessitating closer monitoring (Mitchell et al., 2013). Patients with prior thrombosis, stroke, or cardiovascular disease represent high-risk groups requiring aggressive management (Haddad & Sharma, 2007).

6.2 Antithrombotic Prophylaxis

Antithrombotic prophylaxis is central to managing hypercoagulability in high-risk patients. The ACCP guidelines recommend low-dose aspirin or low-molecular-weight heparin (LMWH) for VTE prevention in high-risk populations (ACCP, 2012). Decisions to initiate antithrombotic therapy should balance bleeding risks against clot prevention benefits, emphasizing individualized care.

6.3 Low-Dose Aspirin

Low-dose aspirin (81-100 mg daily) reduces arterial thrombosis risk, especially in patients with metabolic syndrome or cardiovascular disease. While its role in VTE prevention is less established, it may benefit schizophrenia patients on SGAs who present with dyslipidemia or insulin resistance (Haddad & Sharma, 2007).

6.4 Low-Molecular-Weight Heparin

LMWH, such as enoxaparin, is effective for preventing VTE in high-risk patients, including those immobilized or with a history of VTE. Compared to unfractionated heparin, LMWH has a better safety profile, with lower bleeding risks and easier administration. It is particularly useful during hospitalization or extended bed rest (Millar et al., 2010).

6.5 Direct Oral Anticoagulants (DOACs)

DOACs, including apixaban and rivaroxaban, are effective in preventing venous and arterial thromboembolism. However, their use requires careful consideration of potential drug-drug interactions with antipsychotics. Regular renal and hepatic function monitoring is essential for patients on DOACs (Hor & Taylor, 2010).

6.6 Monitoring Coagulation Markers

Routine monitoring of coagulation markers helps identify patients at increased risk of thromboembolism. Elevated biomarkers such as D-dimer, fibrinogen, and prothrombin fragments can indicate ongoing clot formation (Meyer & Stahl, 2009). Regular laboratory assessments of these markers in patients on antipsychotics like clozapine or olanzapine enable early detection and intervention (Millar et al., 2010).

6.7 Non-Pharmacologic Interventions

Non-pharmacologic strategies, including lifestyle modifications, are vital for reducing hypercoagulability risks. The metabolic side effects of antipsychotics, such as weight gain, insulin resistance, and dyslipidemia, significantly contribute to hypercoagulability (De Hert et al., 2012). Addressing these factors through diet, exercise, smoking cessation, and weight management is crucial.

6.8 Dietary Modification

A heart-healthy diet is foundational for managing metabolic syndrome. Patients should consume diets rich in fruits, vegetables, whole grains, and lean proteins while limiting saturated fats, trans fats, and refined sugars. Omega-3 fatty acids, found in fatty fish, may reduce platelet aggregation and systemic inflammation, providing additional anticoagulant benefits (Protopopova et al., 2019). Lowering sodium intake can also help control blood pressure, further decreasing thromboembolic risk.

6.9 Physical Activity

Regular aerobic exercise improves endothelial function, supports weight management, and enhances insulin sensitivity. Moderate-intensity activities, such as walking or cycling for at least 150 minutes per week, can yield significant cardiovascular and metabolic health benefits. Encouraging schizophrenia patients to engage in consistent physical activity is essential (Stubbs et al., 2015).

6.10 Smoking Cessation

Smoking is a well-documented risk factor for hypercoagulability and metabolic syndrome. Providing resources and support for smoking cessation can significantly reduce thrombotic and cardiovascular risks. Smoking cessation programs tailored to individuals with schizophrenia may improve adherence and outcomes (Mitchell & Lord, 2012).

6.11 Weight Management

Weight management is critical for minimizing thromboembolic risks. Patients should have access to dietary counseling and weight management programs, particularly those on SGAs, which are associated with significant weight gain. Addressing antipsychotic-induced metabolic side effects through weight management can significantly reduce hypercoagulability risk (Haddad & Sharma, 2007).

6.12 Integrated Care Strategies

Managing hypercoagulability in schizophrenia patients requires integrating pharmacologic and non-pharmacologic strategies into routine care. Clinicians should prioritize risk stratification, ensuring high-risk patients receive appropriate antithrombotic prophylaxis and are regularly monitored for coagulation abnormalities. Lifestyle interventions, including diet, exercise, and smoking cessation, should be emphasized as complementary strategies to reduce thromboembolic risks. A comprehensive approach to addressing these factors allows for safer long-term management of schizophrenia and mitigates complications associated with antipsychotic treatment.

7. Conclusion

In conclusion, while antipsychotic drugs remain essential in managing schizophrenia, they may contribute to a hypercoagulable state, increasing the risk of thromboembolic events. Schizophrenia itself is linked to systemic inflammation and metabolic disturbances, which can be further exacerbated by antipsychotics. The mechanisms driving these risks include endothelial dysfunction, platelet activation, and inflammation. Clinical studies suggest an elevated incidence of venous thromboembolism and stroke in patients receiving antipsychotic treatment. Therefore, clinicians must adopt a balanced approach in prescribing antipsychotics, incorporating regular coagulation monitoring and lifestyle modifications to mitigate the thrombotic risks, while prioritizing the psychiatric benefits for patients.

Author contributions

D.H., D.A., and M.A. contributed significantly to the research, drafting, and revision of the manuscript. D.H. conceptualized and designed the study. D.A. was responsible for data collection and analysis. M.A. contributed to the interpretation of the results and manuscript editing. All authors reviewed and approved the final manuscript.

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Competing financial interests

The authors have no conflict of interest.

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