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-. Trihexyphenidyl. [Updated 2017 Jul 20].
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Trihexyphenidyl

Updated: July 20, 2017.

OVERVIEW

Introduction

Trihexyphenidyl is an oral anticholinergic agent used predominantly in the symptomatic therapy of Parkinson disease and movement disorders. Trihexyphenidyl has not been associated with serum enzyme elevations during treatment, but has been implicated in rare cases of acute liver injury.

Background

Trihexyphenidyl is an anticholinergic agent that blocks the central cholinergic receptors, helping to balance cholinergic transmission in the basal ganglia. Trihexyphenidyl may also block dopamine reuptake and storage in central sites thus increasing dopaminergic activity. The exact mechanism(s) by which the anticholinergic agents are beneficial for symptoms of Parkinson disease is unknown. They are used largely in early Parkinsonism and as adjunctive therapy with levodopa or more potent antiParkinson disease agents. Trihexyphenidyl was approved for use in the United States in 1949 and has been in use since. Current indications include therapy of symptomatic Parkinson disease, as well as spastic disorders and extrapyramidal disorders due to medications. Trihexyphenidyl is available in tablets of 2 and 5 mg, and as an elixir of 2 mg/5 mL in generic forms and formerly under the brand name Artane. The recommended dose is 2 to 5 mg three times daily. Common side effects are due to its anticholinergic activity and include nervousness, confusion, drowsiness, tachycardia, blurred vision, constipation, dry mouth, nausea and urinary retention.

Hepatotoxicity

Trihexyphenidyl has not been reported to cause serum aminotransferase elevations, but it has not been evaluated for effects on serum enzyme levels in a prospective manner. Trihexyphenidyl was cited as the cause of two cases of acute liver injury resulting in death in the Japanese literature, but few details were given and there have been no other reports of such injury in the literature in the subsequent 40 years. Thus, trihexyphenidyl must be a very rare cause of liver injury, if it occurs at all.

Likelihood score: E* (unproven but suspected cause of clinically apparent liver injury).

Mechanism of Injury

The metabolism of trihexyphenidyl has not been well defined; it appears to be metabolized in the liver to a small extent.

Drug Class: Antiparkinson Agents

Other Drugs in the Subclass, Anticholinergic Agents: Benztropine, Biperiden

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Trihexyphenidyl – Generic, Artane®

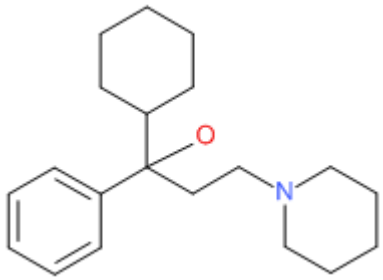
DRUG CLASS

Antiparkinson Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Trihexyphenidyl	144-11-6	C20-H31-N-O	

ANNOTATED BIBLIOGRAPHY

References updated: 20 July 2017

Zimmerman HJ. Antiparkinsonism drugs. In, Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999, pp. 715-7.

(Expert review of hepatotoxicity published in 1999; among anticholinergic agents, "only trihexyphenidyl has been incriminated in hepatic injury"; other antiparkinsonism drugs discussed include levodopa, lergotrile [no longer available], pergolide and bromocriptine).

Larrey D, Ripault MP. Hepatotoxicity of psychotropic drugs and drugs of abuse. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier Inc, 2013, pp. 443-62.

(Review of hepatotoxicity of agents acting on the central nervous system).

Standaert DG, Roberson ED. Treatment of central nervous system degenerative disorders. In, Brunton LL, Chabner BA, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 12th ed. New York: McGraw-Hill, 2011, pp. 609-28.

(Textbook of pharmacology and therapeutics).

McDowell F. Symposium on levodopa in Parkinson's disease. Clinical and pharmacological aspects. Clinical laboratory abnormalities. Clin Pharmacol Ther 1971; 12: 335-9. PubMed PMID: 4102803.

(Retrospective analysis of laboratory abnormalities arising in 974 patients with Parkinson disease treated with levodopa; AST elevations occurred in 9% of 5427 determinations, but were usually mild and transient returning to normal in 1-2 months without dose adjustment; AST levels rose to 1600 U/L in one patient who later died of complications of diabetes).

Lambert D, Waters CH. Comparative tolerability of the newer generation antiparkinsonian agents. Drugs Aging 2000; 16: 55-65. PubMed PMID: 10733264.

(Review of mechanism of action, tolerability and safety of selegiline, pramipexole, ropinirole, tolcapone and entacapone in Parkinson disease).

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 attributed to agents used for Parkinson disease).

Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation, and outcomes in patients with drug-induced liver injury in the general population of Iceland. Gastroenterology 2013; 144: 1419-25,1425. PubMed PMID: 23419359.

(In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, but none of the 96 were attributed to an agent used to treat Parkinson disease).

Drugs for Parkinson's disease. Treat Guidel Med Lett 2013; 11 (135): 101-6. PubMed PMID: 24165688.

(Concise review of recommendations for therapy of Parkinson disease with description of mechanisms of action, efficacy and adverse events).

Hernández N, Bessone F, Sánchez A, di Pace M, Brahm J, Zapata R, A Chirino R, et al. Profile of idiosyncratic drug induced liver injury in Latin America: an analysis of published reports. Ann Hepatol 2014; 13: 231-9. PubMed PMID: 24552865.

(Among 176 reports of drug induced liver injury from Latin America published between 1996 and 2012, none were attributed to an agent to treat Parkinson disease).

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. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury from the US enrolled in a prospective database between 2004 and 2012, none were attributed to an agent used to treat Parkinson disease).