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Anticoagulation Therapies, Low Molecular Weight 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.

Low Molecular Weight (LMW) Heparin

Fast Facts

- Low molecular weight (LMW) heparin is the anticoagulant of choice for most pediatric patients.
- Advantages include:
  - Minimal monitoring requirements.
  - Reduced interference of other drugs and diet.
  - Reduced heparin induced thrombocytopenia (HIT) risk vs. heparin.
  - Reduced risk of osteoporosis with long term use vs. heparin.
- Predictability of the anticoagulant effect is less than in adults, presumably due to altered plasma binding.
- Available products at CMH:
  - Enoxaparin (Lovenox®)
  - Dalteparin (Fragmin®) with hematology consult.
- Enoxaparin half life is 6 hours.
- Enoxaparin has 110 anti-factor Xa units/mg.
- LMW heparin usually does not prolong the PTT.
- LMW heparin levels are followed using a LMW heparin level based on an anti-factor Xa methodology. LMW heparin levels should be ordered to monitor the effects of LMW heparin.
- LMW heparin is also referred to as fractionated heparin in many references.
- Do not confuse the heparin LMW heparin level with that for regular heparin.

Antithrombin III (AT III) is a cofactor for activity of the LMW heparins and therefore inadequate serum AT III might be a cause for poor response to LMW heparin.

Indications for LMW Heparin

- Treatment/prevention of DVT and PE.
- Treatment/prevention of arterial thrombosis.

Content the same for Initiation and Maintenance AND Duration of Therapy boxes.

Initiation of enoxaparin therapy

Obtain blood for baseline CBC, PT, PTT.

Calculate **enoxaparin dose (mg)** based on age, weight and indication. See Table 1

Table 1 - Initial Dosing of Enoxaparin:

LMW heparin indication	< 2 months of life	≥ 2 months of life
Treatment dose q 12 hours SQ	**1.5 mg/kg**	**1 mg/kg**
Prophylaxis dose q 12 hours SQ	**0.75 mg/kg**	**0.5 mg/kg**

Maximum dose without a Hematology consult is 2 mg/kg q 12 hours

Dosing for impaired renal function

If CrCl is <30ml/min/1.73m2, consider use of heparin as an alternative and consult Hematology for dosage recommendations.

Maintenance and monitoring of enoxaparin

Table 2 - Target LMW heparin levels:

Treatment	0.5-1 units/ml
Prophylaxis	0.1-0.3 units/ml
Patients with **new thrombosis or extension of thrombus** while on enoxaparin	0.8-1.2 units/ml with hematology consult

Table 3 - Adjustment of treatment dose and monitoring based on LMW heparin level:

Adjustment of dose & timing of levels based on LMW heparin level where target is treatment			
	First level obtained 4 hours after **3rd** dose		
	After **first level** is received, subsequent adjustments are made based on the following table:		
LMW heparin level (units/ml)	**Hold next dose?**	**Dose change?**	**Repeat LMW heparin level**
< 0.35	No	↑ by 25%	4 hours after 2nd dose
0.35-0.49	No	↑ by 10%	4 hours after 3rd dose

0.5-1	No	No	4 hours after dose then 1x per week once 2 therapeutic levels are attained
1.1-1.5	No	↓ by 20%	4 hours after next dose
1.6-2	No	↓ by 30%	4 hours after next dose
> 2	Yes	↓ by 40%	q 12 hours until < 0.5

- After initiation of therapy, the first LMW heparin level is drawn 4 hours after the 3rd dose of enoxaparin. Adjustment to the initial dose should not be made until the LMW heparin level obtained 4 hours after the 3rd dose is known.
- Enoxaparin dosing will be adjusted to standard administration times by nursing (8am & 8pm). This adjustment will be complete by the 3rd dose, so timing of lab draws for enoxaparin will usually be set for 1200 or 0000 depending on which time the 3rd dose would be given.
- If rapid anticoagulation is required the LMW heparin level may be drawn 4 hours after each dose until a therapeutic level is attained. [*Rapid anticoagulation ONLY*].
- Adjust treatment dose and further monitoring based on the LMW heparin level using Table 2.
- **This table applies only if there is no bleeding.**
- Additional monitoring is NOT required for prophylaxis dosing.
- Infants frequently require higher Enoxaparin doses: up to 1.7 mg/kg for term infants and 2 mg/kg for preterm infants. **Maximum does without a Hematology consult is 2 mg/kg q 12 hours.**

Potential Drug Interactions

- Increased potential for hemorrhage:
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    - Thrombolytic agents; Urokinase, streptokinase, alteplase.
    - Drugs affecting platelet function: Aspirin, NSAIDs, dipyridomole, clopidogrel, ticlopidine & cilostazol.
    - Complementary/alternative medications known to have potential to *increase* bleeding include danshen, devil's claw, dong quai, feverfew, gingko biloba and papain.

