

Vitamin C and kidney stones: facts or fiction

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Widely circulating opinions, especially among the medical community, link vitamin C intake to an increased risk of kidney stones. It appears that this comes from the interpretation of vitamin C metabolism which includes the formation of oxalate, a compound found in kidney stone crystals. However, the kidney stones formation is a quite complex process, and some studies even suggest that moderate dietary intake of vitamin C may be associated with a reduced risk of kidney stones. Individual factors, such as diet, genetics and underlying health conditions, can influence the kidney stone risk.

Vitamin C-kidney stones controversy is another example of bias in scientific and medical research as well as in media reporting. Media has been playing an important role in communicating health information to the public at large without taking much responsibility for being truthful and presenting facts. Various media platforms often enhance expectations of the efficacy of drugs while being negatively prejudiced to nutritional supplements. This is not surprising considering their well-known financial dependency on pharmaceutical advertisers and strong influence of pharma business on medical profession. Already many years ago, Dr. Marcia Angell, former editor-in-chief of the New England Journal of Medicine, declared that it is “no longer a science journal.”

It is a pity that many doctors, having received training that vitamin C causes kidney stones, do not scrutinize this topic and by advising their patients against vitamin C intake, they may involuntarily contribute to depriving them of health benefits of this essential nutrient without decreasing their risk of kidney stones.

Here we evaluate in more detail the scientific evidence available on vitamin C-kidney stones connection including our comments on this topic so our readers can make informed health decisions and understand better the nature of this controversy.

Closer look at the origins of perception linking vitamin C to kidney stones

The vitamin C-kidney stones risk controversy has been continuing for many decades. In 1998 in the review article published in the Journal of the American Medical Association (JAMA), the medical doctors Goodwin and Tangum scrutinized scientific

references quoted in various research papers stating causative effect of vitamin C on kidney stones.

Among others, they examined a scientific review "The Toxic Effects of Water-Soluble Vitamins." published in Nutrition Review in 1984. This article supported the statement that vitamin C promotes kidney stones by seven references. What were these references? One of them was not a clinical study, but a letter to editor published in Lancet in 1973, which described a few case reports from individual observation. Another reference was an error and had nothing to do with the subject. Five other references were coming from books, not from experimental data. Even more, only two of these five books cited a reference for the statement that high doses of vitamin C can cause kidney stones. However, one of these referenced referred to another chapter in another book, while the other used the 1973 letter to the editor.

This illustrates that upon closer examination no scientific basis really existed in supporting the far-reaching conclusion that vitamin C intake causes kidney stones, but the statement fell on a fertile ground in the media and was spread easily.

It is important to understand what the kidney stones are

Kidney stones are crystals of mineral or organic origin which precipitate in the kidneys. They can range in size from the diameter of a grain of rice to the width of a golf ball. They can be confined to the kidneys or travel along the urethra and during their passage large or irregularly shaped crystals can cause pain.

Main types of kidney stones:

1. Stones made of mineral salts

Calcium phosphate stones are quite common and can easily dissolve in acidified urine. Since ascorbic acid (vitamin C) can make the urine more acidic, it supports dissolving already existing phosphate stones and prevents their formation. Incidence of this type of kidney stones: 24-30% in children and 8-18% in adults (75% in pregnant women)

Magnesium ammonium phosphate (struvite) stones are much less common, often appearing after urinary tract or kidney infection. They can grow very large and may harm the kidneys more than other stones. They also dissolve in urine acidified by vitamin C. Both the infection and the stones are virtually preventable with daily consumption of much-greater-than-RDA amounts of vitamin C. Their frequency is 7-13% in children and 2-4% in adults. These stones affect women more than men.

2. Stones that combine mineral and organic molecules

Calcium oxalate stones made of organic molecule- oxalic acid- and a mineral- calcium- are the most common as about 60% of all stones are of this type. They do not completely dissolve in acidic urine, while more alkaline urine favors the

formation of insoluble complexes of oxalic acid with calcium and other minerals. This type of stones may form in people who have chronic inflammation of the bowel or who have had an intestinal bypass operation, or stoma surgery. Incidence: 45-65% in children and 56-61% in adults.

3. Stones made up of organic molecules only

Uric acid stones result from a problem in metabolizing purines (the chemical base of adenine, xanthine, theobromine [in chocolate] and uric acid). Their risk increases in gout. Incidence: 2-4% in children and 9-17% in adults

Cystine stones result from hereditary inability to reabsorb cystine. Often children develop this type of stones, but these are rare. Incidence 5-8% in children and 1% in adults.

