

Star fruit intoxication in chronic kidney disease patients: from the first clinical description to caramboxin

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In August of 1990, 18 patients on dialysis for chronic kidney disease and the medical staff of the Hospital of the São Paulo State University's School of Medicine at Botucatu were inadvertently given a crate of star fruits. Ten patients ingested some fruit. Eight had hiccups within 12 hours of eating the fruit and two had hiccups before undergoing hemodialysis. None of the patients who refused to eat star fruit had hiccups. And none of the members of the medical staff had hiccups.

Martin *et al.*¹ were the first to describe the toxic effects of star fruit intake in patients with chronic kidney disease (CKD), in a paper published in the Brazilian Journal of Nephrology in 1993. Back then, the only findings published in the literature to support medical treatment were the reports of an experimental study published in a journal in Malaysia, in which normal rats given intraperitoneal injections of star fruit extract had neurotoxic manifestations.² In the cases described in Botucatu, hemodialysis alone reversed the clinical symptoms. These and other manifestations observed in the patients led the authors to suggest that star fruit possibly contained a dialyzable substance excreted through the kidneys associated with the symptoms.¹ However, only in 1998 the neurotoxic effects of star fruit poisoning were confirmed with the description of six cases by researchers

from the School of Medicine of Ribeirão Preto,³ with insomnia, hiccups, psychomotor agitation, and death listed among symptoms and outcomes. Four years later, the same group reported the cases of 32 dialysis patients suffering from star fruit poisoning with a roster of clinical manifestations, the most frequent of which being hiccups and vomiting, and a few severe cases of poisoning, of which seven had seizures and three died.⁴ This paper proved hemodialysis was the preferential treatment for star fruit poisoning. The same group made a breakthrough contribution by elucidating the mechanisms of neurotoxicity caused by star fruit intake and isolating a toxin called caramboxin, a phenylalanine-like molecule and an agonist of glutamatergic ionotropic receptors, which explains its neurotoxicity,⁵ that functions regardless of the high levels of oxalic acid seen in star fruit.

It is clear that Brazilian nephrologists and researchers have made the most significant contributions to the clinical and pharmacological descriptions of star fruit poisoning as it affects patients with CKD, with the Brazilian Journal of Nephrology (JBN) as the vehicle in which the event was described for the first time.¹

Today there is greater awareness over the risks of star fruit intake for patients with CKD. Recommendations around what to do in such cases

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have been published in scientific journals and discussed in the media in general. A Municipal Act in effect in the city of Jaú, São Paulo, and a State Law enacted in the state of Mato Grosso do Sul require restaurants, diners, and other similar facilities to alert patrons over the risks of drinking star fruit juice for individuals with kidney disease.

In a recent issue of the JBN, nutritionists from the Federal University of Juiz de Fora made a relevant contribution in the form of a systematic review comprising papers published between 2000 and 2014 on the effects of star fruit intake by patients with CKD. The review included eight trials, two reviews, and three experimental studies.⁶ The symptoms and clinical evolution of 110 patients were described, with intractable hiccups and mental confusion ranking atop all reported manifestations. A significant portion of these individuals died (24.5%), while seizures were associated with poor outcome. Three of the included trials described cases of acute kidney injury among individuals with normal renal function who ingested excessive amounts of star fruit. The review also sheds light on the mechanisms involved in star fruit neurotoxicity.

The knowledge acquired since the first description of cases of star fruit poisoning in

patients on dialysis unequivocally shows the relevance of hypotheses and questions derived from daily clinical observation and the potential contributions they may offer to the development of scientific knowledge. The systematic review published today confirms previous observations over the risk and the severity of the symptoms associated with star fruit intake for patients with CKD and the risk of acute kidney injury linked to excessive ingestion of star fruit. This review, therefore, brings important contributions to the medical staff involved with nephrology care.

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