1.8. Unfractionated Heparin and Low Molecular Weight Heparins

Heparin Dosing and Monitoring Strategies for Confirmed Venous Thromboembolism*

- Bolus with 80 units/kg IV of unfractionated heparin (UFH) and start maintenance infusion at 18 units/kg/hr or with a low molecular weight heparin (LMWH). Dosing for enoxaparin is 1 mg/kg subcutaneously (SC) every 12 hours or 1.5 mg/kg SC daily. For patients with creatinine clearance <30 mL/min, the dose of enoxaparin is 1 mg/kg SC daily.
- Initiate a vitamin K antagonist such as warfarin together with UFH or LMWH or on the first treatment day once a rise in the aPTT has been observed (with UFH).
- For UFH therapy, check aPTT at 4–8 hours and adjust dose as needed to maintain a range corresponding to a therapeutic heparin concentration.
- For UFH therapy, check platelet count prior to starting therapy and then daily. Patients who first receive UFH and are switched to LMWH, platelet count monitoring every 2–3 days from days 4 to day 14 is suggested (if therapy continues that long).
- Discontinue UFH after a minimum of 4–5 days (5–7 days for LMWH) and when the international normalized ratio (INR) is stable and above 2.0.

Pharmacokinetic/Pharmacodynamic Dosing Approach for UFH Using Activated Clotting Time (ACT)

The infusion rate (R_2) for a target ACT (ACT_2) can be estimated from an initial steady state ACT (ACT_1) on a known UFH dosing rate (R_1) using the formula:

$$R_2 = R_1 \times \left(\frac{\log\left(\frac{ACT_2}{ACT_0}\right)}{\log\left(\frac{ACT_1}{ACT_0}\right)} \right)$$

where ACT_0 is the patient's baseline ACT prior to treatment, ACT_1 is the ACT measured at steady state on the heparin infusion given at rate R_1. R_2 is the new infusion rate to produce the desired ACT (ACT_2). Monitoring aPTT is suggested prior to large dose changes if conventional weight-based dosing is initially used.

Table 1.8-1. aPTT and Weight-Based Dosing Adjustment Scheme for UFH[1,2,a]

aPTT (seconds)	Infusion Change (units/kg/hr)	Next Action	Repeat aPTT
<35 (<1.2 times normal)	+4	Re-bolus with 80 units/kg	6 hours
35–45 (1.2–1.5 times normal)	+2	Re-bolus with 40 units/kg	6 hours
46–70 (1.5–2.3 times normal)	0	0	6 hours[b]
71–90 (2.3–3.0 times normal)	–2	0	6 hours
>90 (>3 times normal)	–3	Hold infusion 1 hour	6 hours

[a]Initial dosing: Loading dose is 80 units/kg; maintenance infusion is 18 units/kg/hr (aPTT in 6 hours).

[b]During the first 24 hours, repeat aPTT every 6 hours. Thereafter, monitor aPTT once every morning unless it is outside of the therapeutic range.

Table 1.8-2. Protamine Doses for Reversal of LMWH

LMWH	<8 hr	8–12 hr	>12 hr
Dalteparin	1 mg/100 anti-Factor Xa units	0.5 mg/100 anti-Factor Xa units	Not necessary
Enoxaparin	1 mg/1 mg of enoxaparin	0.5 mg/1 mg of enoxaparin	Not necessary
Tinzaparin	1 mg/100 anti-Factor Xa units	0.5 mg/100 anti-Factor Xa units	Not necessary

References

1. Raschke RA, Reilly BM, Guidry JR, et al. The weight-based heparin nomogram compared with a "standard care" nomogram: a randomized controlled trial. *Ann Intern Med*. 1993;119(9):874–881.

2. Cruickshank MK, Levine MN, Hirsh J, et al. A standard heparin nomogram for the management of heparin therapy. *Arch Intern Med*. 1991;151(2):333–337.

Self-Assessment Problems

1. A 69-year-old, 160-lb female presents to the emergency department (ED) with a swollen left calf, which was painful and warm. A Doppler ultrasound confirms diagnosis of deep vein thrombosis (DVT). Prior to presentation her medication therapy included conjugated estrogens 0.625 mg daily, multiple vitamin once daily, and vitamin E 400 IU daily.

   A. Prior to initiating warfarin therapy, would you begin therapy with a heparin agent? Why or why not?

   B. Complete the following order sets for the patient's UFH therapy:

      1) IV bolus dose of unfractionated heparin (units) _____

      2) IV infusion of unfractionated heparin (initial infusion – units/hr) _____

      3) Check aPPT every ____ hours until therapeutic and then every ____ hours thereafter until heparin is discontinued.

      4) Check platelets every _____ hours until heparin discontinued.