Drinking Water Composition and Incidence of Urinary Calculus

Introducing a New Index

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Introduction. We searched for a pathophysiologically based feature of major water electrolytes, which may define water quality better than the water hardness, respecting urinary calculus formation.
Materials and Methods. Utilizing a multistage stratified sampling, 2310 patients were diagnosed in the imaging centers of the provincial capitals in Iran between 2007 and 2008. These were composed of 1755 patients who were settled residents of 24 provincial capitals. Data on the regional drinking water composition, obtained from an accredited registry, and their relationships with the region's incidence of urinary calculi were evaluated by metaregression models. The stone risk index (defined as the ratio of calcium to magnesium-bicarbonate product in drinking water) was used to assess the risk of calculus formation.
Results. No correlation was found between the urinary calculus incidence and the amount of calcium, bicarbonate, or the total hardness of the drinking water. In contrast, water magnesium had a marginally significant nonlinear inverse relationship with the incidence of the disease in the capitals ($R^2 = 26\%$, $P = .05$ for a power model). The stone risk index was associated nonlinearly with the calculus incidence ($R^2 = 28.4\%$, $P = .04$).
Conclusions. Urinary calculus incidence was inversely related with drinking water magnesium content. We introduced a new index constructed on the foundation of a pathophysiologically based formula; the stone risk index had a strong positive association with calculus incidence. This index can have therapeutic and preventive applications, yet to be confirmed by clinical trials.

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INTRODUCTION

Urolithiasis is a very complex disease. An understanding of the epidemiology, particularly the interactions between different factors, may help define approaches that reduce the risk of calculus formation. People's concern is that public water supply may contribute to urinary calculus formation. Mineral content may widely vary in tap water depending on the geological characteristics of the aquifer site. Water hardness is defined as the molar sum of calcium and magnesium found in water, and is expressed as grains per gallon (gpg), parts per million (ppm) or weight per volume (mg/L).[1] Assuming a daily water intake of 2 L, people in areas with very hard water receive as much as 360 mg of calcium (30% of the reference daily intake), and 170 mg of magnesium (40% of the reference daily intake) via drinking water.

Previous investigations that tried to find a correlation between the water hardness and urolithiasis have led to contradictory results. Similarly, there is no consensus on the effects of mineral content of fresh water such as calcium and bicarbonate on the urinary calculus incidence.[2-12] Certain pathophysiological studies have demonstrated an inhibitory effect of magnesium on calcium oxalate calculus formation.[13-16] Accordingly, magnesium supplements have been suggested for calcium oxalate calculus metaphylaxis.[17-20] However, in epidemiological studies, magnesium-calcium ratio in tap water was shown to be inversely related with the incidence of the calcium-containing urinary calculus.[21,22] The present study was aimed to address whether there is a correlation between the urolithiasis incidence and water supply ingredients in different provinces of Iran. We searched for a pathophysiologically based feature among major water electrolytes which may define water quality better than the water hardness, respecting urolithiasis incidence.

MATERIALS AND METHODS

This study was conducted as part of a nationwide epidemiological research conducted at 787 radiology centers in 24 provinces of Iran between 2007 and 2008, according to an *epsem scheme* (equal probability selection method) sampling.[23] In order to evaluate the burden of the disease, among referrals to imaging centers in defined periods of time, all imaging-proven urolithiasis patients who had their first or a new symptomatic episode of the disease were labeled as new cases and cumulative pooled incidence rates were estimated accordingly based on weighted values (a full description of the method is published elsewhere).[23]

The regional drinking water composition at the same time was obtained from an accredited national registry. Water hardness had been measured directly using the ethylenediamine tetraacetic acid titration test. Consistent with the Water Quality Association classification, water hardness data were classified in 5 groups of soft (< 17.1 ppm), slightly hard (17.1 ppm to 60 ppm), moderately hard (60 ppm to 120 ppm), hard (120 ppm to 180 ppm), and very hard (> 180 ppm).[24] Seasonal variations were observed in the amount of total hardness along with calcium and magnesium contents of water resources in some capital cities. Thus, we used the

Table 1. Incidence of Urinary Calculi in Provincial Capitals of Iran and Tap Water Data*

