



Valerian

Updated: November 25, 2013.

OVERVIEW

Introduction

Valerian is a botanical extract derived from the roots of *Valeriana officinalis*, which is widely used in herbal medicine for insomnia, anxiety and digestive and urinary problems. Valerian has been linked to rare instances of clinically apparent liver injury.

Background

Valerian (va ler' ee an) is the common name of the plant genus *Valeriana*, several species of which are used in herbal medicine, most typically *Valeriana officinalis*. Valerian has been used for centuries in Europe, usually for digestive and urinary problems. The name valerian derives from the Latin word *valere*, which means "to be in good health." Valerian is claimed to have sedative, hypnotic, anxiolytic, anticonvulsant, antispasmodic and antidepressant activities. Presently, it is used most commonly as a sleeping aid and for therapy of stress. The basis for its sedative effects is believed to be valepotriates (which are terpene alcohols) and volatile oils (including monoterpenes and sesquiterpenes). Components of valerian are believed to interact with the gamma amino butyric acid (GABA) receptor in a manner similar to the benzodiazepines. The typical dosage of valerian is 300 to 600 mg at bedtime for sleep or taken 3 times daily for stress. Valerian is found in many relaxation drinks. Valerian has few side effects, which are mostly mild and transient and include sedation, dizziness and withdrawal symptoms on stopping.

Hepatotoxicity

Valerian has been implicated in a small number of cases of clinically apparent liver injury, but usually in combination with other botanicals such as skullcap or black cohosh. In view of its wide scale use, valerian has to be considered a very rare cause of hepatic injury. In published cases, the latency to onset ranged from 3 to 12 weeks and the pattern of enzyme elevations was usually hepatocellular or mixed hepatocellular-cholestatic. The liver injury was usually mild-to-moderate in severity with recovery within 2 to 4 months of stopping. Immunoallergic and autoimmune features were not present. Severe cases with features of hepatic failure have been described, but usually in association with other potentially hepatotoxic herbals.

Mechanism of Injury

The cause of the liver injury associated with valerian use is not known. Valerian extracts contain multiple ingredients, but none have been shown to be specifically hepatotoxic.

Outcome and Management

Hepatotoxicity from valerian is usually mild-to-moderate in severity and self-limiting. Only a small number of cases of liver injury attributed to valerian have been published, and there have been no instances of chronic hepatitis, cirrhosis or vanishing bile duct syndrome attributed to its use, and no convincing case of acute liver failure.

Other Names: All-heal, Garden heliotrope, Tagara, Valeriana officinalis, Common valerian, Garden valerian, Indian valerian

Drug Class: Herbal and Dietary Supplements

CASE REPORT

Case 1. Acute hepatitis due to valerian.

[Modified from case 1 of: MacGregor FB, Abernethy VE, Dahabra S, Cobden I, Hayes PC. Hepatotoxicity of herbal remedies. *BMJ* 1989; 299: 1156-7. [PubMed Citation](#)].

A 57 year old woman developed fatigue one week after starting an herbal medication for stress (Neurelax: believed to contain valerian, hops, asafetida and gentian). Two weeks later, 3 weeks after starting the botanical, she developed jaundice. She had no history of liver disease or risk factors for viral hepatitis. She drank socially, averaging 1 to 2 alcoholic beverages daily, and took no other medications except indapamide (a nonthiazide diuretic) which she had taken for many years. Physical examination showed jaundice, but no fever, rash or signs of chronic liver disease. Laboratory tests showed marked elevations in serum bilirubin (18.4 mg/dL) and ALT levels (1165 U/L) (Table). There was no mention of results of testing for viral or autoimmune hepatitis. Ultrasonography showed no evidence of biliary obstruction. Despite stopping the herbal, she deteriorated clinically over the next few weeks, developing ascites and hepatic encephalopathy. The jaundice persisted for 4 months but eventually resolved. A liver biopsy showed evidence of chronic hepatitis and fibrosis. Ten months after initial presentation, she was well enough to return to work, but serum ALT levels were still slightly elevated.

Key Points

Medication:	Neurelax (Valerian)
Pattern:	Hepatocellular (R=12.7)
Severity:	4+ (jaundice, hospitalization, hepatic decompensation)
Latency:	1 week to fatigue, 3 weeks to jaundice
Recovery:	10 months (incomplete)
Other medications:	Indapamide chronically

Laboratory Values

Time After Starting	Time After Stopping	ALT (U/L)*	Alk P (U/L)	Bilirubin (mg/dL)*	Other
Started herbal (including skullcap and valerian)					
3 weeks	0	1165	232	18.4	INR=1.9
4 weeks	1 weeks	890		22.8	
6 weeks	3 weeks	200		23.4	
8 weeks	5 weeks	210		28.7	

Table continued from previous page.

