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Original Article

Urine specific gravity and water hardness in relation to urolithiasis in persons with spinal cord injury

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Study design: A matched case-control study.
Objectives: To clarify the influence of urine specific gravity and drinking water quality on the formation of urinary stones in persons with spinal cord injury (SCI).
Setting: A rehabilitation center within a university hospital.
Methods: Between 1992 and 1998, 63 stone cases (31 kidney, 27 bladder, and five both) and 289 age-duration-matched controls were recruited from a cohort of SCI patients enrolled in an on-going longitudinal study. Data on urine specific gravity and other characteristics of study participants were retrieved from the database and medical charts. Community water supply information was provided by the Alabama Department of Environmental Management. Multivariable conditional logistic regression analysis was performed to evaluate the association with stone formation.
Results: SCI individuals who had urinary stones were more likely than control subjects to use indwelling catheters and have decreased renal function. The occurrence of stones was not significantly related to gender, race, severity of injury, urinary tract infection, nor urine pH. After controlling for the potential confounding from other factors, a continuously increasing stone occurrence with increasing specific gravity was observed ($P=0.05$); this association was stronger for kidney (odds Ratio [OR] = 1.8 per 0.010 g/cm^3) *versus* bladder stones (OR = 1.2) and for recurrent (OR = 2.0) *versus* first stones (OR = 1.5). Increased water hardness was not significantly associated with a decreased stone occurrence.
Conclusions: Study results suggest that maintaining urine specific gravity below a certain level might reduce the occurrence of urinary stones. This could be easily achieved by using a dipstick for self-feedback along with appropriate fluid intake. For persons with SCI who are at an increased risk of a devastating stone disease, this prophylactic approach could be very cost-effective; however, this requires further confirmation.
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Keywords: spinal cord injury; calculi; specific gravity; hardness

Introduction

Urinary stone disease is a frequent complication of spinal cord injury (SCI). It has been estimated that within 8 years after injury, approximately 7% of SCI patients would develop their first kidney stones,[1] whereas 36% would have bladder stones.[2] Urinary calculi can lead to obstruction, sepsis, deterioration of renal function, and even loss of the affected kidney.[3,4] An effective method to prevent stones is necessary to alleviate the threat, which they pose to the health and welfare of many SCI survivors.

The high stone incidence in the SCI population has been thought to be attributable to immobilization hypercalciuria and an increased susceptibility to urinary tract infection (UTI).[1] Most injury-related determinants of urinary stones, including years since injury, severity of injury, and methods of bladder management, may reflect one or both of these pathways. However, because UTI is much more common than urinary stones in persons with SCI, infection may be a necessary component, but not sufficient, to cause stone formation. Similarly, immobilization hypercalciuria is not a necessary or a sufficient factor. The return to normal urinary calcium after SCI patients become ambulatory is not accom-

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panied by cessation of stone occurrence and recurrence.

The majority of stones that afflict the SCI population are struvite stones (magnesium ammonium phosphate),[5] whereas calcium stones account for more than 70% of total stones in the general population.[6] It is unknown if the risk factors that have been identified in the general population are similar to those in the SCI population. Whether the prophylactic treatments recommended in the general population are appropriate to the SCI population remains speculative.

Increased fluid intake has been advocated as a dietary management for the prevention of any type of stones. The hydration status, nevertheless, could be monitored by urine specific gravity.[7] The use of urine specific gravity test strips as a self-feedback tool has been shown to be more successful in increasing fluid intake than a simple dietary instruction.[8] However, the influence of urine specific gravity on stone formation has never been examined.

Prior ecological investigations conducted in the general population have observed an increased incidence rate of kidney stones in areas containing soft water.[9] A similar geographic association was observed in a national cohort of SCI subjects.[10] However, the study of SCI individuals, rather than in an ecological unit, is absent regarding the impact of drinking water hardness and mineral content on stone occurrence.

The present study was, therefore, conducted to elucidate the roles of urine specific gravity and drinking water quality on the development or urinary stones among persons with SCI. We examined the distribution of urine specific gravity between SCI individuals with stones and without stones to determine whether increased specific gravity was associated with a greater frequency of stone presentation. We also assessed whether increasing hardness due to calcium carbonate in the community water supply was associated with a decreased occurrence of urinary stones. As part of this study, we collected data on other potential risk factors for stones both to control for possible confounding and to investigate the potential role of these factors in stone formation.