How common are kidney stones

Kidney stones incidence is less prevalent than heart disease, cancer or diabetes, but it affects between 5-10% of the population in different countries. In general, people of white race are more prone to develop kidney stones than blacks with higher frequency observed in men than women. Kidney stones increase in men entering their 40s and continue to rise into their 70s. For women, the prevalence of kidney stones peaks in their 50s. However, in recent times, the stone formation appears to be affecting younger people. Now about 13% of all male and almost 20% of all female stone-formers experience their first stone before the age of 20 compared with 4.7% and 4.0% respectively in 1975. Pregnancy increases the risk of kidney stones which is 3x more likely to be calcium phosphate than oxalate stones. Once a person gets more than one stone, other stones are likely to develop.

A closer look at calcium oxalate stones

Since stones made of calcium and oxalic acid are more frequent than other types of kidney stones it is important to learn more about oxalate in our body. Most oxalate in urine may come from our diet and metabolic processes occurring in our body and only a small fraction originates from metabolic conversion of vitamin C.

1. Sources of dietary oxalate

Oxalic acid is contained in many foods common in our diet, including spinach (100-200 mg oxalate per 28g of spinach), rhubarb (from 570-1900 mg in 100 g), almonds (122 mg in 3g) , 1cup of beets provides 152 mg of oxalate and 100 g of wheat bran has 220 mg. Tea and coffee are thought to be the largest source of oxalate in the diet of many people, providing up to 150-300 mg/day. Typically, daily oxalate intake by an adult is in the range of 80-150 mg/d, but it can range from 44-1000 mg/d in individuals who eat a typical Western diet. This is considerably more than 20-30 mg that would likely be generated by taking 1000 mg of vitamin C/day.

2. Early interventions in decreasing oxalate absorption in the GI track

Dietary oxalic acid is readily absorbed from the intestine into the bloodstream with estimated about 2-15% of oxalic acid absorbed from different foods. One of the ways to decrease the amount of oxalate getting to our blood and reaching the kidneys is by binding it in our intestinal track to calcium. This results in forming insoluble calcium oxalate crystals that are eliminated in the stool. The preferred calcium form to reduce oxalate is calcium citrate taken with each meal, because citrate also inhibits oxalate absorption from the intestinal tract.

Also, probiotics may be helpful in decreasing oxalate absorption by promoting oxalate degradation in the intestine. In addition to *Oxalobacter* strain also *Bifidobacterium lactis* and *Lactobacillus acidophilus* have enzymes that degrade oxalates and individuals with low amounts of this types of bacteria are much more susceptible to kidney stones.

3. Sources of metabolic oxalate in blood and urine

It has been estimated that blood that reaches kidneys contains on average about 0.4-0.9 mg/dl oxalate coming from dietary sources and created during our body metabolism.

Oxalate formed in the liver. The main metabolic source of oxalate in our body is the liver from which it gets into bloodstream and is excreted in urine. Oxalate comes from metabolic conversion of amino acids (glycine, hydroxyproline, tryptophane), sugars (glucose, fructose, pentose sugars), vitamin C and glyoxal (from the breakdown of carbohydrates, proteins, and fats). Glyoxal can be further converted to glyoxylate, a precursor to oxalate (J. Knight, 2010). It is interesting that both glyoxal and oxalate synthesis are associated with oxidative stress.

Contribution of vitamin C metabolism to oxalate formation. Only a small percentage of vitamin C (1-1.5%) in the body cells is converted to oxalate. In practice, it is not likely that vitamin C promotes formation of oxalate stone for several reasons. For once vitamin C in the urine tends to bind calcium decreasing its availability to bind oxalate. Also, vitamin C makes urine more acidic which further reduces the binding of calcium with oxalate and consequently, stone formation. In addition, the diuretic effect of vitamin C increases flow of urine, thereby reducing urine stagnation necessary for stone formation. "Fast moving rivers deposit little silt".

