Strategy to Control Catheter Encrustation With Citrated Drinks: A Randomized Crossover Study

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Abbreviations and Acronyms

pH_n = nucleation pH

pH_v = voided urine pH

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Purpose: Nucleation pH is the pH at which Ca and Mg come out of urine to form crystals. If the safety margin between voiding pH and nucleation pH could be increased, it would increase the possibility of an alternative to controlling the activity of urease producing bacteria as a strategy to control catheter encrustation.

Materials and Methods: We performed a 6-week randomized crossover study in 24 patients with catheter blockage who were randomly allocated to a specific sequence of 3 consecutive available treatments, including increased fluid intake, lemon juice and potassium citrate. Each patient received all available regimens. At the end of each week 24-hour urine samples were analyzed for voiding and nucleation pH, citrate, Ca and Mg.

Results: Mean ± SD nucleation pH increased from 7.45 ± 0.60 at baseline to 7.93 ± 0.50, 7.68 ± 0.64 and 7.96 ± 0.37 in the lemon juice, increased fluid intake and potassium citrate groups, respectively ($p < 0.0001$). Mean urinary citrate increased significantly ($p < 0.0001$), in particular due to lemon juice and potassium citrate effects. The association between treatment and Ca was weak ($p = 0.12$) while that of Mg was negative due to lemon ($p < 0.001$). Average increase in the safety margin (nucleation pH minus voiding pH) beyond baseline was 0.84 (95% CI 0.63–1.04), 0.57 (95% CI 0.37–0.78) and 0.41 (95% CI 0.20–0.61) for lemon juice, increased fluid intake and potassium citrate, respectively. A strong treatment effect on the safety margin was apparent even when controlling for study design ($p < 0.001$).

Conclusions: Increased fluid intake with lemon juice may be a simple, inexpensive, effective strategy to control catheter encrustation.

Key Words: urethra, urinary catheterization, hydrogen-ion concentration, potassium citrate, Proteus mirabilis

A common complication in the care of patients undergoing long-term indwelling catheterization is catheter encrustation.[1] This may lead to emergency referrals of patients in discomfort who are in urinary retention or incontinent of urine due to sudden catheter blockage.[2] The problem stems from infection by urease producing bacteria, particularly Proteus mirabilis. These organisms colonize the catheter, forming extensive biofilm communities.[3] Bacterial urease generates ammonia from urea, increasing the pH of urine and biofilm. As urine pH increases, crystals of Ca and Mg phosphates come out of solution. The pH at which this occurs is known as pH_n.[4] Thus, in patients with urease producing bacteria infection pH_v may increase above pH_n and crystallization can occur in urine and biofilm. Contin-

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ued development of this crystalline biofilm blocks the urine flow.[3] All available types of indwelling catheters are vulnerable[5] and currently no effective procedures are available for its control.[6]

Hedelin et al noted little encrustation in patients with mean urinary pH less than 6.8 and suggested this as the critical pH above which crystal formation occurs.[7] Choong et al reported that mean urine pH_n was 7.58 in patients with a blocked catheter but mean pH_v was 7.85, clearly explaining why encrustation occurred.[8] Subsequently in a prospective study Mathur et al found a significant positive correlation between pH_n and catheter life span ($p = 0.004$).[9] The higher the urinary pH_n and the greater the safety margin between pH_n and pH_v, the longer it took catheters to become blocked. Also, urine pH_n varied among individuals and among weeks in any single individual. If pH_n can be manipulated to increase the safety margin, there is a possible alternative to inhibiting the activity of urease producing bacteria as a strategy to control catheter encrustation.

In a study of healthy volunteers Suller et al found that simply by increasing fluid and citrate intake urine pH_n could be increased to values that are rarely achieved even in P. mirabilis infected urine.[10] Subsequent experiments in a laboratory model infected with P. mirabilis confirmed that when models were supplied with dilute citrate containing urine with pH_n greater than 8.3, crystalline biofilms did not form.[11] We determined whether increasing the fluid intake with citrated drinks would increase pH_n and the safety margin between pH_n and pH_v in patients infected with P. mirabilis who had recurrent catheter blockage.

