Heparin-Induced Thrombocytopenia
Steven A. Baroletti, PharmD; Samuel Z. Goldhaber, MD

Patients receive blood thinners (anticoagulants) to treat or prevent blood clots. The most commonly used intravenous anticoagulant is heparin. This Cardiology Patient Page focuses on heparin-induced thrombocytopenia (HIT), a complication of heparin therapy. This complication of heparin is often confusing because in HIT, heparin does the opposite of what it is supposed to do: It forms rather than prevents new blood clots.

What Is Heparin-Induced Thrombocytopenia?
Ordinarily, heparin prevents clotting and does not affect the platelets, components of the blood that help form blood clots. Triggered by the immune system in response to heparin, HIT causes a low platelet count (thrombocytopenia).

Two distinct types of HIT can occur: nonimmune and immune-mediated. Nonimmune HIT, which occurs most frequently, is characterized by a mild decrease in the platelet count and is not harmful. The second type, immune-mediated HIT, occurs much less frequently but is dangerous. Immune-mediated HIT causes much lower platelet counts. Paradoxically, despite a very low platelet count, patients who suffer from HIT are at risk for major clotting problems.

After heparin is administered to a patient, an immune complex can form between heparin and a specific blood factor (platelet factor 4, or “PF4”) that is released by platelets. The body views this “heparin-PF4” complex as a foreign substance. Therefore, an antibody is formed against the heparin-PF4 complex. The antibody binds to this complex and the platelets are destroyed.

This disruption of platelets can lead to the formation of new blood clots in patients with immune-mediated HIT. The result can be a deep vein thrombosis (in the veins of the thigh or pelvis), pulmonary embolism, or even a heart attack or stroke. However, this does not seem to occur with the mild decrease in platelets associated with nonimmune HIT.

When Does HIT Occur?
Immune-mediated HIT usually occurs between 5 to 14 days after first beginning heparin therapy. However, there are exceptions, with HIT developing infrequently either early (after a recent previous exposure to heparin) or late after heparin exposure.

How Is HIT Diagnosed?
HIT can often be diagnosed by measuring the platelet count and PF4 antibody level in the blood. Symptoms of new blood clot formation may suggest HIT.

Symptoms of deep vein thrombosis include pain or tenderness, sudden swelling, discoloration, visibly large veins, and skin that is warm to the touch. Dislodgement of clot from the deep leg veins and passage into the lungs (pulmonary embolism) may present as shortness of breath, a change in heart rate, sharp chest pain, dizziness, or feelings of anxiety and excessive sweating. Severe indicators of HIT are skin changes that present as bruising or blackening around the heparin injection site as well as the fingers, toes, and nipples that may progress to gangrene. The extremities are especially susceptible to the small clots that form because of HIT. If you have any of these signs or symptoms, call your doctor.

How Is HIT Treated?
The first step is to discontinue heparin on suspicion of HIT. The next step is to treat HIT using an alternative type of anticoagulant. Even though the platelet count is low, it is important to avoid platelet transfusions, which can “add fuel to the fire.”

Medications
Direct thrombin inhibitors (DTI) are a class of anticoagulant medications that do not cause HIT. These drugs are administered by continuous intrave-
nous infusion. Three DTIs have been approved by the Food and Drug Administration: lepirudin, argatroban, and bivalirudin. You may also be treated with another class of injectable anticoagulant medication called fondaparinux instead of a DTI (Table). After several days, your blood will be tested to make sure that the platelet count has returned to normal. At that point, the oral blood thinner warfarin (commonly called by its trade name, Coumadin) may be prescribed in addition to the fondaparinux or DTI. The DTI or fondaparinux is overlapped with warfarin for about 5 days, until a target value is achieved on a blood test (known as international normalized ratio, or INR) that measures the level of anticoagulation from warfarin. Your doctor or an anticoagulation clinic staff member will monitor your INR and warfarin dosing closely for as long as you need to continue the medication (usually at least 1 to 3 months). Warfarin use has been described previously in another Cardiology Patient Page.2

What if I Need Anticoagulants in the Future?

Although HIT is caused by a reaction to heparin that is similar to other allergic reactions, it is not a true allergy. In contrast to many allergies to other medications or foods, the allergy to heparin is not long-lasting. The PF4 antibody that causes HIT will usually disappear after approximately 3 months. Thereafter, heparin may be considered for use if a new clot did not develop from HIT and if the PF4 antibody test is negative.

If you have been told that you have HIT or an allergy to heparin, inform your doctor before taking any form of heparin. It is extremely helpful to write down when you were exposed to heparin and when HIT occurred. Helpful information for your healthcare provider is shown in the Figure.

Early identification of HIT and avoidance of inappropriate heparin therapy can help promote a safe and effective anticoagulation strategy.

Acknowledgments

We thank Suellen Breakey, RN, PhD, for her contribution to the figure.

Disclosures

None.

References

Heparin-Induced Thrombocytopenia
Steven A. Baroletti and Samuel Z. Goldhaber

Circulation. 2006;114:e355-e356
doi: 10.1161/CIRCULATIONAHA.106.632653
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2006 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/114/8/e355

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation is online at:
http://circ.ahajournals.org/subscriptions/