

Effects of Traditional Hmong Herbal Tea on Urinary Parameters Associated with Kidney Stones

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ABSTRACT

Uric acid kidney stones were common in Hmong-Americans diagnosed with kidney stones in La Crosse, WI. A plant-based tea that the Hmong use for kidney problems may affect uric acid metabolism and transport in the kidneys to alter stone formation conditions. We aimed to determine effects of consumption of this tea in humans and to develop an animal model to study the effects of tea extracts on uric acid metabolism and transport. In a random order, crossover design, with tea and water (control) consumption, 24-hour urinary uric acid (UUA) was measured in men ($n=10$, 20 ± 1 years) supplied a high-purine diet (2154 kcal, 146 gram high biological value protein). UUA in humans was 547 ± 99 mg/day with water and 630 ± 92 mg/day with tea consumption. Specific gravity, pH, and urine volume were also assessed. Anesthetized rats were infused with tea extract or vehicle with time 0, 30, 60, and 90 serum (SUA) and urine measurements of uric acid. We found rat SUA and UUA to be quite variable, despite control of diet, sleep-wake cycle and surgical preparation for study. But UUA to SUA ratio may provide useful information for future extract testing. Our results, thus far, indicate that longer consumption studies and further development of an appropriate animal model to study active fractions of tea extracts are needed.

INTRODUCTION

Kidney stones are formed from the crystallization of chemicals in the urinary tract and can cause severe pain, obstruction of urine flow, and kidney damage. Stone prevalence varies with gender (males > females), ethnicity, and diet. Formation of stones is promoted by reduced urine production, blocked flow, and/or excesses of specific chemicals in the urine. Some stones may be prevented or treated with dietary changes and adequate amounts of fluid intake. Certain foods contain chemicals that promote stone formation, while others may reduce stone formation. The second most common stone is made of uric acid and is associated with high purine foods and improper urate transport in the kidneys.

Purines are present in meat and other select foods and their metabolism results in uric acid production. Uric acid is a weak acid that dissociates to yield the hydrogen cation and urate anion. In the blood, uric acid may serve as an antioxidant and may reduce aging and extend life, but when urate transport is inefficient, high levels of urate appear in the urine and, in an acidic urine, can lead to uric acid crystal formation. During purine (adenine and guanine) metabolism, nucleotides are oxidized to xanthine, which is further oxidized to uric acid. Most mammals have an enzyme called "uricase", which allows their body to convert uric acid into allantoin. Humans lack uricase and have transporters, such as the URAT1 transporter, that reabsorb urate instead.

Urine analysis following a high purine diet and tea versus control conditions should shed light on tea effects on uric acid transport in our human study. Blood and urine analysis following tea extract versus control injections should shed light on tea extract effects on uric acid transport in our animal study.

METHODS

Our human research protocol was approved by the UW-L Institutional Review Board for the Protection of Human Subjects (IRB). Subjects were recruited primarily through print advertisement. Ten healthy male volunteers were randomly assigned to consume either 14 oz control solution (water) or tea and then crossover.

Tea and control (water) solutions and all meals (approx. 2154 kcal, 146 gram high biological value protein and purines) were provided to human subjects on each trial day and subjects were instructed to consume only what was provided. Herbs for tea (and extracts) were obtained from Thailand and provided by Mr. Fang Ger Yang. One cup

of homogenized herbs was brought to boil in a covered pan with 96 ounces of tap water and steeped for 30 minutes. The tea was strained and 14 oz was provided to tea recipients

Urine was analyzed for volume, pH and uric acid levels via quantitative colorimetric kit (QuantiChrom™DIUA-250, BioAssay Systems, Hayward, CA) at 590 nm with a SpectramaxPLUS plate reader (Molecular Devices, Sunnyvale, CA). Briefly, 5µl sample or standard is added to a reagent containing 2,4,6,-tripirydyl-s-triazine, which forms a blue color complex with iron in the presence of uric acid. The intensity of the color is proportional to the amount of uric acid in the sample or standard. All samples and standards were run in duplicate.