Time After Starting	Time After Stopping	ALT (U/L)*	Alk P (U/L)	Bilirubin (mg/dL)*	Other
4 months	10 weeks	90		6.1	
5 months	16 weeks	95		2.3	
7 months	24 weeks	100		1.2	
Normal Values		<40	<100	<1.2	

* Some values estimated from Figure 1. Bilirubin levels converted by formula: 17.1 $\mu\text{mol/L}$ =1.0 mg/dL.

Comment

While this case was convincing as an example of drug induced liver injury, the herbal responsible for the injury was somewhat unclear and it is always possible that the hepatic injury was due to a contaminant of the product. The clinical pattern was of an acute viral hepatitis-like illness with acute liver failure, but eventual spontaneous recovery.

PRODUCT INFORMATION

REPRESENTATIVE TRADE NAMES

Valerian – Generic

DRUG CLASS

Herbal and Dietary Supplements

SUMMARY INFORMATION

[Fact Sheet at National Center for Complementary and Integrative Health, NIH](#)

[Fact Sheet at Office of Dietary Supplements, NIH](#)

CHEMICAL FORMULA AND STRUCTURE

DRUG	CAS REGISTRY NUMBER	MOLECULAR FORMULA	STRUCTURE
Valerian	8008-88-6	Herbal mixture	No Structure

ANNOTATED BIBLIOGRAPHY

References updated: 25 November 2013

Zimmerman HJ. Unconventional drugs. Miscellaneous drugs and diagnostic chemicals. In, Zimmerman, HJ. Hepatotoxicity: the adverse effects of drugs and other chemicals on the liver. 2nd ed. Philadelphia: Lippincott, 1999: pp. 731-4.

(Expert review of hepatotoxicity published in 1999; hepatotoxicity of herbals is discussed, but valerian is not specifically mentioned).

Seeff L, Stickel F, Navarro VJ. Hepatotoxicity of herbals and dietary supplements. In, Kaplowitz N, DeLeve LD, eds. Drug-induced liver disease. 3rd ed. Amsterdam: Elsevier, 2013, pp. 631-58. *(Review of hepatotoxicity of*

herbal and dietary supplements [HDS] Valerian is listed as a potential cause of hepatitis but is not specifically discussed

).

Valerian. In, PDR for Herbal Medicines. 4th ed. Montvale, New Jersey: Thomson Healthcare Inc. 2007: pp. 872-6.

(Compilation of short monographs on herbal medications and dietary supplements).

MacGregor FB, Abernethy VE, Dahabra S, Cobden I, Hayes PC. Hepatotoxicity of herbal remedies. BMJ 1989; 299: 1156-7. PubMed PMID: 2513032.

(Four cases of hepatitis attributed to herbals, all women, ages 41-57, developed jaundice 2-8 weeks after starting herbals for stress ["Neurelax" and "Kalms"], believed to contain skullcap and/or valerian [bilirubin 13.5-28.3 mg/dL, ALT 293-1165 U/L, Alk P 97-730 U/L], resolving 2-19 months after stopping: Case 1).

Shepherd C. Sleep disorders. Liver damage warning with insomnia remedy. BMJ 1993; 306: 1477. PubMed PMID: 8357398.

(Letter in response to a review on the medical uses of valerian pointing out recent reports of hepatotoxicity [MacGregor 1989]).

Caldwell SH, Feeley JW, Wieboldt TF, Featherston PL, Dickson RC. Acute hepatitis with use of over-the-counter herbal remedies. Va Med Q 1994 Winter; 121: 31-3. PubMed PMID: 8142493.

(53 year old woman developed jaundice 4 weeks after starting an herbal containing skullcap and valerian [4 capsules nightly] for sleep [bilirubin 9 mg/dL, ALT 1208 U/L, Alk P 298 U/L, protime 13.5 sec], resolving in 3 months).

Chan TY, Tang CH, Critchley JA. Poisoning due to an over-the-counter hypnotic, Sleep-Qik(hyoscine, cyproheptadine, valerian). Postgrad Med J 1995; 71: 227-8. PubMed PMID: 7784284.

(Study of 23 patients who took an overdose of "Sleep-Qik", a botanical containing valerian, demonstrated no evidence of ALT elevations or liver injury).

Shaw D, Leon C, Kolev S, Murray V. Traditional remedies and food supplements. A 5-year toxicological study(1991-1995). Drug Saf 1997; 17: 342-56. PubMed PMID: 9391777.

