INCIDENCE AND RISK FACTORS OF DE NOVO NEPHROLITHIASIS AFTER CHEMOTHERAPY IN PATIENTS WITH LYMPHOPROLIFERATIVE OR MYELOPROLIFERATIVE DISORDERS
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(Presentation to be made by Dr. Mirheydar)

Purpose: To describe the incidence and risk factors of de novo nephrolithiasis among patients with lymphoproliferative or myeloproliferative diseases who have undergone chemotherapy.

Materials and methods: From 2001 to 2011, patients with lymphoproliferative or myeloproliferative disorders treated with chemotherapy were retrospectively identified. The incidence of image proven nephrolithiasis after chemotherapy was determined. Demographic and clinical variables were recorded. Patients with history of nephrolithiasis prior to chemotherapy were excluded. Primary outcome was incidence of nephrolithiasis, and secondary outcomes were risk factors predictive of de novo stone. Comparative statistics were used to compare demographic and disease specific variables for patients who developed de novo stones versus those who did not.

Results: 1316 patients were identified and the incidence of de novo nephrolithiasis was 5.5% (72/1316; symptomatic stones 1.8% 24/1316). Among patients with nephrolithiasis, 72.2% had lymphoproliferative disorders, 27.8% had myeloproliferative disorders, and 25% utilized allopurinol. The median urinary pH was 5.5, and the mean serum uric acid, calcium, potassium and phosphorus levels were 7.5, 9.6, 4.3, and 3.8 mg/dL, respectively. In univariate analysis mean uric acid (p=0.013), calcium (p<0.001), and potassium (p=0.039) levels were higher in stone formers. Diabetes mellitus (p<0.001), hypertension (p=0.003), and hyperlipidemia (p<0.001) were more common in stone formers. In multivariate analysis, diabetes mellitus, hyperuricemia, and hypercalcemia predicted stone.

Conclusions: We report for the first time the incidence of de novo nephrolithiasis in patients who have undergone chemotherapy. Moreover, we identified risk factors that may assist in identifying patients who might require medical therapy to prevent upper tract stone.

Keywords: Nephrolithiasis, urolithiasis, urate nephropathy, myeloproliferative disorder, lymphoproliferative disorder, chemotherapy

Source of Funding: None
A DROSOPHILA MELANOGASTER MODEL IDENTIFIES A CRITICAL ROLE FOR ZINC IN INITIATING URINARY STONES

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(Presentation to be made by Dr. Chi)

Purpose: Calcium hydroxyapatite serves as a nidus for a variety of mineralized deposits and structures across phyla and species including plaques seen in atherosclerosis, neurodegenerative disorders, and kidney stone disease. It has been postulated to drive the formation of human urinary stones but initiating factors for the calcification process are poorly understood. We utilized a Drosophila model for urinary stone disease to examine elements that might play a critical role in the early events leading to stone formation.

Materials and Methods: Drosophila melanogaster Malpighian tubule calcified concretions and human renal biopsy material were collected. Synchrotron radiation-based analytical techniques and electron microscopy were utilized in both sets of samples to look for common elements. Genetic manipulation in the fly was then utilized to confirm potential therapeutic targets for treatment of urinary stone disease.

Results: Synchrotron radiation-based analysis demonstrated that the presence of Zn$^{2+}$ in mineralized material was consistent across both species, leading us to hypothesize that Zn$^{2+}$ plays an important, previously unrecognized role in the initiation of human urinary stones. Using genetic methods to mitigate Zn$^{2+}$ transport in Drosophila, we demonstrated that these interventions significantly reduced stone formation in the fly.

Conclusions: Our results implicate Zn$^{2+}$ as a critical component for initiating calcification and a potential therapeutic target for treating human kidney stone disease.

Funding: This research was supported by the K12-DK-07-006: Multidisciplinary K12 Urologic Research Career Development Program. This work was also supported in part by a grant from the AUA Foundation Research Scholars Program and Boston Scientific Corporation, The Endourological Society, and the “Friends of Joe” (T.C.).
Purpose: The alpha 1A-adrenoceptor (AR) has been shown to play a role in phenylephrine-induced human ureteral contraction. We evaluated the efficacy of silodosin, a selective alpha 1A AR antagonist, in the medical expulsion of proximal, mid, and distal ureteral calculi.

Methods: Two hundred forty-six patients with a unilateral ureteral calculus (4-10 mm) were randomized to receive either silodosin 8 mg or placebo once daily for up to 4 weeks in a double-blind design. If there was no stone passage after 4 weeks, or if the patient required intervention at any point, the patient was discontinued from the study. Two hundred thirty-two patients received study medication and completed the study follow-up. Univariate logistic regression was utilized to compare the primary endpoint of stone passage at 4 weeks with intention-to-treat analysis. Secondary endpoints included time to stone passage, need for emergency department visits, surgical intervention, pain assessment scores, and analgesic use.

Results: For patients with distal ureteral stones, treatment with silodosin resulted in a significant improvement in the spontaneous expulsion rate at 4 weeks (69.2% vs 45.8%, p=0.0138) and time to stone passage was lower (approaching statistical significance). A trend towards improved passage rate was also observed in patients treated with silodosin for all ureteral calculi combined but not for proximal or mid ureteral calculi subsets. In addition, patients with distal ureteral stones receiving silodosin reported significantly greater improvements in average pain scores at study exit. Among all patients, larger stones (6-10 mm) had higher passage rates with silodosin than with placebo (33% vs 9.1%, p=0.0573).

Conclusions: Silodosin significantly improved the spontaneous expulsion rate of distal ureteral stones and resulted in greater improvements in average pain scores and time to passage for these patients. Additionally, silodosin improved the passage rate of large ureteral stones. Our findings indicate that silodosin provided advantages over placebo in medical expulsion therapy of ureteral calculi.

