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-. Pentamidine. [Updated 2014 Jan 10].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Pentamidine

Updated: January 10, 2014.

OVERVIEW

Introduction

Pentamidine is a potent, broad spectrum antiinfective agent with activity against several parasitic worms, protozoa and fungi that has been used mainly in the treatment and the prophylaxis of Pneumocystis jiroveci (formerly carinii) infection in immunodeficient persons. Pentamidine is relatively toxic and therapy requires careful monitoring. Pentamidine has been associated with transient serum aminotransferase elevations during therapy and with rare instances of clinically apparent liver injury.

Background

Pentamidine (pen tam' i deen) is an aromatic diamine that is active against a broad spectrum of infectious agents. Its mechanism of action is unknown, but it appears to be taken up and concentrated within microorganisms where it inhibits DNA, RNA and protein synthesis. Pentamidine has a broad spectrum of activity against several cestodes, trematodes and protozoan parasites such as Giardia, Cryptosporidium and Entamoeba. Pentamidine is also active against Pneumocystis jiroveci (formerly known as P. carinii), which is now considered a fungal agent. Pentamidine was approved for use in the United States in 1984 at which time a major indication was the prophylaxis and therapy of Pneumocystis jiroveci infection. In intervening years, pentamidine has been replaced by better tolerated and less toxic agents in treating Pneumocystis such as trimethoprim/sulfamethoxazole or dapsone with atovaquone. Pentamidine is also an alternative, second line therapy for leishmaniasis and trypanosomiasis. Pentamidine is not absorbed well by the oral route and is available in aerosol forms (300 mg) under the brand name of Nebupent and as a solution for injection under the name Pentam 300. For treatment of pneumocystis pneumonia, the recommended regimen is 3-4 mg/kg intravenously or intramuscularly once daily for 14 to 21 days. For pneumocystis prevention, the recommended regimen is 300 mg in nebulized form every 4 weeks. Pentamidine therapy is highly toxic and the side effects of intravenous therapy are often severe and can be fatal. These side effects include nausea, abdominal discomfort, dizziness, hypotension, tachycardia, headache, rash, fever, hypoglycemia, hyponatremia, renal insufficiency and allergic reactions, including Stevens Johnson syndrome.

Hepatotoxicity

Pentamidine has been associated with serum aminotransferase elevations in 9% to 15% of patients receiving 2 to 3 weeks of therapy for pneumocystis pneumonia. Clinically apparent liver injury has also been reported with its use, but always in association with multiple other severe complications, such as respiratory or renal failure and pancreatitis. The onset of injury is within days of starting therapy and is characterized by acute hepatic necrosis,

marked elevations in serum aminotransferase levels, rapid development of prolongation of prothrombin time and minimal or no jaundice. Recovery is typically rapid and usually complete.

Mechanism of Injury

Pentamidine interferes with polyamine synthesis and RNA polymerase activity, which may account for its multiorgan toxicity.

Outcome and Management

Pentamidine is not very well tolerated, but its major toxicities are not hepatic, and the predominance of these other dose limiting toxicities may be the reason that liver injury is not more common. Pentamidine has not been associated with fatal acute liver failure or chronic liver injury.

Drug Class: Antifungal Agents

Pentamidine is not a typical antifungal agent and has a broad spectrum of activity that does not fit neatly into any antimicrobial class. Other agents used to treat or prevent Pneumocystis jiroveci pneumonia: Sulfamethoxazole/Trimethoprim, Dapsone, Atovaquone, Primaquine, Clindamycin

Drug Class: Antihelmintic Agents

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Pentamidine – NebuPent® [Aerosol]

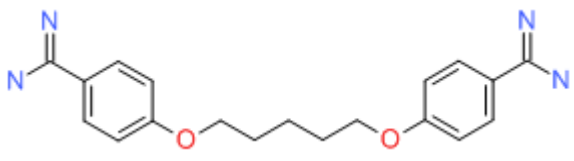
DRUG CLASS

Antifungal/Antihelmintic Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Pentamidine	100-33-4	C19-H24-N4-O2	

ANNOTATED BIBLIOGRAPHY

References updated: 10 January 2014

Zimmerman HJ. Antifungal agents. Hepatic injury from antimicrobial agents. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 609-11.

(Expert review of hepatotoxicity of antifungal agents written in 1999; severe cases of liver injury have been reported in patients with AIDS receiving pentamidine).

Phillips MA, Stanley SL Jr. Pentamidine. Chemotherapy of protozoal infections. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 1434-5.

(Textbook of pharmacology and therapeutics).

Waalkes TP, Denham C, Devita VT. Pentamidine: clinical pharmacologic correlations in man and mice. Clin Pharmacol Ther 1970; 11: 505-12. PubMed PMID: 5310706.

(Analysis of pharmacokinetics and toxicity of pentamidine in 7 patients with cancer being treated for P. jiroveci pneumonia; minor changes in liver enzymes were noted in some patients).

Western KA, Perera DR, Schultz MG. Pentamidine isethionate in the treatment of Pneumocystis carinii pneumonia. Ann Intern Med 1970; 73: 695-702. PubMed PMID: 5312203.

(Among 164 patients with P. jiroveci pneumonia treated with pentamidine, 42% had side effects including 12 [7%] with abnormal liver tests; AST 48-170 U/L, but 1 patient had jaundice and AST 2000 2 weeks after stopping, ultimately resolving at least in part).

Picon M, Causse X, Gelas P, Retornaz G, Trépo C, Bouletreau P. [Pentamidine-related acute hepatitis during pneumocystosis treatment in acquired immunodeficiency syndrome]. Gastroenterol Clin Biol 1991; 15: 463-4. French. PubMed PMID: 2070975.

(27 year old with HIV infection and severe P. jiroveci pneumonia developed renal insufficiency, pancreatitis [amylase 623 U/L] and acute hepatic necrosis after 6 days of intravenous pentamidine, with ALT 2000 U/L and decrease in prothrombin time with rapid recovery upon stopping).

Balslev U, Nielsen TL. Adverse effects associated with intravenous pentamidine isethionate as treatment of Pneumocystis carinii pneumonia in AIDS patients. Dan Med Bull 1992; 39: 366-8. PubMed PMID: 1526188.

(Retrospective analysis of side effects of pentamidine therapy in 21 patients with AIDS and P. jiroveci infection; serum enzyme elevations occurred in 3 patients but were minor; major side effects [n=5] included hypoglycemia, pancreatitis and cardiac arrest).

O'Brien JG, Dong BJ, Coleman RL, Gee L, Balano KB. A 5-year retrospective review of adverse drug reactions and their risk factors in human immunodeficiency virus-infected patients who were receiving intravenous pentamidine therapy for Pneumocystis carinii pneumonia. Clin Infect Dis 1997; 24: 854-9. PubMed PMID: 9142782.

(Retrospective analysis of adverse drug reactions to intravenous pentamidine therapy of Pneumocystis jiroveci pneumonia, identified 174 events in 72% of 106 patients treated with pentamidine; most common were nephrotoxicity [48%], hypoglycemia [24%], hyperkalemia [19%] and serum enzyme elevations [15%]).

http://aidsinfo.nih.gov/guidelines/

(Web site with recent guidelines on management and prevention of opportunistic infections including P. jiroveci in persons with HIV infection).