(Five year experience of a Medical Toxicology Unit in London including 1297 enquiries and 37 for liver injury; 9 cases described, 5 due to valerian).

Menecier D, Saloum T, Dourthe PM, Bronstein JA, Thiolet C, Farret O. [Acute hepatitis after phytotherapy]. Presse Med 1999; 28: 966. French. PubMed PMID: 10366933.

(63 year old woman developed fatigue followed by jaundice several weeks after starting valerian as a sleep aid [bilirubin 4.2 mg/dL, ALT 352 U/L, Alk P 739 U/L], resolving in 3 months after stopping).

Plushner SL. Valerian: Valeriana officinalis. Am J Health Syst Pharm 2000; 57: 328-35. PubMed PMID: 10714969.

(Review of the uses, pharmacology, clinical efficacy and safety of valerian with mention of report of 4 cases of possible hepatotoxicity [MacGregor 1989]).

Stevinson C, Ernst E. Valerian for insomnia: a systematic review of randomized clinical trials. Sleep Med 2000; 1: 91-9. PubMed PMID: 10767649.

(Systematic review of efficacy and safety of valerian for insomnia concluded that evidence for efficacy of valerian is promising, but not fully conclusive; no mention of hepatotoxicity).

Stickel F, Seitz HK, Hahn EG, Schuppan D. [Liver toxicity of drugs of plant origin]. *Z Gastroenterol* 2001; 39: 225-32, 234-7. German. PubMed PMID: 11324140.

(Review of hepatotoxicity of botanicals including pyrrolizidine alkaloids, germander, celandine, chaparral, Chinese herbs and pennyroyal).

Stedman C. Herbal hepatotoxicity. *Semin Liver Dis* 2002; 22: 195-206. PubMed PMID: 12016550.

(Review and description of patterns of liver injury due to herbals, including discussion of potential risk factors, and herb-drug interactions; valerian is listed as potentially causing abnormal liver tests).

Whiting PW, Clouston A, Kerlin P. Black cohosh and other herbal remedies associated with acute hepatitis. *Med J Aust* 2002; 177: 440-443. PubMed PMID: 1238154.

(6 cases of severe hepatitis in patients taking herbal medications, including one on black cohosh alone and 5 taking multiple herbals including skullcap [n=3], valerian [n=2], chaparral [n=1], and greater celandine [n=1] for 1 to 14 weeks, presenting with jaundice [bilirubin 9.9-62.7 mg/dL, ALT 1293-3764 U/L, Alk P 80-219 U/L], the one on black cohosh alone requiring emergency liver transplantation, the other 5 resolving in 7-25 weeks, 3 treated with prednisone for prolonged cholestasis).

Pittler MH, Ernest E. Systematic review: hepatotoxic events associated with herbal medicinal products. *Aliment Pharmacol Ther* 2003; 18: 451-71. PubMed PMID: 12950418.

(Systematic review of published cases of hepatotoxicity due to herbal medications listing 52 case reports or case series, most common agents being celandine [3], chaparral [3], germander [8], Jin Bu Huan [3], kava [1], Ma Huang [3], pennyroyal [1], skullcap [2], Chinese herbs [9], valerian [1]).

Schiano TD. Hepatotoxicity and complementary and alternative medicines. *Clin Liver Dis* 2003; 7: 453-73. PubMed PMID: 12879994.

(Review of herbal associated hepatotoxicity, including common patterns of presentation; valerian is listed as having hepatotoxic potential).

Hadley S, Petry JJ. Valerian. *Am Fam Physician* 2003; 67: 1755-8. PubMed PMID: 12725454.

(The root of valerian is used mostly commonly as a sleeping aid, and secondarily as an anxiolytic; review of clinical trials; no discussion of hepatotoxicity).

Russo MW, Galanko JA, Shrestha R, Fried MW, Watkins P. Liver transplantation for acute liver failure from drug-induced liver injury in the United States. *Liver Transpl* 2004; 10: 1018-23. PubMed PMID: 15390328.

(Among ~50,000 liver transplants reported to UNOS between 1990 and 2002, 270 [0.5%] were performed for drug induced acute liver failure, including 7 [5%] attributed to herbal medications, but valerian not mentioned as a cause).

Seeff LB. Herbal hepatotoxicity. *Clin Liver Dis* 2007; 11: 577-96. PubMed PMID: 17723921.

(Review of herbal induced hepatotoxicity, with a review of the case series of acute liver injury attributed to valerian [MacGregor 1989]).

