Formulary Flash

Volume 06, Issue 1 January 19, 2006

A PUBLICATION OF THE PHARMACY AND THERAPEUTICS COMMITTEE (P&T) AND THE DEPARTMENT OF PHARMACY

Optimizing Diagnosis and Treatment of Heparin-Induced Thrombocytopenia

A Pilot Monitoring Service

Background

Unfractionated heparin (UFH) and low molecular weight heparins (LMWH) are commonly used anticoagulants for the prevention and treatment of thrombi. Paradoxically, these medications can cause an immune-mediated thrombocytopenia and possible thrombosis known as heparin-induced thrombocytopenia (HIT).[1,2] This thrombosis may occur in light of thrombocytopenia. The incidence of HIT is reported to be less than 1% with LMWH and up to 5% with UFH[1] and the clinical consequences can be devastating when thrombosis does occur.

Clinical Features of HIT

Two key clinical features can be easily overlooked when detecting HIT. The first feature is the definition of significant thrombocytopenia, which is a ≥ 50% decline in platelet count from baseline, even if platelets remain in the normal range (≥ 150 X 10^9/L).[2-4] In patients not exposed in the last 100 days, baseline platelet count is considered day 4 after initiation of UFH or LMWH therapy.[3]

The second feature is the timing of thrombocytopenia. In the vast majority of patients, typical onset occurs 5 to 14 days after initiation of UFH or LMWH therapy.[1-4] In patients who have received UFH or LMWH therapy in the preceding 100 days, rapid onset can occur within 24 hours of beginning UFH or LMWH therapy.[2,4] This underscores the need for an accurate patient history.

Diagnosis of HIT

The proper diagnosis of HIT requires both clinical and laboratory features.[1-4] Strong clinical suspicion for HIT prompts a HIT antibody laboratory test for confirmation. However, a positive laboratory test alone is not diagnostic for HIT.[2]

A pretest clinical risk assessment scoring system for HIT has been developed, which can be useful for properly assessing the clinical scenario. The scoring system uses the clinical features of HIT (Thrombocytopenia, Timing, Thrombosis and Other causes of thrombocytopenia).[1] The pretest score gives a probability of high, intermediate, or low risk for HIT, refer to Table 1. The pretest probability score can be used as a tool for determining treatment and ordering a HIT antibody test.

Treatment of HIT

If HIT is strongly suspected, heparin or LMWH should be stopped immediately. The patient should be anticoagulated with a non-heparin anticoagulant until a diagnosis can be confirmed or denied.[1,2,4] The direct thrombin inhibitors (DTI), lepirudin (Refludan®) and argatroban, are the only FDA-approved treatments for HIT. Dosing guidelines and anticoagulation goals appear in Table 2.

Warfarin should not be the initial treatment of HIT.[1,2,4,5] Initial treatment with warfarin depletes the natural anticoagulants protein C and protein S, which can promote thrombosis in HIT.[5] Warfarin therapy may be initiated after a patient has been properly anticoagulated with a DTI and the platelet count has increased to at least 100 x10^9 /L.[4,5] Warfarin and DTI therapy should be overlapped for at least 4 to 5 days, and the INR should be therapeutic when the DTI is discontinued.[4,5]

Pilot Monitoring Service

During the months of January and February, a monitoring service for HIT will be piloted. The monitoring service will be run by Jason Jokerst, Pharm.D., a Pharmacy Practice Resident with the Department of Pharmacy Services, in association with the Pathology and Hematology Departments.

When an order is placed for a HIT antibody assay or a new order is placed for a DTI, the monitoring service will contact the ordering physician. Together they will perform the pretest clinical risk assessment and determine a probability score. After the probability score has been determined, the physician can decide whether to continue with the HIT antibody assay or cancel the order. A HIT antibody assay will not be performed by the laboratory until a probability score has been assigned.

The monitoring service will also follow patients being treated with a DTI for suspected or confirmed HIT. Dosing recommendations will be given to maintain therapeutic anticoagulation, please refer to aPTT goals in Table 2.

Table 1 -- Clinical Risk-Assessment Scoring System for HIT

	2 Points	1 Point	0 Points
Thrombocytopenia (% fall from baseline platelet count)	> 50%	30% - 50%	<30%
Timing of platelet count fall	Onset within 5-14 days OR < 1 day of re-exposure if heparin received within 100 days	No clear onset of fall in platelet count (i.e., no baseline count); OR Onset after 14 days	Onset < 5 days with no previous heparin exposure
Thrombosis or other sequelae	New thrombosis; acute systemic reaction following bolus	Progressive or recurrent thrombosis; erythematous skin lesions; thrombosis suspected but not proven	No thrombosis, skin necrosis or lesions observed
Other causes of thrombocytopenia	No other known etiology	Other etiologies may be present (e.g., DIC, infections, dilution, medications, bone marrow failure, etc.)	Known etiology is present

Add total points from each of the four categories: Total points _____

0 - 3 points = low; 4 - 5 points = intermediate; 6 - 8 points = high
Risk level (check one):
____High Risk (6-8 points): Continue with HIT antibody test. Stop all heparin and anticoagulate with either lepirudin or argatroban until results of HIT antibody test are in.
____Intermediate Risk (4-5 points): Do not continue with HIT antibody test, unless a compelling indication is present. If HIT antibody test is ordered, stop all heparin and continue anticoagulation with either lepirudin or argatroban until results of HIT antibody test are in.
____Low Risk (0-3 points) Do not continue with HIT antibody test at this time. Heparin may be continued.

Table 2 -- Direct-Thrombin-Inhibitor (DTI) Initial Dosing Guidelines

Lepirudin was removed from US market in 2012.
The full P&T approved Argatroban guideline can be viewed on the Clinical Pathways and Guidelines page, under Anticoagulation

1. Target aPTT: 45-90 seconds (as of 10/2016)

2. **Argatroban**:
   - Dose at **1 mcg/kg/min** (lower than manufacture's recommendation).
   - Dosing in hepatic impairment: **0.5 mcg/kg/min**
   - Adjusting dose based on the aPTT
     - If aPTT is 3-3.5 times greater than normal, reduce argatroban dose by 0.5 mcg/kg/min, then recheck aPTT in 2 hours.
     - If aPTT is >3.5 times normal, stop infusion for 15 minutes then decrease dose by 1 mcg/kg/min, then recheck aPTT in 2 hours.

3. **Warfarin**:
   - Initiate warfarin after platelets have rebounded (≥100 x 10^9).
   - **Overlap** warfarin and DTI therapy at least 5 days.
   - Discontinue DTI when INR is therapeutic (range of 2 - 3) for at least 2 days.

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Contributors: Jason Jokerst PharmD
Reviewers: Colleen Barthol PharmD; Pamela Maxwell, PharmD; RCGarcia RPh, Department of Pharmacy
Editors: Alexander Shepherd MD, Chairman, P&T Committee, Yolanda Laurel, Director of Pharmacy Services, University Health System.

Revised: 9/2009, 7/2012,10/2016