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Desirudin

Updated: January 3, 2018.

OVERVIEW

Introduction

Desirudin is a parenterally administered, selective thrombin inhibitor that is used to decrease the risk of deep vein thrombosis and pulmonary embolus in patients undergoing hip replacement surgery. Desirudin has not been linked to serum enzyme elevations during therapy or to clinically apparent liver injury with jaundice.

Background

Desirudin (des" i roo' din) is a recombinant 65 amino acid peptide analogue of hirudin, the naturally occurring anticoagulant found in the salivary glands of leeches (Hirudo medicinalis). Hirudin is a mixture of similar peptides that actively bind to and inactivate thrombin. Like human antithrombin, hirudin binds to both circulating and fibrinogen bound thrombin and thus both prevents and dissolves clots and thrombi. In clinical trials, desirudin given during and after hip replacement surgery was equivalent or slightly better than heparin in decreasing the frequency of deep vein thrombosis and pulmonary emboli during the perioperative period. Desirudin was approved for use in the United States in 2003 and has been used in limited numbers of patients. Current indications are limited to reduction of the risk of deep vein thrombosis and pulmonary embolization after elective hip replacement surgery. Desirudin is available in single use vials of 15.75 mg under the commercial name Iprivask. The usual dose is an injection of 15 mg subcutaneously immediately before surgery and twice daily for 8 to 12 days. The most common side effect is bleeding; other side effects are not common, but can include hypersensitivity reactions, including anaphylaxis. Hypersensitivity reactions are particularly common and more likely to be severe in persons who have been previously treated with desirudin or other hirudin analogues such as bivalirudin.

Hepatotoxicity

In the large prelicensure clinical trials of desirudin, serum aminotransferase and alkaline phosphatase elevations were not reported. Furthermore, there have been no case reports of clinically apparent liver injury attributable to desirudin therapy. There have been reports of hypersensitivity reactions to desirudin therapy and hepatic involvement often occurs during severe drug induced hypersensitivity reactions.

Likelihood score: E (unlikely cause of clinically apparent liver injury).

Mechanism of Injury

Desirudin is a recombinant protein and is unlikely to have intrinsic hepatotoxicity. Liver injury during desirudin therapy is clearly rare, if it occurs at all, and would most likely be part of an immunologic reaction to the foreign protein.

Outcome and Management

There appears to be cross sensitivity to allergic reactions to various preparations of recombinant hirudins and retreatment with desirudin should be avoided.

Drug Class: Antithrombotic Agents, Anticoagulants

Other Drugs in the Subclass, Anticoagulants, Thrombin Inhibitors: Dabigatran

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Desirudin – Iprivask®

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
Desirudin	120993-53-5	Protein	Complex Polypeptide

ANNOTATED BIBLIOGRAPHY

References updated: 03 January 2018

Zimmerman HJ. Platelet aggregation inhibitors. Drugs used in cardiovascular disease. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 639-412.

(Textbook of hepatotoxicity published in 1999; heparin, low molecular weight heparins and ticlopidine are discussed, but not desirudin).

De Marzio DH, Navarro VJ. Hepatotoxicity of cardiovascular and antidiabetic drugs: antihypertensives. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013, p. 528.

(Review of hepatotoxicity of cardiovascular drugs does not discuss anticoagulants or desirudin).

Weitz JI. Blood coagulation and anticoagulant, fibrinolytic, and antiplatelet drugs. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 849-76.

(Textbook of pharmacology and therapeutics).

Eriksson BI, Ekman S, Kälebo P, Zachrisson B, Bach D, Close P. Prevention of deep-vein thrombosis after total hip replacement: direct thrombin inhibition with recombinant hirudin, CGP 39393. Lancet 1996; 347 (9002): 635-9. PubMed PMID: 8596376.

(Among 1119 patients undergoing hip replacement surgery who were treated with one of 3 doses of desirudin or heparin for 8-11 days, thromboembolism was less frequent in desirudin treated subjects [18%-24% vs 34%], with no difference in rate of bleeding; no mention of hepatotoxicity or ALT elevations).

Eriksson BI, Ekman S, Lindbratt S, Baur M, Bach D, Torholm C, Kälebo P, Close P. Prevention of thromboembolism with use of recombinant hirudin. Results of a double-blind, multicenter trial comparing the efficacy of desirudin (Revasc) with that of unfractionated heparin in patients having a total hip replacement. J Bone Joint Surg Am 1997; 79: 326-33. PubMed PMID: 9070519.

(Among 445 patients undergoing hip replacement surgery, deep vein thrombosis occurred in 7% of those treated with desirudin for 8-11 days vs 23% given heparin, with no difference in rates of bleeding; no mention of ALT elevations or hepatotoxicity).