MATERIALS AND METHODS

Study Participants

The study was performed in the BioMed Centre, Bristol Urological Institute, and approved by the local ethical committee. All patients had had a long-term indwelling catheter (urethral or suprapubic and hydrogel coated or silicone) for greater than 3 months and were known to have had greater than 3 episodes of catheter blockage less than 4 weeks in duration each. Only patients with positive urine cultures for P. mirabilis were included in the study. Patients needing antibiotics were excluded from analysis.

Specimen Analysis

Urine samples were analyzed for pH_v, pH_n, citrate, Ca and Mg. The pH_v of urine in each patient was measured upon sample collection using a glass electrode pH meter. Evaluation of pH_n was based on the method described by Choong et al.[4] Samples were centrifuged at 4,000 rpm for 5 minutes and maintained in a water jacketed chamber at 37C. Urinary pH was decreased to 5.0 by adding concentrated HCl. The sample was alkalinized in increments of 0.25 pH U up to pH 10 using 10 M NaOH solution. At each increment optical density was measured at 540 nm using a spectrophotometer. We determined pH_n from the resulting plot of pH against optical density. We defined pH_n by an abrupt change in the slope of the graph, showing an increase in turbidity caused by the precipitation of Ca and Mg containing salts. Plotting pH vs optical density produced 2 straight line segments intersecting at pH_n. Regression lines were calculated by the least squares method for these 2 portions of the graph and used to determine pH_n at the intersection. Ca^{2+} and Mg^{2+} were measured using atomic absorption spectroscopy. Citrate was measured using a citrate assay kit.

Study Design

The study was a randomized crossover design (fig. 1). In control week 1 baseline data were collected on routine fluid intake in each patient. Before week 2 patients were randomly assigned to a particular sequence of 3 experimental treatments, allowing a 1-week washout period at the routine fluid intake between each treatment. Thus, each patient was self-administered all 3 regimens in random order.

In study arm 1 patients were maintained on 1 l water, in addition to the routine intake. On study arm 2 they were started on 1 l lemon juice, in addition to the daily fluid intake. The lemon drink contained 60 ml concentrated PLJ lemon juice (Martlet, Wellingborough, United Kingdom) in 1 l water. In study arm 3 participants were given 1 l potassium citrate solution (6 gm/l) in addition to the routine fluid intake. During the washout week they returned to the baseline fluid intake. To assess compliance patients were provided with charts to document fluid intake and urine output. Participants were asked to collect a 24-hour urine sample on day 7 each week.

Statistical Analysis

For each urine sample pH_n minus pH_v was calculated and termed the safety margin. Descriptive data are shown as the mean ± SD or as the point estimate and 95% CI. ICCs were derived for pH_n, pH_v and the safety margin to assess

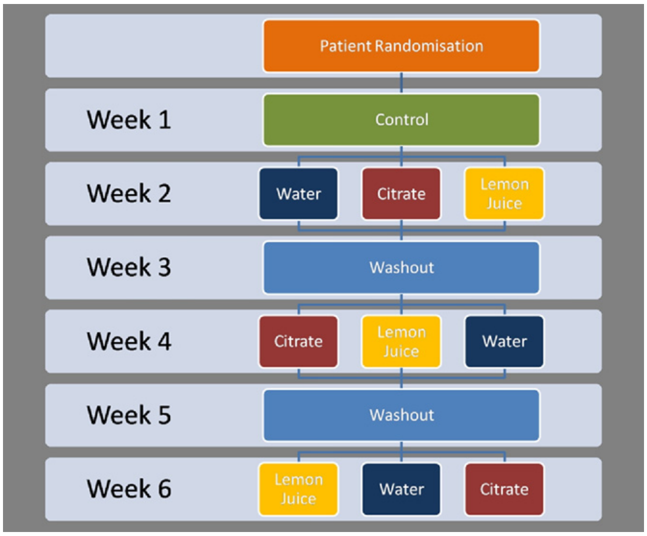

Figure 1. Study design