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Anticoagulation Therapies, Standard Heparin

Children's Mercy Kansas City

These guidelines do not establish a standard of care to be followed in every case. It is recognized that each case is different and those individuals involved in providing health care are expected to use their judgment in determining what is in the best interests of the patient based on the circumstances existing at the time. It is impossible to anticipate all possible situations that may exist and to prepare guidelines for each. Accordingly, these guidelines should guide care with the understanding that departures from them may be required at times.

Standard Heparin Management
Care Process Model
Revised May 2016

Fast facts

- This guideline is intended for the use of heparin for therapeutic (not prophylactic) indications. This guideline is not intended for heparin use to maintain patency of arterial or central venous catheters or hemodialysis/extracorporeal circuits.
- Activated partial thromboplastin time (aPTT- reported in Cerner as PTT) and heparin levels are used to monitor the effects of standard heparin.
- Standard heparin is also referred to as *unfractionated* heparin in many references.
- Heparin levels are performed on arrival in the lab (no specific batch time for this test).
- Antithrombin III (ATIII) levels are automatically ordered and reported with every heparin level.
- The ***optimal sample*** for aPTT and heparin levels is a ***fresh venipuncture site***.
    - Alternate sites may be considered but present limitations with interpretation of the aPTT or heparin levels.
    - Capillary samples are not appropriate.
    - Samples should never be drawn from an IV containing heparin intended for *therapeutic anticoagulation*.
    - If aPTT is highly variable, heparin level may provide a more reliable measure.
    - Ensure sample is not contaminated by heparin from a heparinized IV line (1/2 or 1 unit/mL heparin) by drawing adequate waste volume to clear line before obtaining the sample to be tested.
- Do not confuse the heparin level with that for *fractionated* heparin or LMW heparin level.
- ATIII is a cofactor for activity of heparin and therefore inadequate serum AT III might be a cause for poor response to heparin.

This guideline is not intended for patients on ECMO, cardiac bypass pump, hemodialysis or continuous renal replacement therapy. Refer to specific guideline for these situations.

Indications

- Treatment of venous thromboembolism (VTE).
- Treatment of arterial thrombosis.

Initiation, Maintenance and Duration of Therapy

Initiation of therapy

- Obtain blood for CBC, PT, and aPTT.
- **Loading heparin dose: 75-100 units/kg** IV over 10 minutes.
  - **Loading dose may not be indicated in certain clinical situations with increased bleeding risk**
- Calculate initial maintenance heparin dose based on age and weight.

Initial maintenance dose:

≤ 1 year 28 units/kg/hour IV
> 1 year 20 units/kg/hour IV

- Obtain blood for aPTT and/or heparin level **4 to 6 hours** after administration of the loading dose (no earlier).
- Adjust heparin to maintain the aPTT at **60-85 sec** (or an aPTT which usually correlates to a heparin level of 0.35 to 0.7) using **Table 1.**
- Obtain blood for aPTT and/or heparin level **4 to 6 hours after every** change in infusion rate.
- Use heparin level to calibrate aPTT levels. If aPTT is highly variable, heparin level may provide a more reliable measure. Obtain aPTT at least daily if using heparin levels to titrate dosing.

Table 1 - Heparin Adjustment

PTT (seconds)	**Bolus** (units/kg)	**Hold infusion** (minutes)	**Rate change** (units/kg/hour)	**Repeat PTT**
≤ 50	50	0	↑10%	4 hours
50-59	0	0	↑ 10%	4 hours
60-85	0	0	no change	24 hours
86-95	0	0	↓10%	4 hours
96-120	0	30	↓10%	4 hours
≥ 120	0	60	↓15%	4 hours

Maintenance and monitoring

- Once a therapeutic aPTT or heparin level is achieved obtain blood for CBC, PT, aPTT and/or heparin level at least daily.
- Measure platelet counts daily. If platelet count decreases below 150,000/microL or drops by ≥ 50%, determine if the decrease in platelet count is related to the underlying disorder or is potentially due to heparin therapy. If likely due to heparin, discontinue heparin; initiate an alternative therapy and consult hematology. The risk for **heparin-induced thrombocytopenia** (HIT) is greater after 5 days of heparin.
- Heparin therapy should be administered in an IV and must not be stopped or interrupted for any other medications. If the infusion is interrupted for more than 1 hour, re-establish the heparin maintenance infusion at the previous rate and obtain aPTT and heparin level 4-6 hours later. Once the aPTT level is available, adjust the infusion rate as indicated by **Table 1.**
- Heparin should be discontinued 6 hours prior to any **invasive procedures** such as lumbar puncture or **surgery** unless the clinical situation requires an emergent intervention. For conditions necessitating more emergent intervention, utilize protamine as described in the section Heparin Antidote. Restart 12-24 hours after the procedure or surgery and when hemostasis has been achieved.

