

THE THERAPEUTIC ADVANTAGE OF SOFT VERSUS HARD WATER IN CALCIUM STONE-FORMERS TREATED WITH HYDROCHLOROTHIAZIDE IS DEPENDENT UPON CONCOMITANT OXALATE RESTRICTION

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Summary

The optimal quality of water to drink for calcium stone-formers treated by thiazides remains a matter of controversy, mainly because their calcium and magnesium content are correlated and their oxalate excretion is inversely correlated to hardness of the water. In 22 calcium stone-formers treated by thiazides, dairy product restriction and low oxalate diet, urinary excretion of calcium, magnesium and oxalate were measured after three months with soft water and three months with hard water. Calciuria was lower, the UMg/UCa ratio higher and the probability of being a stone-former (PSF of Robertson taking into account both calcium and oxalate) was lower with soft water. Thus, soft water appears more optimal to drink than hard water in patients treated by thiazides. However, this is true only when oxalate restriction is strictly observed as when an oxalate load of 1g is ingested, the probability of being a stone former is higher on soft water than on hard water because of the dramatic increase in oxalate absorption and excretion.

Introduction

Hydrochlorothiazide and high fluid intake are well established therapeutic measures for calcium nephrolithiasis, the optimal quality of water to drink however, remains a matter of controversy. On one hand, hard water as drinking water appears to be inappropriate since in the absence of thiazide therapy, it has been shown to induce an increase in calcium excretion and has been incidentally incriminated to favour stone recurrence [1]. On the other hand, soft water may not be optimal either for two reasons: (a) its magnesium content is very low and may be therefore less beneficial than hard water with high magnesium content since oral magnesium has a protective effect against calcium crystallization in the urine [2]; (b) in patients on a low calcium diet because of the dairy product restriction and of soft water drinking, a sharp increase of urinary oxalate is

induced when oxalate rich foods are ingested, so that the propensity to stone formation is dramatically increased [3]. Furthermore, in the United States, a higher frequency of stones has been reported in areas with low calcium soil and soft water [4].

Because of these controversies, it seemed to us important to study the variations of the most significant urinary risk factors, i.e. urinary excretion of calcium, oxalate and magnesium in patients treated by thiazides during two successive three month periods, during which water of different hardness was used to assure a high diuresis.

Patients and methods

Twenty-two calcium stone-formers performed the study. Specific causes of urolithiasis such as primary hyperparathyroidism had been excluded by a prior evaluation. During the protocol, patients were treated daily with 50mg of hydrochlorothiazide and were asked to observe a low calcium diet providing less than 500mg of calcium daily without taking into account the calcium content of water. Oxalate restriction was performed by exclusion of foods with high oxalate content (<100mg/100g material).

Two therapeutic periods of 3 months, one with hard water intake (Ca=11.25; Mg=2.7mmol/L) and one with soft water intake (Ca=0.25; Mg=0.25mmol/L) were performed, the volume of water ingested being maintained at a constant daily amount of 1.5 litre. The sequence of the two periods was randomly determined.

At the end of the two periods, patients collected 24 hour urine on two days. At noon of the second day of urine collection, they ingested 1g of oxalate as 200g spinach. In urine collections we measured sodium, calcium, magnesium, creatinine by Auto-Analyser and oxalate by gas liquid chromatography. The probability of being a stone-former (PSF of Robertson) linked to calcium and oxalate was calculated for each urine collection with a method previously described, using our own control and patient data [2].

The urinary magnesium/calcium ratio was also calculated. Assuming that oxalate is not catabolized after absorption [4], the percentage of absorbed oxalate from the orally ingested oxalate load was calculated for each patient during therapeutic period as follows:

$$\frac{24 \text{ hours urinary oxalate excretion after oxalate load} - 24 \text{ hours urinary oxalate excretion during low oxalate diet}}{\text{oxalate load per 24 hours}} \times 100$$

Statistical differences were assessed by Student's 't' test for paired data.

Results

The results are summarized in Table I. There were no significant differences between hard water and soft water intake for urine output sodium, creatinine and magnesium excretions.

