

Dietary Sodium and Kidney Stones: Literature Research on PubMed

Calcium urolithiasis, blood pressure and salt intake	1
Changes in urinary stone risk factors in hypocitraturic calcium oxalate stone formers treated with dietary sodium supplementation.	2
Effect of renin-angiotensin-aldosterone system inhibition, dietary sodium restriction, and/or diuretics on urinary kidney injury molecule 1 excretion in nondiabetic proteinuric kidney disease: a post hoc analysis of a randomized controlled trial.	3
Sodium-sensitive variability of the antiproteinuric efficacy of RAS inhibitors in outpatients with IgA nephropathy	3
Impact of urine sodium on urine risk factors for calcium oxalate nephrolithiasis	4
Benefits of dietary sodium restriction in the management of chronic kidney disease	5
DASH-style diet associates with reduced risk for kidney stones	5
Role of postnatal dietary sodium in prenatally programmed hypertension	6
Salt-resistant blood pressure and salt-sensitive renal autoregulation in chronic streptozotocin diabetes	6

Calcium urolithiasis, blood pressure and salt intake

Blood Press. 2003;12(2):122-7. Timio F, Kerry SM, Anson KM, Eastwood JB, Cappuccio FP. Department of Community Health Sciences, St George's Hospital Medical School, London, UK.

Objectives: To determine whether stone-formers have higher BP than controls drawn from the general population and matched for age, sex and ethnic origin and to compare the relationship between sodium and calcium excretion in the two groups.

Patients and Methods: Thirty-six patients [mean (+/-standard deviation, SD) = 49.0 +/- 11.7 years; range 27-70 years] with kidney or ureteric stones and 108 controls (mean age of 49.6 +/- 6.8 years; range 39-61 years), matched for gender, ethnic origin and age group were studied. Patients and controls underwent physical measurements, a venous blood sample and they were asked to collect a 24-h urine sample for sodium, potassium, calcium and creatinine.

Results: Stone-formers were significantly heavier and had higher BP than age-, sex- and ethnic-matched population controls. Whilst the difference in systolic BP was independent of the difference in body mass index [16.8 mmHg (7.2-26.4 mmHg), p = 0.001], the difference in diastolic BP was attenuated after adjustment for body mass [1.8 (-3.4 to 7.1), p = 0.49]. Stone-formers passed less urine than controls [-438

ml/day (95% CI -852 to -25), $p = 0.038$]. They had higher urinary calcium than controls [$+3.7$ mmol/day (2.8-4.6 mmol/day), $p < 0.001$], even when expressed as ratio to creatinine [$+0.20$ (0.11-0.29), $p < 0.001$]. Sodium excretion was positively associated with urinary calcium in both stone-formers and in controls. The slopes were comparable (0.92 vs 0.98 mmol Ca/100 mmol Na) so that for any level of sodium excretion (or salt intake), stone-formers had a higher calcium excretion than controls.

Conclusions: In stone-formers, the BP is higher than in controls. Stone-formers excrete more calcium than controls do. In stone-formers and controls, the relationship between urinary sodium and calcium is similar. Since this relationship results from an effect of sodium on calcium, a reduction in salt intake may be a useful method of reducing urinary calcium excretion in stone-formers. However, the "relative" hypercalciuria seen in stone-formers is independent of salt intake and may well reflect an underlying genetic predisposition.

Changes in urinary stone risk factors in hypocitraturic calcium oxalate stone formers treated with dietary sodium supplementation.

J Urol. 2009 Mar;181(3):1140-4. Epub 2009 Jan 18. Stoller ML, Chi T, Eisner BH, Shami G, Gentle DL. Department of Urology, School of Medicine, University of California-San Francisco, San Francisco, California, USA.

Purpose: We investigated the effects of supplemental dietary sodium on risk factors for urinary stone disease in stone forming patients with hypocitraturia.

