

Letter

SUCCESSFUL USE OF PRASUGREL, AN ALTERNATIVE ANTIPLATELET AGENT, IN A PATIENT WITH CLOPIDOGREL ALLERGY

Clopidogrel is a widely used antiplatelet agent indicated for patients who require coronary stent placement.¹ Available data also support its use in secondary prevention of atherothrombotic disease.²

Clopidogrel is a thienopyridine prodrug that requires bioactivation before it can achieve its antiplatelet effects. It undergoes metabolism using the cytochrome P450 system. The active metabolite of clopidogrel irreversibly inhibits adenosine diphosphate and antagonizes P2Y₁₂, allowing for maximal platelet inhibition and preventing platelet aggregation.³⁻⁵

Allergic reactions, commonly a rash, have been documented to occur in approximately 1% of patients taking clopidogrel.¹ When clopidogrel cannot be used, alternative thienopyridines, such as ticlopidine, are considered. Newer P2Y₁₂ receptor blockers have been developed and include prasugrel and ticagrelor. Currently, there are not enough data on cross-reactivity between these agents.

We report a case in which prasugrel was well tolerated as an alternative treatment option for a patient with clopidogrel hypersensitivity.

A 62-year-old man who presented with acute coronary syndrome and a history of coronary artery disease, hypertension, hyperlipidemia, allergic rhinitis, and chronic obstructive pulmonary disease was transferred to our institution for cardiac catheterization. In 2003 the patient underwent cardiac catheterization and was treated with clopidogrel, 75 mg orally daily for 3 days, during hospitalization with no reaction observed. The patient went home, took his first dose of clopidogrel, and within minutes developed hives, pruritus, facial swelling, and eye swelling. He denied shortness of breath, dyspnea, or hypotension. He was given diphenhydramine, and the reaction resolved. The clopidogrel was discontinued and never resumed.

The patient then required additional cardiac catheterization, and the cardiology inpatient team requested input from the allergy and immunology department. This was thought to be a clopidogrel allergy because medication review did not reveal other new medications. Skin testing was not performed given the time constraint and necessity for catheterization. Therefore, we recommended its avoidance and did not think ticlopidine was a good alternative given the significant risk of cross-reactivity. Prasugrel was then considered, which is in the same family as clopidogrel. The patient was pretreated before cardiac catheterization with prednisone, 50 mg orally 13 hours before, 7 hours before, and 1 hour before prasugrel use. Diphenhydramine, 50 mg, and ranitidine, 150 mg orally, were also administered 1 hour before prasugrel use. Pretreatment was given to significantly reduce the possibility of a reaction because clopidogrel and prasugrel share a common ring structure. Cardiac catheterization was performed successfully, and 2 drug-eluting stents were placed in the right coronary artery. The patient was given

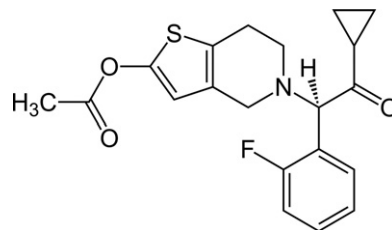


Figure 1. Structure of clopidogrel and prasugrel. Both structures share the thiophene and pyridine ring.

prasugrel, 60 mg orally, and diphenhydramine, 25 mg intravenously, after stent placement in the catheterization laboratory with no reaction. The following day the patient tolerated prasugrel, 10 mg orally, and was discharged with no adverse events. He continued to take prasugrel, 10 mg orally daily, and has tolerated the medication for 12 weeks.

Although hypersensitivity to clopidogrel is uncommon, it can result in challenging dilemmas when it occurs in patients with significant cardiovascular disease. Clopidogrel is approved for prevention of vascular ischemic events in patients with symptomatic atherosclerosis, with acute coronary syndrome without ST-segment elevation, with ST-segment elevation myocardial infarction, and after placement of drug eluting stents.

Alternatives to clopidogrel are members of the same family, thienopyridines. Ticlopidine has a wide adverse effect profile that includes pancytopenia, agranulocytosis, and rash. In addition, a recent study suggested there might be a 27% risk of recurrence of allergic reactions in patients treated with ticlopidine.¹ Clopidogrel desensitization in a monitored setting is another option; however, it has significant risk. There are case reports of a severe hypersensitivity syndrome to clopidogrel on rechallenge, which includes neutropenia, rash, fever, tachycardia, nausea, and vomiting.⁶

Prasugrel is a newer agent that was approved by the Food and Drug Administration on July 10, 2009. It is a thienopyridine adenosine diphosphate receptor inhibitor that irreversibly binds to the P2Y₁₂ receptor. It has been shown to act more quickly and potently than clopidogrel.⁷ It has a structure similar to clopidogrel because they both contain a thiophene and pyridine ring (Fig 1).⁸

There has been one case report of clopidogrel hypersensitivity with prasugrel as an alternative in The Netherlands; however, to our knowledge, our case is the first case report published in the United States. Although the authors did not premedicate their patients, we thought it was in our patient's best interest given his previous reaction and the possibility of cross-reactivity.

Clopidogrel is a medication used by many patients for conditions ranging from cardiac to neurologic disease, and given the incidence of hypersensitivity to clopidogrel, more investigation is necessary.

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Disclosures: Authors have nothing to disclose.

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doi:10.1016/j.anai.2011.08.003

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