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Comparison of Hispanics to Caucasians in Metabolic Evaluation of Nephrolithiasis

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ABSTRACT

Introduction

It is well-known that nephrolithiasis is related to urinary metabolic abnormalities. However, it is not known what, if any, difference exists between Caucasians and Hispanics in regards to metabolic stone disease. The Southwest United States offers a unique patient population to compare these two groups.

Materials and Methods

A retrospective study was performed at a single institution of all patients that underwent 24 hour urine stone risk studies over a 5-year period. All urine studies were performed by Litholink. Age, ethnicity, BMI, 24 hour urine parameters, serum electrolytes, Parathyroid hormone (PTH) level and stone composition were evaluated. Ethnicity was determined by patient self-selection. Patients that did not select Hispanic or Caucasian were excluded. Differences in the metabolic evaluation of these patients in regards to the risk of nephrolithiasis were analyzed.

Results

A total of 208 patients with 349 urine studies were included in the study. There were 122 Caucasians (Group A) and 87 Hispanics (Group B) with 206 and 143 urine studies respectively. BMI was not statistically different between Group A (28.3) and Groups B (29.1), p=0.4. However, there were more women in Group B (64.4%) than Group A (50%). Group A had significantly higher urinary volume, oxalate, potassium, phosphorus, sulfate, urine urea nitrogen and 24 hour creatinine compared to Group B but lower urinary citrate, supersaturation of calcium phosphate and magnesium levels. Group B had higher PTH compared to Group A (69.7 *vs.* 42.6, respectively, p=0.048). Group B also had a higher percentage of Calcium phosphate stones.

Conclusion

Our results suggest that there is a difference in metabolic evaluation between Caucasians and Hispanics. Caucasians have an increased risk of stone formation due to increased oxalate excretion while Hispanics demonstrate increased risk due to lower urinary volumes and elevated supersaturation of calcium phosphate.

Keywords
Nephrolithiasis; Metabolic evaluation.

INTRODUCTION

The Hispanic population is the largest minority group in the United States and constitutes 17% of the population.[1] Projections show that by 2060, Hispanics will make up 31% of the US population.[1] Little is known regarding Hispanic-Americans in regards to the metabolic risk of stones and how this compares to the Caucasian-American population, which is traditionally the largest group of stone formers. [2,3,4]

Our Institution is located within a state where Hispanics are the majority and that has the highest percentage of Hispanics

in the country at 47.3%.1This allows for a unique comparison of Hispanics to Caucasians within one geographic region.

MATERIALS AND METHODS

After institutional IRB approval, a retrospective review was performed at our single tertiary care center. All patients diagnosed with kidney stones who underwent a 24 hour urine stone risk analysis at our institution from 2008-2013 were evaluated. All 24 hour stone risk urine tests were performed by Litholink. Pediatric patients (age <18-years-old) were excluded from analysis as this population has a greater risk of underlying metabolic disease.

Patients were divided into 2 groups based on self-reported ethnicity. Group A included Caucasian patients and group B included Hispanic patients. Other racial/ethnic groups and those who did not designate were excluded. In addition to the urinary stone risk evaluation, stone composition, serum metabolic evaluations, past medical history, patient demographics and body mass index (BMI) were evaluated. The two groups were compared with each other to determine any differences between ethnicities.

RESULTS

A total of 224 patients with 370 urine studies were identified. Fifteen patients with 21 urine studies were excluded because their race/ethnicity was not Caucasian or Hispanic or they did not self-identify a race/ethnic group. This left 208 patients with 349 urine studies including 122 Caucasians (Group A) and 87 Hispanics (Group B) with 206 and 143 urine studies, respectively.

Group B was significantly younger with an average age of 45.6 (18-78) compared to 50.3 (19-74) in Group A (p=0.02). BMI was not statistically different (p=0.4) between the Group A and Group B (28.3 *vs.* 29.1, respectively). There were equal numbers of men and women in Group A, yet proportionately more women in Group B (64.4%). Equal percentage of patients within each group had family history (defined as 1st or 2nd degree relatives) of stones (42.6% in Group A and 41.4% in Group B). There were slightly more patients with hypertension in Group A at 31.1% compared to 26.4% in Group B but equal number of diabetics (21.3% for Group A *vs.* 23.0% in Group B). Table 1 demonstrates the patient demographics of each group.

