Animal Protein and the Risk of Kidney Stones: A Comparative Metabolic Study of Animal Protein Sources

Chad R. Tracy, Sara Best, Aditya Bagrodia, John R. Poindexter, Beverly Adams-Huet, Khashayar Sakhaee, Naim Maalouf,* Charles Y. C. Pak and Margaret S. Pearle†

From the Departments of Urology, University of Iowa (CRT), Iowa City, Iowa, and University of Wisconsin-Madison (SB), Madison, Wisconsin, and Departments of Urology (AB, MSP) and Internal Medicine (BA-H, KS, NM) and Jane and Charles Pak Center for Mineral Metabolism and Clinical Research (JRP, CYCP, MSP), University of Texas Southwestern Medical Center, Dallas, Texas

Purpose: We compared the effect of 3 animal protein sources on urinary stone risk.

Materials and Methods: A total of 15 healthy subjects completed a 3-phase randomized, crossover metabolic study. During each 1-week phase subjects consumed a standard metabolic diet containing beef, chicken or fish. Serum chemistry and 24-hour urine samples collected at the end of each phase were compared using mixed model repeated measures analysis.

Results: Serum and urinary uric acid were increased for each phase. Beef was associated with lower serum uric acid than chicken or fish (6.5 vs 7.0 and 7.3 mg/dl, respectively, each $p < 0.05$). Fish was associated with higher urinary uric acid than beef or chicken (741 vs 638 and 641 mg per day, $p = 0.003$ and 0.04, respectively). No significant difference among phases was noted in urinary pH, sulfate, calcium, citrate, oxalate or sodium. Mean saturation index for calcium oxalate was highest for beef (2.48), although the difference attained significance only compared to chicken (1.67, $p = 0.02$) but not to fish (1.79, $p = 0.08$).

Conclusions: Consuming animal protein is associated with increased serum and urine uric acid in healthy individuals. The higher purine content of fish compared to beef or chicken is reflected in higher 24-hour urinary uric acid. However, as reflected in the saturation index, the stone forming propensity is marginally higher for beef compared to fish or chicken. Stone formers should be advised to limit the intake of all animal proteins, including fish.

Key Words: kidney, calculi, risk, dietary proteins, diet

Abbreviations and Acronyms

CaOx = calcium oxalate

CTRC = Clinical and Translational Research Center

SI = saturation index

TA = urinary titratable acidity

UA = uric acid

Accepted for publication January 8, 2014.

Study received institutional review board approval.

Supported by Grant UL1TR000451 from the National Center for Advancing Translational Sciences, National Institutes of Health.

* Financial interest and/or other relationship with Takeda.

† Correspondence: Department of Urology, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd., J8.106, Dallas, Texas 75390-9110 (telephone: 214-648-6853; FAX: 214-648-8786; e-mail: Margaret.pearle@utsouthwestern.edu).

For another article on a related topic see page 260.

Kidney stone disease is a significant health problem in the United States.[1] Despite highly successful surgical treatments to remove stones a successful medical prophylactic program has the potential to prevent the morbidity of stone related events and avoid the need for surgical intervention. Although a number of medications decrease the likelihood of stone recurrence,[2] patient compliance with drug regimens is poor.[3] Consequently, recent efforts have focused on dietary measures in the hope of improving patient compliance while decreasing the stone recurrence rate.[4–6]

Various dietary measures have been evaluated for the effect on urinary stone risk factors or stone

0022-5347/14/1921-0137/0
THE JOURNAL OF UROLOGY®

http://dx.doi.org/10.1016/j.juro.2014.01.093
Vol. 192, 137-141, July 2014
Printed in U.S.A.

formation.[4,7,8] Animal protein lowers urinary pH and increases urinary UA, which are risk factors for UA and calcium stone formation.[9,10] A large epidemiological study in men showed a positive correlation between animal protein intake and initial stone formation.[11] Also, a randomized trial of stone forming men with hypercalciuria showed a lower rate of stone recurrence in those who adhered to a low animal protein, low sodium, normal calcium diet compared to those on a low calcium diet.[7] However, despite compelling evidence that excessive animal protein consumption enhances the risk of stone formation, the effect of different sources of animal protein has not been explored.

Fish is widely recognized as the healthiest of animal proteins and stone formers are commonly advised to restrict the intake of beef to decrease stone risk. We report a randomized, crossover metabolic study comparing the effect of different animal proteins (beef, fish and chicken) on urinary stone risk factors.

