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Side Effects of Star Fruit Consumption in Patients with Chronic Renal Failure

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ABSTRACT

The present study aimed to make a literature review about the toxic effects caused by the consumption of star fruit by individuals with chronic kidney failure. The articles were selected from the SciELO, ScienceOpen and PubMed databases based on the descriptors "carambola", "insuficiência renal crônica", "toxicidade;", "toxicity", "chronic kidney failure" and "star fruit". Within the searched parameters, 13 studies were brought together in order to assess the side effects presented. The results show that caramboxin and calcium oxalate present in high levels in the body, trigger neurotoxic and nephrotoxic effects, causing from incoercible hiccups and mental confusion to even coma and death. Therefore, consumption of the fruit should be avoided.

Keywords

Chronic kidney failure, Star fruit, Renal Replacement Therapy, Toxicity.

Introduction

Chronic renal failure (CKD) is the most advanced stage of chronic kidney disease (CKD), characterized by the irreversible and progressive loss of kidney functions, which makes it impossible for the kidneys to maintain adequate renal filtration levels. The disease is marked by the presence of elevated levels of protein in the urine (>150 mg/day) and/or reduced glomerular filtration capacity (< 60 ml/min) for more than three months [1].

According to the Brazilian Society of Nephrology [2], CKD is defined by the injury to the renal parenchyma (with normal renal function) and/or renal functional decrease present for a period equal to or greater than three months and is associated with some chronic non-communicable diseases (NCDs), such as hypertension and diabetes mellitus. Studies indicate that these NCDs act as factors to increase the risk of mortality in patients with CKD, since data confirm that patients under 50 years of age have a 5-year survival rate of 62% and for those over this age and diagnosed with diabetes mellitus, survival is only 23% [2].

Because it is a disease with high morbidity and mortality rates, with an increase in its incidence and prevalence in terminal stages progressively year after year, CKD has become a public health problem in Brazil and worldwide [1]. The prevalence of chronic kidney disease worldwide is 7.2% for individuals over 30 years of age and 28% to 46% in individuals over 64 years of age [2]. In Brazil, it is estimated that more than ten million people have the disease, and of these, 90 thousand are on dialysis, a number that has grown more than 100% in the last ten years. According to data from the Brazilian Dialysis Census2 in 2010 there were about 2 million patients on dialysis in the world, and it is estimated that this figure will double by 2030, according to the analysis of data from the decade.

For treatment, patients may depend on advanced technology, such as hemodialysis and Renal Replacement Therapy (RRT), which is a blood filtration process that removes excess fluid and metabolites [3]. In this process, patients experience psychosocial and clinical changes that interfere with quality of life, and psychic manifestations such as changes in social interaction and

psychological imbalances are common, not only for the patient, but also for the family that accompanies him [4].

In addition to these changes, during the course of treatment, it is known that patients may present impairment in their nutritional status, due to dietary and water restrictions and not only due to constant inappetence, but also to metabolic disorders resulting from this phase, such as infections, bleeding and hydroelectrolytic spoliation [5].

Therefore, nutritional control is necessary, associated with a good quality of life and good dialysis treatment of CKD. Among the dietary recommendations associated with CKD, the prohibition of the consumption of star fruit (*Averrhoa carambola*) stands out, since recent studies have shown that the ingestion of the fruit is associated with complications in chronic kidney patients, due to the presence of a neurotoxin capable of causing severe neurological changes in chronic nephropathy patients [6].

According to Moreira [6], star fruit is a fruit of the oxalidaceous family, species *Averrhoa carambola*, and is believed to have originated in Sri Lanka, cultivated in Southeast Asia and Malaysia for several centuries and acclimatized in several tropical countries, including Brazil. The literature indicates that there are two types of fruits: the sourest, which contain a high value of oxalic acid, and the sweetest, with a lower content.

Data show that star fruit arrived in the country in the eighteenth century, in the Northeast through the French agronomist Paul Germain. Although it is not native, its cultivation occurs throughout the Brazilian territory, especially in areas where there is no incidence of frost, and it is currently cultivated in the tropics in both hemispheres [6].

Its characteristics are bittersweet in taste, and its color varies from green or yellow depending on its degree of ripeness. The fruit has five very pronounced longitudinal segments, which provide the shape of a star when sliced crosswise [7]. Its pulp is abundant and rich in soluble fiber, and its skin is rigid, translucent and smooth-shiny. Star fruit has calcium, iron, potassium and vitamins A, C, B1 and B2 as its main nutrients [8].

Data reports the first case of star fruit poisoning dating back to 1980, through the work of Muir and Lam [9]. The first clinical observations related to the ingestion of this fruit were reported by Martin [10], who described an outbreak of incoercible hiccups in chronic kidney patients undergoing hemodialysis treatment in 1993.