Methods

Identification of cases and controls

The SCI Urology Database, launched by the Spain Rehabilitation Center in the University of Alabama at Birmingham, was designed to provide an opportunity to understand the clinical course of urinary tract complications in persons with SCI. All SCI patients admitted to the Spain Rehabilitation Center within a year post injury, discharged alive, and with discernible neurologic deficits are eligible for the planned follow-up program. Since 1979 when the program began, data have been collected on sociodemographic variables, injury-related characteristics, urologic complications and management, and laboratory findings of all participants during initial hospital care and annually thereafter.

Stone cases consisted of all nondeceased participants enrolled in the SCI Urology Database who had a diagnosis of urinary calculi between 1992 and 1998 ($n=63$; 31 kidney, 27 bladder, and five both; 30 recurrent and 33 first onset). Stone cases were defined as those participants who had an abnormal concretion in the kidney, ureter, or bladder documented by X-ray, ultrasound, or cystoscopy performed during the annual surveillance. In very few occasions when there is no evidence regarding the origin of the stones based on history and laboratory tests, those spontaneously passed stones reported by participants were arbitrarily assigned as bladder stones in the data collection process, even though they might have been renal in origin. For each stone subject we randomly selected, at most, five participants from the database to serve as controls ($n=289$). They were currently alive, had never had stones since injury, and were matched on age (10-year strata) and years since injury (1, 2–3, 4–10, >10) with an index case.

Data collection

The laboratory examination of urine specific gravity has been routinely tested for all SCI patients enrolled in the database on a yearly basis by using a routine urine sample since 1988. An extensive medical chart review was conducted to obtain results of all urinalysis tests performed at any clinic visits prior to the reference date. For stone cases, the reference date was the date of diagnosis of calculi; for control subjects, it was the date that corresponded to the date of the diagnosis of the matched stone case. An average of the last three tests since entry to the study was computed to indicate the hydration status likely predisposing to stone occurrence. Data on urine pH were also obtained using the same procedure. The majority ($>70\%$) of these urinalysis tests obtained were done within 3 years prior to the reference date.

According to the participants' residency or water company during the year prior to the reference date, the information concerning hardness, alkalinity, calcium, and magnesium level of their water supplies was retrieved from the Alabama Department of Environment Management. The laboratory in the Alabama Department of Environment Management has monitored the mineral content of public water supplies periodically as part of its ongoing water quality program. To account for the potential variation with time, the last measurement of water quality before the reference date was used in this analysis.

Data on other potential risk factors for stones were retrieved from the SCI Urology Database, which included age, gender, race, level and completeness of injury, method of urinary drainage, UTI, and renal function. In this study, we classified neurologic level into three categories: normal or functional motor incomplete lesion (American Spinal Injury Association [ASIA] Impairment Scales D or E); paraplegics with complete, sensory incomplete, or non-functional motor incomplete lesion (ASIA A, B, or C); and tetraplegics with ASIA A, B or C. UTI was evaluated by self-reported symptoms (fever and chills) and urine cultures tested within 3 years before the reference date. Significant bacteriuria was defined as a bacterial count $\geqslant$100 000 colonies per ml for clean-catch urine and $\geqslant$1000 colonies for urine samples obtained by urethral catheterization. The measure of renal function was the total effective renal plasma flow (ERPF) as determined by renal scan, which has been performed annually during the first few years after injury and every other or third year for later years. Because of time-varying characteristics, the last measurements of renal function and bladder management prior to the reference date were used.

