

Severe Complications of Herbal Medicines

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Abstract

Herbal medicines are being increasingly used for treatment of variety of disorders. Herbal medicines are generally thought to lack severe side effects. Despite of the general belief, herbal medicines are known to cause serious side effects and toxicities. On the other hand, physicians' knowledge of herbal

medicines and their potential toxicities are generally limited. Neurotoxicity, cardiac toxicity, pulmonary toxicity, hepatotoxicity, and nephrotoxicity are potential severe complications of herbal medicines. The subject of severe herbal medicine complications is reviewed.

Key words: Herbal medicine; alternative medicine; side effect

Introduction

Herbal medicines are commonly used for treatment of variety of health conditions. Herbal medicines are generally believed to lack serious side effects. Lower costs compared to conventional medications are other likely attraction to these treatments. Despite of the general belief, herbal medicines can cause serious complications and even death. These complications are potentially caused by use of inherent toxic herbs, misidentification of herbs, or contamination or adulteration of herbal medicines with heavy metals or conventional medicines [1-3].

Physicians have limited knowledge regarding potential herbal medicine side effects. Physicians have little training in herbal medicines and their potential serious complications and they usually do not treat herbs in the same manner as conventional medicines. Familiarity of physicians with potential severe complications of herbal medicines is important to identify and treat these conditions [4-6]. This review discusses reported severe complications reported after use of herbal medicines.

Cardiac Complications

Severe cardiac side effects can occur in patients that are taking herbal medicines that include bradycardia, heart block, and tachyarrhythmia (**Table1**) [7-23].

Erycibe henryi Prain (*Ting Kung Teng*) is an herb used in Chinese medicines to treat musculoskeletal discomfort. *Erycibe henryi* Prain exhibits cholinergic activities and lacrimation, salivation, rhinorrhea, diarrhea, vomiting, and miosis develop shortly after consumption. Cardiovascular manifestations are bradycardia, ventricular tachyarrhythmia, and hypotension. The management is supportive. Gastrointestinal decontamination, and in severe cases administration of intravenous atropine, could be life saving [7,8].

Complete atrioventricular block due to consumption of *Nerium oleander* containing cardiac glycoside has been reported. *Nerium oleander* is an evergreen shrub that grows in United States, China, India, Portugal, and Mediterranean region. This plant contains oleandarin and neriine that are cardiac glycosides. Despite its potential toxicity, *Nerium oleander extract* is used in mixed herbal medicines [9-11].

Caowu (*Aconitum kusnezoffii*) and Chuanwu (*Aconitum carmichaeli*) are Oriental herbal medicines that are used to treat arthritis. These herbs contain the highly toxic diterpene alkaloid: aconitine. Aconitine is a cardiotoxin. Aconitine poisoning may manifest by

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gastrointestinal upset, generalized weakness, hypotension, and ventricular arrhythmias. The management of aconitine poisoning is mainly supportive. Close cardiac monitoring is necessary to detect and treat arrhythmias [12-16].

Anticholinergic syndrome may develop after ingestion of herbal teas like Angel trumpet lily tea, Lime tea mixed with *Datura innoxia*, and Paraguay tea (*Ilex paraguariensis*). Belladonna alkaloids and atropine are alkaloids responsible for the anticholinergic syndrome. Clinical manifestations include dry mucus membranes, hyperthermia, sinus tachycardia, mydriasis, cycloplegia, decreased gastrointestinal and bladder motility, and central nervous system (CNS) symptoms. Complete heart block, circulatory collapse, respiratory failure, and coma have been described with high doses. Treatment of anticholinergic syndrome is generally supportive. The use of anticholinesterase agents like tacrine hydrochloride has been suggested in severe toxicities [17-22].