García-Cortés M, Borraz Y, Lucena MI, Peláez G, Salmerón J, Diago M, Martínez-Sierra MC, et al. [Liver injury induced by “natural remedies”: an analysis of cases submitted to the Spanish Liver Toxicity Registry]. *Rev Esp Enferm Dig* 2008; 100: 688-95. Spanish. PubMed PMID: 19159172.

(Among 521 cases of drug induced liver injury submitted to Spanish registry, 13 [2%] were due to herbals, one attributed to valerian, onset in 1 week [bilirubin 16.9 mg/dL, ALT and Alk P normal], resolving in 6 months).

Chalasani N, Fontana RJ, Bonkovsky HL, Watkins PB, Davern T, Serrano J, Yang H, Rochon J; Drug Induced Liver Injury Network (DILIN). Causes, clinical features, and outcomes from a prospective study of drug-induced liver injury in the United States. *Gastroenterology* 2008; 135: 1924-34. PubMed PMID: 18955056.

(Among 300 cases of drug induced liver disease in the US collected between 2004 and 2008, 9% of cases were attributed to herbal medications, but none were attributed to valerian).

Cohen DL, Del Toro Y. A case of valerian-associated hepatotoxicity. *J Clin Gastroenterol* 2008; 42: 961-2. PubMed PMID: 18431248.

(27 year old woman developed fatigue and abdominal pain 10 weeks after starting valerian root [bilirubin 0.9 mg/dL, ALT 820 U/L, Alk P 278 U/L], resolving within 4 weeks of stopping).

Navarro VJ. Herbal and dietary supplement hepatotoxicity. *Semin Liver Dis* 2009; 29: 373-82. PubMed PMID: 19826971.

(Overview of the regulatory environment, clinical patterns, and future directions in research with HDS; valerian is listed as having been linked to hepatotoxicity).

Vassiliadis T, Anagnostis P, Patsiaoura K, Giouleme O, Katsinelos P, Mpoumponaris A, Eugenidis N. Valeriana hepatotoxicity. *Sleep Med* 2009; 10: 935. PubMed PMID: 19138557.

(50 year old woman found to have ALT elevations without symptoms 3 weeks after starting valerian tea [ALT 246 rising to 564 U/L with normal bilirubin and Alk P], resolving 10 months after stopping).

Müller Z, Sárkány A, Altorjay A, Szilágyi A, Tura T, Ozsvár Z. [Liver failure a la Eastern Europe]. *Orv Hetil* 2009; 150: 555-7. Hungarian. PubMed PMID: 19275973.

(50 year old woman with alcoholism who took valerian intermittently developed cirrhosis and portal hypertension, the authors suggesting that valerian exacerbated the underlying alcoholic cirrhosis).

Jacobsson I, Jönsson AK, Gerdén B, Hägg S. Spontaneously reported adverse reactions in association with complementary and alternative medicine substances in Sweden. *Pharmacoepidemiol Drug Saf* 2009; 18: 1039-47. PubMed PMID: 19650152.

(Review of 778 spontaneous reports of adverse reactions to herbals to Swedish Registry does not mention valerian or skullcap).

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 [11%] were attributed to drug induced liver injury, of which 12 [9%] were due to herbals including usinic acid [2], thermoslim [1], Ma Huang [1], horny goat weed [1], black cohosh [1], Hydroxycut products [1] and unspecified herbals [4], but none were attributed to valerian specifically).

Stacy S. Relaxation drinks and their use in adolescents. *J Child Adolesc Psychopharmacol* 2011; 21: 605-10. PubMed PMID: 2136095.

(Review of relaxation drinks which now include more than 300 bottled beverages available in the US, some of which include valerian as an anxiolytic and sleeping aid with names such as Bula, Drank, iChill, Marley Mellow Mood, miniCHILL, Slow Cow).

Teschke R, Wolff A, Frenzel C, Schulze J, Eickhoff A. Herbal hepatotoxicity: a tabular compilation of reported cases. *Liver Int* 2012; 32: 1543-56. PubMed PMID: 22928722.

(A systematic compilation of all publications on the hepatotoxicity of specific herbals identified 185 publications on 60 different herbs, herbal drugs and supplements including two publications on valerian [MacGregor 1989, Mennecier 1999]).

Bunchorntavakul C, Reddy KR. Review article: herbal and dietary supplement hepatotoxicity. *Aliment Pharmacol Ther* 2013; 37: 3-17. PubMed PMID: 23121117.

(Systematic review of literature on HDS associated liver injury mentions that valerian has been implicated in causing clinically apparent hepatotoxicity [Cohen 2008]).

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. (In a population based study of drug induced liver injury from Iceland, 96 cases were identified over a 2 year period, including 15 attributed to herbals or dietary supplements, but none specifically to valerian). PubMed PMID: 23419359.