Therapeutic Dosing of Unfractionated Heparin – Pediatric – Inpatient – Clinical Practice Guideline

Cover Sheet

Target Population: Inpatient

CPG Contact:
   Name: Sara Shull, PharmD, MBA, Drug Policy Manager
   Phone Number: 608-262-1817
   Email address: SShull@uwhealth.org

Guideline Author(s):
   Anne Rose, Pharm.D.
   Nicole Lubcke, Pharm.D

Coordinating Team Members:
   Carol Diamond, MD
   Scott Hagen, MD

Review Individuals/Bodies:
   Inpatient Anticoagulation Committee

Committee Approvals/Dates:
   Anticoagulation Committee: July 2012; June 2013
   Pharmacy and Therapeutics: August 2012; July 2013

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Clinical Practice Guideline (CPG)
Executive Summary

Guideline Title:
Therapeutic Dosing of Unfractionated Heparin – Pediatric – Inpatient – CPG

Guideline Overview
The following guideline provides recommendations for how to initiate, dose adjust and
monitor a therapeutic unfractionated heparin infusion in pediatric patients.

Practice Recommendations
1. Initial Heparin Bolus
   1.1. Initial bolus dose of 75 units/kg will result in a therapeutic anti-Xa in 90% of children
   1.1.1. Bolus doses are based on actual body weight
   1.2. Boluses should be used with caution or avoided in patients with the following:
      1.2.1. Neonates and premature neonates
      1.2.2. Stroke
      1.2.3. Active bleeding
      1.2.4. High bleeding risk

2. Initiation of Heparin Infusion
   2.1. Initial infusion rate is based on the age of the child
   2.2. Document infusion rates in units/kg/hr

Table 1. Initial Heparin Infusion Rates

<table>
<thead>
<tr>
<th>Age</th>
<th>Bolus Dose (units/kg)</th>
<th>Maximum Bolus (units)</th>
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<td>80</td>
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3. Algorithm for adjusting therapeutic heparin infusion

Table 2. Heparin Infusion Dose Adjustments

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<tr>
<th>Heparin Level by Anti-Xa (IU/mL)</th>
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A. Scope
1. Hospitalized patients receiving intravenous unfractionated heparin intended for therapeutic dosing

B. Methodology
1. A modified Grading of Recommendations Assessment, Development and Evaluation (GRADE) developed by the American Heart Association and American College of Cardiology (Figure 1.) has been used to assess the Quality and Strength of the Evidence in this Clinical Practice Guideline.¹

<table>
<thead>
<tr>
<th>LEVEL A</th>
<th>Multiple populations evaluated*</th>
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<tbody>
<tr>
<td>Data derived from multiple randomized clinical trials or meta-analyses</td>
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Suggested phrases for writing recommendations:³

- should be recommended
- is indicated
- is useful/effective/beneficial
- is reasonable
- may/might be considered
- may/might be reasonable
- usefulness/effectiveness is unknown/unclear/uncertain or not well established
- is not recommended
- is not indicated
- should not
- is not useful/effective/beneficial

C. Definitions
1. **Therapeutic range** - No outcome studies have determined a therapeutic range for unfractionated heparin in pediatric patients. With the absence of pediatric specific range information, extrapolation of the adult therapeutic range is appropriate.²
   1.1 **Unfractionated heparin infusion:** heparin level by anti-Xa of 0.3-0.7 units/mL.²
   1.2 **Low molecular weight heparin:** heparin level by anti-Xa of 0.5-1.1 unit/mL based on twice daily dosing.²

2. Heparin levels by anti-Xa levels have been preferred in pediatric intensive care units due to the potential lack of correlation between anti-Xa and aPTT levels.²

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D. Introduction
   Neonates and children differ in their pharmacologic response to medications. The following guideline provides recommendations for how to initiate, dose adjust and monitor a therapeutic unfractionated heparin infusion for a pediatric patient.

E. Recommendations
1. Therapeutic heparin infusions should be ordered by an order set that includes a dose adjustment algorithm, specified lab monitoring, and patient assessment: **(Class I, Level C)**
   1.1. While discouraged, if patient circumstances require heparin dosing that differs from established algorithms, specific orders must be written.
   1.1.1. Consider consulting pediatric hematology for patients who may not fit into the standard algorithm **(Class I, Level C)**
   1.2. Separate heparin order sets are available for patients on extracorporeal membrane oxygenation.

