U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Heparin. [Updated 2017 Nov 13].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Heparin

Updated: November 13, 2017.

OVERVIEW

Introduction

Standard or unfractionated heparin is a complex mixture of naturally occurring glycosaminoglycans and is used as an anticoagulant to treat venous thrombosis or to prevent thrombosis in high risk patients. Heparin therapy is associated with frequent elevations in serum aminotransferase levels that are typically transient and not associated with clinical symptoms or significant liver injury.

Background

Heparin (hep' a rin) is a complex mixture of naturally occurring glycosaminoglycans that have potent anticoagulant activity. Heparin has been used to treat or prevent venous thromboses for more than 50 years. Multiple generic forms of heparin are available, usually in ampoules or vials of 1000 to 40,000 units per mL. Heparin is typically given initially as 5000 to 10,000 units intravenously, followed by intravenous or subcutaneous boluses every 4 to 12 hours to keep the activated partial thrombin time in the range of 1.5 to 2 times the control value. Common side effects of standard heparin include dizziness, fatigue, headache, indigestion, nausea, excess bleeding, ecchymoses, rash and urticaria.

Hepatotoxicity

Heparin has been associated with transient serum aminotransferase elevations in 10% to 60% of patients, but values are usually less than 5 times the upper limit of normal and are rarely associated with symptoms or jaundice. Values above 5 times the upper limit of normal occur in ~2% of those receiving the high doses of heparin. In contrast, serum bilirubin and alkaline phosphatase levels usually do not change. The aminotransferase elevations are usually asymptomatic, mild and self-limited arising within the first 4 to 8 days of therapy and decreasing thereafter, rarely requiring dose modification or discontinuation. In the rare instances of mild, clinically apparent liver injury attributed to heparin reported in the literature, other possible causes of liver injury were usually present (shock, heart failure, sepsis, other potential hepatotoxins). The serum enzyme elevations generally resolve fully within 4 to 10 days of stopping heparin. Allergic features (rash, fever, eosinophilia) and autoantibodies are generally not present.

Mechanism of Injury

The cause of the serum aminotransferase elevations during heparin therapy is not known, but it is likely due to a direct hepatotoxic effect on the liver. The elevations may be accompanied by decreases in platelet counts, another know side effect of heparin therapy.

Outcome and Management

The serum aminotransferase elevations that occur on heparin therapy are usually self-limited and do not require dose modification or discontinuation of therapy. No convincing instances of clinically apparent, severe acute liver injury have been linked to heparin therapy in the published literature.

References to hepatotoxicity of standard heparin and low molecular weight heparins are given at the end of the overview section entitled Heparins.

Drug Class: Antithrombotic Agents, Anticoagulants

Other Drugs in the Subclass, Anticoagulants: Dabigatran, Desirudin, Apixaban, Edoxaban, Fondaparinux, Rivaroxaban, Heparins, Warfarin

Other Drugs in the Subclass, Heparins: Dalteparin, Enoxaparin, Tinzaparin

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Heparin – Generic

DRUG CLASS

Antithrombotic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Heparin	9005-49-6	Unspecified	No Structure