

Dietary citrate substitution in urolithiasis patients

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Stone formation is dependent on supersaturation of urinary salts and urinary crystal retention. Urinary promoters (protein aggregates, cell debris) and inhibitors (citrate, magnesium, urinary macromolecules such as glycosaminoglycans and proteins) are involved in the process of stone formation [1].

Hypocitraturia is one of the most common pathogenetic mechanisms involved in stone formation; in patients with stone recurrence the prevalence of hypocitraturia is between 20 and 60%.

Citrate has received a lot of attention in basic research and in clinical applications. It is a weak organic tribasic acid and has been widely reported to be an important factor in the prevention and development of calcium urinary stones [1].

Citrate retards urinary stone formation by:

- (i) Inhibiting calcium oxalate (CaOx) and calcium phosphate (CaP) crystal growth and aggregation.
- (ii) Forming intestinal complexes with calcium thereby decreasing calcium excretion which reduces ion activity products (supersaturation) of CaOx and CaP [2].

Urinary pH plays an important role in citrate concentration; in fact, a low pH reduces renal citrate excretion through the activity of sodium-dependent dicarboxylate transporter (NaDC-1), which is responsible for the reabsorption of citrates in distal renal tubules, and of successive integration into the Krebs cycle [3], while alkalosis induces a reduction of citrate absorption, resulting in increased urinary citrate excretion.

Serum concentration of citrate ranges from 0.05mM to 0.3mM. This concentration is relatively constant and is controlled by the activity of NaDC-1 which has been found in renal tubules as well as in the small intestine and colon. There is strong evidence for intestinal absorption of citrate after an oral citrate load with a significant increase in serum citrate [4].

Most international guidelines suggest

the use of alkaline-citrates (such as potassium citrate, sodium-citrate, potassium-magnesium citrate, etc.) for the medical therapy of stone-formers with hypocitraturia and for prevention of stone recurrence.

Therapy with citrate preparations is limited however by relatively high treatment costs and side-effects such as epigastric discomfort. So, how about the dietary application of citrate?

Dietary intervention for hypocitraturia

Dietary manipulation is important for the control of acid-base balance; indeed the major dietary source of alkali is the conjugate base of potassium salts present in vegetables, fruits and their juices. Food containing amino acids with sulphur moieties (meat, poultry, fish and eggs), represents the primary intake of dietary acid.

Several studies have demonstrated that a diet with a high intake of fruit juice can increase citrate excretion and reduce stone recurrence [5].

The most important fruit juices that may help increase the serum concentration of citrate are:

Lemon juice

Lemon juice can considerably increase urinary citrate levels. In many of these studies a reduction of the urinary calcium excretion was observed without increase in the oxalate levels in urine [6,7]. Comparative studies between orange juice and potassium citrate administration suggest that lemon juice is less effective in increasing urinary citrate [8,9].

Orange juice

The use of orange juice resulted in a considerably higher urinary citrate excretion when compared to lemon juice; but with orange juice the urinary oxalate concentration was notably higher. In some studies, the difference of saturation of calcium oxalate was favourable after consumption of orange juice compared to the lemon juice, albeit not significantly so [10].

Grapefruit juice

Grapefruit juice, pink or red, appreciably increased urinary citrate but also urinary oxalate concentrations. The increase in oxalate excretion, which would promote lithogenicity, is contrasted by the increase in citrate excretion [11].

Lime juice

In an experimental study in stone formers a solution containing lime powder consistently increased urinary citrate, pH, and potassium [12].

Melon juice

The consumption of melon juice, a non-citrus fruit, has a positive effect in increasing citraturia as compared to citrus fruits [13].

Sport drinks

Performance®, a sport drink without fruit, increased citrate concentration of urine and pH in non-stone former patients to a similar degree observed in some studies using lemon juice. Another sport drink, Gatorade®, did not considerably change urinary parameters [14].

Soda drinks

The use of soda drinks showed no important variations of citrate urinary concentration. In any case, high volumes of these beverages for long-term citrate replacement is not recommended, due to the high caloric content of many such preparations [15].

Conclusions

Dietary interventions, as an alternative or supplement to medical treatment could represent a good option for the prevention of stone recurrence in patients with hypocitraturia. Many citrus fruit juices (lemons, oranges, grapefruit, and lime) and non-citrus fruit juices (melon) are natural sources of citrate, and numerous studies have shown their ability to increase urine citrate levels. Although there are no prospective randomised trials in the literature on dietary treatment of urolithiasis with hypocitraturia as an endpoint, in clinical practice there may be a role for this from the limited evidence we have at the present time.

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