City	Calculus Incidence, per 100 000/y	Water Hardness, ppm	Calcium, mg/L	Bicarbonate, mg/L	Magnesium, mg/L	Stone Risk Index
Ilam	3222	233.4	60	176.7	17.5	0.0194
Sanandadj	1420	159.3	56	178.3	6.1	0.0515
Bushehr	854	558.5	60	...	...	...
Sari	577	412.7	64	379.1	36.7	0.0046
Birjand	564	298.8	55	...	...	...
Rasht	506	382.8	53	175.3	42.0	0.0072
Shahrekord	500	277.3	67	246.8	34.8	0.0078
Urmia	471	57.4	55	168.8	13.3	0.0245
Arak	449	359.2	52	...	...	...
Semnan	379	571.1	56	26.2	65.1	0.0328
Tabriz	374	227.6	62	234.7	20.8	0.0127
Kermanshah	302	212.9	58	187.5	11.9	0.026
Gorgan	298	367.1	56	260.2	28.7	0.0075
Mashhad	294	278.8	55	...	...	...
Ardabil	253	419.9	56	406.0	20.9	0.0066
Qom	234	443.7	63	152.9	40.4	0.0102
Hamedan	233	193.1	60	157.8	19.2	0.0198
Bojnourd	213	554.6	55	380.4	96.4	0.0015
Qazvin	202	135.0	60	...	...	...
Ahwaz	171	371.6	65	...	...	...
Kerman	138	281.7	55	...	...	...
Zahedan	98	874.7	53	...	...	...
Shiraz	79	468.0	53	311.9	58.6	0.0029
Esfahan	52	223.4	58	...	...	...

*Ellipses indicate not available. Data of 6 provincial cities of Iran were not available. Tehran was excluded because of its multiple sources of tap water.

mean of each parameter. Tehran city was excluded from our study because it had numerous water resources with different compositions which could cause misinterpretation. In houses, water softeners are not usual in Iran and drinking bottled water is not a common practice; thus, tap water is the major source of drinking water in Iran.

The incidence of the urinary calculi was estimated either with all detected cases in capitals or based on the settled or permanent residents of the cities (as presented in the Table 1). The *stone risk index* (SRI) was defined as the ratio of calcium concentration to the magnesium-bicarbonate product:

SRI = calcium (mg/L)/(magnesium [mg/L] × bicarbonate [mg/L])

The relation between the regional drinking water composition and the related regional urolithiasis incidence as well as the amount of calculated SRI was evaluated by metaregression with linear and nonlinear models that were designed for each mineral. The models were compared with respect to their R^2 values, the sum of squares for the model, and the residual, standard error, F statistics, and the related *P* value. The significance level for *P* value was assumed to be less than .05.

RESULTS

Of 6127 imaging-proven cases of urinary calculi detected out of 117 956 referrals to the radiology centers of all provinces, 2310 were diagnosed in the imaging centers of the provincial capitals. These were composed of 1755 patients who were settled residents of the large cities including 1325 permanent residents, ie, who had lived for at least 2 years in those capital cities in 24 provinces. The incidence was widely diverse as illustrated in Table 1. The mean age of the patients was 41.5 years old, and 57.5% of them were male.

The calcium level of the tap water ranged from 52 mg/L to 67 mg/L (mean, 57.7 ± 4.1 mg/L); magnesium level, from 6.1 mg/L to 96.4 mg/L (mean, 34.1 ± 24.1 mg/L); and bicarbonate level, from 26 mg/L to 403 mg/L. We did not have access to the magnesium data in 9 of the capital cities. The water hardness ranged from 57 ppm to 874 ppm (mean, 348 ± 176 ppm). More importantly, over 87% of the cities had a very hard (> 180 ppm) water supply (Table 1). There was no city with soft water and only 4.2% had slightly hard water. None of the cities had moderately hard water, and 8.3% of the cities had hard water supply.

Taking into account the city incidence of the disease as a dependent variable, a power model was compatible with the water magnesium concentration (R^2 = 26%, *P* = .05; Figure 1). When only settled or permanent residents in the cities were taken into account, the model became marginally nonsignificant (R^2 = 21%, *P* = .08); however, the estimated curve remained constant (Table 2).