When comparing the two groups for all tests completed, several 24 hour urine parameters were significantly different. Table 2 shows the urinary parameter measurements for each group. Group A had a higher mean urine volume of 2.24 liters compared to 2.21 liters in Group B (p=0.006). Group A had significantly higher urinary oxalate, potassium, phosphorus, sulfate, urine urea nitrogen and 24 hour creatinine compared to Group B. Group A had lower urinary citrate, supersaturation of calcium phosphate and magnesium levels. Remaining urinary parameters were not significantly different.

Table 1. *Patient Demographics*

	Group A (Caucasians)	Group B (Hispanics)	*p* value
Number	122	87	
Number of 24 hour collections	206	143	
Age (range)	50.3±14.06 (19-74)	45.6±15.12 (18-78)	0.022
Gender (M:F)	61:61	31:56	
BMI	28.34±6.869	29.13±6.584	0.412
Positive Family history	52 (42.6%)	36 (41.4%)	
Presence of hypertension	38 (31.1%)	23 (26.4%)	
Presence of diabetes mellitus	26 (21.3%)	20 (23.0%)	

Table 2. *Comparison of all 24 hour Urine Parameters*

	Group A	Group B	*p* value (*=significance)
Volume (Liters)	2.24±1.065	1.95±0.886	0.0062*
SS CaOx	6.48±3.254	6.78±3.920	0.456
Calcium (mg/day)	219.84±120.653	217.93±120.409	0.884
Oxalate (mg/day)	39.69±16.590	34.14±13.789	0.0008*
Citrate (mg/day)	586.58±386.808	512.75±307.483	0.0485*
SS CaP	1.15±0.896	1.46±1.210	0.0091*
pH	6.20±0.666	6.27±0.534	0.299
SS UA	0.78±0.837	0.68±0.798	0.267
Uric acid (g/day)	0.61±0.195	0.61±0.219	0.909
Sodium (mmol/day)	172.30±72.313	182.22±82.307	0.246
Potassium (mmol/day)	65.63±32.537	53.77±23.076	0.0001*
Magnesium (mg/day)	101.74±48.342	90.61±40.936	0.0220*
Phosphorus (g/day)	0.92±0.337	0.79±0.343	0.0004*
Ammonium (mmol/day)	31.62±19.051	29.06±12.424	0.134
Chloride (mmol/day)	164.44±68.205	168.04±73.774	0.647
Sulfate (mEq/day)	38.82±15.179	34.98±14.576	0.0185*
Urea Nitrogen (g/day)	10.73±3.645	9.55±3.566	0.0029*

SS CaOx=supersaturation of calcium oxalate, SS CaP–supersaturation of calcium phosphate, SS UA=supersaturation of uric acid

Further analysis was done to evaluate only the first collection, taken prior to any dietary or medical therapy was commenced. Group A remained significantly higher in urinary oxalate, potassium, magnesium, phosphorus, ammonium and 24 hour creatinine when compared to Group B. Group B continued to have significantly higher supersaturation of calcium phosphate.

The urine volume was not significantly different between the two groups. Table 3 lists the urinary parameters of the first urine collection.

Table 3. *Comparison of First Urinary Collection*

	Group A	Group B	*p* value (* = significance)
Volume (Liters)	2.08±1.061	1.87±0.889	0.107
SS CaOx	6.82±3.470	6.71±3.608	0.818
Calcium (mg/day)	217.45±135.288	202.75±109.187	0.387
Oxalate (mg/day)	39.08±16.917	32.17±14.061	0.0035*
Citrate (mg/day)	559.66±334.364	501.45±303.009	0.191
SS CaP	1.11±0.937	1.46±1.278	0.034*
pH	6.10±0.647	6.20±0.510	0.219
SS UA	0.94±0.925	0.76±0.876	0.149
Uric acid (g/day)	0.60±0.181	0.60±0.223	0.868
Sodium (mmol/day)	169.92±76.040	178.28±83.894	0.462
Potassium (mmol/day)	60.19±28.718	50.21±22.011	0.0051*
Magnesium (mg/day)	100.16±51.188	83.30±34.143	0.0050*
Phosphorus (g/day)	0.92±0.337	0.79±0.331	0.0045*
Ammonium (mmol/day)	33.01±20.325	28.05±12.405	0.031*
Chloride (mmol/day)	162.09±70.827	163.20±75.774	0.915
Sulfate (mEq/day)	36.69±14.483	34.01±15.029	0.202
Urea Nitrogen (g/day)	10.45±3.677	9.15±3.586	0.011*

