Impact of Prolonged Fasting on the Risk of Calcium Phosphate Precipitation in the Urine: Calcium Phosphate Lithogenesis during Prolonged Fasting in a Healthy Cohort

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Purpose: Intermittent fasting and curtailing water intake for extended periods were likely common in Paleolithic times. Today it occurs for religious and dietary reasons. This restriction in intake should cause a decrease in the urine flow rate while raising the concentration of certain substances in urine to the point of precipitation. In this study we measured the risk of $CaHPO_4$ precipitation following 18 hours of food and water deprivation.

Materials and Methods: Urine samples were periodically collected from 15 healthy subjects who fasted and abstained from drinking any liquid for 18 hours. The urine constituents Ca^{2+}, HPO_4^{2-} and pH involved in $CaHPO_4$ formation were measured at various times throughout the fasting day. A comparison was made with control data, which consisted of diurnal urine collections taken throughout a separate nonfasting day prior to the fasting day.

Results: The mean ± SEM urine flow rate decreased significantly from 0.93 ± 0.1 ml per minute in the control group to 0.37 ± 0.05 ml per minute in the fasting group ($p < 0.05$). Mean Na^+ and Ca^{2+} excretion rates decreased significantly from 127 ± 12 to 54 ± 13 μmol per minute and from 3.2 ± 0.4 to 0.80 ± 0.21, respectively. Mean urinary Na^+ and Ca^{2+} concentrations also decreased from 161 ± 11.6 to 122 ± 16.0 mmol/l and from 3.7 ± 0.5 to 2.0 ± 0.55, respectively. Urinary pH and the concentration of phosphate, citrate and magnesium were not significantly affected.

Conclusions: Although the steady decrease in the urine flow rate was statistically significant during 18 hours of food and water deprivation, there was no evidence that the calculated risk of $CaHPO_4$ precipitation in the healthy subjects had increased.

Key Words: kidney calculi, fasting, water deprivation, calcium phosphate, citric acid

Abbreviations and Acronyms

BP = blood pressure
Ksp = solubility product constant
PCT = proximal convoluted tubule
RAAS = renin-angiotensinogen-aldosterone system
UFR = urine flow rate
WD = water and food deprivation

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GIVEN the recent popularity of intermittent fasting, studies have attempted to investigate the health benefits and risks associated with this behavior.[1] Despite studies indicating the positive effects of intermittent fasting[2] the decreased fluid intake during fasting are speculated to impact the process of nephrolithiasis. Early humans were likely water and food deprived for extended periods and it would have been devastating to survival if they were affected by kidney stone sequelae.[3]