Therefore, the objective of this study was to analyze the main toxic effects of star fruit ingestion by patients with CKD, elucidating the side effects and symptoms caused.

Methods

The present study is a systematic review of literature. For this, a bibliographic search was elaborated having as concepts analyzed, scientific studies on the toxicity of star fruit in patients with chronic renal failure. The descriptors used in Portuguese were "carambola", "chronic renal failure" and "toxicity; The English terms were "toxicity", "chronic kidney failure" and "star fruit".

The search strategy was based on articles in English and Portuguese, published between 2000 and 2021, in the SciELO, ScienceOpen and PubMed databases. As an inclusion criterion, studies carried out with human beings of any age group, race and gender were gathered. Among the exclusion factors, review articles, studies in languages other than those considered, and studies carried out with animals were not considered.

The work was separated into two phases, the first of which followed the criteria of searches and readings of titles and articles related to the theme for analysis in the inclusion and exclusion criteria, and the second phase was based on the development of the study, the results and their resolutions, based on the study criteria.

Results

From the literature search and based on the search parameters, 13 studies were compiled. Of these studies, four are original articles and nine are case reports, which evaluated nephropathy patients with poisoning after ingestion of star fruit and their respective clinical conditions.

Table 1 presents the characteristics of the studies, as well as the side effects and symptoms presented by the patients, the amount of fruit that was consumed, the treatment used and its duration, and whether the patient recovered or not.

Among the articles gathered, 85 people were evaluated, with a mean age of 55 years, ranging from men (58%) to women (42%). It is noted that in 11 of the 13 studies, renal replacement therapy (RRT) was used as a form of treatment. Regarding the amount of fruit consumed, there is a great variation: from half a fruit to 50 units, either fresh or in the form of juice. It is observed that, of the 13 studies evaluated, 10 present incoercible hiccups as a common symptom and, 09, mental confusion. The mortality and recovery rate of patients was 32% (28 deaths) and 68% (57 recovered), respectively.

Being able to observe a greater number of patients and symptoms presented compared to the other studies cited, the study by Neto [11], which evaluated 32 uremic patients, shows that the most common symptoms were persistent and intractable hiccups, vomiting, varying degrees of disturbance of consciousness (mental confusion, psychomotor agitation), decreased muscle power, numbness of the limbs, insomnia and convulsions. Laboratory tests showed elevated urea and creatinine, and the patients were treated by hemodialysis and dialysis, ranging from 13 hours to 12 days of treatment. Of these treated patients, 17 recovered and 15 died.

Wang [12] presented the management of star fruit-induced neurotoxicity and seizures in an 84-year-old patient with chronic renal failure, who consumed 3 units of star fruit. The patient initially presented speech disorders, then became disoriented and

confused; On the third day, he was admitted to the hospital after losing consciousness. On the fifth day of hospitalization, he fell into a coma. The tests showed elevated creatinine and urea, and the patient was treated with hemodialysis and propofol, but died.

Stumpf [13] reported a case of a patient who consumed 50 units of star fruit. The symptoms present in this case were paresis on the right side of the body and mental confusion, as well as hypovolemia and anuria. The treatment consisted of four days of dialysis, with the patient's recovery.

For a better survey of symptoms, the most commonly presented symptoms were classified as mild, moderate and severe. Mild symptoms include hiccups, vomiting, and insomnia; moderate patients comprise agitation, numbness, paresthesia, paresis, and mild mental confusion; Severe mental confusion, seizures, status epilepticus, coma, hemodynamic instability, and shock.

Table 1: Study characteristics.

Author	N	Age	QFC	Symptoms/side effects	Treatment	Duration	Deaths	Recovered
Auxiliadora et al. [14]	1	53	NR	Moderates; Graves and Coma	Hemodialysis	5 days	1	0
Neto et al. [11]	32	49 (average)	0.5-10 pcs. and 200-500ml	Light; moderate and severe	Hemodialysis and dialysis	1pm-12 days	15	17
Chang et al. [15]	1	64	2 units	Mild; Moderate	Dialysis	2 hours	0	1
Chang et al. [16]	20	36-71	NO	Mild; Serious	Hemodialysis and dialysis	1-4 days	8	12
Moreira et al. [6]	1	56	4 units	Leves; Graves and bradycardia	Hemodialysis	NO	1	0
Neto et al. [17]	5	34-67	12-15 pcs. and 300-1500ml	Mild	NO	NO	0	5
Wang et al. [12]	1	84	3 units	Moderates and Eats	Hemodialysis and propofol	5 days	1	0
Herbland et al. [18]	6	51-81	NO	Light; Moderate; Graves and coma	Medic. antiepileptic drugs and SRB	5-38 days	2	4
Neto et al. [19]	4	30-70	0.5-6 units	Light; Moderate; and loss of consciousness	Hemodialysis	4 days	0	4
Abeysekera et al. [20]	2	56 and 60	200 ml e 6 unid. - 4 unid.	Light and moderate	Prednisolone in a patient	2-3 weeks	0	2
Herath et al. [21]	4	28-55	3-6 units	Mild	Hemodialysis	Hemodialysis for a week, and a month in total for everyone.	0	4
Tse et al. [22]	7	NR	NR	Light and moderate	Hemodialysis and dialysis	NR	0	7
Stumpf et al. [13]	1	51	50 units	Moderate	Dialysis	4 days	0	1