Materials and Methods: Ten patients diagnosed with recurrent isolated hypocitraturic calcium urolithiasis were identified. Baseline 24-hour urinalysis was performed with patients on their regular diet, including citrate replacement with 20 mEq potassium citrate 3 times per day. Strict daily dietary logs were kept for a 7-day period, during which patients had normal oral intake and potassium citrate replacement. Patients then received supplemental sodium chloride for 1 week (1 gm orally 3 times per day), in addition to their regular diets and potassium citrate supplementation. Dietary logs were continued and 24-hour urinalysis was performed at the end of 1 week of supplemental sodium. Risk factors for urinary stone disease were compared using the Student t test and ANOVA.

Results: Two patients were unable to comply with sodium supplementation based on 24-hour urinalysis and, therefore, they were excluded from study. The remaining 8 patients were analyzed. Patients on supplemental dietary sodium demonstrated significantly increased mean urinary voided volume (933 ml per day above baseline, $p < 0.05$) and mean urinary sodium excretion (66 mEq per day above baseline, $p < 0.05$). There was no statistically significant change in urinary calcium, oxalate or uric acid. The urinary supersaturation relative risk ratio decreased for calcium oxalate stones (0.93 vs 0.63, $p < 0.05$), while those of brushite, struvite and uric acid were not different before vs after supplemental sodium.

Conclusions: Dietary sodium supplementation resulted in an increased voided urine volume and decreased the relative risk supersaturation ratio for calcium oxalate stones in patients with a history of hypocitraturic calcium oxalate nephrolithiasis. Urinary calcium excretion as well as other urine parameters that are risk factors for nephrolithiasis was not changed. Sodium restriction may be inappropriate in patients with hypocitraturia and recurrent urinary stones. Sodium supplementation may be beneficial in these patients because it results in voluntary increased fluid intake

Effect of renin-angiotensin-aldosterone system inhibition, dietary sodium restriction, and/or diuretics on urinary kidney injury molecule 1 excretion in nondiabetic proteinuric kidney disease: a post hoc analysis of a randomized controlled trial.

[Am J Kidney Dis. 2009 Jan;53\(1\):16-25](#). Epub 2008 Sep 27. Waanders F, Vaidya VS, van Goor H, Leuvenink H, Damman K, Hamming I, Bonventre JV, Vogt L, Navis G. Department of Nephrology, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

Background: Tubulointerstitial damage plays an important role in chronic kidney disease (CKD) with proteinuria. Urinary kidney injury molecule 1 (KIM-1) reflects tubular KIM-1 and is considered a sensitive biomarker for early tubular damage. We hypothesized that a decrease in proteinuria by using therapeutic interventions is associated with decreased urinary KIM-1 levels.

Study Design: Post hoc analysis of a randomized, double-blind, placebo-controlled, crossover trial.

Setting & Participants: 34 proteinuric patients without diabetes from our outpatient renal clinic.

Intervention: Stepwise 6-week interventions of losartan, sodium restriction (low-sodium [LS] diet), their combination, losartan plus hydrochlorothiazide (HCT), and the latter plus an LS diet.

Outcomes & Measurements: Urinary excretion of KIM-1, total protein, and N-acetyl-beta-d-glucosaminidase (NAG) as a positive control for tubular injury. **RESULTS:** Mean baseline urine protein level was 3.8 +/- 0.4 (SE) g/d, and KIM-1 level was 1,706 +/- 498 ng/d (increased compared with healthy controls; 74 ng/d). KIM-1 level was decreased by using placebo/LS (1,201 +/- 388 ng/d; P = 0.04), losartan/high sodium (1,184 +/- 296 ng/d; P = 0.09), losartan/LS (921 +/- 176 ng/d; P = 0.008), losartan/high sodium plus HCT (862 +/- 151 ng/d; P = 0.008) and losartan/LS plus HCT (743 +/- 170 ng/d; P = 0.001). The decrease in urinary KIM-1 levels paralleled the decrease in proteinuria (R = 0.523; P < 0.001), but not blood pressure or creatinine clearance. 16 patients reached target proteinuria with protein less than 1 g/d, whereas KIM-1 levels normalized in only 2 patients. Urinary NAG level was increased at baseline and significantly decreased during the treatment periods of combined losartan plus HCT only. The decrease in urinary NAG levels was not closely related to proteinuria.

