CHAPTER 3

UNFRACTIONATED HEPARIN

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INTRODUCTION

Unfractionated heparin (UFH) is one of the most commonly used parenteral anticoagulants. Heparin is used in a wide variety of settings to prevent or treat thromboembolism. It can be used systemically, instilled in catheters, used to sustain device functions, or coat artificial surfaces and lines to prevent thrombotic complications. As one of the oldest anticoagulant agents in use, many of its applications developed over time and had limited assessment of efficacy from rigorous trials. Despite availability of newer anticoagulants, UFH remains frequently used due to its quick onset and offset and ease to reverse.

PHARMACOLOGY[1,2]

- UFH is a highly sulfated mucopolysaccharide, heterogeneous compound of which one-third contains the pentasaccharide unit responsible for anticoagulant activity.
- UFH is an indirect-acting anticoagulant that forms a complex with antithrombin, increasing the affinity and anticoagulant activity of antithrombin against clotting factors IIa (18 saccharide sequence required) and Xa (5 saccharide sequence required). Factors IXa, XIa, and XIIa are also inactivated.
- At higher concentrations, heparin chains unrelated to the pentasaccharide sequence can catalyze thrombin by inhibiting thrombin via heparin cofactor II, or separately by factor Xa generation through antithrombin and heparin cofactor II.
- UFH will not dissolve a formed clot but will prevent its propagation and growth.
- No differences in antithrombotic activity have been demonstrated between the various UFH preparations.

INDICATIONS

Approved indications for UFH are listed in **Table 3-1**.

PHARMACOKINETICS/PHARMACODYNAMICS

The pharmacokinetic properties of UFH are listed in **Table 3-2**.

- The pharmacokinetics of UFH can be altered by factors such as age, thromboembolism location, hepatic or renal impairment, and obesity.

TABLE 3-1: **Approved Indications for Unfractionated Heparin**

- Anticoagulant in blood samples for laboratory purposes
- Anticoagulant in blood transfusions, extracorporeal circulation, dialysis procedures
- Atrial fibrillation with embolism
- Diagnosis and treatment of acute and chronic consumptive coagulopathies (disseminated intravascular coagulation [DIC])
- Prevention of clotting in arterial and cardiac surgeries
- Prophylaxis and treatment of peripheral arterial embolism
- Prophylaxis and treatment of venous thromboembolism

Clinical Pearls

- *The activated partial thromboplastin time (aPTT)/anti-factor Xa activity from UFH can be checked to verify appropriateness of the dose for a particular treatment dosing interval. For subcutaneous administration with higher treatment goals, a 12-hour (trough) value can be assessed. If this value is too low, an 8-hour dosing interval may be considered. Similarly, if an 8-hour trough value is in the upper portion of the target range or higher, a 12-hour dosing interval can be considered for ease of use. A repeat trough value can be considered to validate the regimen. Risk assessment for thrombosis, bleeding, and compliance should be considered when determining a subcutaneous dosing regimen.*
- *Intramuscular administration is not recommended due to erratic absorption and risk of hematoma formation.*

Change in Calibrators for UFH and Potency

In 2009, the United States Pharmacopeia (USP) updated the monograph for heparin to be consistent with the World Health Organization (WHO) standards. This update resulted in up to a 10% reduction in heparin potency (potency per USP unit of heparin was up to 10% less than International Units). This conversion created a concern among clinicians for a potential underdosing of heparin. Consensus to date suggests that impact of this change on clinical outcomes is minimal.[6]