N: number of samples; RRT: renal replacement therapy; CFQ: amount of fruit consumed; AEB: alteration in biochemical tests; NR: not reported.

Discussions

It was possible to perceive from the analyzed studies that most studies on star fruit poisoning in nephropathy patients show that the symptoms begin hours after consumption, and that the most common symptoms are incoercible hiccups, mental confusion and alteration in motor functions.

Patients with chronic kidney disease are vulnerable to drug or toxin poisoning, and star fruit is probably the only natural fruit associated with neurotoxicity in these individuals according to Auxiliadora [14], due to the carambuxine present in the fruit. However, Chang [15] reports that star fruit poisoning can also occur in patients without advanced chronic renal failure.

Present in star fruit, caramboxine is a low molecular weight, water-soluble and thermostable neurotoxin, which has renal excretion and is able to cross the blood-brain barrier. Patients with impaired renal function do not excrete it properly, and consequently the serum elevation inhibits the GABAergic system, leading to cerebral hyperexcitability, causing neurological symptoms such as hiccups, paresis and paresthesia, mental confusion, seizures and coma, which may even result in death [16-23].

Star fruit is also a fruit rich in oxalates, which can obstruct the renal tubules by calcium oxalate crystals, generating tubular obstruction and kidney damage due to increased apoptosis of epithelial cells. According to Abeysekera [19], it can be postulated that prolonged consumption of star fruit may cause recurrent occult renal damage, resulting in chronic interstitial nephritis and chronic nephropathy even in individuals without previous renal impairment. Calcium oxalate is one of the most reactive crystals that can evoke inflammatory response, leading to interstitial fibrosis, nephron

loss, and eventually chronic renal failure.

According to Neto [11], the neurotoxic effects of star fruit can be classified into three levels of intoxication that can provide useful guidance for the institution of appropriate treatment: (I) mild intoxication: with the clinical presence of hiccups, vomiting and insomnia; (II) moderate intoxication: with the clinical presence of psychomotor agitation, numbness and paresthesias of the limbs, and mild mental confusion; and (III) severe intoxication: with clinical presence of moderate to severe mental confusion, progressing to coma, seizures progressing to status epilepticus, and hemodynamic instability progressing to hypotension and shock.

As analyzed, the treatment depends on the severity of the clinical condition. According to Tse [22] and Neto [11], hemodialysis is the most effective treatment, especially in the most severe cases, and is currently the most used treatment method in these cases; It should be noted that peritoneal dialysis should not be used in these cases because it is inefficient. According to the data collection, there is no significant difference in relation to the gender and age of the patients, and in relation to the consumption of the fruit, it is observed that the amounts ingested are varied, making it difficult to measure whether there is a portion of the fruit that can be ingested without causing unwanted reactions.

According to the present review, elevated creatinine levels are present in 92% of the cases in the aforementioned studies, as they are indicative signs of impaired renal function. Among the 85 patients mentioned in the study, 36 were on hemodialysis and 16 were on peritoneal dialysis. Of the 52 patients who underwent RRT, 23 died. So it can be identified that 82% of the patients who died were on RRT.

Regarding the limitations faced, it can be pointed out the scarcity of current original studies on the toxicity of the fruit in humans, with a large sample number, and case reports have to be used. Therefore, it is suggested that new studies be carried out to clarify issues that are still little studied.

Conclusions

The results presented in this study show that star fruit poisoning can be fatal in patients with chronic renal failure, because nephropathy patients have difficulty excreting caramboxin, and thus, the neurological system is compromised, causing symptoms such as hiccups, paresis and paresthesia, mental confusion, seizures and coma. In addition to caramboxin, another risk factor is the oxalates present in star fruit, which can obstruct the renal tubules, inflaming the kidneys and can lead to interstitial fibrosis, loss of nephrons and eventually chronic renal failure in individuals with previously normal renal function.

Due to the scarcity of new research and more detailed studies, it was not possible to identify the amount of fruit that can be consumed without the risk of intoxication, but it can be said that the consumption of fruit can be lethal, so it is recommended that the fruit not be consumed by patients with CKD.

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