2. Baseline Laboratory Monitoring
   2.1. STAT anti-Xa and PT/INR if not available **(Class Ia, Level B)**
   2.2. STAT CBC and platelet, if not available **(Class Ia, Level B)**
   2.3. Labs must be drawn prior to initiating the heparin infusion
      2.3.1. Optimal sample is from a fresh venipuncture site

3. Initial Heparin Bolus
   3.1. Initial bolus dose of 75 units/kg will result in a therapeutic anti-Xa in 90% of children\(^2\) **(Class IIb, Level C)**
      3.1.1. Bolus doses are based on actual body weight
   3.2. Boluses should be used with caution or avoided in patients with the following: **(Class IIb, Level C)**
      3.2.1. Neonates and premature neonates
      3.2.2. Stroke
      3.2.3. Active bleeding
      3.2.4. High bleeding risk
   3.3. Round the bolus dose to the nearest 10 units for ease of preparation
   3.4. Document the administered bolus in the flow sheet
   3.5. Use heparin 1000 units/mL vial for bolus from floor stock

4. Initiation of Heparin Infusion
   4.1. Initial infusion rate is based on the age of the child\(^2\) **(Class Ia, Level B)**
   4.2. Document infusion rates in units/kg/hr

**Table 1. Initial Heparin Infusion Rates**

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5. Titration of Heparin Infusion **(Class Iib, Level C)**
   5.1. Do **NOT** monitor the heparin infusion with both aPTT and anti-Xa
   5.2. Check STAT anti-Xa after initiation of the infusion and after any rate change
      5.2.1. Every 8 hours for children < 1 year of age
      5.2.2. Every 4 hours for children ≥ 1 year of age
   5.3. Use Table 2 for dose adjustments
   5.4. Once 3 consecutive anti-Xa levels are therapeutic it is recommended to check anti-Xa level every 24 hours with the am labs
5.5. If a rate adjustment becomes necessary or the infusion is held for any reason and restarted, recheck anti-Xa level and repeat the above process.

6. Algorithm for adjusting therapeutic heparin infusion (Class IIb, Level C)

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6.1 If a therapeutic goal is not reached within 24 hours with correct titration the patient may not be an appropriate candidate for adjustments based on the heparin algorithm. Recommend consultation with Pharmacy and/or Hematology for assistance with dosing. (Class IIb, Level C)

7. Maintenance Laboratory Monitoring (Class I, Level A)

7.1 Optimal sample is from a fresh venipuncture site

7.1.1 Sample should not be drawn from an IV infusing therapeutic heparin

7.2 Hemoglobin and platelets must be followed 24 hours after initiating heparin therapy and every other day thereafter for up to 14 days or until therapy is discontinued.

8. Patient Assessment (Class IIb, Level C)

8.1 Every eight hours: Inspect line/surgical/wound sites for bleeding and check patient for symptoms indicating bleeding such as hematomas, bruising, and respiratory symptoms. Contact MD for any signs of bleeding.

9. Provider should be notified if: (Class I, Level C)

9.1 Baseline anti-Xa > 0.1 unit/mL or baseline INR > 1.2

9.2 Platelet count decreases > 50% from baseline or if count falls below 100 x10^9/L

9.3 Hemoglobin decreases by > 2 g/dL from baseline

9.4 Anti-Xa level is < 0.1 IU/mL or > 0.9 IU/mL

9.5 Patient has any deterioration in neurologic status

10. Therapeutic heparin infusions should be used with caution in patients with: (Class I, Level C)

10.1 Hypersensitivity to heparin

10.2 Increased risk for hemorrhagic complications

10.3 Active bleeding

10.4 Thrombocytopenia

10.5 Less than 72 hours post surgical procedure
A. References

B. Benefits/Harms of Implementation
1. Benefit:
   1.1. Provides a standardized approach for management and monitoring of therapeutic unfractionated heparin
   1.2. Minimize adverse drug reactions with a high risk medication in a patient population without standardized therapy
2. Harms:
   2.1. Kinetics are diverse in pediatric populations, individual patients may not fit into this algorithm

C. Qualifying Statements - No clinical studies have determined a therapeutic range for UFH in pediatric patients. Therapeutic ranges have been extrapolated from therapeutic ranges used in the adult population.

D. Implementation Strategy –
1. Recommendations provided by this guideline will be disseminated to clinical staff through the use of implementation tools outlined below.

E. Implementation Tools/Plan –
1. Email notification to hospital staff through the Clinical In-brief and Health Link PRN
2. Notification to physician groups (residents, heme/onc, peds ICU, surgery, renal) by physician leads
3. Development of self study packets to be disseminated to nurses who practice in pediatrics
4. Notification to the hospital pharmacists at staff and team meetings
5. Creation of decision support within health link through the development of pediatric therapeutic heparin infusion order sets

F. Disclaimer
It is understood that occasionally patients will not match the conditions considered in the guideline and clinical judgment should be used when developing a treatment plan.