Source of Funding: Watson Laboratories
EXTRACORPOREAL LITHOTRIPSY USING ULTRASOUND PULSES
WITHOUT SHOCK WAVES: IN VITRO RESULTS

(Presentation to be made by Dr. Maxwell)

Purpose: Shockwave lithotripsy (SWL) remains a first line of treatment for renal calculi. However, the high retreatment rate associated with SWL is shifting clinical preference towards other approaches in many centers. We are developing a new form of extracorporeal lithotripsy using focused ultrasound pulses without shock waves, which may provide a more effective alternative to SWL. This study investigated stone fragmentation under different ultrasound exposures.

Materials and Methods: Uric acid, struvite, cystine, and calcium oxalate stones removed during percutaneous nephrolithotomy, as well as artificial stones (Begostone, 6x10-12mm) with acoustic properties similar to calcium oxalate were used in experiments. Stones were adhered to a thin plastic membrane and aligned with the focus of the ultrasound transducer in a bath of degassed water. The transducer was driven between 170-255 kHz to output 10-cycle sinusoidal pulses. Pulses were delivered at a rate of 200 Hz with focal pressure amplitude $p \leq 6.5$ MPa. Time to complete fragmentation was recorded and the resulting debris was collected to determine the size distribution.

Results: Fragmentation starting at the proximal stone surface and progressed distally during treatment. The minimum focal pressure to initiate fracture of artificial stones was between $p = 2.3 - 2.8$ MPa. Artificial stones treated at 170 kHz and $p = 6.5$ MPa achieved comminution in 10.9 +/- 2.5 minutes (n=6). Stone composition and size affected the fragmentation time of human stones exposed to the same parameters, ranging from 10 seconds (5mm, uric acid) to 21 minutes (12mm, cystine). The size of the resulting fragments had an inverse relationship with the applied ultrasound frequency.

Conclusions: Focused ultrasound pulses can fragment artificial and human kidney stones in vitro without shock waves. The fragment size generated may be controllable through choice of ultrasound frequency.

Sources of Funding: Work supported by NIH 2T32DK007779-11A1, 2R01EB007643-05, 2P01DK043881-15, 1R01DK092197-02, and NSBRI through NASA NCC 9-58.
MULTICENTER VALIDATION OF S.T.O.N.E. NEPHROLITHOMETRY
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(Presentation to be made by Dr. Okhunov)

Objective: The STONE nephrolithometry was previously developed as a stone complexity scoring system and prospectively validated in a single center percutaneous nephrolithotomy (PCNL) cohort. We evaluated the nephrolithometry score in a multicenter database of patients undergoing PCNL.

Methods: We performed a multicenter retrospective study of patients undergoing PCNL. Preoperative CT images were reviewed and STONE score was assigned to each patient. The association of STONE score with patient demographics, stone characteristics and surgical outcomes was performed.

Results: Of the 425 patients who underwent PCNL in 4 institutions between 2009 and 2012, 197 (46%) had complete data and were included in the analysis. Patient demographics are provided in Table 1. The mean overall nephrolithometry score was 8.3 (SD=1.8). Overall stone-free rate after was 69%. STONE score was significantly associated with postoperative stone-free status (P<0.001). Stone-free patients had lower STONE scores than patients with residual stones (mean STONE score=7.8 vs. 9.4, respectively; P<0.001). There were 29 (17%) complications with postoperative sepsis and bleeding being most frequent ones. STONE score was significantly associated with overall complication rate (P=0.015), estimated blood loss (P=0.003), operative time (P<0.001), and fluoroscopy time (P=0.016, Table 3).

Conclusions: In this multicenter study including data from multiple surgeons, STONE nephrolithometry accurately predicted surgical outcomes following PCNL, including stone-free rate and complications. The easy-to-use STONE scoring system obtained from computed tomography imaging may be utilized in preoperative patient counseling, surgical planning, and as standardized measure to evaluate surgical outcomes across different studies and institutions.

Source of Funding: None
Purpose: Ureteroscopy patients with are exposed to significant amounts of radiation during their initial work-up, surgical treatment, and follow-up. In an effort to reduce patient exposure to ionizing radiation, a technique for ureteroscopy was developed that eliminated the need for intraoperative fluoroscopy. The purpose of this study was to compare outcomes of this technique with a cohort of conventional ureteroscopic patients.

Materials and Methods: A retrospective review of 50 consecutive patients undergoing ureteroscopy using a completely fluoroless technique between January 2009 and November 2012 was performed. Fluoroless procedures were performed by inserting guidewires and instruments using tactile feedback, direct visualization, and external visual cues to substitute for fluoroscopy. This cohort was compared to 50 conventional ureteroscopies performed during this same period. Patient characteristics, perioperative factors, complication rates, and stone-free rates were compared.

Results: All fluoroless ureteroscopies were successfully performed without image guidance. In the fluoroless group the mean operative time was 59.2 minutes (25-120 min.), overall stone burden was 91.5 mm² (2-480 mm²), complication rate was 4%, and repeat procedure rate was 8%. When compared to conventional ureteroscopy, there was no statistical difference between operative time, complication rate, repeat procedure, age, gender, ASA, BMI, and laterality. The fluoroless patients had statistically larger stone burden 91.5 vs. 56.5 mm² (p = 0.042). Average conventional fluoroscopy time was recorded at 38.6 seconds.

Conclusions: In this comparison we demonstrate that fluoroless ureteroscopy results in similar patient outcomes as conventional ureteroscopy, but results in dramatically reduced fluoroscopy time. This technique may be particularly uselful in younger or pregnant patients, in whom risk from ionizing radiation is highest. Further study and comparison with conventional approaches will be necessary to establish optimal patient selection criteria.

Source of Funding: None