

Intravenous vitamin C as a primary cause of renal failure is not supported by the evidence base

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A couple of recent *Otago Daily Times* articles have made reference to a patient having died (more than a decade ago) from kidney stones and eventual renal failure due to high-dose intravenous (IV) vitamin C administration.^{1,2} This statement is not supported by the evidence-based literature. Despite cases of acute renal failure ascribed to IV vitamin C being reported in the literature,³ as with any case report there is no control comparator and there are invariably confounders such as disease- or medication-related complications.

In a United States (US) survey of nearly 10,000 patients who received IV vitamin C, adverse events were reported in only 1%, and were mostly minor.³ One patient only had renal failure as a “*not confirmed (possible)*” complication as the “*patient had partial renal failure and cancer metastases to the kidneys*”; thus, likely a complication of the disease rather than the vitamin C therapy.³ Further interrogation of the US Food and Drug

Administration (FDA) Adverse Event Reporting System database for patients treated with IV vitamin C was inconclusive due to the inability to eliminate confounders.³

Although vitamin C (ascorbic acid) can be converted to oxalate, and has been implicated in oxalosis and calcium oxalate nephrolithiasis, this reaction requires multiple oxidation steps (Figure 1). Oxalate formation also often occurs as an *ex vivo* artefact in urine samples rather than *in vivo* due to the numerous endogenous reduction mechanisms that convert the oxidised vitamin (dehydroascorbic acid) back to ascorbic acid.⁴ In support of this, a prospective case series study of 157 adults with 1-year follow-up carried out in a New Zealand setting indicated no reported renal stones with high-dose IV vitamin C administration, despite 8% of the patients having a history of renal stones.⁵

Calcium oxalate crystals are quickly passed in healthy individuals; however, intratubular

Figure 1: Pathway for vitamin C (ascorbic acid) conversion to oxalic acid.

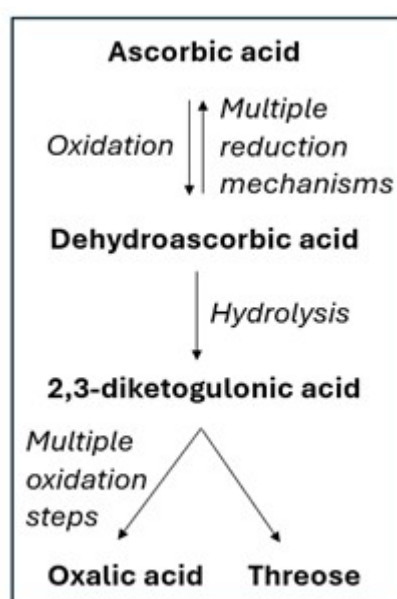


Table 1: Alternate risk factors for renal failure and secondary oxalosis reported in the literature.

Renal failure risk factors	Secondary oxalosis risk factors
Medications causing crystal deposition (e.g., ceftriaxone and amikacin, and other antibiotics, darunavir, triamterene, etc.)	Medications (e.g., methoxyflurane, orlistat, xylitol, topiramate, indinavir and other antivirals, etc.)
Renal transplantation failure (e.g., antibody-mediated rejection, reoccurrence of disease)	Excessive intake (e.g., ethylene glycol, specific foods)
Direct infection of kidneys (e.g. SARS-CoV-2/ACE2 interaction)	Increased absorption (e.g., gastrointestinal diseases, gastrointestinal surgery)
Septic shock/severe burns (e.g., renal hypoperfusion, cytokine storm, vasopressor administration, drug toxicity, mechanical ventilation)	Decreased excretion (e.g., dehydration/diarrhoea, acute and chronic renal failure, chronic haemodialysis)
Chronic diseases (e.g., diabetes, hypertension, autoimmune diseases)	Vitamin deficiencies (e.g., thiamine, pyridoxine)

retention is believed to occur in areas of damaged and regenerating tubular epithelium, where molecules with potential crystal-binding capacity are expressed.⁶ High-dose IV vitamin C administration produces high (millimolar) peak concentrations in the circulation,⁷ which are normally cleared by functioning kidneys with a half-life of approximately 2 hours.⁸ Pre-existing renal failure, however, results in sustained high circulating concentrations of the vitamin, which may have untoward side effects.

There are numerous risk factors for renal failure (e.g., drug toxicity, renal transplantation failure, infection and septic shock, severe burns, chronic diseases—see Table 1) as well as many alternate risk factors for secondary oxalate nephrolithiasis, such as certain medications, excessive intake of specific foods, increased absorption due to gastrointestinal diseases/surgery, decreased elimination due to dehydration or renal failure and specific vitamin deficiencies (Table 1).⁹ As such, vitamin C administration should not be automatically ascribed to renal failure due to oxalate nephrolithiasis in patients who happen to be receiving IV vitamin C therapy,

particularly if there are other pre-existing risk factors.

This premise also applies to studies that have reported associations between vitamin C intake or oral supplementation and kidney stones;¹⁰ not all of the possible confounders are able to be taken into account. Furthermore, vitamin C plasma concentrations are limited in these cases by the regulated intestinal uptake of oral vitamin C via specialised vitamin C transporters, meaning that only a specific proportion of the ingested vitamin is absorbed,¹¹ thereby minimising its potential toxicity.

Overall, IV vitamin C-dependent oxalate nephrolithiasis appears to be a result of pre-existing renal dysfunction, and the inability of the kidneys to adequately clear high plasma concentrations of the vitamin, rather than the vitamin being the primary cause of the renal failure. Thus, it is vital for renal function to be assessed prior to administration of IV vitamin C, and high doses of the vitamin not administered if pre-existing renal dysfunction is apparent, or be discontinued if renal function should decline due to disease- or medication-related complications.

COMPETING INTERESTS

A C Carr has received honoraria from Pascoe for conference presentations (2025), and support for conference attendance, paid to institution, from Pascoe (2025), National Institute of Integrative Medicine (2024) and Linus Pauling Institute (2023).

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