Limitations: Post hoc analysis.

Conclusions: Urinary KIM-1 level was increased in patients with nondiabetic CKD with proteinuria and decreased in parallel with proteinuria by using losartan, sodium restriction, their combination, losartan plus HCT, and the latter plus sodium restriction. These results are consistent with the hypothesis of amelioration of proteinuria-induced tubular damage. Long-term studies are warranted to evaluate whether targeting treatment on KIM-1 can improve outcomes in patients with CKD with proteinuria

Sodium-sensitive variability of the antiproteinuric efficacy of RAS inhibitors in outpatients with IgA nephropathy

Clin Nephrol. 2009 Oct;72(4):274-85. Suzuki T, Miyazaki Y, Shimizu A, Ito Y, Okonogi H, Ogura M, Utsunomiya Y, Kawamura T, Hosoya T. Division of Kidney and Hypertension, Department of Internal Medicine, Jikei University School of Medicine, Nishishinbashi, Minato-ku, Tokyo, Japan.

Aims: Inhibition of the renin-angiotensin system (RAS) decreases proteinuria in IgA nephropathy and often retards disease progression. However, its antiproteinuric efficacy varies considerably among patients or

different stages in a single patient. We sought for the factor(s) underlying the variation in urinary protein excretion in RAS inhibitor-treated outpatients with IgA nephropathy.

Patients: 43 patients with biopsy-proven IgA nephropathy, moderate proteinuria (0.5 - 3.5 g/day), normal to moderately-low estimated GFR (eGFR) (28.6 - 114.2 ml/min/1.73 m²) and normal blood pressure, prehypertension or mild hypertension (systolic/diastolic blood pressures < 160/100 mmHg) were placed on RAS inhibitors following diagnosis.

Method: Excretion of urinary protein (UprV) and sodium (UNaV), estimated protein intake (EPI) and the mean blood pressure (MBP) were determined on 12 consecutive visits for an average duration of 17.6 months. Analyses were performed to determine which factor(s) influenced the variation in UprV.

Results: 14 patients (32.6%) showed a significant correlation between UprV and UNaV, whereas UprV correlated significantly with EPI or MBP in 7 (16.3%) and 3 patients (7.0%), respectively. The 14 patients were characterized by lower eGFR and more extensive glomerulosclerosis and tubulointerstitial damage at baseline than the other 29 patients. The UprV-UNaV correlation was significant in 8 of 12 patients (66.7%) with eGFR < 60 ml/min/1.73 m² and in 6 of 29 patients (19.4%) with eGFR ≥ 60 ml/min/1.73 m² (p < 0.05). The UprV/UNaV regression lines were significantly steeper with more extensive glomerulosclerosis (p < 0.05) and tubulointerstitial damage (p < 0.05) at baseline. The lines also tended to be steeper with lower baseline eGFR (p = 0.062).

Conclusions: These results showed that the antiproteinuric effect of RAS inhibitors becomes susceptible to an increase in urinary sodium excretion as renal function and functioning nephron mass decline with the progression of renal histological damage. Stringent dietary sodium restriction is required to maximize the antiproteinuric effect of RAS inhibitors in outpatients with IgA nephropathy.

Impact of urine sodium on urine risk factors for calcium oxalate nephrolithiasis

[J Urol. 2009 Nov;182\(5\):2330-3](#). Epub 2009 Sep 16. Eisner BH, Eisenberg ML, Stoller ML. Department of Urology, University of California-San Francisco, San Francisco, California 94143, USA. eisnerbh@urology.ucsf.edu, eisnerbh@urology.ucsf.edu

Purpose: Increased sodium intake is thought to promote nephrolithiasis by dietary sodium hypercalciuric effects. However, equivocal data exist on whether increased urine sodium actually increases the nephrolithiasis risk. We examined the relationship between urine sodium and urine risk factors for nephrolithiasis.