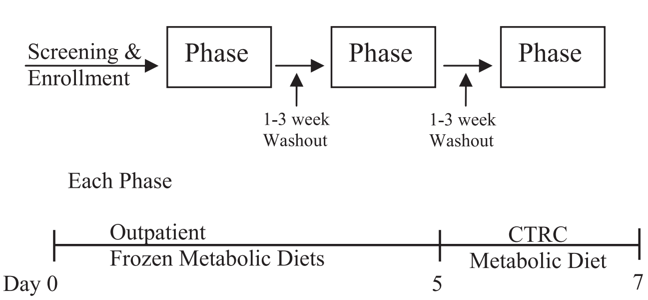
METHODS

Study Population

After receiving institutional review board approval healthy volunteers 18 to 70 years old were recruited for participation. Study exclusion criteria included a history of kidney stones or any medical condition predisposing to stone formation (eg gout, congenital hyperuricemia, chronic diarrhea, insulin resistance, neoplastic disorders, hyperparathyroidism or renal tubular acidosis). Vegetarians, vegans and individuals with an aversion to specific types of meat were also excluded. Eligible subjects underwent screening serum and urine studies, including urine dipstick and serum electrolytes, and UA measurement. Those with any abnormal screening tests were excluded from study. Informed consent was obtained from qualified individuals.

Dietary Intervention

Subjects participated in 3 phases of study, each lasting 1 week and differing according to the type of animal protein provided, that is beef, chicken or fish (see figure). The order of phases was randomly assigned using SAS® Proc Plan with Latin squares. A minimum 1-week washout period between phases was imposed. However, for women participants a 3-week washout period was used to assure that each phase was performed during the same phase of the menstrual cycle.



Randomization scheme for each study phase

For the first 4 days of each phase (outpatient) frozen meals were provided by the CTRC metabolic kitchen. On the evening of day 5 subjects were admitted to the CTRC for the remaining 2 study days and all meals were provided on site. Blood and urine studies were obtained under close scrutiny during the inpatient stay.

During each phase subjects consumed a standard metabolic diet matched for calories, protein, sodium and calcium, and indexed to body weight. The diet included beef, chicken or fish and 3 L fluid daily. Fish diets comprised salmon and cod, chicken was provided as breast meat and beef diets contained ground beef or tenderloin. Diets were isocaloric for each patient throughout the study and only the protein source varied among study phases. Dietary protein intake was matched across phases by protein weight based on the average intake of Americans at ages 19 to 50 years (1.4 gm/kg ideal body weight per day)[12] rather than by purine content. Dairy was not considered in daily animal protein calculations but was kept constant between phases. The metabolic diet consisted of low sodium and oxalate content (100 mEq per day and 100 to 150 mg per day, respectively) and 600 to 800 mg per day Ca. Because of significant variability in phosphorus content among meat sources, we could not keep phosphorus constant among phases.

Study Phases, Test Procedures and Laboratory Methods

During each phase fasting venous blood samples were obtained on the morning of days 6 and 7, and analyzed for pH, serum electrolytes, blood urea nitrogen, creatinine, glucose and UA. On the last 2 days of each phase subjects collected 2, 24-hour urine specimens, which were analyzed for urine volume, pH, sodium, potassium, chloride, ammonium, phosphate, sulfate, creatinine, calcium, oxalate, citrate and UA. TA was calculated as previously described.[13] Net acid excretion was calculated as (NH_4^+ + TA) − (HCO_3^- + ionized citrate) in mEq. Net gastrointestinal absorption of alkali was calculated as [urine ($Na^+ + K^+ + Ca^{+2} + Mg^{+2}$ mEq per day) − (Cl^- mEq per day + $1.8 \times PO_4^{-3}$ mmol per day)] in mEq per day. Urinary saturation of CaOx, UA and brushite was calculated as the SI using JESS (Joint Expert Speciation System, Mayhem Unit Trust and Council for Scientific and Industrial Research, Pretoria, South Africa).[14]

Statistical Analysis

Sample size calculations were based on the results of similar metabolic studies[10] with the goal of identifying a clinically significant difference in urinary UA of 100 mg per day among the 3 diets. Based on these calculations 10 subjects were required to identify a difference of 0.03 in urinary pH, 100 mg per day in UA, 50 mg per day in undissociated UA and 0.5 in SI of UA or CaOx with a power ($\alpha = 0.05$) of 0.89 to 0.96. Allowing for 20% dropout we planned to enroll at least 14 patients. Repeated measures analysis was applied to evaluate the effect of