Statistical analysis

The descriptive statistics of study factors were compared between SCI individuals with stones and without stones by using a two-tailed Student's *t*-test and chi-square statistics, as appropriate. Conditional logistic regression analysis was conducted to evaluate the effects of specific gravity and water quality on stone formation while simultaneously adjusting for other potential risk factors. This statistical procedure was chosen because the present design involved individual matching and because unequal numbers of controls were assigned for each case. Also that subjects within the same matching set are dependent, violates the assumptions of the usual unconditional logistic regression analysis. The adjusted odds ratios (OR) are used to indicate the degree of association. An OR of 1.0 suggests there is no relation for the particular variable with stone occurrence. An OR$>$1.0 implies an increased risk, whereas an OR $<$1.0 implies a decreased risk. The 95% confidence intervals (CI) around an OR is used to measure the precision and statistical significance of the OR estimate. Separate analyses were also performed for kidney, bladder, first, and recurrent stones.

To account for potentially skewed non-normal distribution and to assess the dose-response relation, continuous variables of primary interest were further classified into three levels either using tertiles (alkalinity, calcium, magnesium, and magnesium-to-calcium ratio) or based on prior knowledge (specific gravity and hardness). According to a prior investigation, specific gravity at or less than 1.010 was estimated to be equivalent to a total daily urine output of two liters or more; specific gravity greater than 1.017 was estimated to be approximately equal to urine volume less than one liter per day.[8] We therefore classified specific gravity into these three levels.

Results

As presented in Table 1, the average age and years since injury were similar between 63 stone cases and 289 age- and duration-matched controls. Although SCI individuals who had urinary stones tended to have more severe neurologic deficits and were more likely to be women and Caucasians, the differences were not statistically significant ($P>0.10$). Neither the frequency of symptomatic UTI, significant bacteriuria, and urine pH differed significantly between the two groups.

A higher proportion of stone cases used indwelling or intermittent catheter, whereas more control subjects voided satisfactorily (Table 1; $P<0.0001$). Compared with users of indwelling catheterization, the odds of stone formation was lower for persons who were catheter-free (OR = 0.1, 95% CI: 0.03–0.4) or on condom catheterization (OR = 0.3, 95% CI: 0.1–0.5). A nonsignificant difference was observed for those with intermittent catheterization (OR = 0.5, 95% CI: 0.2–1.2).

The renal function assessed at a median of 1 year before the reference date was significantly higher in controls than cases (Table 1; $P=0.0008$). With an increase of 100 ml/min total ERPF, the odds of stone formation decreased 30% (OR = 0.7, 95% CI: 0.6–0.9); this association remained relatively consistent for kidney (OR = 0.7, 95% CI: 0.5–0.9), bladder (OR = 0.8, 95% CI: 0.6–1.1), first (OR = 0.8, 95% CI: 0.6–1.1), and recurrent stones (OR = 0.6, 95% CI: 0.5–0.9).

The urine specific gravity was greater for cases than for controls (Table 2; $P=0.02$). Given the comparability of age, years since injury, gender, race, neurologic level, bladder management, significant bacteriuria, urine pH, and renal function, we noted a continuously increasing trend in stone occurrence with an increasing level of specific gravity (Table 3; $P=0.05$). Although this study size was not sufficient to examine the effect of urine specific gravity on the different types of stones, interestingly, this positive relation seemed to be stronger for recurrent (OR = 2.0) than for first stones (OR = 1.5) and stronger for kidney (OR = 1.8) than for bladder stones (OR = 1.2; Table 4).

The overall quality of community water supply did not differ significantly between SCI individuals with stones and without stones (Table 2; $P>0.25$). In the multivariable analysis, we categorized the level of water quality for assessing the potential dose-response relation. As summarized in Table 3, a decreasing stone occurrence with increasing water hardness was observed, but not statistically significantly ($P=0.48$).

Discussion

Increased fluid intake has been considered a standard prophylactic strategy for stone occurrence and recurrence. The effect of total fluid intake against stone formation has been supported by some studies,[11,12] but not others.[13–15] This inconsistent evidence suggests