Materials and Methods: We retrospectively reviewed the records of 880 patients evaluated at a metabolic stone clinic to determine the relationship between urine sodium and urine calcium, volume and calcium oxalate supersaturation. Patients were separated into sodium excretion quintiles. Tests of linear trend were performed by examining the linear contrast in coefficients and using Cuzick's nonparametric linear trend test. Multivariate linear regression with urine sodium as a continuous variable was done to assess the relationship between urine sodium and other urine variables.

Results: Tests of linear trend showed that urine calcium and volume increased with increasing urine sodium (each p < 0.01) but urine calcium oxalate supersaturation decreased with increasing urine sodium (p < 0.01). Multivariate linear regression was adjusted for age, sex, body mass index and urine constituents. Urine sodium was positively associated with urine calcium (beta = 0.28, 95% CI 0.15 to 0.41, p < 0.001) but negatively associated with urine calcium oxalate supersaturation (beta = -0.013, 95% CI -0.016 to -0.011, p < 0.001). There was a trend toward a positive association of urine sodium and volume (beta = 0.001, 95% CI -0.00019 to 0.002, p = 0.10).

Conclusions: Increasing urine sodium does not appear to increase the risk of calcium oxalate nephrolithiasis. Global sodium restriction may not necessarily alter the risk of stone formation, ie cause changes in calcium oxalate urine supersaturation, in patients with a history of nephrolithiasis.

Benefits of dietary sodium restriction in the management of chronic kidney disease

[Curr Opin Nephrol Hypertens. 2009 Nov;18\(6\):531-8.](#) Krikken JA, Laverman GD, Navis G. Department of Internal Medicine, Division of Nephrology, University Medical Center Groningen, Groningen, The Netherlands.

Purpose of Review: To evaluate the role of restricting dietary sodium intake in chronic kidney disease (CKD) and its complications.

Recent Findings: A consistent line of evidence shows that high dietary sodium intake is a determinant of therapy resistance to blockade of the renin-angiotensin-aldosterone system (RAAS). Addition of sodium restriction to RAAS blockade or to RAAS blockade combined with a diuretic permits a further reduction in urinary protein excretion of approximately 30%, which could be expected to reduce long-term renal risk by 25%.

Summary: High sodium intake increases blood pressure and proteinuria, induces glomerular hyperfiltration and blunts the response to RAAS blockade. Although recommended in international guidelines, sodium restriction is not a spearhead in treating renal patients. Sodium status is only rarely mentioned in recent large intervention studies in CKD. Sodium intake in CKD is similar to that in the general population. Reduction of sodium intake to the target of 50-85 mmol/24 h in patients with CKD reduces blood pressure and proteinuria, the latter by approximately 30%, and should be actively pursued to improve outcome in CKD.

DASH-style diet associates with reduced risk for kidney stones

[J Am Soc Nephrol. 2009 Oct;20\(10\):2253-9.](#) Epub 2009 Aug 13. Taylor EN, Fung TT, Curhan GC. Renal Division and Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts 02115, USA. entaylor@partners.org

The impact of the Dietary Approaches to Stop Hypertension (DASH) diet on kidney stone formation is unknown. We prospectively examined the relation between a DASH-style diet and incident kidney stones in the Health Professionals Follow-up Study (n = 45,821 men; 18 yr of follow-up), Nurses' Health Study I (n = 94,108 older women; 18 yr of follow-up), and Nurses' Health Study II (n = 101,837 younger women; 14 yr of follow-up). We constructed a DASH score based on eight components: high intake of fruits, vegetables, nuts and legumes, low-fat dairy products, and whole grains and low intake of sodium, sweetened beverages, and red and processed meats. We used Cox hazards regression to adjust for factors that included age, BMI, and fluid intake. Over a combined 50 yr of follow-up, we documented 5645 incident kidney stones. Participants with higher DASH scores had higher intakes of calcium, potassium, magnesium, oxalate, and vitamin C and had lower intakes of sodium. For participants in the highest compared with the lowest quintile of DASH score, the multivariate relative risks for kidney stones were 0.55 (95% CI, 0.46 to 0.65) for men, 0.58 (95% CI, 0.49 to 0.68) for older women, and 0.60 (95% CI, 0.52 to 0.70) for younger women. Higher DASH scores were associated with reduced risk even in participants with lower calcium intake. Exclusion of participants with hypertension did not change the results.