Neurological Complications

Herbal medicines can cause severe neurological symptoms including weakness, seizure, and intracranial bleeding. *Cimifuga racemosa*, *Cicuta douglasii*, *Arcostaphylos uva-ursi*, *Herba ephedrae*, *Piper mysticum*, *Pausinystalia yohimbe*, *Acontium sp.*, *Ginkgo biloba*, *Strychnos nux-vomica*, *Nerium oleander*, herbal teas are known to be associated with seizures in humans. Possible mechanisms for this association include reduced seizure threshold, interaction with anti-convulsive medications, direct neurotoxicity, strychnine poisoning, and cardiovascular collapse. *Ginkgo biloba* potentially inhibits platelet activating factor and prolongs bleeding time after its consumption. Subdural hematoma and intra-cerebral bleeding have been associated with *Ginkgo biloba* [24-29].

Pulmonary Complications

Severe pulmonary complications may result after use of herbal medicines. Anaphylactic reactions, asthma exacerbation, severe interstitial pneumonitis, non-cardiogenic pulmonary edema, acute eosinophilic pneumonia, and small airway disease are discussed briefly in this section.

Peumus boldus, *Echinacea*-containing herbal remedies, and *willow bark*-containing dietary supplements are associated with anaphylactic reactions. Respiratory

support, antihistamines, epinephrine, and corticosteroids are mainstay of therapy [30-32].

Green tea has been shown to induce asthma. Green tea contains a low molecular component epigallocatechin gallate (EGCG) that is the culprit in inducing asthma. Patients with green tea-induced asthma demonstrate dose-dependent histamine release to epigallocatechin gallate challenge. IgE-mediated mechanism has also been suggested to play a role in green tea-induced asthma [33-35].

Interstitial pneumonitis in patients taking kampo medicines has been well described. Kampo medicines are mixture of several herbal agents and are used to treat a wide variety of disorders (**Table2**). The clinical presentation of kampo-induced pneumonitis is nonspecific and include fever, cough, and shortness of breath. Pneumonitis is usually detected 2 to 3 months after continues use of kampo medicines. Elevated C-reactive protein, erythrocyte sedimentation rate, serum lactic dehydrogenase, transaminases, and leukocytosis are nonspecific laboratory findings that are frequently seen in drug-induced pneumonitis. Pulmonary function testing shows carbon monoxide diffusion capacity. Chest computed tomography can findings include diffuse ground-glass opacities with patchy consolidation. The clinical course of kampo-induced pneumonitis seems to be benign. Cessation of medication may result in complete resolution of pneumonitis in several months. In more severe cases, a course of corticosteroid therapy may be reasonable [36-48].

Noncardiogenic pulmonary edema and respiratory failure have also been reported after use of kampo medicines. Although there are no data to support the use of corticosteroids, high-dose methylprednisolone has been used empirically with some success [49-51].

Acute eosinophilic pneumonia can develop after taking Shosaiko-to and Shoseiryu-to. Patients present with fever, dyspnea, hypoxemia, peripheral and BAL eosinophilia, and diffuse or peripheral pulmonary infiltrates. Resolution of pulmonary disease and hypoxemia is expected after corticosteroid therapy [52-54].

Sauropus androgynus is an Asian shrub leaf that was a commonly ingested vegetable for weight loss in Taiwan. An endemic of obstructive pulmonary disease in

young otherwise healthy women have now been attributed to *Sauropus androgynus*. These patients presented with dyspnea, obstructive pattern on pulmonary function testing, and normal chest radiographs. The obstructive lung disease is due to presence of bronchiolitis obliterans. Bronchiolitis obliterans is a pathological diagnosis. Small airways (2-4 mm) often showed segmental, partial, or completely circumferential, necrosis of the walls, with inflammatory infiltrates. Bronchiolitis obliterans is irreversible damage and conventional modalities in treatment of COPD were ineffective. Many patients developed respiratory failure and required lung transplantation [55-60].

