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Response of urinary sodium excretion to elevated intravesical pressure

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Summary. This experimental study was designed to investigate the possibility of an interaction between elevated intravesical pressure and urinary sodium excretion. Fourteen male New Zealand rabbits were used. After performing a ureterocutaneous diversion, urinary sodium excretion was measured in two situations: with the bladder empty and with the bladder overdistended and an intravesical pressure of 60 cm H_2O. There was a significant decrease in urinary sodium excretion at an elevated intravesical pressure. The urinary sodium excretion returned to normal after relief of the pressure. The results suggest the existence of a neurogenic pathway activated by the elevated intravesical pressure.

Key words: Elevated intravesical pressure – Urinary sodium excretion – Vesicorenal reflexes

Regulation of urinary sodium excretion is not completely understood. Many factors can affect glomerular and renal tubular function and, as a consequence, sodium excretion.

Both anatomical factors and functional derangements can cause obstruction to the outflow of urine from the bladder resulting in elevation of intravesical pressure and, in the case of vesico-ureteric reflux, in elevation of the pressure within the ureter and renal pelvis. Whether elevated intravesical pressure without vesico-ureteric reflux can affect renal function is still controversial [5–7, 10–13, 15, 16].

The aim of the present experimental study was to evaluate the response of urinary sodium excretion to elevated intravesical pressure when there is no transmission of the pressure to the kidneys and the urine flows freely.

Materials and methods

Fourteen male New Zealand white rabbits weighing 2.3–3.5 kg were used for the experiments. A supravesical ureterocutaneous urinary diversion was performed on the animals to disconnect the bladder

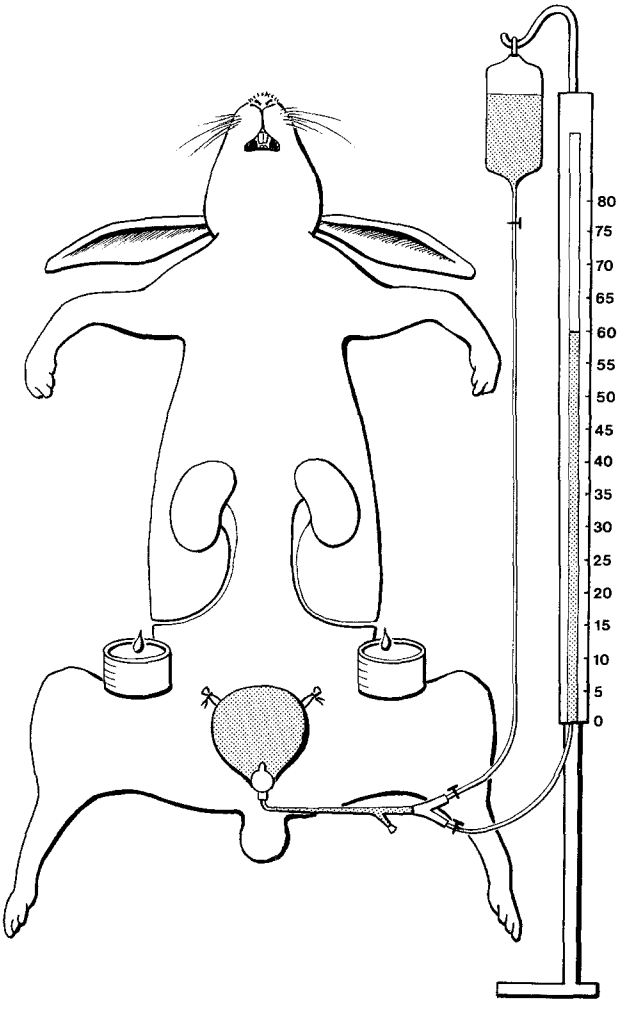

Fig. 1. Schematic drawing of the experimental design

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Table 1. Urinary sodium excretion with intravesical pressure 0 ($NaUIP_0$) and 60 cm H_2O ($NaUIP_{60}$)

