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Pergolide

Updated: July 20, 2017.

OVERVIEW

Introduction

Pergolide is an oral dopamine receptor agonist used predominantly in the therapy of Parkinson disease. Pergolide therapy is associated with low rate of transient serum enzyme elevations during treatment and has been implicated in rare cases of acute liver injury.

Background

Pergolide (per' goe lide) is an ergot derivative similar to bromocriptine which acts as a dopamine receptor agonist. Pergolide, unlike bromocriptine, has agonist activity on both D1 and D2 dopamine receptors and acts directly on the substantia nigra. Pergolide was approved for use in the United States in 1988 and has been in use since in the therapy of symptomatic Parkinson disease, usually in combination with levodopa/carbidopa. Pergolide is available in tablets of 0.05, 0.25 and 1.0 mg in generic forms and under the brand name of Permax. The typical initiating dose of pergolide is 0.05 mg once daily for the first 2 days, with gradual increase thereafter based upon tolerance and effect. The average therapeutic dose in clinical studies was 3 mg per day given in 3 divided doses. Common side effects include profound hypotension (with the first dose), somnolence, fatigue, vivid dreams, insomnia, anxiety, confusion, depression, dizziness, headache, nausea and gastrointestinal upset.

Hepatotoxicity

Pergolide has been reported to cause serum aminotransferase elevations in a small proportion of patients, but these abnormalities are usually mild, asymptomatic and self-limiting even without dose adjustment. In addition, pergolide has been implicated in a small number of cases of clinically apparent, acute liver injury, but the frequency, severity, clinical characteristics and typical pattern of enzyme elevations have not been characterized. Thus, pergolide is may be a rare cause of clinically apparent liver injury.

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

Mechanism of Injury

Pergolide is metabolized extensively by the liver and metabolic byproducts excreted rapidly in the urine.

Outcome and Management

Most instances of suspected hepatotoxicity of pergolide have been mild and self-limited. There have been no published reports of acute liver failure or chronic hepatitis due to pergolide. There is likely cross sensitivity to hypersensitivity reactions among the different ergot alkaloids, such as bromocriptine.

Drug Class: Antiparkinson Agents

Other Drugs in the Subclass, Dopamine Receptor Agonists: Apomorphine, Bromocriptine, Pramipexole, Ropinirole, Rotigotine

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Pergolide – Generic, Permax®

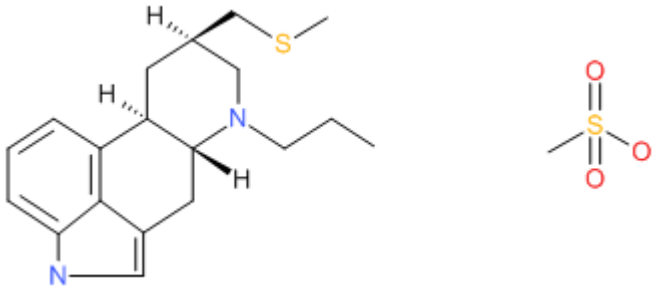
DRUG CLASS

Antiparkinson Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Pergolide	66104-23-2	C19-H26-N2-S.C-H4-O3-S	

REFERENCES

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).

LeWitt PA, Ward CD, Larsen TA, Raphaelson MI, Newman RP, Foster N, Dambrosia JM, et al. Comparison of pergolide and bromocriptine therapy in parkinsonism. Neurology 1983; 33: 1009-14. PubMed PMID: 6348585.

(27 patients with Parkinson disease were treated with either pergolide or bromocriptine in a double-blind cross over study and 11 were continued on pergolide for up to one year; the two drugs had comparable effects and side effects, one patient developed mild ALT elevations [59 U/L] that resolved despite continuing bromocriptine).

Lieberman AN, Gopinathan G, Neophytides A, Goldstein M. Management of levodopa failures: the use of dopamine agonists. Clin Neuropharmacol 1986; 9: S9-21. PubMed PMID: 3297319.

(Among 278 patients with Parkinson disease failing to respond to levodopa and treated with a dopamine agonist, 61% improved but adverse events requiring discontinuation occurred in 46%; no discussion of hepatotoxicity).

Langtry HD, Clissold SP. Pergolide. A review of its pharmacological properties and therapeutic potential in Parkinson's disease. Drugs 1990; 39: 491-506. PubMed PMID: 2184010.

(Review of the mechanism of action, pharmacology, efficacy and safety of pergolide in Parkinson disease; side effects lead to discontinuation of pergolide in 27% of patients; ALT elevations and hepatotoxicity are not mentioned).

Barone P, Bravi D, Bermejo-Pareja F, Marconi R, Kulisevsky J, Malagù S, Weiser R, Rost N. Pergolide monotherapy in the treatment of early PD: a randomized, controlled study. Pergolide Monotherapy Study Group. Neurology 1999; 53: 573-9. PubMed PMID: 10449123.

(In a controlled trial of 3 months of pergolide vs placebo in 105 patients with Parkinson disease, side effects included anorexia, nausea, vomiting and dizziness and led to discontinuation in 12% of pergolide vs 4% of placebo patients; no mention of ALT elevations or hepatotoxicity).

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).

Bonuccelli U, Colzi A, Del Dotto P. Pergolide in the treatment of patients with early and advanced Parkinson's disease. Clin Neuropharmacol 2002; 5: 1-10. PubMed PMID: 11852289.

(Review of the mechanism of action, pharmacology, efficacy and safety of pergolide in Parkinson disease; no mention of ALT elevations or hepatotoxicity).

Oertel WH, Wolters E, Sampaio C, Gimenez-Roldan S, Bergamasco B, Dujardin M, Grosset DG, et al. Pergolide versus levodopa monotherapy in early Parkinson's disease patients: The PELMOPET study. Mov Disord 2006; 21: 343-53. *(* PubMed PMID: 16211594.

In a controlled trial of pergolide vs levodopa in 294 patients with early Parkinson disease, adverse events led to discontinuation in 18% of pergolide vs 10% of levodopa treated patients; no mention of ALT elevations or hepatotoxicity).

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).