Hepatotoxicity

Acute hepatitis has been described in patients taking herbal medicines. Extracts of *Kavalactones* are used as a remedy for anxiety and tension. *Atractylis gummifera* is a Mediterranean thistle and *Callilepis laureola* is a remedy for stomach upset and cough. The *chaparral leaf* has been used for treatment of cancer, gastrointestinal complaints, respiratory diseases and sexually transmitted diseases. *Germander* is generally consumed in tea or capsule form for weight loss. *Ma-huang* is a traditional Chinese medicine, has been commonly used in the western civilization as a weight loss aid. *Syosaiko-to* is a kampo medicine, which has been used in the treatment of chronic liver disease. Clinical manifestations usually

develop 1 to 4 months after taking the herbal medications and include nausea, vomiting, abdominal discomfort, and jaundice. Elevate transaminases are found on initial laboratory work-up. Clinical course is usually benign and most patients improve after stopping the medicines. More severe cases may progress to hepatic failure and need intensive supportive care. Orthoptic liver transplant has been performed in patients with herb-induced fulminant hepatic failure [61-68].

Nephrotoxicity

Rhizoma Rhei extracts, *Aristolochia manshuriensis*, *Cape aloes*, and *Ajuga nipponensis* *Maniko* are known nephrotoxins. Acute renal failure, acute interstitial nephritis, metabolic acidosis, rhabdomyolysis, and tubular dysfunction have been described [69-75].

Heavy Metal Poisoning

Heavy metal contamination of herbal medicine has commonly been reported. Lead, arsenic, thallium, and uranium are common contaminants. Patients may present with a variety of clinical manifestations including gastrointestinal upset, hepatitis, polyarthritis, encephalopathy, ataxia, or change of mental status. Heavy metal poisoning should be considered in patients taking herbal medications and unexplained symptoms [76-80].

TABLE 1. CARDIAC COMPLICATIONS OF HERBAL MEDICINES.

Herbal Medicine	Clinical Manifestations
Erycibe henryi Prain (Ting Kung Teng)	Cardiac: bradycardia, ventricular tachyarrhythmia, and hypotension Other: lacrimation, salivation, rhinorrhea, diarrhea, vomiting, and miosis
Nerium oleander	Cardiac: Complete Heart Block Other: Drowsiness, Tremor, Seizure
Aconitum sp.	Cardiac: Hypotension, Ventricular arrhythmias, QT-prolongation Other: Gastrointestinal Upset, Generalized Weakness
Angel trumpet lily tea Datura innoxia Ilex paraguariensis	Cardiac: Sinus Tachycardia, Complete Heart Block, Circulatory Collapse Other: Dry Mucus Membranes, Hyperthermia, Mydriasis, Cycloplegia, Constipation, Urinary Retention, CNS Symptoms.

TABLE 2. PULMONARY TOXICITIES ASSOCIATED WITH COMPLEMENTARY MEDICINES

Herbal Medicine	Pulmonary Complication
Bakumondo-to	Interstitial Pneumonia
Bofutsusho-san	Interstitial Pneumonia
Byakkokaninjin-to	Interstitial Pneumonia
Daisaiko-to	Interstitial Pneumonia
Gosha-jinki-gan	Interstitial Pneumonia
Hangeshashin-to	Interstitial Pneumonia
Kamishoyo-san	1. Interstitial Pneumonia 2. Non-cardiogenic Pulmonary Edema
Mokuboui-to	Interstitial Pneumonia
Otsuji-to	1. Interstitial Pneumonia 2. Non-cardiogenic Pulmonary Edema
Ouren-gedoku-to	Interstitial Pneumonia
Pien Tze Huang	Interstitial Pneumonia
Rikkunshi-to	Interstitial Pneumonia
Saiboku-to	Interstitial Pneumonia
Sairei-to	1. Interstitial Pneumonia 2. Non-cardiogenic Pulmonary Edema
Shosaiko-to	1. Interstitial Pneumonia 2. Non-cardiogenic Pulmonary Edema 3. Pulmonary infiltrates with eosinophilia
Shoseiryu-to	1. Interstitial Pneumonitis 2. Pulmonary infiltrates with eosinophilia
Auopus androgynus	Bronchiolitis
Green tea	Asthma exacerbation

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