Excessive fluid intake as a novel cause of proteinuria

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We are currently conducting a longitudinal population cohort study in the community of Walkerton, Ontario, to determine health outcomes after the municipal water supply was contaminated with Escherichia coli O157:H7 and Campylobacter in 2000. We identified 100 adults who had proteinuria and polyuria but no medical history or medication use to explain their condition. Fifty-six of the 100 participants underwent both initial and confirmatory urine concentration tests, which showed that their urine osmolality could reach normal levels. We then instructed them to reduce their fluid intake to less than 2 L/d for 1 week. The proteinuria and polyuria were largely reversed by this manoeuvre. We do not know at this time whether the proteinuria associated with excessive fluid intake in these otherwise healthy people will affect their kidney function in the long term.

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Research letter

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Abstract

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We attempted to discern the cause of the unexplained proteinuria and polyuria. Of the 100 people, 63 agreed to confirmatory 24-hour urine collection to measure protein excretion, followed by a urine osmolality measurement after overnight water deprivation. The 24-hour confirmatory urine samples had a mean protein content of 0.43 g (standard deviation [SD] 0.21 g, 95% confidence interval [CI] 0.36–0.49 g), and the mean volume of urine was 3.7 L (SD 1.2 L, 95% CI 3.3–4.1 L). This group was similar to the overall cohort of 2253 adults in terms of age (mean 47 [range 15–72] and 47 [range 15–92] years, respectively), sex (68% and 61% women), history of hypertension (28.0% and 35.2%) and gastroenteritis (61.0% and 60.4%).

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not differ significantly between the 56 people who participated in the complete testing (39 who required only 1 test plus 17 who completed 2 tests) and the 44 people who did not participate in the complete testing.

The 56 participants were then asked to voluntarily reduce their total daily fluid intake to fewer than 8 large glasses (< 2.0 L/d) for 1 week, on the last day of which they provided another 24-hour urine sample. The mean urine volume following the voluntary water-reduction intervention decreased to 1.81 L in 24 hours (95% CI 1.54–2.07 L), and the amount of protein excreted decreased to a mean of 0.16 g in 24 hours (95% CI 0.12–0.20 g) (Table 2). The mean urine creatinine level did not change significantly from the baseline level before or after the intervention (Table 2). The relation between urine volume and protein excretion was similar for the 56 participants regardless of whether they had had symptoms of gastroenteritis at the time of the water contamination in 2000.

When asked about their fluid consumption, the 56 participants indicated that they were drinking large volumes of fluid because they perceived it to be a healthy lifestyle choice. The water contamination and resultant temporary switch to bottled water may have led some to assume a habit of overconsumption. However, most said that their overconsumption preceded the water contamination. Although our participants did not fit the classic description of the compulsive water drinker, their attenuated concentration response did.

Our unexpected finding of a 4.4% rate of proteinuria associated with polyuria in seemingly healthy people stemmed from observations that had been made during a community-based screening program. The reversible nature of the proteinuria and polyuria after reduction of the total fluid intake to less than 2 L/d makes any explanation other than voluntary excessive fluid intake unlikely. In a study of the effect of water loading on urinary albumin excretion in 18 healthy volunteers, Viberti and colleagues* noted that water loading was associated with a short-lived but significant increase in urine albumin levels. We did not characterize the proteinuria, nor do we know at this time whether the reversible proteinuria associated with large fluid intake in these otherwise healthy people could affect their kidney function in the long term.7–11 If the proteinuria was largely tubular in origin, owing to tubular washout, rather than glomerular in origin, one might pre-

| Test                                      | No. of participants | Osmolality, mOsm/kg |
|-------------------------------------------|---------------------|---------------------|
| Overnight water deprivation (n = 63)       |                     |                     |
| Concentrated urine                         | 39                  | 451–1069            |
| Unconcentrated urine                       | 24                  | 59–450              |

*Seventeen of the 24 participants who initially had unconcentrated urine (osmolality ≤ 450 mOsm/kg) agreed to undergo a repeat overnight water-deprivation test 1 week after the first, followed by an 8-hour observed water-deprivation test. The observed water-deprivation test ended as soon as patients demonstrated concentrated urine; the number of participants achieving this at each point is shown.

| Test                                      | Time of measurement; mean value (95% confidence interval) |
|-------------------------------------------|----------------------------------------------------------|
| Measurement                               | At baseline | Before intervention | After intervention |
| Urine volume, L                           | 3.69 (3.44–3.95) | 3.35 (2.89–3.82) | 1.81 (1.54–2.07) |
| Protein level, g                          | 0.41 (0.36–0.45) | 0.38 (0.31–0.46) | 0.16 (0.12–0.20) |
| Creatinine level, mmol                    | 10.61 (10.08–11.14) | 12.04 (11.14–12.94) | 12.50 (10.56–14.44) |
| Protein:creatinine ratio                  | 0.04 (0.04–0.04) | 0.03 (0.03–0.04) | 0.02 (0.01–0.02) |
sume that progressive kidney injury would be less likely.⁹ Until such data are available from our longitudinal study, it may be advisable to discourage otherwise healthy people from consuming large volumes of fluid.

This article has been peer reviewed.

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