SS CaOx=supersaturation of calcium oxalate, SS CaP–supersaturation of calcium phosphate, SS UA=supersaturation of uric acid

Of the 208 patients, 195 (93.7%) had a basic metabolic panel (BMP). There were 111 (90.1%) patients in Group A and 84 (96.6%) patients in Group B who completed a BMP. Serum potassium was higher in Group A (4.15) compared to Group B (4.02). Twenty-eight patients in Group B (32%) had a PTH level and on average the level was higher compared to the 32 patients (26%) in Group A (69.7 *vs.* 42.6, respectively, p=0.048). Table 4 shows the serum results for the two groups. The remaining serum levels were not significantly different between the two groups.

Stone analysis was collected on 117 patients overall. A stone was classified as the predominant stone type if there was more than 80% of that compound present. It was classified as mixed composition if there was less than 80% predominant compound. Stone analysis was performed in 71 (58.2%) of the patients in Group A. Of these 71 patients, 41 (57.7%) had calcium oxalate, 4 (5.6%) had calcium phosphate, 4 (5.6%) had uric acid, 3 (4.2%) had cysteine, 17 (23.9%) had mixed stones. There were no struvite stones present. Stone analysis was performed in 46 (52.3%) of the patients in Group B. Of these 46 patients, 18 (39.1%) had calcium oxalate, 12 (26.1%) had calcium phosphate, 3 (6.5%) had uric acid and 12 (26.1%) had mixed stones. There were no struvite or cysteine stones present. Table 5 shows the stone analysis data.

Table 4. *Comparison of Serum Results*

	Group A	Group B	*p* value
Sodium	139.51±2.586	139.63±2.610	0.775
Potassium	4.15±0.392	4.02±0.394	0.022*
Chloride	105.23±3.246	105.76±3.535	0.279
Bicarbonate	24.68±2.848	24.02±3.065	0.126
Blood urea Nitrogen	15.84±5.800	14.83±6.201	0.253
Creatinine	1.01±0.425	1.81±8.027	0.367
Calcium	9.24±1.038	9.26±0.631	0.855
Magnesium	2.00±0.349	1.91±0.232	0.067
Parathyroid hormone	42.63±28.625	69.74±63.400	0.0486*
Uric acid	5.81±2.209	5.09±1.388	0.202
Vitamin D 25(OH)	29.39±14.411	25.27±14.758	0.286

Table 5. *Stone Analysis by Group*

	Group A (71 patients)	Group B (46 patients)
Calcium Oxalate	41 (57.7%)	18 (39.1%)
Calcium Phosphate	4 (5.6%)	12 (26.1%)
Uric Acid	4 (5.6%)	3 (6.5%)
Cysteine	3 (4.2%)	0
Struvite	0	0
Mixed	17 (23.9%)	12 (26.1%)

DISCUSSION

To the best of our knowledge, we report the first direct comparison in the literature of metabolic evaluation for urolithiasis between Hispanic and Caucasian populations. Our institution is located within a state with nearly equal Hispanic and Caucasian populations. Our unique demographic allowed us to evaluate differences between these two groups who are exposed to the same environment and relatively similar diets.

The analysis showed that Caucasians are more likely to have higher oxalate levels than Hispanics. However, neither group demonstrated overall hyperoxaluria (>40 mg/day) on average. Yet certainly it is known that higher urinary oxalate is associated with increased stone formation.[5] Higher oxalate levels may be a more significant cause of stone formation in Caucasians and therefore should be a focus point when counseling and evaluating these patients.