TABLE I. Excretions (Mean \pm SEM) of urine output, creatinine (UCrV), sodium (UNaV), calcium (UCaV), magnesium (UMgV), oxalate (UOxV) and values of PSF and magnesium/calcium, urinary ratio (UMg/UCa)

Urinary Excretion 24 hours	HARD WATER Dietary oxalate		SOFT WATER Dietary oxalate	
	Restriction	Load	Restriction	Load
Diuresis l	2.6 \pm 0.17	2.6 \pm 0.14	2.7 \pm 0.21	2.7 \pm 0.17
UCrV mmol	14.4 \pm 0.72	14 \pm 0.87	13.5 \pm 0.62	14 \pm 0.78
UNaV mmol	184 \pm 19	164 \pm 17	190 \pm 16	175 \pm 0.78
UCaV mmol	8.9 \pm 0.7	8.6 \pm 0.9	5.3 \pm 0.8**	5 \pm 0.7
UMgV mmol	5.8 \pm 0.2	5.7 \pm 0.3	4.8 \pm 0.5	4.8 \pm 0.5
UMg/UCa	0.7 \pm .08	0.7 \pm .08	0.95 \pm 0.22***	0.99 \pm 0.21
UOxV	0.235 \pm 0.01	0.274 \pm 0.02†	0.293 \pm 0.02**	0.453 \pm 0.03††
PSF	0.63 \pm 0.05	0.64 \pm 0.05	0.51 \pm 0.05*	0.72 \pm 0.05††

Significance of the difference between Hard Water intake and Soft Water intake:

*p<0.05, **p<0.01

Significance of the difference before and after oxalate load during each therapeutic period:

†p<0.05, ††p<0.01

Calcium excretion was significantly lower and oxalate excretion significantly higher during soft water intake. But the probability of being a stone-former taking into account these two parameters was lower with soft water intake in the absence of an oxalate load. Urinary magnesium/calcium ratio was found higher during soft water intake.

The oxalate load induced a significant increase in oxalate excretion with soft water and hard water intake, but the increase of oxalate excretion was more dramatic during soft water intake so that there was a significant increase of the probability of being a stone-former after oxalate load only during soft water intake. The percentage of oxalate absorbed was significantly greater during soft water intake (2 \pm 0.1% versus 0.5 \pm 0.35%; p<0.05).

Discussion

Our study shows that in calcium stone-formers on chronic thiazide therapy, calcium excretion is lower when drinking soft water than hard water. The difference cannot be explained by a sodium-dependent hypocalciuric effect because sodium excretion was similar with both waters. In fact, in spite of the hypocalciuric effect of thiazide which may decrease calcium excretion by 50 per cent [6], calciuria is still dependent upon calcium intake during chronic thiazide therapy. This may be the reason for which the only controlled study (versus placebo) that has proved the efficiency of thiazides in the prevention of stone recurrence, is the one which has paid attention to control the calcium intake [7].

Our data show a tendency to a higher magnesium output during hard water intake. The lack of a significant difference might be linked to the magnesuric effect of thiazide which could blunt a difference in magnesium excretion in

relation to a difference in magnesium intake with the two kinds of water. Nevertheless, the importance of magnesium in inhibiting calcium crystallization depends on the concentration of magnesium in relation to calcium rather than on the absolute amount of this ion. For this reason, soft water appears to be the most optimal water to prevent recurrence when considering magnesium excretion because the important decrease of calcium excretion offsets fully the decrease in magnesium excretion so that the UMg/UCa ratio is more suitable with soft water than with hard water to prevent crystallization. However, the duration of the magnesuric effect of thiazide treatment seems to disappear after one year [2]. So it remains to check whether this more favourable urinary magnesium/calcium ratio is still observed with soft water intake after one year of thiazide therapy.

This work confirms our previous data observed in patients not taking thiazides: compliance to oxalate restriction is critical in stone-formers on calcium restriction in order to prevent an increase in the probability of being a stone-former linked to an increase in oxalate excretion [8]. With soft water intake, the dramatic decrease in calcium excretion offsets fully a moderate increase in oxalate excretion, so that the probability of being a stone-former observed with soft water intake is significantly lower when compared to the probability of being a stone-former observed with hard water intake. But with soft water intake, an oxalate load induces a dramatic increase in oxalate excretion and consequently the probability of being a stone-former whereas this is not observed with hard water intake. So, when taking into account oxalate and calcium excretion together, soft water is best for calcium stone-formers only when oxalate restriction is observed.

In conclusion: 1) even under treatment with thiazide, calciuria remains dependent upon calcium intake; 2) after three months, when considering the optimal UMg/UCa , soft water appears to be more suitable than hard water but this judgement has to be re-evaluated after one year when the effect of thiazide on magnesuria has vanished; 3) when considering the probability of being a stone-former, which takes into account calcium and oxalate excretions, soft water is still more suitable than hard water but only if oxalate restriction is strictly observed.

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