Oxalate triggered by some infections: Some amounts of oxalate can be generated in people affected by fungi infections i.e. *Aspergillus*

Type of evidence used in evaluating risk of kidney stones by Vitamin C

Vitamin C – kidney stones connection remains inconclusive. There are no large, well-controlled studies showing directly that a regular intake of the specific amount of

vitamin C caused the development of kidney stones. Most evidence in support and against such a connection comes from retrospective epidemiological studies. Such studies involve individuals monitored for longer periods (a few years). Their vitamin C intake is usually reported in self-assessed questionnaires submitted at different times (often every few years) that recall a person's lifestyle, dietary habits, supplement intake, etc. which can be biased or prone to reporting errors. Other studies involve indirect evidence demonstrating increased oxalate secretion in urine in some individuals consuming vitamin C, but not straightforward evidence of the presence of stone.

1. Clinical evidence showing that Vitamin C intake is NOT linked to kidney stones formation

In the large (45,251 men) Harvard Prospective Health Professional Follow-Up Study (HPFS), the groups of men with greater than 1,500 mg/day vitamin C intake had a lower risk of kidney stones than men with the lowest vitamin C intake. (Curhan et al., 1996)

Mega-evaluation of the results from the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS) showed that Vitamin C intake up to 1 g/day had no association with kidney stones in women, but it had in men (by 19%) Ferraro et al., 2016). These conclusions were drawn based on food frequency questionnaires and did not include stone compositions. Also, the study in men had a low statistical significance.

A large-scale, prospective study involving 85,557 women followed for 14 years found no evidence that vitamin C causes kidney stones. There was no difference in the occurrence of stones between people taking less than 250 milligrams per day and those taking 1.5 grams or more. The authors of these large studies stated that restriction of higher doses of vitamin C because of the possibility of kidney stones is unwarranted (Curhan, et al., 1999; Curhan, et al., 1996).

Tsao and Salimi (Tsao et al., 1984) evaluated oxalic acid levels in urine samples in healthy people taking 10 g of vitamin C daily for at least two years. Among the six subjects tested, five had no significant change in urinary oxalate excretion, oxalate was elevated in one individual, but its level was within the range of urinary oxalate content from consuming normal diet.

Gerster stated that vitamin C has no contribution to oxalate type kidney stone formation (Gerster, 1997)

2. Studies linking Vitamin C intake to kidney stones formation

A prospective study in men published in *JAMA Internal Medicine* in 2013 claimed that vitamin C supplements increased the risk of developing kidney stones. The study stated that the stones were most likely of an oxalate type, which can be formed from vitamin C metabolic conversion, but it did not analyze the kidney stones of

participants. Instead, it relied on a different study of kidney stones where ascorbate was not tested.

This type of poorly organized study does not help the medical profession or the public but instead causes confusion. The study acknowledges that accurate details of vitamin C dosage were not available, and that the results need to be confirmed in other studies.

Another study followed 23,355 Swedish men for a decade. Study participants were divided into two groups: one that did not take any supplements (22,448) and a smaller group (907) that took vitamin C. The average diet for each group was recorded, but not in much detail. It appeared that the group that took vitamin C had a greater risk of kidney stones. This extra risk was very low, 147 per 100,000 person-years, or only 0.15% per year.

This was observational, not a randomized controlled study, in which vitamin C would be given to a group selected at random. This type of observational study has limitations that make its conclusion unreliable. Also, the correlation between vitamin C supplementation and kidney stones could not be determined, because of a lack of detailed information on each patient's diet and a chemical analysis of each stone to provide a hint about the probable cause. Drawing conclusions from such a study can hardly be a good example of "evidence-based medicine".

Massey's study (Massey et al., 2005) included 29 stone formers and 19 non-stone formers supplemented with 2 grams of vitamin C. After five days on a low-oxalate diet, the subjects consumed 136 mg oxalate, including 18 mg oxalic acid. They remained on a low oxalate diet for the remainder of the day. At the end, 12 stone formers and 7 non-stone formers showed increased oxalate excretion by over 10% after supplementation. Interestingly, seven of the subjects who showed an increased level of oxalate were not-stone formers. The important question of why some people are prone to forming kidney stones, and others do not, was neatly sidestepped.

The only thing that this study proved was that "the absorption of dietary oxalate" was increased with supplementation of 2g of vitamin C. While the authors were anxious to conclude that Vitamin C would increase the risk of kidney stones in fact they did not see any single kidney stone in the study! What is ironic is the fact that in 1946, physician William McCormick used vitamin C to prevent and eliminate some kidney stones stating that "There is no evidence that vitamin C causes kidney stones. Indeed, in some cases, high doses may be curative" (McCormick, 1946).