Group 1				Group 2			
Rabbit no.	$NaUIP_0$ (meq/h)	$NaUIP_{60}$ (meq/h)	Change (%)	Rabbit no.	$NaUIP_{60}$ (meq/h)	$NaUIP_0$ (meq/h)	Change (%)
1	1.87	1.32	−29.5	1	2.96	3.32	+10.8
2	2.06	1.65	−19.9	2	1.87	2.47	+24.2
3	1.50	1.12	−25.3	3	2.67	3.06	+12.7
4	0.89	0.83	− 6.7	4	3.50	4.20	+16.6
5	1.20	0.97	−19.1	5	1.60	1.90	+15.0

Group 3					
Rabbit no.	$NaUIP_0$ (meq/h)	$NaUIP_{60}$ (meq/h)	Change (%)	$NaUIP_0$ (meq/h)	Change (%)
1	2.65	1.96	−26.0	2.72	+27.9
2	1.86	1.40	−24.7	2.05	+31.7
3	3.46	2.82	−18.5	3.25	+13.2
4	4.61	3.87	−16.0	4.95	+21.8

from the upper urinary tract and to ensure free urine flow. The design of the experiment is represented schematically in Fig. 1. The animals were anaesthetized with an intravenous injection of thiopental sodium, 10 mg/kg body weight (Pentothal, Abbott, North Chicago, ILL.) into the dorsal vein of the ear. Through two small lateral incisions the ureters were exposed and divided; the distal end was ligated and the proximal ureter brought to the skin surface, a No. 21 silicon catheter being inserted and connected to a 20-ml bottle for urine collection. The bladder was catheterized with a 6 Ch Foley catheter which was firmly attached to the distal urethra so as to avoid leakage. Forty-eight hours after the operation, and after the animals had been fasted for 12 h, the bladder catheter was connected to a bottle containing sterile water for instillation to enable differing intravesical volumes and pressures to be measured. The time lapse of 48 h after the operation was to avoid any effects from the anaesthesia. After the operation the rabbits were randomly divided into three groups. In the first group (5 rabbits) urinary sodium excretion was measured initially with the bladder empty and then with the bladder full and an intravesical pressure of 60 cm H_2O. Each phase had a duration of 3 h. In the second group (5 rabbits) the experimental protocol was reversed and urinary sodium was measured initially with the bladder full and an intravesical pressure of 60 cm H_2O and then with the bladder empty. A duration of 3 h for each period was necessary to collect an adequate amount of the excreted urine. In the third group (4 rabbits) urinary sodium excretion was measured initially with the bladder empty, then with the bladder full and an intravesical pressure of 60 cm H_2O, and finally with the bladder empty again.

Statistical analysis on sodium excretion was done on absolute values using Student's *t*-test for paired data in each group separately. A probability level of <0.05 was considered significant.

Results

An effective increase in bladder pressure was achieved in all cases. This varied from 54 to 66 cm H_2O (mean value 60 H_2O). Minimal leakage around the catheter resulted in a transient drop in pressure that was corrected with further infusion. The results are shown in Table 1, and represented schematically in Fig. 2. A significant decrease in sodium excretion was observed in all cases when the bladder was overdistended. In the first group this varied between 6.7% and 29.5% ($P<0.05$). In the second group, in which the reverse experiment was performed, a significant increase in sodium excretion followed the release of bladder pressure ($P<0.01$). This varied between 10% and 24.2%. In the third group it was found that: (1) there was significant reduction in sodium excretion when the bladder was overdistended ($P<0.01$); (2) release of bladder pressure was always followed by a return of sodium excretion values to their initial levels; (3) there was no significant difference in sodium excretion between control and recovery periods.

Significantly lower values were observed in animals 3, 4 and 5 in the first group, animals 2 and 5 in the second group and animal 2 in the third group. Because the only stimulation between the two phases of the experiment was the elevation in intravesical pressure and the response was identical, these animals were not excluded from the study. For the same reason the results were analysed as paired data.

