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Pilocarpine

Updated: June 24, 2020.

OVERVIEW

Introduction

Pilocarpine is an orally available cholinergic agonist that is used to treat symptoms of dry mouth in patients with keratoconjunctivitis sicca (Sjögren syndrome) or with xerostomia (dry mouth) due to local irradiation. Pilocarpine has not been linked to serum enzyme elevations during therapy or to instances of clinically apparent liver injury.

Background

Pilocarpine (pye" loe kar' peen) is a cholinergic agonist that stimulates muscarinic receptors, resulting in an increase in parasympathetic activity. Engagement of the cholinergic receptors causes increased secretion from exocrine glands, including sweat, salivary, lacrimal, gastric, pancreatic and intestinal glands, as well as increased tone and motility of smooth muscle cells in the eye, respiratory and gastrointestinal tract. Use of daily oral doses of pilocarpine has been shown to improve symptoms of dry mouth and increase salivary flow in patients with Sjögren syndrome and with xerostomia due to local irradiation therapy. Pilocarpine for oral use was approved for use in the United States in the 1990s and is currently available in generic forms as tablets of 5 mg. Pilocarpine is also available as ophthalmologic drops for therapy of glaucoma and ocular hypertension. The typical oral dose is 5 mg 2 to 4 times daily. Side effects are usually mild and largely attributable to cholinergic stimulation including increased sweating, rhinitis, nausea, diarrhea, headaches, dizziness, visual disturbances and fatigue.

Hepatotoxicity

In clinical trials of pilocarpine, serum enzyme elevations were uncommon and no more frequent than with placebo. Despite, wide scale use, there have been no published reports of acute liver injury attributable to pilocarpine.

Mechanism of Injury

The mechanism by which pilocarpine might cause serum aminotransferase elevations is not known. Pilocarpine is metabolized in parasympathetic synaptic clefts and in plasma and has little hepatic metabolism.

Drug Class: Sjögren Syndrome Agents, Cholinergic Agents

Other Drugs in the Class: Cevimeline

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Pilocarpine – Generic

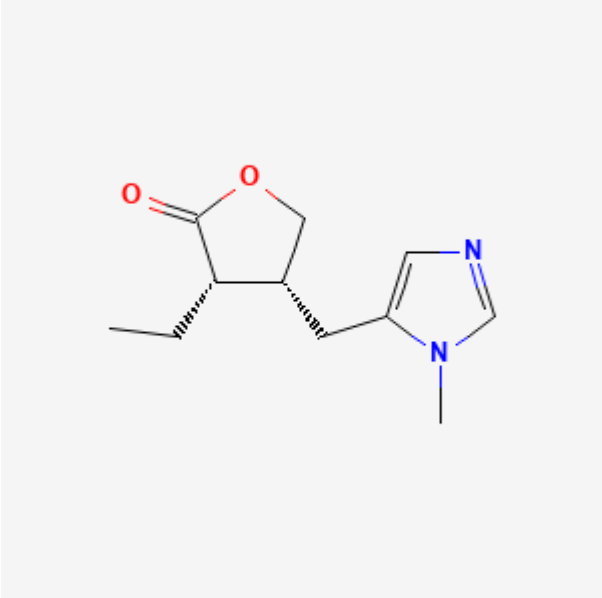
DRUG CLASS

Sjögren Syndrome Agents

COMPLETE LABELING

Product labeling at DailyMed, National Library of Medicine, NIH

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NO.	MOLECULAR FORMULA	STRUCTURE
Pilocarpine	92-13-7	C11-H16-N2-O2	

ANNOTATED BIBLIOGRAPHY

References updated: 24 June 2020

Zimmerman HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999.

(Extensive review of hepatotoxicity published in 1999; cholinergic agents and pilocarpine are not discussed).

Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013.

(Textbook of hepatotoxicity published in 2013; cholinergic agents and pilocarpine are not discussed).

Henderer JD, Rapuano CJ. Ocular pharmacology. In, Brunton LL, Hilal-Dandan R, Knollman BC, eds. Goodman & Gilman's the pharmacological basis of therapeutics. 13th ed. New York: McGraw-Hill, 2018, pp. 1251-70.

(Textbook of pharmacology and therapeutics).

Fox PC, van der Ven PF, Baum BJ, Mandel ID. Pilocarpine for the treatment of xerostomia associated with salivary gland dysfunction. Oral Surg Oral Med Oral Pathol. 1986;61:243–8. PubMed PMID: 3517744.

(Pilot study of single doses of pilocarpine or placebo in 6 patients with Sjögren syndrome demonstrated an increase in salivary flow and decrease in sensation of dry mouth).

Rieke JW, Hafermann MD, Johnson JT, LeVeque FG, Iwamoto R, Steiger BW, Muscoplat C, Gallagher SC. Oral pilocarpine for radiation-induced xerostomia: integrated efficacy and safety results from two prospective randomized clinical trials. Int J Radiat Oncol Biol Phys. 1995;31:661–9. PubMed PMID: 7852133.