Eriksson BI, Wille-Jørgensen P, Kälebo P, Mouret P, Rosencher N, Bösch P, Baur M, et al. A comparison of recombinant hirudin with a low-molecular-weight heparin to prevent thromboembolic complications after total hip replacement. N Engl J Med 1997; 337: 1329-35. PubMed PMID: 9358126.

(Among 1587 patients undergoing hip replacement surgery, deep vein thrombosis occurred in 18% of those treated with desirudin for 8-12 days vs 25.5% given enoxaparin, with no differences in rates of bleeding; other side effects including ALT elevations were not mentioned).

Ewenstein BM. Antithrombotic agents and thromboembolic disease. N Engl J Med 1997; 337: 1383-4. PubMed PMID: 9358134.

(Editorial in response to Eriksson [N Engl J Med 1997]).

Roe MT, Granger CB, Puma JA, Hellkamp AS, Hochman JS, Ohman EM, White HD, et al. Comparison of benefits and complications of hirudin versus heparin for patients with acute coronary syndromes undergoing early percutaneous coronary intervention. Am J Cardiol 2001; 88: 1403-6, A6. PubMed PMID: 11741559.

(Among 1410 patients with acute coronary syndromes undergoing percutaneous interventions who were treated with either hirudin or heparin, myocardial infarction was less frequent with hirudin treatment, but overall survival rates were the same; no discussion of rates of ALT elevations or hepatotoxicity or other nonbleeding side effects).

Chalasani N, Fontana RJ, Bonkovsky HL, Watkins PB, Davern T, Serrano J, Yang H, Rochon J; Drug Induced Liver Injury Network (DILIN). Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. Gastroenterology 2008; 135: 1924-34. PubMed PMID: 18955056.

(Among 300 cases of drug induced liver disease in the US collected between 2004 and 2008, none were attributed to anticoagulants).

Reuben A, Koch DG, Lee WM; Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology 2010; 52: 2065-76. PubMed PMID: 20949552.

(Among 1198 patients with acute liver failure enrolled in a US prospective study between 1998 and 2007, 133 were attributed to drug induced liver injury, but none were due to anticoagulants).

Desirudin (Iprivask) for DVT prevention. Med Lett Drugs Ther 2010; 52 (1350): 85-6. PubMed PMID: 21045759.

(Concise review of the mechanism of action, efficacy and safety of desirudin, a recombinant analog of hirudin which is used to prevent deep vein thrombosis and pulmonary embolization after hip replacement surgery; no mention of hepatotoxicity or ALT elevations).

Antithrombotic drugs. Treat Guidel Med Lett 2011; 9 (110): 61-6. PubMed PMID: 21941228.

(Guidelines on the use of antiplatelet drugs including aspirin, clopidogrel, prasugrel, ticagrelor and ticlopidine mentions that prasugrel appears to be more effective than clopidogrel, but has a greater risk of bleeding; no mention of hepatotoxicity or ALT elevations).

Bergese SD, Minkowitz HS, Arpino PA, Sane DC, Levy JH. Multicenter trial of desirudin for the prophylaxis of thrombosis: an alternative to heparin-based anticoagulation (DESIR-ABLE). Clin Appl Thromb Hemost 2013; 19: 418-23. PubMed PMID: 22802554.

(Among 516 patients with risk factors for deep vein thrombosis [surgical or medical] treated with desirudin for 1-24 days, thromboembolism events occured in 1.6% of patients and none had major bleeding episodes; no mention of ALT elevations or hepatotoxicity and desirudin is not discussed).

Jove M, Maslanka M, Minkowitz HS, Jaffer AK; DESIR-ABLE Investigators. Safety of desirudin in thrombosis prevention after total knee arthroplasty: the DESIR-ABLE study. Am J Ther 2014; 21: 496-9. PubMed PMID: 23344102.

(Analysis of 65 patients treated prophylactically with desirudin from the DESIR-ABLE trial [Bergese] whose surgery was for total hip replacement, showing that none had a major bleeding episode, although 2 had minor episodes and none died or had symptomatic deep venous thromboses; two had asymptomatic thromboses and a nonfatal pulmonary embolus; no mention of ALT elevations or hepatotoxicity).

Chalasani N, Bonkovsky HL, Fontana R, Lee W, Stolz A, Talwalkar J, Reddy KR, et al.; United States Drug Induced Liver Injury Network. Features and outcomes of 899 patients with drug-induced liver injury: The DILIN Prospective Study. Gastroenterology 2015; 148: 1340-52.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, two cases were attributed to anticoagulants (prasugrel and dalteparin), but none to desirudin or the direct thrombin inhibitors or factor Xa antagonists).