RENAL STONE RISK DURING SPACE FLIGHT: ASSESMENT AND COUNTERMEASURE VALIDATION

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NASA has focused its future on exploration class missions including the goal of returning to the moon and landing on Mars. With these objectives, humans will experience an extended exposure to the harsh environment of microgravity and the associated negative effects on all the physiological systems of the body. Exposure to microgavity affects human physiology and results in changes to the urinary chemical composition during and after space flight. These changes are associated with an increased risk of renal stone formation. The development of a renal stone would have health consequences for the crewmember and negatively impact the success of the mission. As of January 2007, 15 known symptomatic medical events consistent with urinary calculi have been experienced by 13 U.S. astronauts and Russian cosmonauts.

Previous results from both MIR and Shuttle missions have demonstrated an increased risk for renal stone formation. These data have shown decreased urine volume, urinary pH and citrate levels and increased urinary calcium. Citrate, an important urinary inhibitor of calcium-containing renal stones binds with calcium in the urine, thereby reducing the amount of calcium available to form calcium oxalate stones. Urinary citrate also prevents calcium oxalate crystals from aggregating into larger crystals and into renal stones. In addition, citrate makes the urine less acidic which inhibits the development of uric acid stones. Potassium citrate supplementation has been successfully used to treat patients who have formed renal stones. The evaluation of potassium citrate as a countermeasure has been performed during the ISS Expeditions 3-6, 8, 11-13 and is currently in progress during the ISS Expedition 14 mission.

Together with the assessment of stone risk and the evaluation of a countermeasure, this investigation provides an educational opportunity to all crewmembers. Individual urinary biochemical profiles are generated and the risk of stone formation is estimated. Increasing fluid intake is recommended to all crewmembers. These results can be used to lower the risk for stone formation through lifestyle, diet changes or therapeutic administration to minimize the risk for stone development. With human presence in microgravity a continuing presence and exploration class missions being planned, maintaining the health and welfare of all crewmembers is critical to the exploration of space.

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Introduction

NASA has focused its future on exploration class missions including the goal of returning to the moon and landing on Mars. With these objectives, humans will experience an extended exposure to the unique environment of microgravity. Exposure to microgravity affects human physiology and results in changes to the urinary chemical composition during and after space flight. These changes are associated with an increased risk of renal stone formation. The development of a renal stone would have health consequences for the crewmember and negatively impact the success of the mission. As of January 2007, 15 known symptomatic medical events consistent with urinary calculi have been experienced by 13 U.S. astronauts and Russian cosmonauts.

Citrate, an important urinary inhibitor of calcium-containing renal stones binds with calcium in the urine, thereby reducing the amount of calcium available to form calcium oxalate stones. Urinary citrate also prevents calcium oxalate crystals from aggregating into larger crystals and renal stones. In addition, citrate makes the urine less acidic which inhibits the development of uric acid stones. Potassium citrate (KCIT) supplementation has been successfully used to treat terrestrial patients who have formed renal stones. The evaluation of potassium citrate in microgravity as a countermeasure has been performed during the ISS Expeditions 3-6, 8, 11-13 and is currently in progress during the ISS Expedition 14 mission. With human presence in microgravity a continuing presence and exploration class missions being planned, maintaining the health and welfare of all crewmembers is critical to the exploration of space.

Methods

- 24-hr urines collected pre-, in- and postflight
- Food, fluid, exercise, and medications monitored before and during the urine collection period
- Ingestion of 2 potassium citrate (KCIT) pills daily (with the last meal of the day) from L-3 days to R+14 days
- Biochemical analysis of urine samples for urinary factors associated with stone formation
- Dietary analysis completed to assess environmental influences on the urinary biochemistry

Significant Findings

- Urinary citrate levels were maintained throughout the in-flight and postflight periods
- Increased urinary pH levels reduced the risk of uric acid stones
- KCIT subjects showed decreased in-flight and early postflight calcium oxalate supersaturation
- Urinary volume is the strongest predictor of renal stone risk
- Educational value of this study to crewmembers was evident by the increased urinary volume and decreased risk in both groups compared to Shuttle-Mir

Results

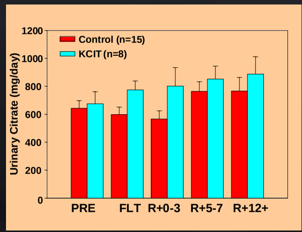

Figure 1. 24 hr urinary citrate excretion in control and treatment group.

