Vitamin C supplementation and kidney stone risk

In a recent research letter published in *JAMA Internal Medicine*, Thomas and coworkers suggest that high-dose vitamin C supplements be avoided due to a two-fold increased risk of kidney stones observed in their cohort of 23,355 Swedish men. This study has been widely reported in the medical literature, however, we would like to present a critique of their findings and emphasise that the findings relate to supplemental vitamin C and not dietary intake of the vitamin.

Concerns for the safety of vitamin C arise from one of its metabolites, oxalate, which is known to be excreted in the urine, although estimates of how much and at what doses of vitamin C have been controversial. A more recent metabolic trial demonstrated small increases of 20 to 33% in urinary oxalate in both normal individuals and kidney stone formers upon supplementation with 2 grams of vitamin C per day, although oxalate levels remained within the normal range.

Because the majority of kidney stones are composed of calcium oxalate, and urinary oxalate is a risk factor for such stones, a number of cohort studies have sought to investigate the association between kidney stone risk and vitamin C intake or supplement use, with differing results. In women, no such relationship has been found. The latest study followed a group of Swedish men with no previous history of kidney stones for up to 12 years, having estimated vitamin C supplement use (along with frequency of use) only at baseline by self-reported questionnaire. The questionnaire was validated; however, with a positive predictive value of 74% for vitamin C use, at least one in four cases are likely to be misclassified at baseline, and even more misclassification is probable given that exposure status was not updated over the 12 year follow up. Additionally, there were only 31 cases of kidney stones in the vitamin C-supplementing group suggesting there is little room for such error.

The study design is observational and, while the authors account for confounders such as dietary intake of vitamin C, calcium and magnesium, and tea and coffee intake, they ignore other prominent risk factors such as dehydration and diuretic use.

Interestingly, randomised control trials, which avoid the issue of confounding, have shown no suggestion of increased risk of kidney stones with vitamin C supplementation even at high doses and for extended periods of time. Additionally, it is important to highlight that the findings in regards to supplemental vitamin C should not be translated to dietary intake of the vitamin given the demonstrated protective effects of other components of the diet such as potassium and also the likely dosage of vitamin C consumed in the study.

The authors have not measured dosage, but state that most of their participants are likely to be consuming 1000 mg tablets. This is significantly higher than the median daily dietary intake of 99 mg for the New Zealand population.
Finally, the authors did not measure plasma levels of vitamin C; intakes whether supplementary or dietary are not necessarily a good reflection of plasma levels, and it is plasma levels that are likely to be a better indicator for kidney stone risk.\(^9\)

Lastly, we would like to point out that the statement “vitamin C supplementation has no benefits” is misleading. Whilst the original randomised control trials found no benefits of supplementation, many of those people would have gained no increase in vitamin C status due to their already saturating levels, and as such further well-conducted studies are required before deciding on the health effects of vitamin C.\(^10\)

We believe the association between ascorbate supplementation and increased risk of kidney stone formation remains controversial, and at this stage should only be of concern to those individuals with a history of kidney stones.

Juliet M Pullar  
Research Fellow

Anitra C Carr  
Research Fellow & Study Co-ordinator

Margreet C M Vissers  
Professor & Associate Dean (Research)

Centre for Free Radical Research, Department of Pathology, University of Otago  
Christchurch, New Zealand

References: