

Case report: Jin bu huan—not so benign herbal medicine

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in bu huan (JBH) is most likely a benign Chinese herbal medicine that has been in use for a long time. It became a poisoned pharmaceutical when marketed as “anodyne tablets” in the 1990s. Though now banned in Canada and the United States, it is still causing hepatitis.

Case description

A 45-year-old white woman consulted her family physician regarding 4 to 6 weeks of nausea and mild pruritus, followed by 2 to 3 days of white stools. She was a smoker with a history of mild asthma, migraine, and back pain attributed to spondylolisthesis* and had last seen her doctor 16 months previously for a complete physical examination.

At this visit, physical findings included a 7-kg weight loss; mild sinus tachycardia; a palpable but non-goitrous thyroid; some spider nevi; and tenderness on palpation of her liver, the border of which was felt 3 cm below the costal margin. She had no history of viral exposure, and there was no reason to suspect alcohol abuse. Results of urinalysis and abdominal ultrasound were normal, but liver enzymes were consistent with a diagnosis of hepatitis: aspartate aminotransferase was 656 U/L, alanine aminotransferase was 1785 U/L, and bilirubin was 46 µmol/L, all markedly elevated, while alkaline phosphatase was 115 U/L, the upper limit of normal. Hemoglobin and white blood cell counts were within normal limits,

with mild lymphocytosis (48% compared with 32% neutrophils) and normal smear results.

Results of screening for hepatitis A, B, and C were negative. Thyroid-stimulating hormone was undetectable and thyroglobulin antibody was negative, but microsomal antibody was slightly elevated at 177 U/L. Creatinine, blood sugar, uric acid, international normalized ratio (INR), serum albumin, and amylase levels were all normal. Specialist recommendations of blood tests to search for a cause of hepatitis included a VDRL test, Epstein-Barr virus, and cytomegalovirus antibody tests, antinuclear factor, antismooth muscle antibody, ceruloplasmin, and ferritin, which were all normal except for a “reactive” high ferritin level of 1349 µg/L.

The patient was advised to avoid both alcohol and large doses of acetaminophen. Stools and results of blood tests returned to normal over the course of the next 6 weeks. Meanwhile the free thyroxine confirmed hyperthyroidism (47 pmol/L), and a subsequent 24-hour radioactive iodine uptake scan confirmed Graves disease.

During the search for the cause of her hepatitis, the patient reported that her son’s grandfather was visiting from Asia but was well and had no history of infection. On a review of medications, she reported having taken JBH for anxiety and insomnia (possibly symptoms of her undiagnosed Graves disease). Jin bu huan is available as a tea or pill from herbalists in Chinatown in Toronto, Ont. Our patient, however, took a formulation that was banned in Canada and the United States in 1994.

Discussion

The decision to ban JBH Anodyne tablets followed reports of toxicity after both acute and chronic use from the Centers for Disease Control in 1993.^{3,4} A literature search from 1994⁵ to 2000 revealed discussion of the cause and mechanism of these reactions as well as suggestions for preventive measures.

*Two of these symptoms, headache and back pain, are among the five most common conditions for which patients use unconventional therapies. Anxiety is a third.^{1,2}

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Cet article a fait l'objet d'une évaluation externe.

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It is now known that JBH Anodyne contains levo-tetrahydro-palmatine, a “sedating dopamine receptor antagonist and calcium channel antagonist,” structurally similar to hepatotoxic pyrrolizidine alkaloids known to cause poisonings in Africa, Asia, and the West Indies.⁶ Not only were the ingredients of the JBH tablets mislabelled but levo-tetrahydro-palmatine is naloxone-resistant. As well, the pill containers were not childproof, and no list of potential side effects was included.

In 1996, Blackwell⁷ emphasized another unique issue: preparation of the “medicine” involved extracting a single chemical from a traditional herb, a non-traditional, untested method that proved unsafe. Despite naming the manufacturer and publicizing the drug’s ban in North America, use of JBH anodyne persists.

Since 1993 in North America, awareness has increased about the potential toxicity of JBH. In the lay press, books and periodicals have cautioned readers against its use.⁸⁻¹² In fact, there is now a recognized list of herbal remedies that might cause liver toxicity: borage (suspected), chaparral tea, coltsfoot, comfrey, *Crotalaria* (apparently contaminated with pyrrolizidine alkaloids), germander (skullcap), maté tea, mistletoe (suspected), pennyroyal oil, sassafras, *Senecio* (groundsel), valerian (suspected), megadose vitamin A, and willow bark (theoretical—contains salicin, which is structurally different from acetylsalicylic acid and therefore unlikely to cause Reye’s syndrome. No clinical adverse effects have been reported). But there is also an equally long list of allopathic prescription drugs that can do the same: allopurinol, erythromycin, fluoroquinolones, halothane, isoniazid, isotretinoin, ketoconazole, nefazodone, nicotinic acid, nitrofurantoin, nonsteroidal anti-inflammatory drugs (NSAIDs), oral contraceptives, statins, tetracyclines, tricyclic antidepressants, trimethoprim-sulfamethoxazole, and valproate.¹³

Patients see alternative remedies as safer, and Blackwell reminds us that most historical remedies are safe:

We should remember that adverse effects from Chinese herbs are rare. In Hong Kong, where the use...is both widespread and unregulated, it has been shown that only 0.2% of the general medical admissions to the Prince of Wales Hospital were due to adverse reactions to Chinese medicine, as compared to 4.4% of admissions caused by Western pharmaceuticals.⁷

Patients anticipate our disapproval when they report using alternative remedies. This will diminish only if we remember to include nonjudgmental questions, such as “Have you found any herbs or vitamins to be helpful?”

Editor’s key points

- This case describes liver toxicity in a woman using Jin Bu Huan Anodyne tablets, a herbal remedy still marketed despite clear evidence that it is toxic.
- Family physicians should be aware of a new federal Natural Health Products Directorate where they can obtain information about herbal medications or report adverse effects.

Points de repère du rédacteur

- Cet article décrit un cas de toxicité hépatique chez une femme qui prenait des comprimés de jin bu huan anodyne, un remède à base de plantes qui est toujours en vente malgré des preuves de ses effets toxiques.
- Les médecins de famille devraient connaître l’existence de la Direction des produits de santé naturels, un nouvel organisme fédéral auquel ils peuvent s’adresser pour obtenir de l’information sur les remèdes à base de plantes et auquel ils peuvent rapporter les effets indésirables de ces produits.

and acknowledge how influenced we all are (doctors and patients) by anecdotal evidence (ie, patients by personal recovery stories and doctors by side effect “horror” stories). Proving efficacy is an important long-term project, but documenting safety is an immediate and more realistic need.

Physicians are encouraged to participate in the voluntary reporting program of the new federal Natural Health Products Directorate (<http://www.hc-sc.gc.ca/hpb-dgps/therapeut>) at Health Canada. In November 1998, the Standing Committee on Health tabled its report on Natural Health Products, which included recommendations that mandatory reporting of adverse reactions be required from the industry, but voluntary reporting only from practitioners and the public. Its working principles included a goal for standards of quality but a clear statement that safety is its primary concern. Health professionals and consumers can now use the toll-free adverse drug reaction line (866) 234-2345 or fax (866) 678-6789 or can call Ottawa directly at (613) 957-0337 or fax (613) 957-0335.

Conclusion

This case study is meant to inform physicians about a benign Chinese herbal remedy that became a manufactured poison. Though banned in 1994, JBH might still be available in Canada. It is not listed in the new Canadian Medical Association’s reference book on herbs.¹⁴ ❁

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Competing interests

None declared

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