228

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EFFECTS OF HIGH-SALT DIET AND POLYURIA ON THE BLADDER

Hypothesis / aims of study

The impact of polyuria on bladder function has been studied in diabetic models, but has not been investigated in a context without hyperglycemia. We have previously demonstrated that the Dahl salt-sensitive (Dahl/SS) rat, a model with hypertension, shows signs of bladder overactivity compared to control rats. Our aim was to determine the effect of a high salt intake in this model on bladder function, and the associated polyuria.

Study design, materials and methods

Dahl/SS rats received either a 4% NaCl (high-salt) diet (n=5), or a normal diet (n=4) for 6 weeks. Water intake and micturition patterns over a 24-hour period were recorded in metabolic chambers. Blood pressure measurements were also recorded. After 6 weeks of the diet, these measurements were repeated. Conscious cystometry was then carried out. Bladders were collected for measurements of contractile force using organ bath experiments, collagen quantification using the Masson's trichrome stain and H&E staining for qualitative comparisons. Paired *t*-tests were used to compare changes between week 0 and week 6 within each group. Unpaired *t*-tests were used for comparisons between normal and 4% NaCl diet for cystometry, organ bath and collagen quantification. $p<0.05$ was considered significant.

Results

Systolic blood pressure significantly increased after 6 weeks with the high-salt diet but not in the rats fed a normal diet (Table 1). Similar water 24-hour intake, as well as micturition patterns were observed initially in all animals. After 6 weeks, the control rats had unchanged measurements from the start of the study. However, rats on the high-salt diet had significantly increased water intake, increased total urine, and higher volume of urine per micturition.

Table 1. Blood pressure and metabolic chamber measurement 6 weeks after normal or 4% NaCl diet. Results show mean values ± SEM.

Parameter	Normal		4% NaCl	
	Week 0	Week 6	Week 0	Week 6
Systolic BP (mmHg)	171.5 ± 6.9	184.4 ± 13.2	169.8 ± 3.9	212.8 ± 6.38**
Water (mL)	18.5 ± 4.3	16.3 ± 3.4	13.5 ± 1.2	47.3 ± 3.9***
Urine (mL)	7.3 ± 1.8	3.1 ± 1.3*	6.9 ± 0.8	25.3 ± 3.3**
Volume/Micturition (mL)	0.29 ± 0.02	0.23 ± 0.02	0.34 ± 0.03	0.78 ± 0.10**

*$p<0.05$; **$p<0.01$; ***$p<0.001$. Paired *t*-tests comparing Week 0 vs. Week 6 in each group.

Cystometry showed significantly higher intercontraction intervals, bladder capacity, micturition volumes and bladder compliance in rats on high-salt diet compared control (Table 2).

Table 2. Selected cystometry values and bladder weights at 6 weeks of normal or 4% NaCl diet. Results show mean values ± SEM.

Parameter	ICI (s)	Bcap (mL)	MV (mL)	Bcom (mL/cmH_2O)	Bladder Weight (g)
Normal	318.8 ± 28.5	0.89 ± 0.08	0.97 ± 0.11	0.03 ± 0.00	248.0 ± 29.3
4% NaCl	656.2 ± 67.6**	1.82 ± 0.19**	2.06 ± 0.26**	0.06 ± 0.01*	285.6 ± 20.7

*$p<0.05$; **$p<0.01$. ICI, intercontraction interval; Bcap, bladder capacity, MV, micturition volume; Bcom, bladder compliance.

No difference in detrusor contractility in organ bath studies was observed between the two groups (Fig. 1).

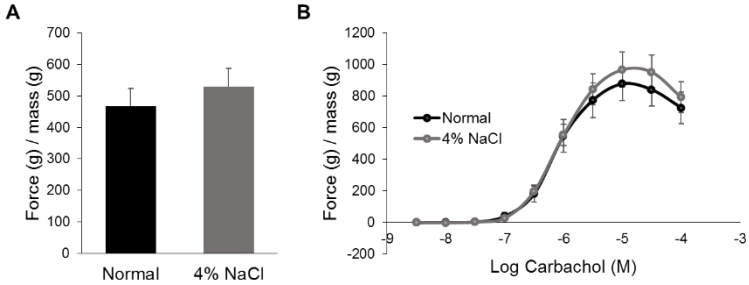

Figure 1. Contractile responses of detrusor strips from rats fed a normal and 4% NaCl diet. A: Response to KCl 60 Mm. B: Dose-response curve to carbachol. Results are expressed as mean values ± SEM.

H&E staining showed an impaired integrity in bladder of animals fed a 4% NaCl diet compared to those fed a normal diet. The animals in the high-salt diet group also had thinner urothelium and detrusor layers (Fig. 2 A-B). Collagen content was significantly increased in the lamina propria of rats fed a high-salt diet, compared to those fed a normal diet ($p<0.05$) (Fig. 2 C-D).

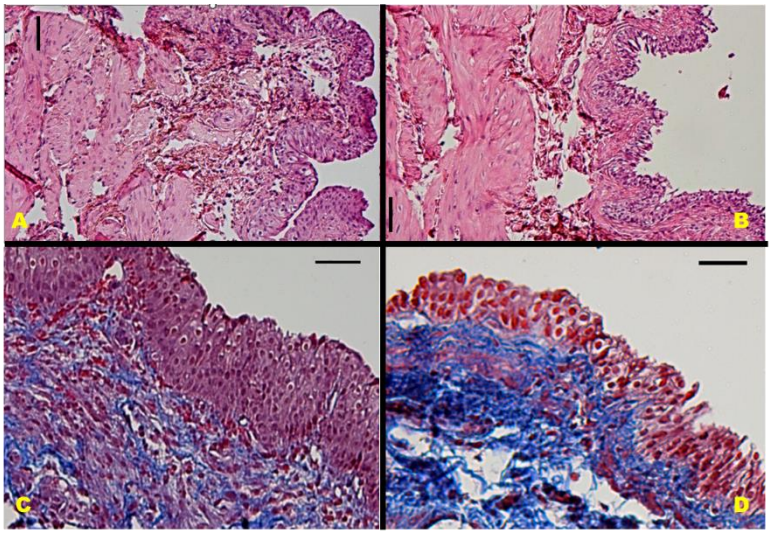

Figure 2. H&E stain of Dahl rats with normal (A) and 4% NaCl (B) diet; scale bar = 100µm. Masson trichrome stain of Dahl rats with normal (C) and 4% NaCl (D) diet; scale bar = 50µm.

Interpretation of results

The high-salt diet led to higher blood pressures in an animal model of hypertension. As a result of increased salt intake, the animals developed polydipsia and polyuria. This disrupted the morphology of the bladder and led to an increase in bladder capacity. In addition, there was an increase in collagen content in the lamina propria due to overstretching of the bladder. While this is an immediate response of the bladder to constant stretch, it may take longer for the detrusor to be affected by changes in collagen content, explaining our organ bath findings.

Concluding message

The polydipsia and polyuria observed in the high-salt diet group led to an increase in bladder capacity in this group. Polyuria in a context of hypertension may lead to changes in bladder morphology and function. These findings may clarify the clinical impact of polyuria on voiding function, specifically in patients of metabolic syndrome.

Disclosures

Funding: FRQS **Clinical Trial:** No **Subjects:** ANIMAL **Species:** Rat **Ethics Committee:** McGill University Animal Ethics Committee