



SIDE EFFECTS OF ANTIPLATELET DRUGS IN ADULTS

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Abstract. Antiplatelet drugs are cornerstone agents in the prevention and management of cardiovascular and cerebrovascular diseases. They play a crucial role in reducing thrombotic events such as myocardial infarction, ischemic stroke, and peripheral arterial disease by inhibiting platelet aggregation through various biochemical pathways. However, these life-saving medications are associated with a spectrum of adverse effects that range from mild gastrointestinal discomfort to severe bleeding and hematologic complications. This article provides a detailed overview of the mechanisms, clinical manifestations, and pathophysiological basis of antiplatelet drug-related side effects in adults. The discussion encompasses both traditional agents such as aspirin and clopidogrel and newer drugs including prasugrel, ticagrelor, and glycoprotein IIb/IIIa inhibitors. Strategies for minimizing adverse reactions through personalized pharmacotherapy, drug monitoring, and risk stratification are also examined.

Keywords: antiplatelet therapy, bleeding, aspirin, clopidogrel, thrombocytopenia, gastrointestinal toxicity, pharmacovigilance.

INTRODUCTION

Antiplatelet drugs occupy a central place in the prevention of thromboembolic events among adults with cardiovascular and cerebrovascular disease. By interfering with platelet activation, adhesion, and aggregation, these drugs reduce the risk of arterial thrombosis that underlies conditions such as myocardial infarction, ischemic stroke, and unstable angina. Yet, the pharmacological mechanisms that make antiplatelet drugs so effective are also responsible for their potential adverse effects. The inhibition of platelet function, though desirable in preventing clot formation, inherently increases the risk of bleeding, both overt and occult. Additionally, systemic exposure to these agents can affect multiple organ systems, leading to gastrointestinal, hematologic, renal, dermatologic, and, in rare cases, immunologic complications [1].

Understanding the side effects of antiplatelet drugs requires an appreciation of their pharmacodynamics and pharmacokinetics. While all antiplatelet agents share a common therapeutic objective—reducing platelet aggregation—they differ in their



sites and mechanisms of action. Aspirin irreversibly inhibits cyclooxygenase (COX-1), suppressing thromboxane A₂ synthesis, while P2Y₁₂ receptor inhibitors such as clopidogrel, prasugrel, and ticagrelor block adenosine diphosphate (ADP)-mediated platelet activation. Glycoprotein IIb/IIIa inhibitors (abciximab, eptifibatide, tirofiban) directly block the final common pathway of platelet aggregation. Each class thus presents a unique pharmacological profile and distinct spectrum of side effects, influenced by factors such as age, comorbidities, genetic polymorphisms, and concomitant medications.

MATERIALS AND METHODS

The gastrointestinal (GI) tract is among the most commonly affected systems during antiplatelet therapy, particularly with aspirin and dual antiplatelet regimens. Aspirin's mechanism of COX-1 inhibition decreases the synthesis of prostaglandins that protect the gastric mucosa by promoting mucus and bicarbonate secretion and maintaining mucosal blood flow. As a result, chronic aspirin use predisposes patients to gastritis, mucosal erosions, and peptic ulcers. The risk of upper gastrointestinal bleeding increases in proportion to dosage and duration, and it is further elevated when aspirin is combined with nonsteroidal anti-inflammatory drugs (NSAIDs) or anticoagulants [2].

Clopidogrel, while less ulcerogenic than aspirin, can still contribute to GI bleeding, particularly when used in dual antiplatelet therapy (DAPT). Dyspepsia, nausea, abdominal pain, and diarrhea are relatively common but generally mild side effects. Gastrointestinal bleeding may be mitigated by co-administration of proton pump inhibitors (PPIs); however, potential drug interactions—especially between clopidogrel and omeprazole, which share CYP2C19 metabolism—must be carefully considered. Ticagrelor and prasugrel also carry gastrointestinal risk, though their reversible and faster pharmacodynamic profiles may slightly modify bleeding tendencies [3].

RESULTS AND DISCUSSION

Bleeding remains the most significant and clinically relevant adverse effect of all antiplatelet drugs. It can occur at any anatomical site—cutaneous, mucosal, gastrointestinal, intracranial, or surgical—and its severity ranges from minor bruising to fatal hemorrhage. The incidence depends on the potency and combination of agents, as well as patient-specific risk factors such as age, renal dysfunction, and concurrent use of anticoagulants or nonsteroidal anti-inflammatory drugs.

Aspirin monotherapy typically causes minor bleeding, manifesting as epistaxis, easy bruising, or prolonged bleeding from cuts. However, in elderly patients and those with



peptic ulcer disease, the risk of major gastrointestinal hemorrhage is substantially increased. In dual antiplatelet therapy, especially with clopidogrel plus aspirin, the rate of major bleeding may rise two- to threefold. Prasugrel and ticagrelor, being more potent P2Y₁₂ inhibitors, are associated with higher bleeding risks compared to clopidogrel, particularly in patients with prior stroke or low body weight [3].