In the Hispanic population, there is a significantly higher

urinary supersaturation of calcium phosphate compared to the Caucasian population. The pH was not significantly higher and there does not appear to be an increased risk of renal tubular acidosis. Interestingly, Hispanics did have a higher PTH level than Caucasians. Other studies have also reported this finding, however, its association with risk for stone disease is unclear.[6,7] There was certainly a higher proportion of female Hispanic patients which may also explain the increased urinary supersaturation of calcium phosphate. It remains unclear at this time how this affects the overall metabolic evaluation in the Hispanic population but we feel this certainly warrants further study and evaluation.

The observed urinary parameter differences seem to correlate with stone type. The higher rate of calcium oxalate stone formation in Group A may be related to the increased urinary oxalate secretion in this group. In addition, Group B did have a higher rate of calcium phosphate stones with the corresponding increased supersaturation of calcium phosphate in the urine. Certainly this study is not designed to evaluate the cause of stone type among these two groups. Yet-further studies are warranted to determine if there is any relationship between the metabolic parameters and stone type, as well as differences in the causes of stone formation between groups.

While we have shown several differences between our two groups, several limitations exist. This is a retrospective review of data which certainly allows for bias to exist. We compared only those patients that actually completed a metabolic evaluation at our institution. There were many patients with stone disease that were seen and treated for urolithiasis but simply did not complete the workup or for whom work up was not recommended. This may explain why we have an overrepresentation of females in our groups when considering urolithiasis is a male dominated disease historically.[3] Because the study was retrospective in nature and took all patients that completed a 24 hour urine study, unfortunately a gender discrepancy was introduced. Interestingly, however, Dell'era et al. reported in a single institution study, a 1:1 ratio male to female presentation of symptomatic upper tract stones in a Hispanic population.[8] It is unclear if there is truly a gender disparity in stone disease within the Hispanic population in our state, or if the observed male to female ratio simply represents a bias error.

Mente et al performed an analysis of multi-ethnic calcium nephrolithiasis formers compared to Caucasians.[9] This study included a very small number of patients from Latin America (34, 3% of the study) which were compared to a European control group. The findings demonstrated an increased risk of calcium stones among those from Latin America but there was little ability to interpret underlying causes for this difference. Our study is not designed to determine if the Hispanic population has an increased overall risk of kidney stones, and certainly further population based studies are warranted.

All of our patients completed at least one 24 hour urine test. While some literature supports two 24 hour urine testing initially, other significant data suggests that one is sufficient.[10,11] Our patients had poor compliance overall with follow up metabolic testing. Only 37.9% (45) of the patients in Group A completed subsequent 24 hour urine tests. Of the patients in Group B, 40.2% (35) completed repeat 24 hour urine testing. Given the small follow-up numbers, we determined that further analysis of a difference in repeat testing may not be valid. In the future however, with the addition of more patients this may be something to investigate.

While we have shown that there are differences in urinary parameters between the two groups, we do not know how this effects overall stone formation. Given the very poor compliance of our patient population it was not possible to evaluate for subsequent stone formation within the study time frame.

LIMITATIONS

This is a retrospective review of all patients completing a 24 hour urine study and this certainly introduces selection bias. We do not know how many patients did not complete the metabolic evaluation and therefore this could change the overall results. The groups are not matched and there is a significantly higher amount of women in the Hispanic group. This may explain the differences in the urinary parameters. However, this may also be a difference between the ethnic groups. Dall'era et al demonstrated that there was a 1:1 presentation of male to female stone patients in the Hispanic population in contrast to 2.5:1 male:female ratio in Caucasians.[8] Further studies are needed to determine if there is a difference in gender ratio in stone disease in the Hispanic population. In addition, a case matches study may be useful to understand any difference between Caucasians and Hispanics in regards to urinary parameters. Our study, simply highlights that there appears to be a difference in the two groups and additional studies are warranted.

CONCLUSION

Our study suggests that there is a metabolic difference between Caucasian and Hispanic populations. Caucasians show an increased risk of stone formation due to increased oxalate excretion with subsequent higher rates of calcium oxalate stone formation. Hispanics show an increased risk of stone formation due to decreased urinary volume as well as increased supersaturation of calcium phosphate with associated higher rates of calcium phosphate stone formation. Further studies are needed to determine if this is applicable to a wider geographic region, and if this is applicable to all stone formers. This information may be useful for more generalized dietary recommendations pertinent to these two population groups.

CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

DISCLOSURE

No competing financial interests exist.

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