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On Drugs and Therapeutics

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IN BRIEF

Poor Metabolizers of Clopidogrel (Plavix)

The FDA has required the manufacturer of *Plavix*, an antiplatelet drug used in addition to aspirin to prevent cardiovascular events in high-risk patients,¹ to add a boxed warning to the package insert about the risk of a poor response to the drug in patients with genetic polymorphisms of the cytochrome P450 enzyme CYP2C19. Clopidogrel is a prodrug and CYP2C19 is mainly responsible for its bioactivation. The Medical Letter reported last year that several studies have found higher rates of cardiovascular events, including stent thrombosis, in patients with these polymorphisms taking clopidogrel.²

At least one genetic polymorphism leading to poor metabolism of clopidogrel has been reported to occur in 15% of Caucasians, 17% of African Americans and 30% of Asians.³ Since many patients take clopidogrel to protect against life-threatening events, and some continue to do so for extended periods of time, it might be worthwhile to test for these polymorphisms. Such tests, requiring small amounts of blood or saliva, are commercially available from clinical laboratories. More directly, patients who are taking clopidogrel could have platelet aggregation assays to determine whether the drug is being activated.

However, the best course of action for patients who prove to be poor metabolizers of clopidogrel is not clear. They could be treated with higher doses of clopidogrel, but the doses that would be safe and effective in such patients have not been established. Alternatively, they could be treated with prasugrel (*Effient*), a similar antiplatelet drug that does not require CYP2C19 for activation, instead of clopidogrel, but prasugrel has a greater effect on platelets and may cause more bleeding.⁴

1. Antiplatelet and anticoagulant drugs. *Treat Guidel Med Lett* 2008; 6:29.
2. PPI interactions with clopidogrel revisited. *Med Lett Drugs Ther* 2009; 51:13.
3. Z Desta et al. Clinical significance of the cytochrome P450 2C19 genetic polymorphism. *Clin Pharmacokinet* 2002; 41:913.
4. Prasugrel (*Effient*) vs. clopidogrel (*Plavix*). *Med Lett Drugs Ther* 2009; 51:69.

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