Heparin and Lovenox
What the Oral and Maxillofacial Surgeon Needs to Know

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KEYWORDS

• Heparin • Lovenox • Fondaparinux • Anticoagulation • Protamine sulfate

KEY POINTS

- Many of our surgical patients are on heparin products during surgery.
- There is no standardized approach to treating anticoagulated patients during oral and maxillofacial surgical procedures.
- When a patient is on heparin therapy, heparin may be stopped 4 to 6 hours before the surgical procedure and resumed once hemostasis is achieved (usually within 24 hours).
- If low-molecular-weight heparin is given, the treatment is generally stopped at least 12 hours before surgery and then resumed once hemostasis is achieved.

INTRODUCTION

Heparin is a naturally occurring glycosaminoglycan anticoagulant found in the secretory granules of mast cells. It is composed of alternating D-glucuronic acid and N-acetyl-D-glucosamine residues.[1] Following synthesis inside the mast cell, a glucuronidase enzyme slowly degrades the glycosaminoglycan chains to various-sized heparin fragments.[2,3] *Unfractionated heparin* is a term for the heterogeneous heparin molecules that have not been separated according to length, which can vary between 5 and 30 kD. By itself, heparin has no intrinsic anticoagulant effect. Antithrombin is a serine protease inhibitor that inhibits several coagulation factors in the intrinsic and common pathway.[2] Antithrombin binds to a specific 5-saccharide sequence on heparin. When antithrombin binds heparin, a conformational change is induced within the antithrombin enzyme. This activated antithrombin then binds coagulation factor Xa with increased affinity and accelerates its inactivation.[2–4] Thrombin (factor II) inhibition occurs when antithrombin and thrombin bind concurrently to adjacent sites on a heparin molecule. Only heparin molecules at least 18-saccharide units long are able to bind both thrombin and antithrombin simultaneously.[3] Heparin then acts as a catalyst to facilitate thrombin binding to antithrombin, forming a ternary complex that causes thrombin inhibition. Interestingly, because of their variety in fragment size, not all heparin molecules have anticoagulant activity. Some molecules may be missing the necessary 5-saccharide sequence required to bind antithrombin, whereas the chains less than 18-saccharide units are not able to span antithrombin and thrombin together to cause thrombin inhibition.[3,4]

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Low-molecular-weight heparins (LMWHs), trade name Lovenox, are derivatives of heparin used for anticoagulation. LMWHs are produced by chemically decreasing the number of the polysaccharide units on heparin, resulting in molecules that average 4 to 5 kD in weight. LMWHs that possess the necessary 5-saccharide chain retain the ability to bind antithrombin and inactivate factor Xa, as described for heparin.[3] LMWHs have inherently less antithrombin activity, however, because they are not of sufficient length to form the ternary complex bridging thrombin to antithrombin for inactivation.[3,5] **Fig. 1** compares the mechanism of action of heparin with LMWH and fondaparinux.

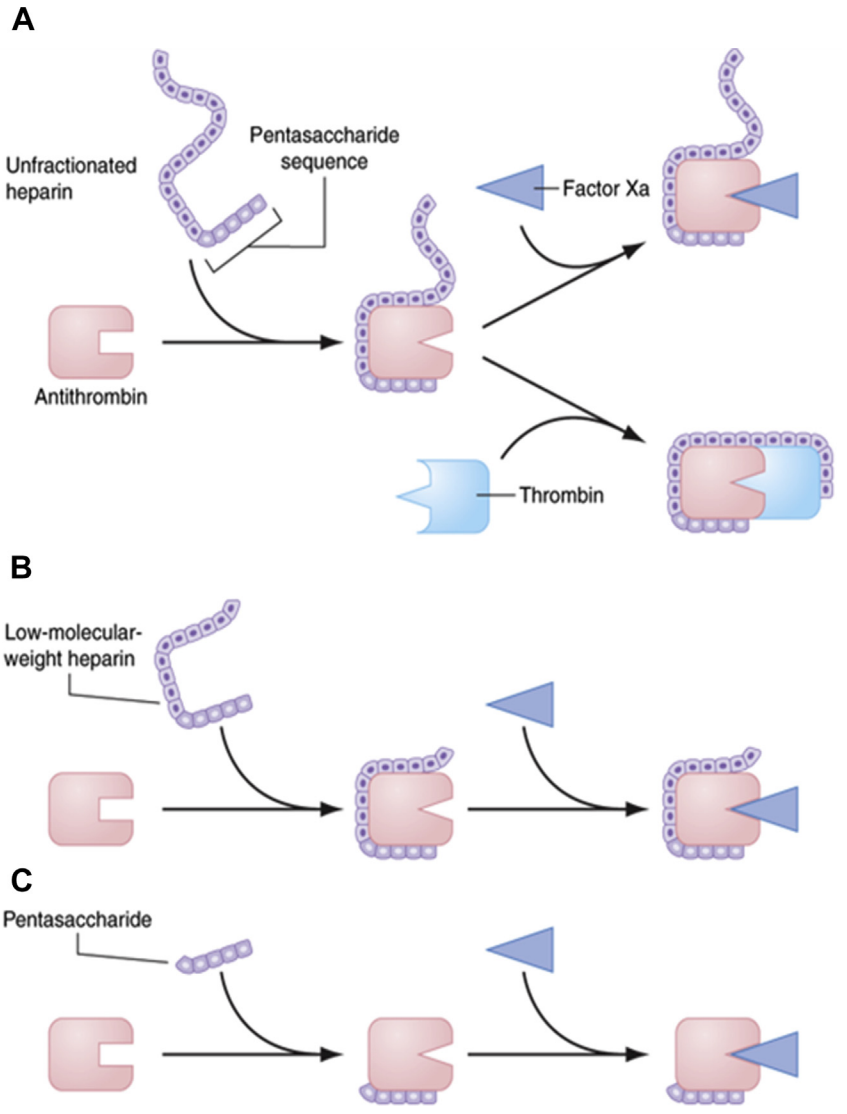

Fig. 1. Mechanism of action of heparin, LMWH, and fondaparinux, a synthetic pentasaccharide. (*A*) Heparin binds to antithrombin via its pentasaccharide sequence. This binding induces a conformational change in the reactive center loop of antithrombin that accelerates its interaction with factor Xa. To potentiate thrombin inhibition, heparin must simultaneously bind to antithrombin and thrombin. Only heparin chains composed of at least 18 saccharide units, which correspond to a molecular weight of 5400 Da, are of sufficient length to perform this bridging function. With a mean molecular weight of 15,000 Da, all of the heparin chains are long enough to do this. (*B*) LMWH has greater capacity to potentiate factor Xa inhibition by antithrombin than thrombin because, with a mean molecular weight of 4500 to 5000 Da, at least half of the LMWH chains are too short to bridge antithrombin to thrombin. (*C*) The pentasaccharide only accelerates factor Xa inhibition by antithrombin because the pentasaccharide is too short to bridge antithrombin to thrombin. *From* Kasper D, Fauci A, Hauser S, et al, editors. Harrison's principles of internal medicine. 19th edition. New York: McGraw-Hill; 2015; with permission.