For tea extracts, plant materials were separated individually into: leaves, barks, chunks and twigs. Individual plant materials were ground and combined with solvents 20X their weight; solvents consisted of: methanol (MeOH), methanol chloride (CH₂Cl₂) and water. Extracts were then stirred overnight with solvents of MeOH and CH₂Cl₂, whereas water solvent extracts were heated for 30 minutes or until boiling. Extracts were then filtered, dried, capped and stored at room temperature in the dark.

Our animal research protocol was approved by the UW-L Institutional Animal Care and Use Committee (IACUC). Sprague Dawley Rats (Harlan Sprague Dawley, Indianapolis, IN) were housed under standard conditions (12:12 light:dark cycle, ad libitum chow and water) at the Health Science Center Laboratory Animal Facility. For the in vivo animal study, 14 rats were anesthetized with isoflurane and femoral veins were catheterized. Seven rats received water control and seven received extract intravenously (Li et al. 2008). Blood and urine samples were taken at 0, 30, 60, and 90 minutes post-infusion and analyzed as detailed above for the human study.

RESULTS AND DISCUSSION

The human study indicated that both water and tea conditions were associated with decreased urinary pH. There was no significant difference in this decrease by condition as shown in Figure 1. The decrease in urinary pH would be expected with a high purine diet. Urine volume was not significantly different with water versus tea consumption. However, fluid intake was only controlled preceding urine collection for subjects' second trials, which was a major limitation of our study. Urinary uric acid was increased with the tea condition compared to water (see Figure 2, below). This does not support the alternative hypothesis that tea may reduce stone formation conditions under the circumstances of our study.

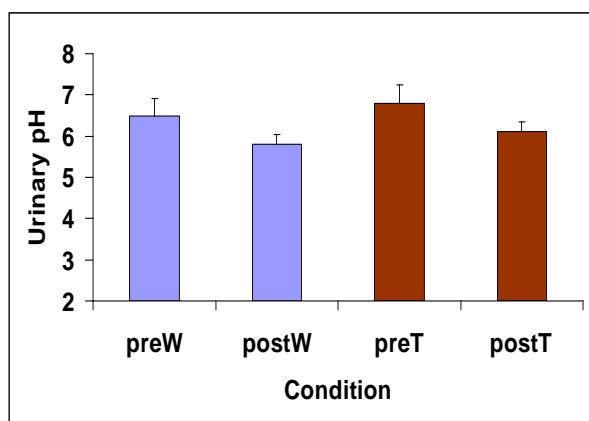


Figure 1. Urinary pH of urine collected before (pre) and after (post) water (W) or tea (T) consumption with a high purine diet.

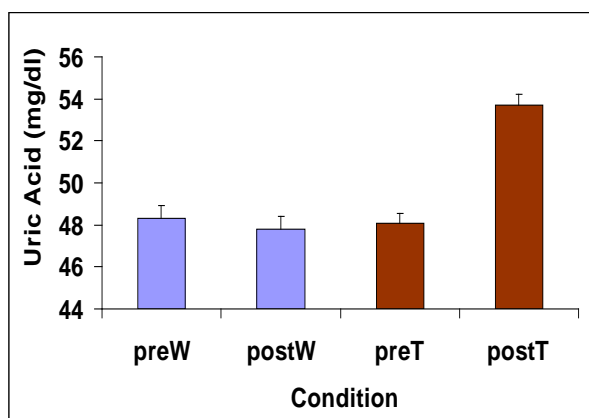


Figure 2. Urinary uric acid of urine collected before (pre) and after (post) water (W) or tea (T) consumption with a high purine diet.

