DRUG-INDUCED HYPERKALEMIA

To the Editor:

In his review article on drug-induced hyperkalemia, Perazella (1) refers to nutritional supplements and herbal remedies as possible precipitants of hyperkalemia. Because the use of these "alternative" medicines is remarkably high in the United States (2), I would like to draw attention to the pathogenesis and clinical impact of one such group of drugs whose use may result in clinically significant hyperkalemia. Extracts from the dried skin of toads (*Bufo*) are used in herbal medicines today by the Chinese (who call it *Chan Su*) and by the Japanese (who call it *Senso*) to treat congestive cardiac failure. *Chan Su* is also a major component of the traditional Chinese medicines *Liu-Shen-Wan* and *kyushin*. Their use dates back to ancient times when physicians prescribed dried toad skins to treat dropsy (edema) and as a cardiotonic, even before digitalis was introduced (3). These drugs are also used to treat tonsillitis, sore throat, and furuncles because of their proposed anesthetic, anti-inflammatory, and antibiotic actions.

The cardioactive bufadienolide steroid aglycones (bufagins) and their derivatives (bufotoxins) isolated from toad skin are structurally analogous to the well-known plant cardiac glycosides, such as digitalis (3). Both have the configuration essential for cardiac activity and, therefore, the same pharmacologic and toxicologic actions (3). Because the chemical structure of bufadienolides is similar to that of digoxin, Chinese medicines containing these toad compounds frequently interfere with digoxin immunoassays (4). The pharmacologic receptor for both toad and plant cardiac glycosides is the membrane-bound Na-K-ATPase (5). Bufadienolides, similar to digitalis in toxic doses, may cause analogous extracardiac effects (like nausea, emesis, diarrhea, and a bitter taste), bradycardia, and ultimately asystole (3,6). Administering commercially available digoxin-specific antibodies may antagonize some of the cardiotoxic effects of toad venoms (7). Significant poisoning from toad toxins may result in hyperkalemia (8), as occurs from acute ingestion of other cardiac glycosides. Although the general population considers these unconventional over-the-counter traditional Chinese medicines to be safe, serious toxic effects including fatalities have been documented in the literature (9,10).

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The Reply:

As noted by Dr. Pantanowitz, a number of herbal or natural remedies may be unsafe for general human consumption. This is particularly true for patients with underlying renal disease. Some herbal products have been noted to cause renal failure (*Aristolochia* spp) and kidney stones (*Ma-Huang-Ephedra* spp) in normal hosts (1,2). However, certain medicinal herbs may induce potentially life threatening hyperkalemia in patients with underlying risk factors (chronic renal insufficiency, hypoaldosteronism, use of other potassium-altering medications) for this electrolyte disorder. Examples include herbs or juices, such as noni juice (*Morindia citrifolia*), alfalfa (*Medico sativa*), dandelion (*Taraxacum officinale*), horsetail (*Equisetum arvense*), and nettle (*Urtica dioica*), that contain large amounts of potassium (3,4). Patients with impaired renal potassium handling can develop severe hyperkalemia after ingesting these substances. In addition to the herbs pointed out by Dr. Pantanowitz, Na-K-ATPase impairment by the digoxin-like substances contained in milkweed, lily of the valley, Siberian ginseng, and hawthorne berries may also precipitate hyperkalemia in at-risk patients (5,6). It is therefore prudent that practitioners who care for patients who consume these products become familiar with the associated adverse effects. Furthermore, the FDA should be allowed to enforce the same drug standards for herbal remedies and natural products available in the marketplace that are required for other medications.

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