Duration of therapy

The duration of heparin therapy is dependent upon the primary problem.

- **General recommendations:**
  - **May start warfarin as early as day 1 if long-term anticoagulation is planned.**
  - **UFH/enoxaparin should be discontinued no earlier than day 6 and after INR has reached goal range for 2 consecutive days.**
  - **May convert to LMW heparin/enoxaparin when clinical situation allows.**

Dietary considerations

- None

Potential drug interactions

- Increased potential for hemorrhage:
  - Concurrent thrombolysis.
  - Drugs affecting platelet function such as aspirin, NSAIDs, dipyridamole, clopidogrel, ticlopidine and cilostazol.
  - Complementary/alternative medications known to have potential to *increase* bleeding include danshen, devil's claw, dong quai, feverfew, gingko biloba and papain.
- Decreased effect of heparin:
  - Digoxin, tetracycline, nicotine, antihistamines, and IV nitroglycerin.

Adverse effects

- Bleeding:
  - Most common adverse effect.
  - Discontinue heparin.
  - Refer to Heparin antidote section for management.
- Osteoporosis:
  - Uncommon.
  - Occurs with prolonged heparin therapy.
  - Monitor bone density if heparin therapy exceeds 3 months.
- Thrombocytopenia due to **heparin-induced thrombocytopenia** (HIT):
  - Risk in children < 2%.
  - May be asymptomatic.
  - May be associated with life threatening or fatal arterial or venous thrombosis.
  - Suspect HIT if platelet count decreases by 50% or decreases below 150,000/microL between day 5 and 10 of heparin exposure (may occur sooner if patient has previously been exposed to heparin).
  - Consult Hematology if HIT is suspected.

Heparin antidote

- Termination of the IV infusion generally will terminate the anticoagulant effect.
- If immediate reversal is required, **protamine** sulfate will result in neutralization of heparin. The dose of protamine is based on the amount of heparin administered in the previous 2 hours using **Table 2**.

Table 2. Protamine sulfate for immediate reversal

Time since last heparin dose	Protamine dose/100 units heparin given
<30 minutes	1 mg
30-60 minutes	0.5-0.75 mg
60-120 minutes	0.375-0.5 mg
>120 minutes	0.25-0.375 mg

- Maximum Protamine dose is 50 mg.
- Protamine should be given IV over 10 minutes. Infusion rate should not exceed 5 mg/min. More rapid infusion may result in hypotension. Patients with hypersensitivity to fish and those who have received protamine-containing insulin or previous protamine therapy may be at risk of hypersensitivity reactions.
- Obtain an aPTT and PT 15 minutes after the administration of protamine.
- Excessive Protamine doses may worsen bleeding potential.

Other considerations

- The ***optimal sample*** for aPTT and heparin levels is a ***fresh venipuncture site***.
  - Alternate sites may be considered but present limitations with interpretation of the aPTT or heparin levels.
  - Capillary samples are not appropriate.
  - Samples should never be drawn from an IV containing heparin intended for *therapeutic anticoagulation*.
  - If aPTT is highly variable, heparin level may provide a more reliable measure.
  - Ensure sample is not contaminated by heparin from a heparinized IV line (1/2 or 1 unit/ml heparin) by drawing adequate waste volume to clear line before obtaining the sample to be tested.
- Avoid aspirin, NSAIDs and other antiplatelet drugs unless required for specific disease management or clinical situation.
- Consider alternative analgesics such as acetaminophen or choline magnesium salicylate (Trilisate®), as clinically appropriate, if analgesia is required.
- Avoid IM injections and arterial punctures.
- Heparin should be discontinued 6 hours prior to any **invasive procedures** such as lumbar puncture or **surgery** unless the clinical situation requires an emergent intervention. For conditions necessitating more emergent intervention, utilize protamine as described in the section Heparin Antidote. Restart 12-24 hours after the procedure or surgery and when hemostasis has been achieved.
- Mobilization should be encouraged as tolerated.

Indications for Hematology consultation (not all inclusive)

- Initiation of therapy for patients
  - Age < 30 days
  - Baseline INR ≥ 1.2 prior to initiation of warfarin
  - Impaired renal function
- Maintenance of anticoagulation therapy with
  - Delay in reaching therapeutic anticoagulation
  - Progression of thrombus
  - Concern for heparin induced thrombocytopenia (HIT)
  - Hemorrhage and need for antidote
- Surgery or invasive procedure in patients with:
  - Mechanical/prosthetic mitral valves
  - Atrial fibrillation
  - Recent/recurrent thromboembolism
- Use of LMW heparin other than enoxaparin

Patient Education

- Patient education will be initiated when heparin infusion is transitioned to warfarin or LMW heparin.

References

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