It must be noted that urine output also changed in each phase of the experiment. In every case urinary sodium excretion was measured on a unit/time basis and not on a unit/volume basis.

Discussion

Overdistension of the urinary bladder leads to stretching of the trigone and an increase in the resistance to flow through the intravesical ureter. If the overdistension is allowed to continue, trigone hypertrophy will occur and ureteral stasis and increased back-pressure on the kidney will result [20]. Whether this is the only mechanism through which increased intravesical pressure can affect renal function is still controversial. Lucas was the first to

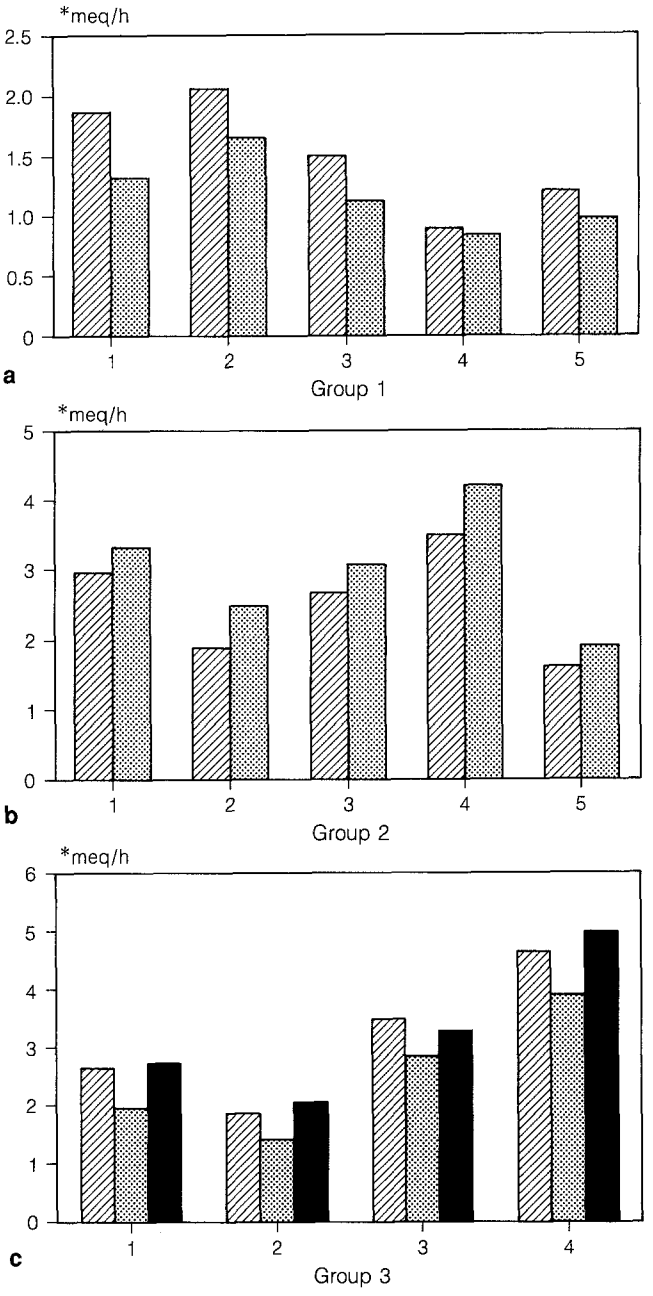

Fig. 2. Urinary sodium excretion (meq/h) with intravesical pressure 0 and 60 cm H_2O (▨ NaUIPO*; ▩ NaUIP60*; ■ NaUIPrec*)

suggest the possibility of a neurogenic interaction between the urinary bladder and the kidneys [11]. Pflaumer reported a decrease in urinary output upon bladder filling [15]. Boeminghaus confirmed Pflaumer's findings and introduced the term "vesicorenal reflex" [5]. This phenomenon has been confirmed by several investigators [6, 10, 12, 16] and contested by a few [7, 13].