Table 1 Selected characteristics of study subjects

	Cases (n=*63*)		*Controls* (n=*289*)		
Characteristics	*Mean*±*SD*	n (%)	*Mean*±*SD*	n (%)	P[a]
Current age (year)	39±13		38±12		0.41
Years since injury	9±6		9±5		0.68
Gender: men		48 (76)		244 (84)	0.12
Race: Caucasian		44 (70)		171 (59)	0.12
Neurologic level					
ASIA D, E		7 (11)		51 (18)	0.21
Paraplegia ASIA A, B, C		29 (46)		144 (50)	
Tetraplegia, ASIA A, B, C		27 (43)		94 (32)	
Bladder management					
Catheter-free		3 (5)		50 (17)	<0.0001
Condom catheter		17 (27)		132 (46)	
Intermittent catheter		15 (24)		49 (17)	
Indwelling catheter		26 (41)		52 (18)	
Other		2 (3)		6 (2)	
Symptomatic UTI		9 (17)		47 (18)	0.89
Significant bacteriuria		50 (79)		217 (75)	0.41
Urine pH	6.5±0.8		6.4±0.7		0.30
Total ERPF (ml/min)	569±142		624±146		0.0008

Data expressed as mean±standard deviation and number (percentage). ASIA, American Spinal Injury Association Impairment Scale; UTI, urinary tract infection; ERPF, effective renal plasma flow. Number of cases and controls for each analysis slightly varied because of incomplete data. [a]Obtained from a two-tailed Student's *t*-test (continuous variables) or chi-square test (categorical variables)

Table 2 Urine specific gravity and drinking water quality between cases and controls

Characteristics	*Cases* (n=*63*)	*Controls* (n=*289*)	P*
Specific gravity (g/cm^3)	1.015±0.006	1.013±0.006	0.02
Hardness as $CaCO_3$ (mg/l)	62.1±38.4	65.9±37.9	0.48
Alkalinity (mg/l)	55.0±61.6	63.4±60.8	0.33
Calcium (mg/l)	18.8±14.7	19.3±12.7	0.76
Magnesium (mg/l)	3.3±2.9	3.8±3.2	0.27
Magnesium-to-calcium ratio	0.24±0.16	0.22±0.14	0.52

Data expressed as mean±standard deviation. Number of cases and controls for each analysis slightly varied because of incomplete data. [a]Obtained from a two-tailed Student's *t*-test

that total fluid intake might not be a sole determinant of stone occurrence. Urine specific gravity, which measures urine density function, may be a better indicator of urinary dilution and a stronger predictor of stone formation.

The present study is the first study that investigates the influence of urine specific gravity on the formation of urinary stones. It provides scientific evidence that increased urine specific gravity is associated with a greater frequency of stone occurrence in persons with SCI regardless of the level of injury and methods of bladder management. This finding is biologically plausible because in addition to lowering the concentration of stone constituent in urine, urinary dilution has the potential to reduce bacterial nutrients, decrease the risk of UTI, and, consequently, lower the likelihood of stone formation.

In the present analysis, urinary dilution seems particularly important for kidney stones and recurrent stones, which are known to be clinically more devastating. The use of urine specific gravity to monitor hydration status and to adjust fluid intake may be of immense benefit for the prevention of stone occurrence or recurrence in persons with SCI. This self-feedback method seems feasible because it is simple, quick, inexpensive, and valid with a high correlation with urine osmolality ($r>0.9$)[16] and total 24-h urine volume ($r=-0.5$).[8]

Hardness is caused primarily by compounds of calcium and magnesium and by a variety of other metals. Increased dietary calcium intake has been reported to decrease stone incidence in the general population.[11] It has been hypothesized that calcium binds with oxalate and interferes with the absorption of oxalate in the gastrointestinal tract, leading to lower concentrations of oxalate in urine and, consequently, a decreased risk of stone formation.[17] Similarly to a study of non-SCI individuals,[18] the present study is unable to provide statistical significance to support findings from ecological studies that persons living in

Table 3 Odds ratios (OR) and 95% confidence intervals (CI) for urinary stones associated with urine specific gravity (USG) and drinking water quality

