

Star fruit as a cause of acute kidney injury

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The star fruit - a.k.a. carambola, family *Oxalidaceae*, species *Averrhoa carambola* - is commonly found in tropical countries and is a popular fruit in Brazil.¹ In 1993, Martin *et al.*² were the first to report clinical observations on the intake of this fruit. The authors described an outbreak of intractable hiccups in patients with chronic kidney disease (CKD) on hemodialysis. In 1998, Moyses Neto *et al.*³ described the cases of six patients on dialysis who, in addition to intractable hiccups, had other neurological symptoms such as mental confusion, psychomotor agitation, coma, and seizures; one of the patients died. Other reports have since confirmed these changes in CKD patients on and off dialysis.⁴⁻⁶ Reviews on the topic available in the literature have comprised years of observations and several case reports.^{7,8} Patients with CKD stages 3 to 5 are susceptible to star fruit poisoning, and initially present hiccups which may progress to neurological symptoms such as mental confusion, coma and seizures, and death. These symptoms have also been observed in uremic patients and may mimic neurological syndromes in some cases.^{9,10} Most patients improve with hemodialysis or, more rarely, with continuous hemodialysis or hemoperfusion.^{7,8} However, some patients die regardless of treatment. Generally, this happens when star fruit poisoning is not timely recognized and the introduction of treatment is delayed. Peritoneal dialysis is not an appropriate course of therapy. A neurotoxin present in the carambola fruit was recently isolated. Caramboxin is a molecule similar to phenylalanine and a strong glutamate receptor which produces cerebral hyperexcitability.¹¹

In addition to exerting neurotoxic effects on patients with CKD, the amount of oxalate in star fruit may cause acute kidney injury in patients with normal renal function. The amounts of soluble oxalate salts in star fruit may range from 80 mg/dL to 730 mg/dL.¹² Therefore, two distinct effects may be triggered: neurotoxicity and nephrotoxicity. The first study describing nephrotoxicity in humans was published in 2001.¹³ The authors looked into two cases of individuals with clinical symptoms of acute kidney injury by oxalate after having massive amounts of star fruit juice. Both patients had to undergo hemodialysis. Their kidney biopsies revealed histological findings consistent with acute oxalate nephropathy. The patients had been fasting and were probably dehydrated. Other cases in humans have been reported since,¹⁴⁻¹⁶ in addition to experimental trials on the matter.¹⁷⁻¹⁹ Oxalic acid and its soluble salts are potentially harmful to humans and animals, contrary to insoluble oxalic acid calcium and magnesium salts.²⁰ When individuals feed, the chances of free oxalic acid binding to calcium or magnesium in the gastrointestinal tract to form insoluble complexes that cannot be reabsorbed are usually increased. Free reabsorbed oxalate binds to circulating calcium and precipitates in the renal tubules, causing acute obstruction and tubular injury.^{13,14,20} Niticharoenpong *et al.*¹⁵ reported the case of a patient with pre-existing CKD and deteriorating renal function who had star fruit for medicinal purposes. Kidney biopsy analysis revealed the individual had acute oxalate nephropathy. The subject's renal function

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returned to baseline levels after star fruit intake was discontinued. The maximum recommended volume of star fruit juice or amount of fruit one can ingest safely has not been determined yet. The levels above which star fruit intake can cause acute oxalate nephropathy have to be defined and considered along with the individual risk factors that may increase the chance of adverse events.^{14,20} The literature contains cases of fasting individuals developing nephropathy after having 300 ml of pure star fruit juice.¹⁴ Patients with previously normal renal function treated with and without dialysis had reportedly good outcomes.^{13,14,16}

However, in some cases of nephrotoxicity, renal function deteriorates and patients may be affected by nephrotoxicity and neurotoxicity.¹⁴ In such cases, acute kidney injury prevents the excretion of caramboxin, a toxin found in star fruit, causing neurotoxic manifestations in the form of hiccups and sometimes mental confusion, all of which subside as soon as renal function is back to normal.¹⁴

In this issue of the Brazilian Journal of Nephrology, Scaranello *et al.* report on a case of star fruit poisoning suggestive of acute kidney injury by oxalate. The patient was prescribed two sessions of hemodialysis and got better, as did other individuals in cases described in the literature. This particular patient had massive amounts of star fruit, which released significant volumes of free oxalate in his gastrointestinal tract. The absorption of free oxalate triggered the onset of acute kidney injury. The case report does not mention hiccups or any other manifestations consistent with neurotoxicity. This case draws the attention of physicians and nephrologists in particular to a condition that is increasingly better known and therefore diagnosed more frequently, and coincides with recent reports of acute oxalate nephropathy caused by another member of the *Oxalidaceae* family, the *Averrhoa bilimbi*.²¹ This oxalate-rich fruit, commonly known as bilimbi, cucumber tree, or tree sorrel, is widely grown in the State of Bahia and can be found in all regions of Brazil.²² We were recently informed of a case occurred in Bahia of a fasting individual who developed non-oliguric acute kidney injury after having bilimbi juice. The patient did not require dialysis and recovered completely from renal injury (anecdotal report by Raphael Paschoalin, December 18, 2013).

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