Kidney stone disease, which is characterized by severe pain, afflicts

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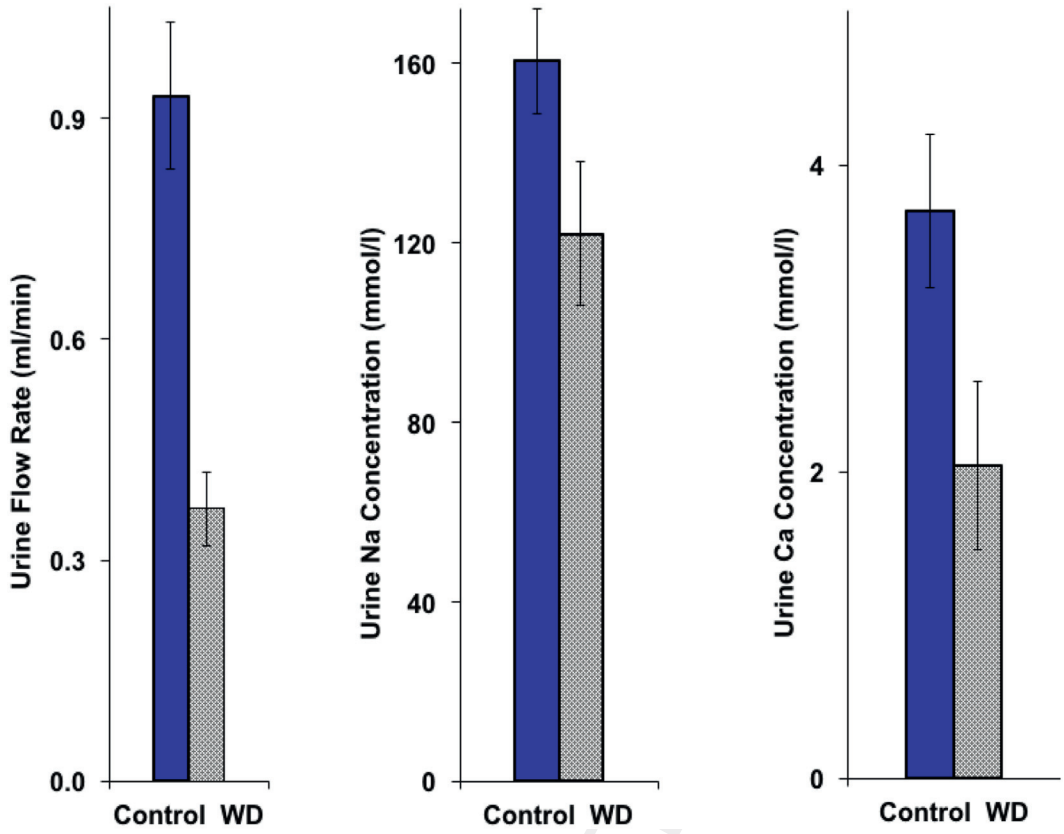

Figure 1. In fasting vs control groups changes in UFR, and Na^+ and Ca^{2+} urine concentrations were significant (all $p < 0.05$). SEM shows variance.

10% to 15% of the general population with a 0.5% increasing prevalence annually in North America and Europe.[4,5] Although urinary lithiasis carries dire health risks, the mechanisms underlying it and the pathology are largely undefined.[6]

We specifically studied $CaHPO_4$ precipitates for certain reasons. 1) They are the main precursors of calcium oxalate monohydrate nucleation and growth, representing the most common stone type with a growing incidence. 2) They can cause renal failure by plugging Bellini ducts.[7,8] Furthermore, $CaHPO_4$ stone formation is associated with 2 measurable lithogenic variables, including ionized Ca^{2+} and divalent phosphate ions (H_2PO_4). Changes in the concentration of either divalent ion may have unfortunate consequences on kidney stone formation.

Precipitation formation is contingent on the solubility product constant of a compound. The risk of $CaHPO_4$ precipitation formation increases when the mentioned divalent ions exceed the Ksp. Supersaturation is the condition in which a product exceeds its normal Ksp.[9] The risk of $CaHPO_4$ precipitation formation decreases with higher levels of urinary citrate and magnesium ions caused by competitive binding and with a decrease in the HPO_4^{2-} concentration caused by decreasing urinary pH.

Prior studies have indicated that a prolonged fasting state leads to lower BP and, thus, to lower renal perfusion as well as lower UFR.[9] As shown by the equation, urine flow rate = excreted effective mOsm per minute/urine effective osmolarity in mOsm/l, UFR is determined by the number of effective osmoles in urine and the changes in urine effective osmolality.[10] Simply, if the decrease in UFR were the only variable, the impact of lower UFR on supersaturation would be exponential since it would raise Ca^{2+} and HPO_4 activity. If the excretion rates of these ions remain constant, the ionic product $CaHPO_4$ should increase fourfold for each halving of UFR.

In this study we assessed the alternative hypothesis that decreased UFR after 18 hours of water deprivation would result in increased renal reabsorption of Na^+ and Ca^{2+}. Therefore, there would be no increased risk of $CaHPO_4$ precipitate formation in normal healthy individuals.

MATERIALS AND METHODS

The St. Michael's Hospital Research Ethics Board approved the study protocols. Written consent was provided by subjects to use their data anonymously. A total of