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EDITORIAL

The clopidogrel story: a cautionary tale of pharmacogenomics and personalized medicine

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Clopidogrel, a widely used antiplatelet drug, has been a cornerstone in the prevention of cardiovascular events in patients with atherosclerotic vascular disease. Clopidogrel works by inhibiting adenine diphosphate (ADP) induce platelet aggregation by binding to P2Y12 receptor. However, the story of clopidogrel serves as a cautionary tale in the era of pharmacogenomics and personalized medicine. The discovery of genetic variations in the *CYP2C19* and *P2Y12* that affect clopidogrel metabolism and efficacy, has significant implications for patient care (1, 2).

Studies have shown that patients with variation in *CYP2C19*, particularly the *2 and *3 alleles, have reduced metabolism of clopidogrel to its active form, resulting in decreased platelet inhibition and a higher risk of adverse cardiovascular events (3). Additionally, genetic variations in the *P2Y12* have also been shown to affect the response to clopidogrel (4). The H2 haplotype of the *P2Y12* has been associated with increased platelet aggregation and reduced response to clopidogrel (5). This phenomenon of reduced clopidogrel response is known as clopidogrel resistance.

Understanding the genetic factors that influence clopidogrel response, including *CYP2C19* and *P2Y12* polymorphisms, can help healthcare providers make more informed treatment decisions and improve patient outcomes (6).

The Clinical Pharmacogenetics Implementation Consortium (CPIC) has published guidelines for the clinical use of pharmacogenetic testing in patients receiving clopidogrel (7). According to these guidelines, patients who are poor metabolizers of clopidogrel, as determined by *CYP2C19* genotype, may benefit from alternative antiplatelet therapy that targets the P2Y12 receptor, such as ticagrelor or prasugrel.

The clopidogrel story highlights the importance of pharmacogenomics in personalized medicine. By tailoring treatment decisions to individual patients based on their genetic profiles, healthcare providers can improve patient outcomes and reduce healthcare costs. Further research and investment in pharmacogenomics are needed to realize its full potential (8).

In conclusion clopidogrel is one of the most important drugs where anti-platelet therapy is required. However, the efficacy of clopidogrel is affected by *CYP2C19* and *P2Y12* polymorphisms. Patients with certain degree of clopidogrel resistance are more prone to develop cardiovascular adverse events. Studies are needed to be focused on identifying which particular polymorphism is highly prevalent in our population that greatly affects clopidogrel net effect. This will help the healthcare provider to choose the best anti-platelet medications for the patients

based on their individual genetic and non-genetic factors thereby reducing the cardiovascular events. This will lower the hospital readmissions and financial burden in future.

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