Practical aspects in preventing kidney stones

Kidney stones are an example of a multifactorial disease and there is not a single factor that can lead to it. Keep in mind that even though a certain part of oxalate in the urine derives from metabolized vitamin C, it does not mean that it causes calcium oxalate kidney stones. At the same time vitamin C, which is not produced in our body, is

critical for our health and life by being essential in collagen formation, antioxidant defense, immunity, absorption of iron and many other processes.

1. Known risks of kidney stones which you can control

- **Low fluid intake** was found to be inversely related to the risk of kidney stones, with a relative risk of 0.71 in men and of 0.61–0.68 in women.
- **Diet high in animal protein** can increase the risk of uric acid kidney stones because it is associated with an increase in urinary calcium and reduction in urinary citrate. Although dairy proteins are associated with higher calcium excretion, they also promote citrate excretion and decrease oxalate and uric acid excreted in urine.
- **Food rich in oxalate** (i.e. spinach, rhubarb, nuts, or beets) can increase oxalate in urine
- Be aware of **fructose consumption** as high fructose containing syrups and sodas have been linked to higher risk of kidney stones since fructose increases urinary excretion of calcium, oxalate, and uric acid, decreases magnesium and affects acidity of urine (Johnson et al., 2018). Intravenous infusion of fructose could increase urinary oxalate excretion by 60% compared to glucose infusion (Nguyen et al., 1995). People with metabolic syndrome and those suffering from heat stress may be especially affected by fructose. Increased the risk of kidney stones by fructose was also confirmed in a meta analysis of several prospective epidemiological studies in men and women (Taylor et al., 2008).
- Kidney stones are also more common in people with **inflammatory bowel disease** such as Crohn disease associated with excessive oxalate secretion in urine and malabsorption of magnesium. Also, patients with resection or a bypass of the small bowel.
- Kidney stones can result from many underlying metabolic conditions, including hyperparathyroidism characterized by excessive secretion of parathyroid hormone (PTH) leading to increased calcium levels in the blood and urine, or diseases affecting kidneys (i.e. 3–20% of people who form kidney stones have medullary sponge kidney).

2. What you can do to decrease your risk of kidney stones

- Be aware of the **risk factors you can control** (see #1)
- **Drink lots of fluids!** Maintaining diluted urine is a key principle for the prevention of kidney stones and high fluid intake has been associated with a 40% reduction in recurrence risk.
- **Beverages** you consume can also affect stone formation. Analysis of the effects of various beverages consumption in 45,289 men, 40-75 years of age, who had

no history of kidney stones followed for 6 years concluded that the risk of stone formation decreased by daily consumption of 240-ml of coffee by 10%; tea by 14%; beer by 21% and wine by 39%. However, the risk of stone formation increased by 35% for apple juice and 37% for grapefruit juice. Curhan et al., 1996)

- Provide your body with **essential minerals**:
 - Potassium – its high dietary intake can increase citrate in urine - an inhibitor of urinary crystal formation.
 - Magnesium either from foods (buckwheat, green vegetables, beans, nuts) or magnesium supplements is important since magnesium is also an inhibitor of urinary crystal formation. Recommended intake at least 300-400 mg/day (more may be desirable to maintain an ideal 1:1 balance of magnesium to calcium). Readily absorbable forms are magnesium citrate, chelate, malate, or chloride. Magnesium oxide is cheap and widely available, however, it is only about 5% absorbed and thus acts mostly as a laxative.
 - Calcium binds with oxalate already in the gastrointestinal tract, thereby preventing its absorption into the bloodstream and reaching the kidneys. The preferred form is calcium citrate because it helps to increase urinary citrate excretion. Calcium supplements should be taken with meals.
- **B-complex vitamins** (B6) and magnesium. Dr Rath B-complex supplement, twice daily, plus about 400 milligrams of magnesium, is usually adequate.
- **Probiotics** containing oxalate metabolizing bacteria: *Oxalobacter formigenes* may help in patients with high oxalate. Studies showed that *Oxalobacter* supplementation decreased oxalate secretion in these patients by 96% (Hatch et al., 2006; Hoppe B et al., 2005). Also, a recent case-controlled study in 58 patients and 29 controls showed benefits of *Oxalobacter* in significantly decreasing oxalate in urine (Tavasoli et al., 2020). Be aware that Antibiotics – (sulfonamides, ampicillin, amoxicillin, quinolones, furans and pyridines) kill many beneficial bacteria including *Oxalobacter*.

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