The animal study indicated that in both the water and tea extract, serum uric acid (SUA) does not change. However, following injections, urinary uric acid increases transiently at 30 with water (UUA-W) and 60 with tea (UUA-T) and the transient increases are greater with tea as shown in Figure 3. This response suggests that the surgical/experimental procedure led to changes in kidney function, which were delayed but enhanced with tea. These results may also suggest that there was surgical stress from damaged tissues, which in return could trigger immune and endocrine responses that alter kidney function. In addition, saline and/or heparin could have resulted in changes in blood volume/blood pressure with hemorrhage or flushes. Low molecular weight heparin has been shown to prevent a rise in serum uric acid when there is glomerulonephropathy in rats and reduce nephrotoxic damage from adriamycin (Deepa 2003). Such changes may affect hormone and local factor control of kidney function. Heparin was used as an anticoagulant in our surgical protocol and may have affected our results.

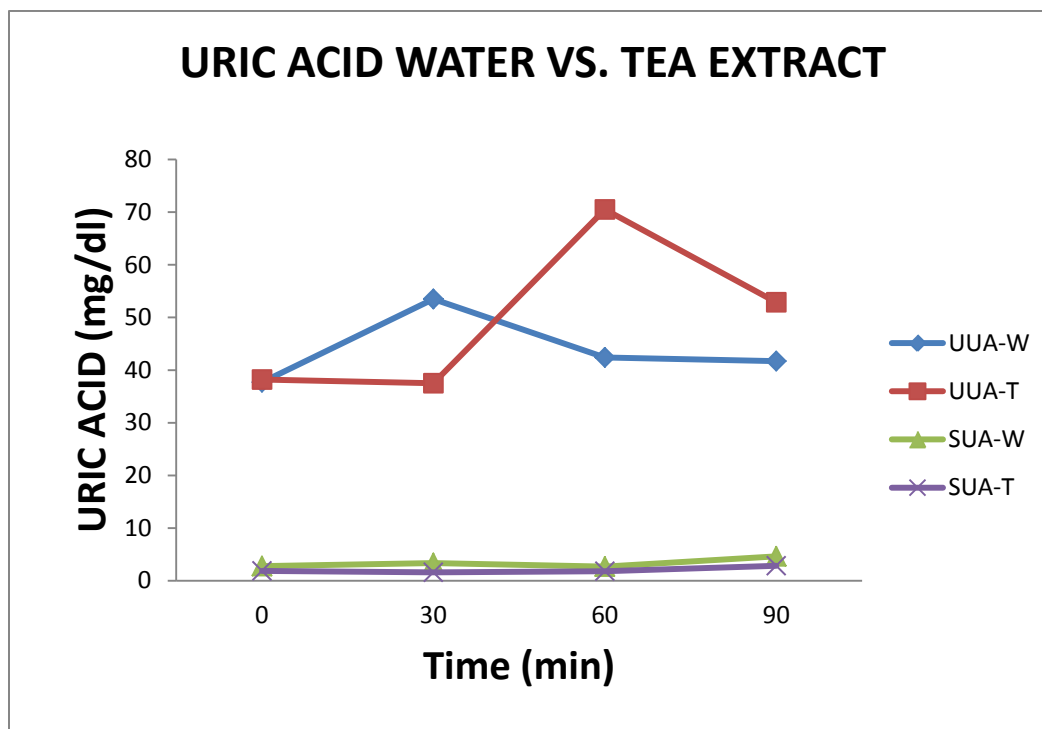


Figure 3. Urinary uric acid in both water (UUA-W) and tea (UUA-T) increases transiently. However, transient increases at 30 with water and 60 with tea. Whereas serum uric acid (SUA) showed similar affect in both conditions.

In conclusion, while the human study results do not support an alternative hypothesis that this tea may reduce favorable conditions for stone formation, our studies do suggest that the tea may affect uric acid metabolism and/or transport in humans with high purine intake but not in the way we originally thought. The animal study suggests that there may be an interaction between the tea extracts and heparin or some other aspect of the surgical or experimental setup. Future studies should include a more defined tea, longer, more controlled consumption studies and further development of an appropriate animal model to study active fractions of tea extracts.

ACKNOWLEDGEMENTS

This research was supported by a University of Wisconsin-La Crosse SAH Dean's Summer Fellowship and the McNair Scholars Program.

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