Now a day Acute Kidney Injury and Chronic Kidney Disease are the two common problems worldwide with increased mortality and morbidity as well as health care cost. Nephrotoxicity and neurotoxicity by the Star fruit, sometimes fatal, is far more frequent than reported. Star fruit belongs to the Oxalidaceae family, species Averrhoa carambola, is a popular fruit among Orientals. The aim of the study is to create awareness among the population regarding star fruit intoxication, to reduce the development of Acute Kidney Injury in general population, to reduce the mortality and burden of morbidity from chronic renal failure, to reduce the mortality of the patients of End stage renal disease taking regular haemodialysis and to reduce the mortality and burden of morbidity of the people suffering from Diabetes mellitus and Hypertension. Star fruit juice produces acute renal injury not only through the obstructive effect of calcium oxalate crystals, but also inducing apoptosis of renal epithelial cells, which may be caused by the levels of oxalate in the fruit. There have been reports of hiccup, confusion and occasional fatal outcomes in uremic patients after ingestion of star fruit. An excitatory neurotoxin from star fruit has been implicated although the exact nature of this toxic substance has not been identified. High quantities of oxalate in empty stomach and dehydrated state may pose an additional risk for development of renal injury. To avoid acute oxalate nephropathy, pure sour carambola juice or mild diluted post pickled juice should not be consumed in large amounts, especially in an empty stomach and dehydrated state. It is recommended that uremic patients should totally abstain from star fruit due the rare but potentially fatal complications.

**Key Words:** Star fruit, Nephrotoxicity, Neurotoxicity, Oxalidaceae

**ABSTRACT**

Now a day Acute Kidney Injury and Chronic Kidney Disease are the two common problems worldwide with increased mortality and morbidity as well as health care cost. Nephrotoxicity and neurotoxicity by the Star fruit, sometimes fatal, is far more frequent than reported\(^2\). Star fruit (Figure: 1,2) belongs to the Oxalidaceae family, species Averrhoa carambola, is a popular fruit among Orientals\(^1\). Star fruit is one of the plant sources that contain highest concentration of oxalic acid; 100 g of fresh fruit contains 50,000-95,800 ppm of oxalic acid\(^2\). Sour carambola juice is a popular beverage in Taiwan. Commercial carambola juice usually is prepared by pickling and dilution processes that reduce oxalate content markedly\(^2\).

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Literature Review

Mechanism of Star fruit induced Acute Renal Failure:

To investigate the mechanisms of star fruit associated acute oxalate nephropathy, the nephrotoxic effect of star fruit was examined in both cellular experiments and animal models. Star fruit juice produces acute renal injury not only through the obstructive effect of calcium oxalate crystals, but also inducing apoptosis of renal epithelial cells, which may be caused by the levels of oxalate in the fruit3,4,5.

Renal Biopsy findings

Renal biopsies (Figure: 3) indicated a typical histological appearance of acute tubular necrosis and oxalate nephropathy. Light microscopy showed oxalate crystals (arrows) within the lumina and tubular walls surrounded by inflammatory infiltration that included lymphocytes, histiocytes and primarily neutrophils. Tubular focal dilation, desquamated cells in the lumina, lining epithelial cell flattening and interstitial oedema were also present. Renal sections were analysed under polarized light and showed colourless oxalate crystals with a pattern of birefringence within the tubular lumina. The oxalate crystals displayed a typical black colour after Von Kossa staining. Light microscopy showing oxalate crystals (arrows) within the lumina and tubular walls surrounded by inflammatory infiltration (Masson's Trichrome, original magnification × 40). Renal section analysed under polarized light showing several colourless oxalate crystals with a pattern of birefringence within the tubular lumina (Haematoxylin and eosin, original magnification ×10). Renal section stained after Von Kossa stain displaying oxalate crystals with a typical black colour (original magnification × 10)2.

Sources of Oxalic acid

Buckwheat, Star fruit, Black pepper, Parsley, Poppy seeds, Rubarb stalks, Amaranth, Spinach, Chard, Beets, Cocoa, Chocolate, Most Nuts, Most Berries, Beans6.

Mechanism of Star fruit induced Status Epilepticus:

Some researchers suspect that there are different toxins in different star fruit subspecies, as well as powerful neurotoxin that can accumulate in blood and cross the blood-brain-barrier in patients with chronic renal disease, eventually causing refractory status epilepticus7,8. Single voxel protein and 31phosphorus MR spectroscopic studies revealed elevation of lactate, elevation of inorganic phosphate and reduced phosphocreatinine and nucleoside triphosphates in the cerebral cortex in an intoxicated patient9. The metabolic changes indicated that neurotoxin could interfere with oxidative phosphorylation and cause energy deprivation. Although the exact nature of star fruit neurotoxin remains obscure, oxalate being abundant in star fruit, has been proposed as a possible candidate for acute nephropathy and neurotoxicity2. More recently, a neurotoxic fraction was obtained from star fruit, which is different from oxalic acid in chemical characterization10. The mechanism of convulsive activity is believed to specifically act on GABA ergic glutamatergic transmission system10.

Effects of Star fruit on Kidney

- Acute kidney injury from acute oxalate nephropathy and acute tubular necrosis.
- Renal stone disease.
- Deterioration of renal function in patients of Chronic kidney disease2,7.