Intracranial bleeding, although rare, represents the most feared complication due to its high mortality rate. The risk is accentuated in hypertensive individuals, those with previous cerebrovascular disease, and in settings of excessive antiplatelet exposure. Clinical vigilance and risk-benefit evaluation are therefore indispensable in tailoring antiplatelet regimens, especially in elderly or frail patients.

In addition to their hemostatic effects, antiplatelet agents can trigger hematologic or immunologically mediated adverse reactions. Thrombocytopenia is a recognized complication of glycoprotein IIb/IIIa inhibitors such as abciximab, eptifibatide, and tirofiban, occurring in approximately 1–2% of treated patients. The mechanism involves the formation of drug-dependent antibodies that target platelet glycoproteins, leading to rapid platelet destruction. This condition can be severe and requires immediate discontinuation of therapy and supportive care.

Thrombotic thrombocytopenic purpura (TTP), although extremely rare, has been reported with thienopyridines like clopidogrel and ticlopidine. TTP is characterized by microangiopathic hemolytic anemia, thrombocytopenia, renal dysfunction, and neurological symptoms, and it can be life-threatening if not promptly recognized and treated with plasma exchange. Additionally, leukopenia, neutropenia, and aplastic anemia have been associated with ticlopidine use, leading to its decline in favor of safer alternatives such as clopidogrel.

Allergic reactions, though uncommon, can manifest as rash, urticaria, or angioedema, particularly with aspirin or ticagrelor. Aspirin-induced asthma, caused by shunting of arachidonic acid metabolism toward leukotriene production, is another notable hypersensitivity reaction, often occurring in individuals with pre-existing respiratory allergies [4].

While antiplatelet drugs are primarily cardioprotective, certain agents can paradoxically provoke cardiovascular or respiratory disturbances. Ticagrelor, for example, is known to cause dyspnea in up to 15% of patients. This side effect is thought to result from ticagrelor's inhibition of adenosine reuptake, leading to increased adenosine-mediated stimulation of pulmonary C-fiber receptors. Though usually benign and transient, dyspnea can be distressing and occasionally necessitates discontinuation of therapy.



Prasugrel, due to its potent antiplatelet activity, may provoke excessive hypotensive responses in some patients, particularly when combined with other vasodilators or antihypertensive drugs. Rarely, aspirin has been implicated in exacerbating hypertension or causing renal impairment in patients with pre-existing kidney disease due to prostaglandin synthesis inhibition and consequent renal vasoconstriction.

The adverse effects of antiplatelet agents are often amplified by pharmacokinetic and pharmacodynamic interactions. The concomitant use of anticoagulants (warfarin, heparins, or direct oral anticoagulants) substantially increases the risk of bleeding. Nonsteroidal anti-inflammatory drugs (NSAIDs) not only enhance bleeding risk through gastric mucosal injury but also compete with aspirin for COX-1 binding sites, reducing its antiplatelet efficacy. Proton pump inhibitors, as mentioned earlier, can attenuate the bioactivation of clopidogrel through CYP2C19 inhibition. Herbal supplements like ginkgo biloba, garlic, and ginseng may further potentiate bleeding by independent antiplatelet effects. Recognizing and managing these interactions form a critical component of safe pharmacotherapy [5].

CONCLUSION

Antiplatelet drugs are indispensable in modern cardiovascular medicine, yet their clinical benefits are counterbalanced by a range of adverse effects that require careful consideration. Bleeding remains the principal and most feared complication, but other side effects — gastrointestinal irritation, hematologic abnormalities, hypersensitivity, and respiratory discomfort — also contribute significantly to patient morbidity and therapy discontinuation. Understanding the pharmacological basis of these reactions allows clinicians to anticipate and prevent complications before they become life-threatening.

Clinical pharmacology teaches that no drug is entirely benign; rather, its value lies in the balance between therapeutic gain and potential harm. In the case of antiplatelet therapy, this balance is particularly delicate because the same mechanisms that prevent thrombosis can, under certain conditions, precipitate hemorrhage. Therefore, optimal antiplatelet management in adults demands individualized dosing, vigilant monitoring, and interdisciplinary coordination between cardiologists, hematologists, and pharmacists.

As the field advances, the emergence of newer agents with more predictable pharmacokinetics, reversible binding properties, and personalized dosing strategies offers hope for safer therapy. The integration of pharmacogenetics and precision medicine will likely redefine antiplatelet management, reducing adverse events while maintaining efficacy. Until then, the clinician's most powerful tools remain



knowledge, vigilance, and the prudent application of pharmacological principles to ensure that the prevention of one disease does not inadvertently give rise to another.

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