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Bromocriptine

Updated: July 20, 2017.

OVERVIEW

Introduction

Bromocriptine is an oral dopamine receptor agonist used predominantly in the therapy of Parkinson disease, but which has other activities including inhibition of prolactin and growth hormone release which has led to its use in acromegaly, infertility and galactorrhea. Bromocriptine 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

Bromocriptine (broe" moe krip' teen) is a semisynthetic ergot alkaloid derivative which acts as a dopamine receptor agonist. Bromocriptine has strong agonist activity on the D2 class of dopamine receptors and partial antagonist of the D1 receptors in central nervous system. Bromocriptine was approved for use in the United States in 1978, the first in this class of agents, and has been in wide use since. Current indications are the therapy of symptomatic Parkinson disease as well as spastic disorders and extrapyramidal disorders caused by medications. Bromocriptine also has inhibitory activity on prolactin and growth hormone release, and its indications also include treatment of amenorrhea and galactorrhea related to hyperprolactinemia, female infertility, acromegaly, Cushing syndrome and premenstrual syndrome. Bromocriptine is available in tablets of 2.5 mg and capsules of 5 mg in generic forms and under the brand name of Parlodel. The recommended dose for Parkinson disease is 10 to 40 mg daily, but it must be introduced gradually and the dose titrated based upon tolerance and effect. In Parkinson disease, it is usually used in combination with levodopa/carbidopa. Common side effects include profound hypotension (with the first dose), somnolence, fatigue, vivid dreams, anxiety, confusion, hallucinations, delusions, depression, dizziness, headache, nausea and gastrointestinal upset, symptoms common with increased dopaminergic activity.

Hepatotoxicity

Bromocriptine 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 rare instances, more marked elevations occur that may require dose modification or discontinuation and which can recur with rechallenge. In addition, bromocriptine has been implicated in a small number of cases of clinically apparent acute liver injury, but the clinical characteristics and typical pattern of enzyme elevations has not been characterized and case reports of hepatic injury due to bromocriptine have not been published. Thus, bromocriptine is a very rare cause of clinically apparent liver injury and has not been implicated in causing acute liver failure or chronic liver injury.

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

Mechanism of Injury

Bromocriptine is rapidly removed from the serum by the liver with extensive first pass metabolism. Bromocriptine is metabolized to inactive forms largely by hydrolysis and excreted rapidly.

Outcome and Management

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

Drug Class: Antiparkinson Agents

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

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Bromocriptine – Generic, Parlodel®

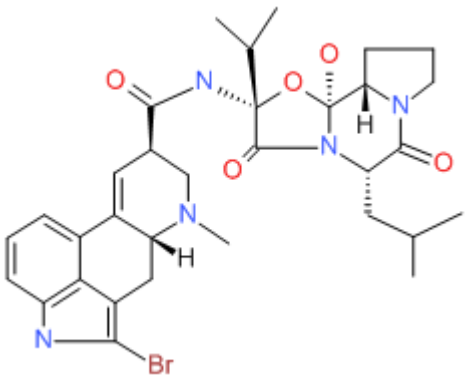
DRUG CLASS

Antiparkinson Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Bromocriptine	25614-03-3	C32-H40-Br-N5-O5	

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).

Calne DB, Plotkin C, Williams AC, Nutt JG, Neophytides A, Teychenne PF. Long-term treatment of parkinsonism with bromocriptine. Lancet 1978; 1: 735-8. PubMed PMID: 76747.

(Retrospective analysis of experience in treating 92 patients with Parkinson disease using bromocriptine and levodopa for up to 30 months, serum enzyme elevations occurred in 6 patients [7%] which were transient in 4, required dose modification in 1 and stopping in 1; no clinically apparent liver injury).

Lieberman AN, Kupersmith M, Gopinathan G, Estey E, Goodgold A, Goldstein M. Bromocriptine in Parkinson disease: further studies. Neurology 1979; 29: 363-9. PubMed PMID: 571981.

(Retrospective analysis of experience in treating 66 patients with Parkinson disease using bromocriptine for 2-24 months; mild Alk P elevations occurred in 22% and one patient developed jaundice after 2 months, biopsy showing a toxic hepatitis and stopping leading to recovery; no details given).

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).

Liberato NL, Poli M, Bollati P, Chiofalo F, Filipponi M. Bromocriptine-induced acute hepatitis. Lancet 1992; 340: 969-70. PubMed PMID: 1357362.

(82 year old man with Parkinson disease developed ALT elevations [peak value ~730 U/L] within 5 days of starting bromocriptine, resolving within 10 days of stopping and recurring [peak value ~750 U/L] within 5 days of restarting; no mention of symptoms or bilirubin levels).

Korczyn AD, Brunt ER, Larsen JP, Nagy Z, Poewe WH, Ruggieri S. A 3-year randomized trial of ropinirole and bromocriptine in early Parkinson's disease. The 053 Study Group. Neurology 1999; 53: 364-70. PubMed PMID: 10430427.

(In a randomized controlled trial in 35 patients with early Parkinson disease comparing ropinirole to bromocriptine, "no significant laboratory abnormalities" or withdrawals because of liver abnormalities were reported).

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).