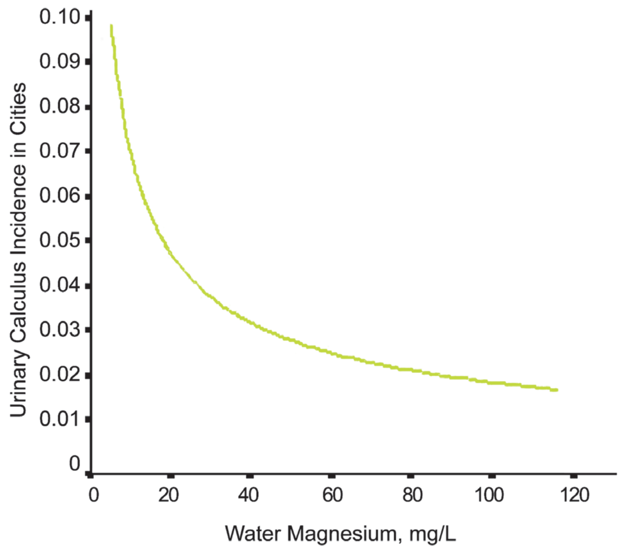

Figure 1. The nonlinear curve demonstrates the relationship between the incidence of urolithiasis in the capital cities and the drinking water magnesium concentration.

Table 2. Nonlinear Regression With Power Models for Associating Various Estimates of Urolithiasis Incidences With Drinking Water Magnesium Composition and Stone Risk Index in the Region*

	Magnesium					Stone Risk Index				
Variable	F	R^2, %	B0	B1	*P*	F	R^2, %	B0	B1	*P*
Province incidence	4.06	22.0	0.0101	-0.395	.06	3.87	21.7	0.011	0.317	.07
Capital city incidence 1	4.58	26.0	0.0290	-0.602	.05	5.16	28.4	0.042	0.511	.04
Capital city incidence 2	3.57	21.5	0.0135	-0.536	.08	4.58	26.1	0.020	0.478	.05
Capital city incidence 3	3.57	21.5	0.0134	-0.541	.08	4.46	25.5	0.020	0.478	.05

*Incidence 1 refers to all positive findings in the capital cities, incidence 2 is restricted to the settled residents in the capital cities, and incidence 3 includes only permanent residents in the capital cities for at least 2 years. F indicates the F statistics; R^2, the amount of variation that could be explained by the model; B0, the intercept; and B1, the regression coefficient.

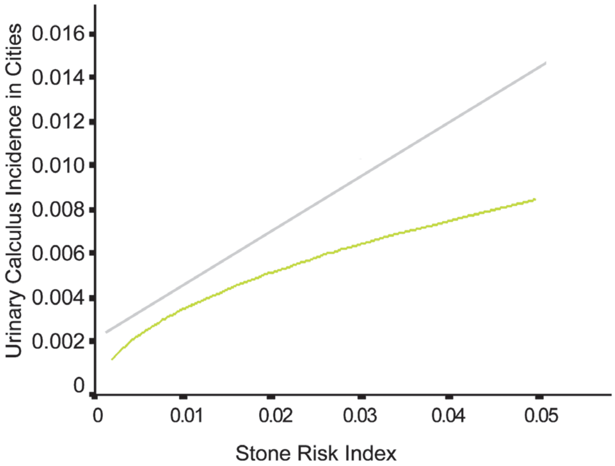

Figure 2. The nonlinear curve demonstrates the relationship between the incidence of urolithiasis in the capital cities and the stone risk index.

The calculated SRI significantly correlated with the city incidence of urolithiasis in a nonlinear power model (R^2 = 28%, *P* = .04). Similar results were obtained with the settled or permanent residents (*P* = .05), though with smaller R^2 (Table 2 and Figure 2).

DISCUSSION

Our study showed no significant correlation between the total hardness of the tap water from various capitals of Iran with the regional incidences of urinary calculus in those areas. Seirakowski and coworkers evaluated 2302 patients admitted to the hospitals with subsequent discharges with a diagnosis of urolithiasis in various geographic regions of the United States and observed an inverse relationship between the water hardness and urolithiasis incidence.[2] Formerly, Churchill and colleagues had evaluated discharge diagnosis with urolithiasis in 1000 general hospitals in the United States from 1948 to 1952 and found a positive correlation with water hardness in that area with urinary calculus.[3] However, Shuster and colleagues showed contradictory results. They conducted a study on 2295 patients from 2 regions of the United States with soft water and high calculus incidence, or hard water and low calculus incidence. Home tap water samples from hospitalizations due to urinary calculi were compared with that of controls. They observed that after adjusting for environmental factors, no significant difference between the two groups was obtained in tap water calcium, magnesium, and sodium concentrations. They concluded water hardness should be a minor concern with respect to urinary calculus formation.[4]

