

New reversible drug shows early promise in preventing dangerous clots

December 17 2015

A new drug that protects against dangerous blood clots in patients undergoing procedures such as angioplasty to restore blood flow through the coronary arteries, appears safe, fast, and the effects are uniquely reversible, according to early testing described in the American Heart Association journal: *Arteriosclerosis, Thrombosis and Vascular Biology*.

Antiplatelet drugs currently available to patients carry an increased risk of bleeding. If a patient needs surgery while taking these medications, they may have a greater risk of complications due to [blood](#) loss. The new antiplatelet drug called PZ-128 is unique because it acts quickly to prevent dangerous blood clots from forming during a coronary artery procedure and its effects are reversible, reducing the risk of excess bleeding.

PZ-128 is a new type of drug called a pepducin. Pepducins enter cells and, from the interior side of the cell membrane, act on a specific receptor that alter the cell's biochemical processes.

This study is the first demonstration of pepducin's potential benefits in humans, said Athan Kuliopulos, M.D., Ph.D., senior author of the study and director of the Center for Hemostasis and Thrombosis Research at Tufts Medical Center in Boston, Massachusetts.

The new drug was given to 31 patients, ages 43 to 74, in a range of doses. More than one-fifth of the patients had [coronary artery disease](#); the rest had risk factors for [coronary artery](#) plaques such as [high blood](#)

[pressure](#), cholesterol, diabetes or smoking. Many of the patients were taking medicines for heart disease including aspirin, or drugs to control blood pressure, cholesterol or blood glucose.

Researchers found that the more PZ-128 a patient received, the better the medicine blocked platelet aggregation—the clumping together of platelets in the blood which can lead to deadly clots. At the highest doses, PZ-128 prevented 80 percent to 100 percent of platelets from clumping together. Moreover, the impact of the PZ-128 was quickly reversed, with the drug completely clearing patients' blood as early as 24 hours (and at least up to 192 hours) after it was given.

Current antiplatelet therapy commonly takes a two-pronged approach, with aspirin and a class of medicines that includes clopidogrel acting in two different ways to inhibit platelet clumping. Yet even with highly potent [antiplatelet drugs](#), about 20 percent of patients suffer recurrent artery blockages within two years, Kuliopulos said, suggesting that aiming at yet another target could further reduce risk.

PZ-128 targets a platelet-activating receptor called PAR1. Blocking PAR1 on the cell's outer surface has been challenging because at that site the receptor is very similar to receptors for related molecules. But that's not the case where PZ-128 acts on the receptor, inside the cell. Currently, no drugs are on the market for blocking PAR1 during procedures when the risk of serious complications like a heart attack is high.

A PAR1-inhibiting pill, vorapaxar, is available for non-acute use in patients who previously had a heart attack or have [peripheral artery disease](#). But the drug, whose effects build slowly and are long-lasting, was not approved for use during cardiac procedures due to a risk of excessive bleeding, Kuliopulos said. By contrast, PZ-128 appears able to block PAR1 fast enough to be used in an urgent procedure, and for a

time short enough to limit bleeding risk afterward, he said.

Researchers cautioned that the research is only a Phase 1 study, whose main goals are gauging the drug's safety and finding tolerable doses. PZ-128 requires more testing before firm conclusions could be drawn about how well it works, he said. The research team is planning a Phase 2 study in up to 600 [patients](#) having angioplasty or with acute blockages of [blood flow](#) to the heart.

Provided by American Heart Association

Citation: New reversible drug shows early promise in preventing dangerous clots (2015, December 17) retrieved 3 May 2024 from <https://medicalxpress.com/news/2015-12-reversible-drug-early-dangerous-clots.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--