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TO FIND THE PATTERN OF BLADDER SENSATION IN HEALTHY VOLUNTEERS USING A WATER LOAD PROTOCOL

Hypothesis / aims of study

A forced diuresis protocol has been developed to evaluate bladder sensation during filling. The original protocol required consumption of 250-300 ml water every 15 minutes to achieve a steady diuresis rate (1). In recent work, the reliability of this protocol to produce a stable and predictable diuresis was proven (2). Variability is reduced with a water load of 300ml/15 minutes instead of 250ml, and any test where the variation in diuresis rate between the two test cycles exceeds 4.5 ml/min should be rejected (2). This study was designed to calculate diuresis rates, confirm test-retest reliability and to compare graphically bladder sensation curves.

Study design, materials and methods

This study was the second of four stages of an observational and experimental study. Twenty-four volunteers were asked to undergo a previously designed diuresis and bladder sensation protocol (1). The protocol allowed the visual recording of bladder sensation by the patient marking sensations on a 10 point visual analogue scale every 5 minutes while drinking an excess of water continually for the duration of the test.

Following ethical approval, informed consent was obtained from participants before obtaining serum to measure glomerular filtration rate to exclude undiagnosed kidney disease. A biomedical impedance test was performed prior to the diuresis test to determine the participant's fluid status. The volume drunk during the test was 300 ml/15 minutes.

Participants were asked to drink 250 ml of water every 15 minutes 1 hour before the test. No verbal cues were given other than to concentrate on the sensation in their bladder and to mark on the data-logging sheet the intensity of this sensation. When they reached the strongest sensation they could bear they were asked to hold on for up to 5 minutes and to remember this as their maximum sensation, marking it as a 10 on their sheet. They were then asked to void and this volume measured (V1). Immediately post void they recorded this as the minimal sensation.

Participants continued to drink and recorded bladder sensation for another entire filling cycle, where the voided volume was measured (V2) and for at least 30 minutes of the next cycle (voided volume V3). The first cycle allowed participants to fix the maximum and minimum sensations in their minds; cycle two was the core part of the experiment where analyses were done, and cycle three was used to confirm a steady diuresis rate has been achieved during cycles two and three (i.e. V2/t2 = V3/t3).

This test was performed twice within 14 days apart. Data were presented as median (range) and compared by Wilcoxon signed rank test or Mann Whitney U test for paired and unpaired data.

Table 1: Voids and diuresis rate at each test.

Factor	Test 1 (n=16)	Test 2 (n=16)	p value#
Void 1 (ml) Median (range)	763 (437-1052)	820 (474-1538)	0.109
Void 2 (ml) Median (range)	788 (400-1136)	796 (502-1489)	0.266
*p value**	*0.776*	*0.756*	
Diuresis rate V2 (ml/min) Median (range)	12.33 (8.43-17.38)	14.40 (9.55-18.75)	0.056
Diuresis rate V3 (ml/min) Median (range)	12.01 (8.30-20.86)	13.28 (7.66-17.80)	0.326
*p value**	*0.255*	*0.215*	

*p: comparison within each test #p: comparison of Test 1 vs Test

Results

Twenty-five healthy volunteers were recruited. 24 underwent the forced diuresis protocol once and 21 twice. Three participants withdrew after first test: one due to medical reasons and two unknown.

Median age was 28 years (19-47years), median BMI 26.3 Kg/m^2 (19.0-39.0 kg/m^2). 21 were female participant and four male. All participants had a glomerular filtration rate >60ml/min and a normal sodium level.

Participants with a difference diuresis rate >4.5ml/min were excluded leaving 16 participants for analysis. In the first test there was no difference in the median voids: first void (V1) 763ml (437-1052ml) and second void (V2) 788ml (400-1136ml) (p=0.776).

Similarly, there was no significant difference in the median diuresis rate between V2 12.33ml/min (8.43–17.38ml/min) and V3 12.01ml/min (8.30-20.86ml/min) (p=0.255). The median difference in diuresis rate between cycle 2 and cycle 3 was 0.725ml/min (0.08-2.88ml/min) (Table 1)

During the second test, there was no difference in the median voids within cycles. The median for V1 is 820ml (474-1538ml) and for V2 is 796ml (502-1489ml) (p=0.756). Equally, the median diuresis rate did not differ between V2 14.40 ml/min (9.55-18.75ml/min) and V3 13.28ml/min (7.66-17.80ml/min) (p=0.215) and the difference in rate between both cycles was 0.91 ml/min (0.08-3.46ml/min) (Table 1)

Importantly, there was no significant difference in the median voids between tests (V1 p=0.109 and V2 p=0.266). Likewise, there was also no change in the diuresis rate between tests with cycle 2 (p=0.056) and cycle 3 (p=0.326) (Table 1)

Area under the curve was calculated from bladder sensation curves and was reproducible: median 404.96 [247.28-557.14] in test 1 vs 418.63 [262.50-596.02] in test 2 (p=0.234).

Interpretation of results

There was no difference in the median voids or diuresis rate between tests and within cycles. These findings allow us to confirm our initial hypothesis from stage 1 (1). By excluding patients with a large difference in the diuresis rate, we are reducing the variability between tests and within cycles. We can now confirm that the upper limit of variability of the diuresis rate between cycles should not be >4.5ml/min to ensure reliability and reproducibility of the diuresis protocol.

Concluding message

The water load protocol achieves a constant high diuresis with rapid, non-invasive bladder filling. The data provide further evidence of reproducibility and provide proof of concept that area under the curve is a valid analysis.

References

1. Medina H, Tincello D. Test-retest and reliability analysis of a water load protocol as a tool to achieve a fixed diuresis rate for investigation into bladder sensation. (Unpublished)
2. Bakali E, Hong J, Gillespie J, Tincello D. Saccharin increases perception of bladder filling in a forced diuresis experiment. Neurourol Urodyn :n/a-n/a.

Disclosures

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