Neurological symptoms of Star fruit intoxication:

Hiccups, Vomiting, Insomnia, Psychomotor agitation, Numbness and paresthesias of the limbs, Decrease muscle power, Mild mental confusion, Severe mental confusion progressing to coma, Seizures progressing to status epilepticus, Hemodynamic instability progressing to hypotension and shock7,11.

Treatment

Haemodialysis, especially on daily basis, is the ideal treatment for star fruit intoxication. In severe cases, continuous methods of replacement therapy may provide a superior initial procedure, since rebound effects are a common event7. Peritoneal dialysis is of no use as a treatment, especially when consciousness disorder ensue7. Sustained low efficiency daily diaffiltration with hemoperfussion as a therapy for severe star fruit intoxication7.
provoked persist convulsions of the tonic-clonic type. It appears that star fruit contains an excitatory neurotoxin\textsuperscript{12}. Other reports have since confirmed these changes in CKD patients on and off dialysis\textsuperscript{7,13}. Reviews on topic available in the literature have comprised years of observations and several case reports.

Tse KC et al, in 2003, showed in their review article that a group of seven patients from the dialysis center of Queen Mary and Tung Wah Hospitals who developed symptoms including hiccup, confusion, vomiting, impaired consciousness, muscle twitching and hyperkalaemia shortly after ingestion of star fruit\textsuperscript{1}. Symptoms of most patients resolved after intensified dialysis or spontaneously and no mortality was observed\textsuperscript{1}.

Neto MM et al, in 2003, showed in their study, that out of 32 uremic patients, 30(93.75\%) patients developed persistent and intractable hiccups, vomiting in 22(68.7\%), variable degrees of disturbed consciousness (mental confusion, psychomotor agitation) in 21(65.6\%), decreased muscle power, limb numbness, paresis, insomnia and paresthesia in 13(40.6\%) and seizure in 7(21.8\%). Patients who were promptly treated with haemodialysis, including those with severe intoxication, recovered without sequelae. Patients with severe intoxication who were not treated or treated with peritoneal dialysis did not survive\textsuperscript{7}.

Signata A et al, 2009, reported two cases with unknown chronic renal insufficiency, who developed severe encephalopathy after ingestion of star fruit. Diffusion-weighted MR imaging showed cortical and thalamic hyper-intense lesions related to epileptic status. They improved after being submitted to continuous hemofiltration which constitutes the most effective treatment in acute phase\textsuperscript{14}.

In a study in Chang Gung Memorial Hospital, Taiwan, in 2005, Tsai MH et al showed that two patients with chronic renal failure at a pre-dialyzed stage who developed refractory status epilepticus after ingestion of star fruit\textsuperscript{15}. In addition, they review 51 cases in the literature. Among 51 patients, 16 patients presented with epileptic seizures (30\%). The mortality rate was as high as 75\% in patients with seizures. On the other hand in patients without seizures the mortality rate was only 0.03\%. Thy proposed that epileptic seizure is significantly associated with poor prognosis and that status epilepticus is an unpredictable and potentially fatal complication in star fruit intoxication\textsuperscript{15}.

Discussion

Many studies from different countries of the world had done on star fruit intoxication. Star fruit is commonly found in tropical countries and is popular fruit in Brazil\textsuperscript{11}. In 1993, Martin et al were the first to report clinical observations on the intake of this fruit\textsuperscript{11}. The authors described an outbreak of intractable hiccups in patients with chronic kidney disease(CKD) on haemodialysis\textsuperscript{11}.

In a study, Neto MM, Robl F, Netto JC, 1998 showed that six patients in a dialysis programme who were apparently intoxicated by ingestion of star fruit. After ingestion of 2-3 fruits or 150-200 ml of the fruit juice, the six patients who had previously been stable in a regular dialysis programme, developed a variety of symptoms ranging from insomnia and hiccups to agitation, mental confusion and (in one case) death\textsuperscript{12}. Preliminary investigations to characterize the hypothetical neurotoxin in the fruit, an extract, when injected intra-peritoneally or intra-cerebroventricularly in rats,
Clen CL et al, 2001, showed in their study that two of the patients developed nausea, vomiting, abdominal pain and backache within hours of ingestion of large quantities of sour carambola juice, then acute renal failure followed. Pathological examinations showed typical changes of acute oxalate nephropathy2.

Niticharoenpong K et al, 2006 showed in their case report, a patient with underlying chronic kidney disease, who developed a rapid increase in serum creatinine and oxalate nephropathy after chronic ingestion of star fruit juice without overt neurotoxicity. The decline in renal function was not fully reversible after stoppage of intake16.

Conclusion

High quantities of oxalate in empty stomach and dehydrated state may pose an additional risk for development of renal injury. To avoid acute oxalate nephropathy, pure sour carambola juice or mild diluted post pickled juice should not be consumed in large amounts, especially in an empty stomach and dehydrated state. People suffering from Hypertension, Diabetes mellitus and obesity, who are at risk of kidney disease or those who have a family history of kidney disease should preferably avoid Kamranga as a precautionary measure. Patients with CKD in any stage or on dialysis should avoid eating star fruit.

Recommendation

It is recommended that uremic patients should totally abstain from star fruit due the rare but potentially fatal complications. Most of the study regarding star fruit intoxication is from other countries of the world. There is no such study among uremic patients in our country. More study as well publicity is required to create awareness of taking star fruit.

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Conflict of Interest

The author has no conflict of interest to anybody.