Formulary Flash

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Heparin Assay to Monitor Unfractionated Heparin

Background

In late May 2009, University Hospital will begin monitoring heparin therapy with the Heparin Assay. This test uses the Anti-Xa assay to measure heparin function, which relates to a heparin level. The heparin assay will replace the aPTT (activated partial thromboplastin time) currently used to monitor patients on therapeutic doses of unfractionated heparin. This change will only affect UHS and not the VA until further notice.

Reason for Transition

Recently, the UHS lab obtained a new instrument and has been working on updating the therapeutic aPTT range, which had previously been 70-100 seconds. A trend in industry to make aPTT reagents more and more sensitive has lead to therapeutic intervals for heparin that often exceed 100 seconds. Physicians are not accustomed to accepting these aPTT values (eg. 120 seconds) as safe, and there may be a tendency to under-anticoagulate patients. Secondly, the availability of more preferable anticoagulants such as the low molecular weight heparins and fondaparinux have dramatically decreased the use of unfractionated heparin, making it difficult for the laboratory to calibrate new aPTT reagents. Given the current situation, monitoring heparin therapy with the heparin assay is a good alternative due to its universal heparin therapeutic range.

Heparin Assay

Monitoring heparin therapy with the heparin assay is well established in the literature.[1-3] The test measures anti-Xa activity and a heparin concentration can then be derived from a calibration curve. The American College of Chest Physicians recommends a target heparin concentration 0.3 to 0.7 U/mL.

While the aPTT is a global coagulation assay, the heparin assay is less complex because it is not affected by levels other blood factors or lupus anticoagulants. An example is the effect of factor VIII levels on aPTT values.

Factor VIII is an acute phase reactant that is commonly elevated in acutely ill patients. The elevated factor VIII will shorten aPTT values, leading to an inappropriate escalation of heparin doses.

Although there is no data supporting better outcomes when monitoring with the heparin assay, there is literature demonstrating a decrease in the number of tests and dose changes when monitoring with the heparin assay.[2]

Changes to Expect

- New heparin dose adjustment nomogram and target range
- Updated heparin protocol posted to the clinical intranet (see page 2)
- Updated heparin order sets (Medicine, ACS Cardiology, Surgery).
    - Heparin assays will replace aPTT
    - Nurse administration directions modified to reflect changes in target
- After this transition takes place, the aPTT will no longer be used to monitor heparin therapy

What Will NOT Change

- Heparin dose recommendations (see protocol page 2).
- Timing of heparin monitoring -- begin 6 hours after initiation, and continue every 6 hours until 2 consecutive therapeutic levels are reached (0.3 - 0.7 U/mL). Then a heparin assay will be drawn **once daily.**
- Direct thrombin inhibitor (argatroban and lepirudin) monitoring with aPTT. (see guidelines on clinical intranet for target aPTT range for these agents)
- The aPTT will continue to be available for evaluation of factor deficiencies and inhibitors such as lupus anticoagulant.

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Unfractionated Heparin Infusion Protocol

Dosing and Monitoring Guidelines

Baseline Labs (within 24 hrs prior to initiation of therapy)
- CBC (Hgb, Hct, platelet count)

Dosing
Determine initial bolus dose and infusion rate
- Initial Bolus dose is **indication specific**, see tables
- Initial max infusion rate is **indication specific**, see tables
- Total body weight (TBW as dry weight) will be used to calculate doses
- **Be sure to not exceed max doses**

Routine Labs and Monitoring
- **Heparin assay** 6 hours after initiating heparin
- **Heparin assay** 6 hours after each dosage change, **until 2 consecutive therapeutic levels** are reached at a constant rate of infusion, then can begin monitoring **once daily**
- **Target therapeutic heparin level by Anti Xa assay is 0.3-0.7 U/mL**
- Order CBC at least every other day and more frequently if deemed medically necessary
- Monitor for signs of HIT (Platelet drop by > 50% OR decrease < 150 K/µL)

Warfarin Bridging
- Overlap heparin and warfarin for at least 4-5 days **and** until 2 therapeutic INRs are achieved 24 hours apart
- If patient will be discharged prior to 4 days, use LMWH to bridge
- **IV heparin to SQ LMWH conversion** - give first LMWH injection, then discontinue heparin immediately after

Treatment of HIT
- Stop **all** sources of heparin
- Refer to **Guidelines for the use of Argatroban and Lepirudin** posted on the clinical intranet

Venous Thromboembolism Treatment (Target 0.3 - 0.7 U/mL)

Initial Bolus: 80 units/kg (Max Bolus 10,000 units)
Initial Infusion Rate: 18 unit/kg/hr (Max initial rate 2,000 units/hr)
Monitor: Heparin Assay 6 hours after initiation and 6 hours after each dosage change

Heparin Assay AntiXa (U/mL)	Action
< 0.15	80 unit/kg bolus, then increase by 4 units/kg/hr
0.15 – 0.29	40 unit/kg bolus, then increase by 2 units/kg/hr
0.3 - 0.7	**No Change**
0.71 - 1	Decrease by 2 units/kg/hr
> 1	Stop infusion 1 hr then decrease by 3 units/kg/hr

Indications - DVT, PE, Atrial fibrillation

Acute Coronary Syndrome Cardiology (Target 0.3 – 0.7 U/mL)

Initial Bolus: 60 units/kg (Max Bolus 5,000 units)
Initial Infusion Rate: 12 units/kg/hr (Max initial rate 1,000 units/hr)
Monitor: Heparin Assay 6 hours after initiation and 6 hours after each dosage change

Heparin Assay AntiXa (U/mL)	Action
< 0.15	80 unit/kg bolus, then increase by 4 units/kg/hr
0.15 - 0.29	40 unit/kg bolus, then increase by 2 units/kg/hr
0.3 - 0.7	**No Change**
0.71 – 1	Decrease by 2 units/kg/hr
> 1	Stop infusion 1 hr then decrease by 3 units/kg/hr

Indications - Non-STEMI, STEMI, Unstable Angina

References

1. Rosborough TK, Shepherd MF. Achieving target anti-factor Xa activity with a heparin protocol based on sex, age, height, and weight. Pharmacotherapy 2004;2004;24(6):713-719.
2. Rosborough TK. Monitoring Unfractionated Heparin Therapy with Antifactor Xa Activity Results in Fewer Monitoring Tests and Dosage Changes than Monitoring with the Activated Partial Thromboplastin Time. Pharmacotherapy 1999;19(6):760-766.
3. Levine MN, Hirsh J, Gent M, et al. A randomized trial comparing activated thromboplastin time with heparin assay in patients with acute venous thromboembolism requiring large daily doses of heparin. Arch Intern Med 1994;154:49-56.
4. Hirsh J, Bauer KA, Donati MB et al. Chest 2008;133(suppl)141S-155S.