Adverse Effects

- Bleeding:
  - Most common adverse effect.
  - Discontinue LMW heparin.
  - Refer to LMW heparin antidote section for management.

- Osteoporosis:
  - Occurs with prolonged LMW heparin.
  - Monitor bone density if LMW heparin therapy exceeds 3 months.
  - For patients receiving LMW heparin therapy > 3 months, consider bone densitometry studies on day 1 and approximately every 12 months to assess for possible osteoporosis.

- Thrombocytopenia due to **heparin-inducedthrombocytopenia** (HIT):
  - May be asymptomatic.
  - May be associated with life threatening or fatal arterial or venous thrombosis.
  - The risk for (HIT) is greater after 5 days of LMW heparin.
  - Suspect HIT if platelet count decreases by 50% or decreases below 150,000/microL.
  - Consult Hematology if HIT suspected.

LMW Heparin Antidote

- Termination of the SQ injection generally will terminate the anticoagulant effect.
- If immediate reversal is required **protamine** sulfate will result in partial neutralization. If the LMW heparin dose has been given within 3-4 hours give **1 mg protamine/1 mg of enoxaparin dose.** If initiating treatment more than 4 hours after last dose given, give 0.5 mg protamine/1 mg of enoxaparin.
- A second dose of **0.5 mgprotamine** /1mg of enoxaparin dose may be given if the PTT remains prolonged 2-4 hours after the initial dose.
- Protamine should be given IV over 10 minutes. More rapid infusion may result in hypotension. Patients with hypersensitivity to fish (vertibrate, not shellfish) and those who have received protamine-containing insulin or previous protamine therapy may be at risk of hypersensitivity reactions.

Other Considerations

- 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. Hold LMW heparin doses for 24 hours prior to **immunizations or invasive procedures** such as lumbar puncture and **surgery** unless the clinical situation requires an emergent intervention. Restart 12 hours after the procedure, surgery or immunization.
- Measure platelet counts weekly until stable on LMW heparin. 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 LMW heparin therapy. If likely due to LMW heparin, discontinue LMW heparin; initiate an alternative therapy and consult Hematology.
- The optimal sample for **LMW heparin** levels is a fresh venipuncture site.
    - Alternate sites may be considered but present limitations with interpretation of the **LMW heparin** levels.
    - Capillary samples are not appropriate.
    - Ensure that the sample is not contaminated by heparin (e.g. from an arterial line).
- Mobilization should be encouraged as tolerated.

Patient education

- CMH Inpatients
    - Direct patient education on LMW heparin will be provided and documented by CMH pharmacists for CMH inpatients. Education will include potential for adverse drug reactions and interactions, as well as training for preparation of dose and administration.
    - The injection aid device, Inject Ease, is often used when doses are dispensed or drawn up in *non-Safety Glide* insulin syringes. Training will be provided for this device if chosen by patient/caregiver. An education kit provided free-of-charge by manufacturer is available and will be provided *when commercially prepared syringes will be used at discharge*. These kits include either a DVD or VHS tape covering key points.
- CMH Outpatients
    - Patient counseling and written materials on LMW heparin will be provided by the CMH Outpatient Pharmacy and/or Children's Mercy Homecare Pharmacy when LMW heparin is dispensed.
    - CMH Med Cards and Lexicomp patient leaflets are available to outpatient clinics for patients who will obtain prescriptions from sources other than the CMH Outpatient or Homecare Pharmacy.

Indications for Hematology consultation

Indications for Hematology consultation with anticoagulant therapy:

- Initiation of therapy for patients
    - Not in critical care unit
    - Age < 30 days
    - Baseline INR ≥ 1.2 prior to initiation of warfarin
    - Impaired renal function
    - May consult Cardiology or Cardiothoracic Surgery service in lieu of Hem/Onc
- 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

References

David, M., et al. Heparin and LMWH in Children. Thrombosis Interest Group of Canada. January 2007. http://www.tigc.org/eguidelines/heparinchild07.htm. Accessed 11/15/08.

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Enoxaparin, http://online.lexi.com/crlsql/servlet/crlonline, Copyright © 1978-2008 Lexi-Comp, Inc, Hudson, OH 44236

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