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Case report

Digoxin toxicity in a 26-year-old woman taking a herbal dietary supplement

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Herbal dietary supplements are often considered by patients to be safe and free from side effects. The case described here shows digoxin toxicity in a patient taking a dietary supplement not normally considered to contain digoxin. In addition to highlighting the risks of herbal supplements, this case also demonstrates the concept that digoxin equivalents are not picked up by the standard digoxin assay.

(Key words: digoxin, dietary supplements)

Use of herbs as dietary supplements has become common in the United States. According to a 1997 survey, 12.1% of the households interviewed were using herbal medicines.¹ The out-of-pocket expense for these medicines was estimated at \$5.1 billion. Unfortunately, many people do not know the possible side effects of these treatments. Too often, patients perceive that because herbal medications are "natural," they are therefore safe to take without fear of side effects.

This case presents an otherwise healthy young female who was taking an herbal supplement for emotional stress. She came to the emergency department because of chest pain, and subsequently became bradycardic and hypotensive. The patient was then found to have an elevated digoxin level.

Report of case

A 26-year-old woman presented to the emergency department via ambulance with chest pain of approximately 7 hours' duration. The patient was a topless dancer who started having the chest pain while at work. The pain was described as a

shooting pain that was "in her ribs" on the left side. She went home after work and continued to have pain, and it eventually became severe enough that she decided to visit the hospital.

She had no known drug allergies. The patient's only medication was birth control pills. Her past medical history was negative, and her past surgical history was negative. The social history was significant in that the patient reported tobacco use (1 pack/day) and reported that she had ingested four alcoholic drinks over the course of her shift at work. The patient denied use of illicit drugs. Review of systems was noncontributory.

Physical examination was significant only for chest pain, which was reproducible to palpation over the left chest, superior to the breast, and approaching the left sternal border. The patient's heart exhibited regular rate and rhythm without murmur. Her lungs were clear to auscultation. Vital signs included temperature, 98.6°F; respirations, 16 breaths/min; heart rate, 76 beats/min; and blood pressure, 112/59 mm Hg. The rest of the examination was unremarkable.

In the emergency department, the patient was given oxygen via nasal cannula, and she was placed on a cardiac monitor—according to standard chest pain protocol. During the course of monitoring, her heart rate dropped to 39 beats/min and her blood pressure dropped

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Table
Digoxin-like "Factors" in Selected Herbs

Herb	μg Digoxin equivalents per 200 mL cup of tea	
	NKA*	RIA†
Cayenne	4.85	0.004
Hops	2.51	0.013
Skullcap	1.84	0.014
Wood Betony	0.656	0.008
Valerian	0.579	0.006
Black Cohosh	0.555	0.013

*NKA = inhibition of Na, K-ATPase ouabain binding.
†RIA = cross-reactivity to digoxin antibody in radioimmunoassay.
Adapted from Longerich et al²

to 59/36 mm Hg. The monitor showed an absence of P waves (Figure 1). The patient was placed in Trendelenburg's position and infused with normal saline. Before a 12-lead EKG could be obtained, the patient's heart rate and blood pressure returned to original baseline. Cardiac laboratory results and urine drug screen results were normal with the exception of a digoxin level of 0.9 ng/mL (normal therapeutic range, 0.5 to 2.0 ng/mL).

Further discussion with the patient revealed that she had been under a great deal of stress recently and that she had been taking an herbal dietary supplement that contained skullcap herb (*Scutellaria lateriflora*), wood betony herb (*Pedicularis canadensis*), black cohosh root (*Cimicifuga racemosa*), hops flowers (*Humulus lupulus*), valerian root (*Valeriana officinalis*), and cayenne pepper fruit (*Cap-sicum annuum*). She denied taking any

more than the indicated dosage of one to two capsules three times a day. Poison control center personnel suggested that the herbs in the patient's supplement could cause bradycardia and hypotension. The recommendation was to observe the patient, provide supportive care, and to instruct her to stop taking the medication. The patient was admitted to telemetry for 24-hour observation. She was discharged in normal sinus rhythm and was lost to subsequent follow-up after this time.

Comments

Use of herbal dietary supplements in the United States has become a multibillion dollar industry.¹ Because many of these products are listed as dietary supplements, no US Food and Drug Administration controls are exerted over the quality or quantity of herbs in any given product. Patients tend to see such products as harmless supplements and therefore rarely inform their physicians of herbal supplement use, unless specifically asked about such use. In this case, the patient was taking an herbal supplement to help relieve her stress—as the product name suggested the supplement would do. The only warning on the product label was one