Factor	*OR*	*Adjusted*[a] *OR*	*95% CI*
USG (g/cm^3)			
$\leqslant$1.010	1.0	1.0	
1.011–1.017	1.5	1.4	0.6–3.4
>1.017	2.0	2.1	0.8–5.6
P^b	0.03	0.05	
Hardness (mg/l)			
Soft ($\leqslant$60)	1.0	1.0	
Moderately hard (61–120)	0.8	0.9	0.4–1.9
Hard and very hard (>120)	0.6	0.6	0.2–1.9
P^b	0.45	0.48	
Alkalinity (mg/l)			
$\leqslant$25.6	1.0	1.0	
25.7–60.3	0.6	0.6	0.3–1.3
>60.3	0.6	0.7	0.3–1.5
P^b	0.34	0.21	
Calcium (mg/l)			
$\leqslant$12.4	1.0	1.0	
12.5–20.8	1.0	1.0	0.4–2.3
>20.8	0.8	0.9	0.4–2.2
P^b	0.72	0.83	
Magnesium (mg/l)			
$\leqslant$1.94	1.0	1.0	
1.95–3.90	0.5	0.5	0.2–1.1
>3.90	0.8	0.9	0.4–1.9
P^b	0.27	0.38	
Magnesium-to-calcium ratio			
$\leqslant$0.14	1.0	1.0	
0.15–0.26	0.7	0.6	0.3–1.4
>0.26	1.0	1.1	0.6–2.4
P^b	0.51	0.39	

Number of cases and controls for each analysis slightly varied because of incomplete data. [a]Adjusted for gender, race neurologic level, bladder management, significant bacteriuria, urine pH and renal function. [b]Significance level for a potential linear relation (continuous variable)

Table 4 Number of stone cases (n), adjusted[a] odds ratios, and 95% confidence intervals for urinary stones associated with urine specific gravity (per 0.010 g/cm^3), stratified by stone type

Stone type	*Kidney*	*Bladder*	*Total*
First	$n=17$	$n=13$	$n=33$
	2.1 (0.5–9.2)	1.1 (0.2–5.0)	1.5 (0.6–3.7)
Recurrent	$n=14$	$n=13$	$n=29$
	1.8 (0.6–5.0)	1.6 (0.3–7.7)	2.0 (0.9–4.4)
Total	$n=31$	$n=26$	$n=62$
	1.8 (0.8–4.1)	1.2 (0.4–3.2)	1.7 (1.0–3.1)

[a]Adjusted for race, neurologic level (American Spinal Injury Association [ASIA] D and E *vs* A, B and C), bladder management (with or without catheter), and renal function

areas with hard and very hard water had a lower stone incidence than those having soft water,[9,10] although the trend we noted is consistent with these investigations. This nonsignificance, nevertheless, might be partly explained by the relatively homogenous distribution in water hardness and mineral content within the same state (more than 50% of study participants used soft water). This range of difference in water quality might not be sufficient to significantly affect stone occurrence. This study did not support the literature of an inverse relation between the magnesium-to-calcium ratio and struvite stones.[19]

Several limitations, however, need to be considered while interpreting the study results. The specific gravity was obtained at three or fewer occasions using a routine urine sample, which might not reflect the hydration status at every time point of a day. Nevertheless, this error, if it exists, is likely to be nondifferential between cases and controls because they were measured under a comparable situation before stone diagnosis. Because of the retrospective nature of this study, we were unable to account for the actual intake of tap water while estimating the impact of hardness and mineral content on stone occurrence. Likewise, this misclassification is likely to be nondifferential, because we have no reason to suspect that cases would have avoided tap water any differently before stone diagnosis.

Another limitation is that the biochemical composition of these 63 stones was not available in the database or medical charts, and the identified factors might not be specific for struvite stones. Nevertheless, the observed association between stone formation and bladder management suggests that the majority of stones we studied were struvite, perhaps mixed with various amounts of calcium components, and were SCI-related. Lastly, this limited study size is unable to provide a sufficient power for studying the risk factors for different types of stones (kidney, bladder, first, and recurrent). This lack of stratification might have attenuated the observed relations if the association varies by stone types.

Conclusion

The present study demonstrates that independent of other factors, the risk of stone formation in persons with SCI is positively associated with urine specific gravity, a measure of an endpoint of fluid intake, water loss, and renal function. As advocated in the general population,[8] using the test dispstick to monitor specific gravity as a self-feedback tool for modifying fluid intake and improving hydration status would be a simple, inexpensive, and risk-free strategy for the prevention of stone occurrence and recurrence. The efficacy of this intervention on stone prophylaxis merits further trials.

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