(Among 369 patients with xerostomia following cancer radiotherapy who were treated with pilocarpine [2.5-10 mg every 8 hours] or placebo for 12 weeks, there were no serious drug related adverse events at any dose).

Vivino FB, Al-Hashimi I, Khan Z, LeVeque FG, Salisbury PL 3rd, Tran-Johnson TK, Muscoplat CC, et al. Pilocarpine tablets for the treatment of dry mouth and dry eye symptoms in patients with Sjögren syndrome: a randomized, placebo-controlled, fixed-dose, multicenter trial. P92-01 Study Group. Arch Intern Med. 1999;159:174–81. PubMed PMID: 9927101.

(Among 373 patients with Sjögren syndrome who were treated with pilocarpine [2.5 or 5 mg 4 times daily] or placebo for 12 weeks, none had serious drug related adverse events; liver function tests were monitored, but there was no mention of ALT elevations or hepatotoxicity).

Wu CH, Hsieh SC, Lee KL, Li KJ, Lu MC, Yu CL. Pilocarpine hydrochloride for the treatment of xerostomia in patients with Sjögren syndrome in Taiwan--a double-blind, placebo-controlled trial. J Formos Med Assoc. 2006;105:796–803. PubMed PMID: 17000452.

(Among 44 patients with Sjögren syndrome treated with pilocarpine [5 mg 4 times daily] or placebo for 12 weeks, the most common side effect was excessive sweating [22%] and there were no serious adverse events or "significant alterations in ...hepatic profiles").

Fox RI. Sjogren's syndrome: evolving therapies. Expert Opin Investig Drugs. 2003;12:247–54. PubMed PMID: 12556218.

(Review of standard and experimental therapies of Sjögren syndrome mentions pilocarpine and cevimeline, but does not discuss its adverse side effects).

Papas AS, Sherrer YS, Charney M, Golden HE, Medsger TA Jr, Walsh BT, Trivedi M, et al. Successful treatment of dry mouth and dry eye symptoms in Sjögren syndrome patients with oral pilocarpine: a randomized, placebo-controlled, dose-adjustment study. J Clin Rheumatol. 2004;10:169–77. PubMed PMID: 17043506.

(Among 250 patients with Sjögren syndrome treated with pilocarpine [20-30 mg daily] or placebo for 12 weeks, there were no serious drug related adverse events or significant changes in laboratory results in comparison to placebo).

Berk L. Systemic pilocarpine for treatment of xerostomia. Expert Opin Drug Metab Toxicol. 2008;4:1333–40. PubMed PMID: 18798702.

(Review of 6 controlled trials of pilocarpine for radiation induced xerostomia; among 261 patients treated long term, side effects included sweating [55%], urinary frequency [11%], rhinitis [10%], headache [8%], increased lacrimation [8%] and diarrhea [6%], with no mention of ALT elevations or clinically apparent liver injury).

Ramos-Casals M, Tzioufas AG, Stone JH, Sisó Bosch X. Treatment of primary Sjögren syndrome: a systematic review. JAMA. 2010;304:452–60. PubMed PMID: 20664046.

(Review of 3 controlled trials of pilocarpine in 673 patients with Sjögren syndrome found improvements in symptoms of dry mouth and dry eyes with a dose of 5 mg every 6 hours, but also a higher rate of excessive sweating, urinary frequency and nausea; no mention of ALT elevations or clinically apparent liver injury).

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 linked to pilocarpine or other cholinergic agents).

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;148:1340–1352.e7. PubMed PMID: 25754159.

(Among 899 cases of drug induced liver injury enrolled in a US prospective study between 2004 and 2013, no cases were attributed to pilocarpine or other cholinergic agents).

Tanigawa T, Yamashita J, Sato T, Shinohara A, Shibata R, Ueda H, Sasaki H. Efficacy and safety of pilocarpine mouthwash in elderly patients with xerostomia. Spec Care Dentist. 2015;35:164–9. PubMed PMID: 25639487.

(Among 40 elderly patients with dry mouth who were treated with pilocarpine or plain water mouthwash for 4 weeks, drop outs were frequent, and common side effects were oral or tongue discomfort, while xerostomia improved with the pilocarpine but not the water mouthwash).

Brito-Zerón P, Retamozo S, Kostov B, Baldini C, Bootsma H, De Vita S, Dörner T, et al. Efficacy and safety of topical and systemic medications: a systematic literature review informing the EULAR recommendations for the management of Sjögren's syndrome. RMD Open. 2019;5:e001064. PubMed PMID: 31749986.

(Systematic review of the literature on therapies for sicca syndrome mentions 5 controlled trials showing improvements in oral dryness and saliva flow with pilocarpine and cevimeline but no evidence for effects from trials of systemic treatments with anakinra, hydroxychloroquine, infliximab or rituximab).