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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-. Loop Diuretics. [Updated 2017 Oct 2].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Loop Diuretics

Updated: October 2, 2017.

OVERVIEW

Introduction

The loop diuretics are potent and widely used agents in the therapy of edematous states and congestive heart failure and less commonly for hypertension. Clinically apparent acute liver injury due to the loop diuretics is exceeding rare, if it occurs at all.

Background

The loop diuretics act by inhibition of the sodium-potassium-chloride symporter present in the thick ascending limb of the loop of Henle causing an inhibition of sodium reuptake. The increase in delivery of sodium to the distal convoluted loop overwhelms its capacity for sodium reabsorption and a brisk sodium diuresis ensues. The loop diuretics are grouped together because of shared mechanism of action, but they have distinct chemical structures. The loop diuretics are more potent than the typical thiazide diuretics and usually have a shorter duration of action. As a result, the loop diuretics are used more for the therapy of edema than long term therapy of hypertension. Common and shared side effects of the loop diuretics include dizziness, headache, gastrointestinal upset, hypernatremia, hypokalemia and dehydration.

Furosemide (fure oh' se mide) was the first loop diuretic to be approved in the United States (1966) and is still widely used with more than 37 million prescriptions filled yearly. Furosemide is available in tablets of 20, 40 and 80 mg in generic forms and under the brand name Lasix. Furosemide is also available as an oral solution and as a liquid solution for injection. The usual adult dose of furosemide is 20 to 320 mg daily, given in one to three divided doses.

Ethacrynic (eth a krin' ik) acid was the second loop diuretic to be approved for use in the United States (1967), but is now rarely used; it remains available in 25 mg tablets and a solution for intravenous use generically and under the brand name Edecrin. The usual oral adult dose is 25 to 100 mg in one to three divided doses daily.

Bumetanide (bue met' a nide) is a potent loop diuretic that was approved for use in the United States in 1983 and continues to be used for the treatment of edema. Bumetanide is available as tablets of 0.5, 1 and 2 mg in generic forms and under the trade name of Bumex. The usual oral adult dose is 0.5 to 2 mg in two or three divided doses daily.

Torsemide (tor' se mide) was approved for use in edema in the United States in 1993 and is still in common use used for both edema and hypertension. Torsemide is available in tablets of 5, 10, 20 and 100 mg in generic forms and under the brand name of Demadex. Solutions are available for intravenous use as well. The usual oral adult dose is 5 to 100 mg daily in one or two divided doses.

Hepatotoxicity

Use of the loop diuretics has not been associated with an increased rate of serum aminotransferase elevations. There have been only rare reported cases of clinically apparent liver injury associated with loop diuretics and most of these reports have not been very convincing. Interestingly, furosemide causes a direct hepatotoxicity in mice and has been used as an animal model of drug induced liver injury. This injury does not appear to occur in humans. Thus, clinically apparent liver injury from the loop diuretics must be exceeding rare, if it occurs at all.

Likelihood score, all loop diuretics: E (unlikely causes of clinically apparent liver injury).

Mechanism of Injury

The cause of the rare occurrence of clinically apparent liver injury associated with the loop diuretics is not known. These agents are metabolized minimally by the liver and generally have rapid renal excretion.

Outcome and Management

Cases of clinically apparent liver injury due to the loop diuretics have been too few to characterize their severity and course. There have been no published instances of acute liver failure or chronic liver injury attributed to any of the loop diuretics. Cross reactivity among the four agents is unlikely because of the variability of their chemical structure.

References to the safety and potential hepatotoxicity of bumetanide, ethacrynic acid, furosemide and torsemide are provided in the overview section on Diuretics (updated October 2017).

Drug Class: Diuretics

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Bumetanide – Generic, Bumex®

Ethacrynic Acid – Generic, Edecrin®

Furosemide – Generic, Lasix®

Torsemide – Generic, Demadex®

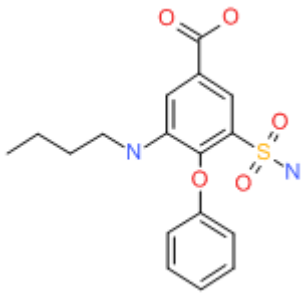
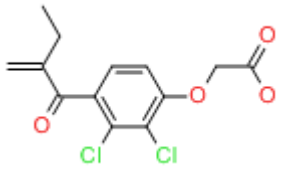
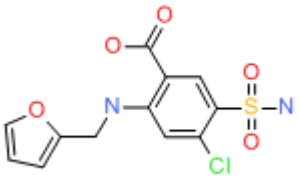
DRUG CLASS

Diuretics

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULAS AND STRUCTURES

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Bumetanide	28395-03-1	C17-H20-N2-O5-S	
Ethacrynic Acid	58-54-8	C13-H12-Cl2-O4	
Furosemide	54-31-9	C12-H11-Cl-N2-O5-S	
Torsemide	56211-40-6	C16-H20-N4-O3-S