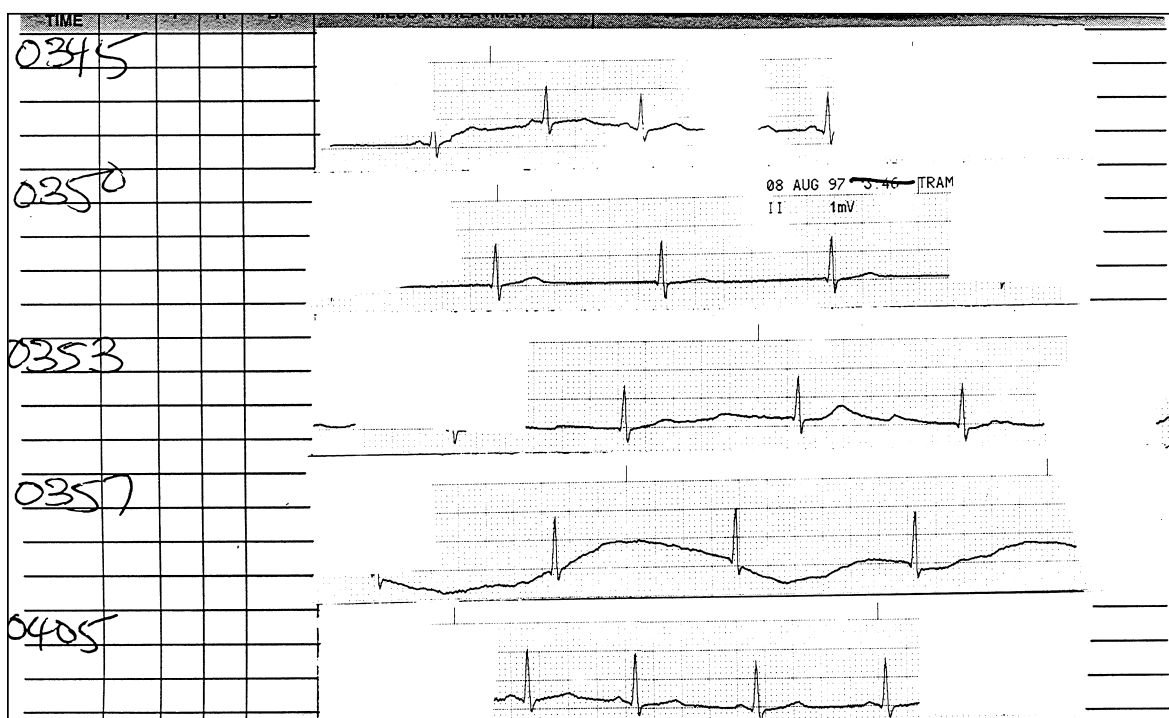


Figure 1.
Emergency room monitor strips.

that stated, "Do not drive or operate machinery while using this product, as drowsiness may result."

Longerich and colleagues² showed that many of the herbs used in teas contain digoxin-like "factors." Like digoxin, these "factors" are cardioglycoside compounds, and they exert the same effect on the myocardium as does digoxin. *Table 1* lists the digoxin activity equivalents for the herbs in the supplement described in this case study. Note that there is a difference between the amounts of digoxin-like "factors" measured by the two methods. This suggests that while the measured amount of "digoxin" in this patient was 0.9 ng/mL, the effective amount of digoxin-like "factors" in the blood may have been much higher.

Digoxin antibody immunoassays only detect those digoxin-like compounds with a chemical structure similar enough to digoxin to bind to the antibody. Such tests do not detect compounds with enough difference in the structure to avoid binding, but which still exhibit significant cardioglycoside activity. This activity is measured by the ouabain Na,K-ATPase binding assay that detects those compounds, which will exert an effect on the digoxin receptor on the myocardium. The assay works by detecting the ability of compounds to displace radio-labeled ouabain from Na,K-ATPase and comparing it to the ability of digoxin to displace the ouabain from the Na,K-ATPase (the site of action for digoxin in the body). While the patient denied taking any more pills than was suggested on the label, actual amounts consumed cannot be verified.

The product the patient had taken was not available for further analysis. Therefore, we could evaluate neither the precise amounts of the specified herbs nor contamination of the product with other herbs. Over the past several years, some herbal supplements have come under increased scrutiny as a result of patient illnesses. A recent report describes digoxin toxicity in two patients taking an herbal supplement for cleansing of the bowel.³ The shipment of plantain used in the supplement was shown to be con-

taminated with *Digitalis lanata*. A number of other plants, including oleander (*Nerium oleander*, a cause of accidental poisoning in children), have been shown to contain cardiac glycosides.⁴ Furthermore, an analysis of traditional Chinese medicines in California showed that 32% contained undeclared compounds.⁵

This case serves to remind us, as physicians, of the importance of discussing alternative medicines with patients. Our patients take a wide variety of herbal medications, including saw palmetto (*Serenoa repens* or *Sabal serrulata*) for prostate problems, ginkgo (*Ginkgo biloba*) for dementia and memory problems, echinacea (*Echinacea purpurea* or *Echinacea angustifolia*) for immunostimulation, pleurisy root (*Asclepias tuberosa*, which also contains high quantities of digoxin-like compounds) for asthma, and so on. Furthermore, many patients take combination products that contain several different herbal compounds. All of these kinds of herbal supplements can potentially interact with medications that patients may be taking.

Depending on the reliability of the source of the herbs, these supplements also may be contaminated with other plants that are not intended to be in the product. Such contamination can significantly interfere with treatments we may be giving outpatients. Such contamination also means the patient may be unknowingly receiving medicinal substances that they do not need or want,

such as digoxin or digoxin-like factors. We must remember to ask our patients not just what medicines they are taking, but also what dietary supplements they may be using.

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