Barkers and Donnan used data of inpatient enquiring in the regions in the United Kingdom. The distribution of upper urinary tract calculus in their study showed a positive correlation with the total hardness of drinking water, since areas of hard water were mainly in south and east of England with a high incidence of nephrolithiasis.[9] Others found no significant relationship in Spain,[10] India,[7] and through the world.[11] However, in our study, this lack of correlation might be partly explained by the nearly homogenous distribution of the water hardness within the provinces in Iran. Around 85% of people who were included in our study lived in the cities with very hard water (above 180 ppm). This amount of variation in water quality is not sufficient to cause significant changes in the calculus occurrence. Although the protective influence of the hard water in urolithiasis could not be proven, our study did not show any extra tendencies toward calculus formation in the people living in areas with harder water either.

Although many pathophysiological studies have shown a prophylactic role for magnesium ingestion and risk for urinary calculus formation,[5,13-20,25,26] the relation between magnesium content of drinking water and urolithiasis incidence is not well clear in epidemiological studies. Many epidemiological studies focused only on the total hardness yet not the individual water magnesium impact.[2-4,9] Others did not observe any significant role for magnesium in the urinary calculus incidence.[5,7] Kohri and coworkers collected tap water in 85 major cities throughout Japan and examined the relationship between the nature of the water and the soil, and the urolithiasis incidences available from a previous epidemiological study. In their study, calcium and magnesium levels of the tap water were not correlated with urinary calculus incidence. Nevertheless, they observed that the magnesium-calcium ratio of the tap water in different geological areas was negatively correlated with the incidence of calcium-containing urinary calculi.[21,22] Our study has shown a marginally significant inverse correlation between the magnesium level of the tap water and the urolithiasis rate of that city. Once considering settled or permanent residents in each city, the power of relation was decreased, and it may be due to the diminished number of people in each group. Despite the results of the Kohri and coworkers' study on the reverse correlation of magnesium-calcium ratio in the drinking water, we found only a marginal impact of the aforementioned ratio in our study. In contrast, a significant correlation was observed between incidence and SRI. This finding emphasizes the value of multivariable models that we suggest for further investigation in prospective research in the future.

The role of calcium amount of ingested fluid in urinary calculus risk has been the subject for some interesting studies. Caudarella and colleagues showed that drinking calcium-rich water increases urinary calcium level. It also causes concomitant hypooxaluria.[8] Nonetheless, Coen and coworkers showed that preventing from urinary calculus recurrences through increasing water intake between meals should preferably be achieved using a relatively low-calcium water, and calcium-rich waters should be avoided.[27] Furthermore, it is suggested that mineral waters containing bicarbonate would lessen the risk of calculus formation in urine.[27] Most of the mentioned studies investigated the correlation of fresh water composition with lithogenic risk factors and urinary average mineral content as a surrogate marker for calculus formation. Our study evaluated the incidence of urolithiasis as an end point in relation to the water composition, based on epidemiological evidence. We did not find any significant difference between the calcium contents of water resources in different provinces, and the relevant urolithiasis incidences. Given the concept that magnesium and bicarbonate intakes have inhibitory effects on urinary calculus formation, we suggested the SRI as a new index in evaluating the water in relation to urinary calculus formation. Since most calculus-forming factors are included in the SRI equation, it seems that its precision boosted. This study merely suggests a nonlinear correlation and a fit model, and further explanation could not be achieved by community studies. The SRI may be validated prospectively in the setting of a population-based individual study design. This index could be used in the evaluation of the mineral waters offered for metaphylaxis of urinary calculi.

CONCLUSIONS

Based on our study, there was no significant relationship between the incidence of urinary calculi and water minerals concentrations in different regions of Iran, which usually have hard or very hard water. Although magnesium content of water had a marginally inverse correlation with calculus incidence, the ratio of calcium to magnesium-bicarbonate product, the SRI, had a stronger positive correlation with calculus incidence. The potential therapeutic and preventive application of the SRI is yet to be confirmed by clinical trials.

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CONFLICT OF INTEREST

None declared.

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