In conclusion, consumption of a DASH-style diet is associated with a marked decrease in kidney stone risk.

Role of postnatal dietary sodium in prenatally programmed hypertension

[Pediatr Nephrol. 2009 Sep;24\(9\):1727-33.](#) Epub 2009 May 7. Stewart T, Ascani J, Craver RD, Vehaskari VM. Louisiana State University Health Sciences Center, 1900 Gravier Street, New Orleans, LA 70112, USA.

In this study we examined the short- and long-term impact of early life dietary sodium (Na) on prenatally programmed hypertension. Hypertension was induced in rat offspring by a maternal low protein (LP) diet. Control and LP offspring were randomized to a high (HS), standard (SS), or low (LS) Na diet after weaning. On the SS diet, the LP pups developed hypertension by 6 weeks of age. The development of hypertension was prevented by the LS diet and exacerbated by the HS diet. Kidney nitrotyrosine content, a measure of oxidative stress, was reduced by the LS diet compared with the HS diet. The modified diets had no effect on control pups. A group of animals on the SS diet was followed up to 51 weeks of age after an early life 3-week exposure to the HS or LS diet. This brief early exposure of LP animals to the LS diet prevented the later development of hypertension and ameliorated the nephrosclerosis observed after early exposure to the HS diet. The LP offspring with early exposure to LS diet had lost their salt-sensitivity when challenged with the HS diet at the age of 43-49 weeks. No effect of early life dietary Na was observed in control animals. These results show that hypertension in this model is salt sensitive and may, in part, be mediated by salt-induced renal oxidative stress and that there may exist a developmental window which allows postnatal "reprogramming" of the hypertension.

In conclusion, we have shown that prenatally programmed hypertension is salt-sensitive and may be "reprogrammable" by varying dietary salt content during a postnatal window. The effect of dietary salt may be mediated, in part, by modulation of intrarenal oxidative stress.

Salt-resistant blood pressure and salt-sensitive renal autoregulation in chronic streptozotocin diabetes

[Am J Physiol Regul Integr Comp Physiol. 2009 Jun;296\(6\):R1761-70.](#) Epub 2009 Apr 1. Lau C, Sudbury I, Thomson M, Howard PL, Magill AB, Cupples WA. Centre for Biomedical Research, University of Victoria, Victoria, British Columbia V8W 3N5, Canada

Hyperfiltration occurs in early type 1 diabetes mellitus in both rats and humans. It results from afferent vasodilation and thus may impair stabilization of glomerular capillary pressure by autoregulation. It is inversely related to dietary salt intake, the "salt paradox." Restoration of normal glomerular filtration rate (GFR) involves increased preglomerular resistance, probably mediated by tubuloglomerular feedback (TGF). To begin to test whether the salt paradox has pathogenic significance, we compared intact vs. diabetic (streptozotocin) Long-Evans rats with normal and increased salt intake, 1 and approximately 3% by weight of food eaten, respectively. Weekly 24-h blood pressure records were acquired by telemetry before and during diabetes. Blood glucose was maintained at approximately 20 mmol/l by insulin implants. GFR was significantly elevated only in diabetic rats on normal salt intake, confirming diabetic hyperfiltration and the salt paradox. Renal blood flow dynamics show strong contributions to autoregulation by both TGF and the myogenic mechanism and were not impaired by diabetes or by increased salt intake. Separately, systolic pressure was not elevated in diabetic rats at any time during 12 wk with normal or high salt intake. Autoregulation was effective in all groups, and the diabetic-normal salt group showed significantly improved autoregulation at low perfusion pressures. Histological examination revealed very minor glomerulosclerosis and modest mesangial expansion, although neither was diagnostic of diabetes. Periodic acid-Schiff-positive droplets found in distal tubules and collecting duct segments were diagnostic of diabetic kidneys. Biologically significant effects attributable to increased salt intake were abrogation of hyperfiltration and of the left shift in autoregulation in diabetic rats.