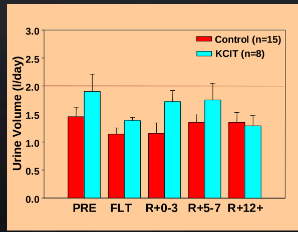

Figure 2. 24- hr urinary output during the pre-, in- and postflight phases of the mission.

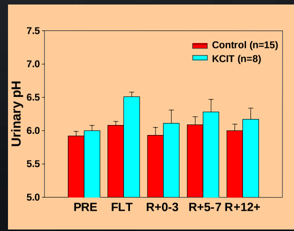

Figure 3. Effect of potassium citrate on 24 hr urinary pH.

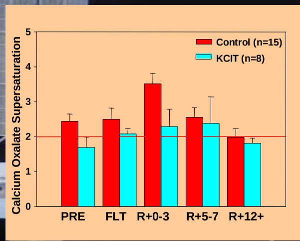

Figure 4. Effect of potassium citrate on the risk of calcium-containing stone formation. Values > 2.0 indicate increased risk.

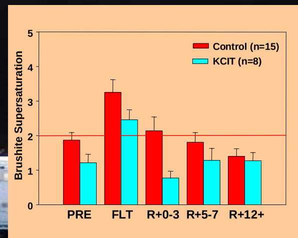

Figure 5. Effect of potassium citrate on the risk of calcium phosphate (brushite) stone formation. Values > 2.0 indicate increased risk.

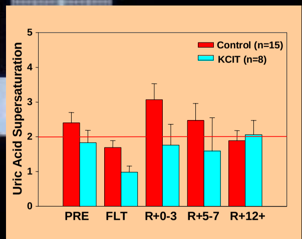

Figure 6. Data represent the risk of uric acid stone formation. Values > 2.0 indicate increased risk.

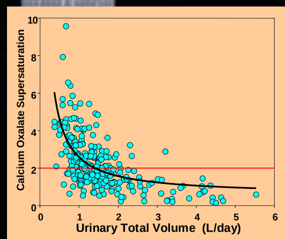

Figure 7. Regression analysis of 24 hr urine volume to risk of calcium oxalate stone formation.

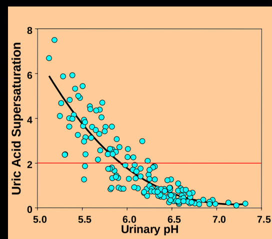

Figure 8. Regression analysis of 24 hr urinary pH on risk of uric acid stone formation.

Discussion

Preliminary results from this investigation suggest that supplementation with potassium citrate decreases the risk of renal stone formation during and immediately after spaceflight. Sample collection and data analysis are continuing at this time. Maintaining the health and well-being of crewmembers during space flight requires a means of minimizing potential detrimental health effects of microgravity. The effects of spaceflight on the urinary biochemistry have shown alterations that may lead to a urinary environment that is conducive to stone formation. Important contributors that decrease the risk of stone formation include the 24 urinary volume and pH. Together with the assessment of stone risk and the evaluation of a countermeasure, this investigation provides an educational opportunity to all crewmembers. Increasing fluid intake is recommended to all crewmembers and can be seen by the increased urinary volume in the ISS crewmember as compared to Mir crewmembers. Prediction of those crewmembers that will develop a renal stone is impossible at this time. Preflight assessment may identify those crewmembers that are at risk and enable measures that may be taken to reduce this risk.