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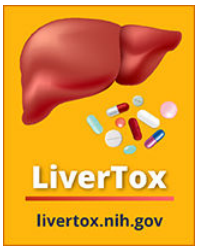
NLM Citation: LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases; 2012-. Atenolol. [Updated 2017 Jan 15].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/



Atenolol

Updated: January 15, 2017.

OVERVIEW

Introduction

Atenolol is a cardioselective beta-blocker that is widely used in the treatment of hypertension and angina pectoris. Atenolol has been linked to rare cases of drug induced liver injury, some of which have been fatal.

Background

Atenolol (a ten' oh lol) is considered a "selective" beta-adrenergic receptor blocker in that it has potent activity against beta-1 adrenergic receptors which are found in cardiac muscle, but has little or no activity against beta-2 adrenergic receptors found on bronchial and vascular smooth muscle. Atenolol was approved for use in the United States in 1981 and is still widely used in the therapy of hypertension and angina pectoris. Atenolol is also used to reduce the risk of cardiovascular mortality in patients with coronary artery disease. Atenolol is available in 25, 50 and 100 mg tablets in generic forms as well as under the trade name of Tenormin. It is also available in fixed combinations with a diuretic such as chlorthalidone (Tenoretic and others). Parenteral formulations for intravenous use are also available. The usual oral dose of atenolol in adults is 25 to 50 mg once daily initially, with subsequent adjustment based upon clinical response and tolerance, but rarely beyond 100 mg daily. Common side effects include bradycardia, hypotension, fatigue, dizziness, depression, memory loss and impotence. At high doses, atenolol is less cardioselective and can cause bronchospasm. As with all beta-blockers, sudden withdrawal can trigger rebound hypertension.

Hepatotoxicity

Atenolol therapy has been associated with mild-to-moderate elevations of serum aminotransferase levels in 1% to 2% of patients. These elevations, however, are usually asymptomatic and transient and resolve even with continuation of therapy. A few instances of clinically apparent, acute liver injury attributable to atenolol have been reported. In view of its wide scale use, atenolol induced liver injury is exceedingly rare. The onset of injury has been within 1 to 4 weeks and pattern of liver enzyme elevations has been hepatocellular or mixed. Symptoms of hypersensitivity (rash, fever, eosinophilia) are uncommon as is autoantibody formation. Most cases are self-limiting and resolve rapidly once atenolol is stopped; however, at least one fatal instance has been reported.

Likelihood score: D (Possible rare cause of clinically apparent liver injury).

Mechanism of Injury

The mechanism of drug induced liver injury from atenolol is not known. The agent has little hepatic metabolism and is excreted largely unchanged in the urine. The few cases of acute liver injury attributed to atenolol were likely idiosyncratic.

Outcome and Management

The severity of liver injury due to atenolol ranges from mild serum aminotransferase elevations to acute hepatitis with jaundice. In large case series of acute liver failure due to medications, atenolol has been listed as a rare cause. Rechallenge has not been reported, but should be avoided. There is little information about cross reactivity among the beta-blockers to hepatic injury. Switching to another beta-blocker after atenolol related acute liver injury should be done with caution and prospective monitoring.

References to the safety and potential hepatotoxicity of atenolol are provided in the overview on Beta-Adrenergic Receptor Antagonists, last updated in June 2019.

Drug Class: Beta-Adrenergic Receptor Antagonists

CASE REPORT

Case 1. Acute liver injury and jaundice from atenolol.

[Modified from a case in the database of the Drug-Induced Liver Injury Network]

A 44 year old man with hypertension was treated with atenolol and 4 weeks later developed nausea, vomiting, light colored stools and weight loss. He was subsequently hospitalized when found to be jaundiced. He admitted to drinking two or three beers per day, but had no history of alcohol problems, liver disease or risk factors for viral hepatitis. Other medications were limited to various vitamins and herbal preparations including coenzyme Q10, omega-3 fatty acids, a vitamin B complex and glucosamine/condroitin which he had taken for several years. On presentation, he had a low grade fever and jaundice, but no rash or peripheral manifestations of chronic liver disease. Serum aminotransferase and alkaline phosphatase levels were both elevated and total serum bilirubin was 5.4 mg/dL (Table). He tested negative for hepatitis A, B, C and E virus infection and autoantibody reactivity. An abdominal ultrasound was unremarkable. A liver biopsy showed multiple epithelioid granulomas and acute hepatic injury with prominence of eosinophils in portal areas, suggestive of a drug reaction. Atenolol was discontinued and he began to improve within a week. When seen in follow up one and 3 months after initial presentation, all liver tests were normal.

Key Points

Medication:	Atenolol (25 mg daily)
Pattern:	Hepatocellular (R=7.5)
Severity:	3+ (jaundice, hospitalization)
Latency:	4 weeks to onset of symptoms and jaundice
Recovery:	4 weeks
Other medications:	Vitamins, glucosamine, chondroitin, omega-3-fatty acids

Laboratory Values

Weeks After Starting	Weeks After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Other
Atenolol stopped after 5 weeks of therapy (25 mg daily)					

Table continued from previous page.

Weeks After Starting	Weeks After Stopping	ALT (U/L)	Alk P (U/L)	Bilirubin (mg/dL)	Other
5	0	497	231	5.4	Eosinophils 9%
5.2	0.3	486	189	5.6	Liver biopsy
5.4	0.4	555	216	3.1	
7	21	41	97	1.2	
9	4	25	71	0.6	
12	7	32	57	1.0	
18	13	19	61	0.5	
Normal Values		**<41**	**<140**	**<1.2**	

Comment

The acute liver injury was typical of what has been described in cases of beta-blocker induced liver injury with a latency of 4 weeks and a mild, self-limited hepatitis and a hepatocellular pattern of serum enzyme elevations. Recovery was prompt once atenolol was stopped. Liver histology also supported the diagnosis. The patient was also taking a variety of over-the-counter vitamins, nutritional supplements and herbal products, but had taken the same formulations for several years and restarted them without incident after recovery from the acute liver injury. This patient had not taken other beta-blockers and had no history of allergy or previous drug induced liver injury.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Atenolol – Generic, Tenormin®

DRUG CLASS

Beta-Adrenergic Receptor Antagonists

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Atenolol	29122-68-7	C14-H22-N2-O3