Food and Chemical Toxicology 107 (2017) 502–519

Contents lists available at ScienceDirect

Food and Chemical Toxicology

journal homepage: www.elsevier.com/locate/foodchemtox

Invited review

Kidney toxicity related to herbs and dietary supplements: Online table of case reports. Part 3 of 5 series

Amy Christine Brown [a, b, *]

[a] Department of Complementary and Alternative Medicine, John A. Burns School of Medicine, 651 Ilalo Street, MEB 223, Honolulu, HI, USA
[b] University of Hawaii at Manoa, Honolulu, HI, USA

ARTICLE INFO

Article history:
Received 22 February 2016
Received in revised form
30 June 2016
Accepted 22 July 2016

Keywords:
Kidney
Renal
Toxicity
Dietary supplement
Herb
Transplant
Death

ABSTRACT

Background: No tabular summary of potentially life-threatening, kidney-toxic dietary supplements (DS; includes herbs) based on PubMed case reports is currently available online and continually updated to forewarn United States consumers, clinicians, and companies manufacturing DS. The purpose of this review was to create an online research summary table of kidney toxicity case reports related to DS.
Methods: Documented PubMed case reports (1966 to May 2016, and cross-referencing) of DS appearing to contribute to kidney toxicity were listed in "DS Toxic Tables." Keywords included "herb" or "dietary supplement" combined with "kidney" to generate an overview list, and possibly "toxicity" to narrow the selection. Case reports were excluded if they involved herb combinations (some exceptions), Chinese herb mixtures, teas of mixed herb contents, mushrooms, poisonous plants, self-harm, excessive doses (except vitamins/minerals), legal or illegal drugs, drug-herbal interactions, and confounders of drugs or diseases. Since commercial DS often include a combination of ingredients, they were treated separately; so were foods. A few foods with kidney-toxic effects were listed in a fourth table. The spectrum of herbal or DS-induced kidney injuries included kidney stones, nephritis, nephrotic syndrome, necrosis, acute kidney injury (AKI; previously known as acute renal failure [ARF]), chronic kidney disease, kidney transplant, and death.
Results: Approximately 7 herbs (minus 4 no longer for sale) and 10 dietary supplements (minus 3 excluded due to excessive doses + germanium that is no longer sold) have been related to kidney injury case reports published in PubMed (+crosslisting) in the last 50 + years (1966 to May 2016). The implicated herbs include Chinese yew (*Taxus celbica*) extract, impila (*Callilepis laureola*), morning cypress (*Cupressus funebris Endl*), St. John's wort (*Hypericum perforatum*), thundergod vine (*Tripterygium wilfordii hook F*), tribulus (*Tribulus terrestris*) and wormwood (*Artemisia herba-alba*). No longer sold in the United States are chocolate vine or mu tong (*Caulis aristolochiae*), guang fang ji (*Aristolochia fangchi*), ma huang (*Ephedra sinica*), and Tenshin Tokishigyaku-ka-goshuyu-shokyo-to. The DS include bile (sheep), chlorella, chromium (Cr), CKLS, creatine, gallbladder (fish), glucosamine, hydrazine, N.O.-Xplode, Spanish fly, and excess intakes of vitamins A, C, and D. Germanium (Ge) is not available for sale. The top two DS with the largest number of reported publications, but not always case reports, in descending order, were the aristolochic acid-containing herbs guang fang ji (mistaken identity) and chocolate vine or mu tong. The remaining DS featured one to three publications over a 50+ year period. Numerous case reports were reported for kidney-toxic foods: djenkol bean, gallbladders (carp fish, pufferfish, & snake), and star fruit (only in chronic kidney disease patients), and uncooked yam powder or juice.
Conclusion: This online "DS Toxic Table" provides clinicians, consumers, and manufacturers with a list of herbs that could potentially contribute to kidney injuries.

* Department of Complementary and Alternative Medicine, John A. Burns School of Medicine, 651 Ilalo Street, MEB 223, Honolulu, HI, USA.
E-mail address: amybrown@hawaii.edu.

http://dx.doi.org/10.1016/j.fct.2016.07.024
0278-6915/

Contents

1. Introduction

This is the third of five review articles investigating dietary supplements (DS; includes herbs): Article one covers DS definitions, usage, efficacy and safety, and an overview of DS regulation in the United States; and articles two through five cover DS medical case reports in tabular form related to liver toxicity, kidney toxicity, heart toxicity, and cancer (Brown, 2017a–e). Interest in complementary and alternative medicine (CAM), also known as functional, integrative, traditional, or holistic medicine, continues to grow, but "natural" is not always safe. Although the majority of botanical products appear inherently safe (Marcus and Grollman, 2002), and some have demonstrated efficacy, this review focuses on the potentially life-threatening DS that increase kidney risk as detected through PubMed case reports. Case reports do not always demonstrate causation or association, but reoccurrences raise concerns (Haaz et al., 2006). In this review, the selected kidney toxicities are defined, the literature search methods employed are described, and a summary table of the results along with a brief discussion of selected DS are presented.

2. Definition

The types of kidney dysfunctions considered in this review are shown in Table 1. The major risk factors for one of the most serious forms of kidney injury, chronic kidney disease, are diabetes mellitus, high blood pressure, heart disease, and a family history of kidney failure (NIH-a, 2014).

The kidney is highly susceptible to toxic insults, and drugs are a common source of acute kidney injury (Garella, 1993; Naughton, 2008). Researchers have suggested that drugs are responsible for as much as 20% of community- and hospital-acquired acute kidney injuries. The most common causes of hospital-acquired renal insufficiency (HARI) were decreased renal perfusion, medications, surgery, and radiographic contrast media (Nash et al., 2002). The highest-risk patients are those older than 60 years and those with pre-existing renal insufficiency (GFR < 60 mL per minute per 1.73 m2), dehydration (volume depletion), history of multiple nephrotoxin exposures, diabetes, heart failure, and sepsis (Naughton, 2008).

In addition to direct nephrotoxicity, various kidney injuries can result indirectly from rhabdomyolysis, the death of muscle cells and subsequent release of their contents into the blood. Acute kidney injury, for example, results when damaged muscle cells release their myoglobin pigment. Potential causes of rhabdomyolysis include excessive exercise, marathon running, heat stroke, "crushing" injuries, polymyositis (muscle inflammation disease), seizures, infections, severe potassium and phosphate depletion, staphylococcal toxins, venoms, viral illness (HIV, Epstein-Barr, influenza, Coxsackie, etc.), and drugs (licit & illicit drugs, including ethanol) (Coco and Klasner, 2004; Weisbord et al., 1997).

Drugs and alcohol cause approximately 81 percent of rhabdomyolysis cases, of which half develop into acute kidney injury