In this experimental study there was no mechanical connection between bladder and kidneys and the urine flowed freely. Consequently, we postulate activation of a vesicorenal reflex by a rise in intravesical pressure as a mechanism for the decrease in urinary sodium excretion in response to elevated bladder pressure. Afferent baroreceptors in the bladder wall convey impulses via the hypogastric nerves to activate the sympathetic renal innervation. Whether the neural effect is direct, i.e. an effect of a neurotransmitter, or indirect, involving the renin-angiotensin, prostaglandin, kallikrein or other humoral system, cannot to determined from this study. The precise pathways of neurogenic transmission as well as possible hormonal factors involved in this reflex have yet to be determined.

Significantly lower values of urinary sodium were observed with an intravesical pressure of 0 in some animals (animals 3, 4 and 5 in the first group, 2 and 5 in the second and 2 in the third). This also resulted in significant differences in mean values of urinary sodium excretion with an empty bladder between the first group and the other two groups. The following factors are most probably involved in these differences. Even though preliminary experiments were performed to standardize a technique, the operation may have affected each animal differently. The possibility of a complication and especially of an infection cannot be ruled out. The food and the water that the animals were allowed to eat and drink for 24 h after the operation may also have contributed to the observed differences. These differences were not considered a flaw in the study. The animals with the low values were included in the final analysis because even though the values were low the response to elevated bladder pressure was identical so that in the other animals. Moreover the study was designed to determine the response of urinary sodium excretion to elevated intravesical pressure and not the normal values of sodium excretion in rabbits. Because the process was the same (bladder filling) and the time interval short, we postulate that the only factor responsible for this natriuretic response is the elevated intravesical pressure – as the reverse experiment and the double test in the third group indicate.

There are observations suggesting a direct neurogenic control of renal tubular sodium reabsorption. Slick and colleagues have found that increases in renal sympathetic nerve activity have a direct effect on tubular sodium reabsorption in situations of low cardiac output and sodium retention [18, 19]. It has also been found that renal sympathetic blockade reverses the antinatriuresis in dogs with chronic heart failure with only minimal changes in renal haemodynamics [2, 3]. Barajas and Müller have demonstrated adrenergic nerve terminals in direct contact with tubular basement membranes of proximal and distal tubular epithelial cells of monkey and rat kidney cortex [1, 14]. La Grange and colleagues identified a level of direct electrical renal nerve stimulation that increased renal venous renin concentration without affecting glomerular filtration rate or renal blood flow. They also observed a 23%–26% decrease in urinary sodium excretion while the filtered sodium load remained constant [9]. These observations suggest a neurogenic control of renal tubular sodium reabsorption.

The fact that a rise in bladder pressure causes a definite increase in arterial pressure has been proved by several investigators [4, 8, 17]. This response may be mediated through the decrease of urinary sodium excretion and can contribute to the hypertension often observed during endourological procedures. For the same reason the acute

retention of urine may be dangerous, especially in patients with renal or heart failure.

Our experimental study was not designed to take into account participation of hormonal factors. As a consequence, any possible hormonal involvement cannot be ruled out. In a relative study Schick and Tanagho have suggested that humoral and nervous factors are involved in vesicorenal reflexes [16].

The observation that elevated intravesical pressure can decrease glomerular filtration rate [12] suggests another mechanism which can result in decrease of urinary sodium excretion. Which of these mechanisms is the more important has yet to be determined.

In conclusion, this experimental study suggests an interaction between elevated pressure and urinary sodium excretion. Specifically an increased intravesical pressure can decrease urinary sodium excretion. Because there were no mechanical connections between bladder and kidneys it appears that the effect is caused by a neurogenic pathway, the details of which have yet to be determined.

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