

## EFFECTS OF TAMSULOSIN ON THE URINARY BLADDER FUNCTION IN RATS WITH PARTIAL OUTLET OBSTRUCTION

### Hypothesis / aims of study

Overactive bladder (OAB) associated with bladder outlet obstruction (BOO) is common in elderly men. However, its exact etiology remains unclear. Tamsulosin is an  $\alpha_1$ -adrenoceptor blocker used in the treatment of symptomatic benign prostatic hyperplasia worldwide, and known to be effective for OAB as well as obstructive symptoms. In this study, we investigated the effects of tamsulosin on the urinary bladder function in conscious rats with partial BOO using a frequency/volume analysis and cystometry.

### Study design, materials and methods

Fifty female SD rats weighing 200-250 gm were used. As a BOO group, partial bladder outlet obstruction was constructed by a ligature of the urethra under laparotomy in 25 rats, and the ligature was removed for the analyses in 4 weeks. As a control group, a sham operation was performed in 25 rats. In the both groups, saline or tamsulosin (2, 4, 8, and 16  $\mu\text{g}/\text{h}/\text{kg}$ ) (n=5, each) was administered subcutaneously using a mini-osmotic pump (Alza, USA). The rat was put into a metabolic cage (Nalge, Italy) connected with PC to record 2-day voiding frequency/volume pattern. The rat had free access to food and water, and was subject to 12/12-hour dark/light photo-cycle. After the frequency/volume analysis, a PE50 polyethylene catheter was inserted into the bladder dome in the 5 rats with 8  $\mu\text{g}/\text{h}/\text{kg}$  of the tamsulosin administration under the anesthesia. Two days later, filling-cystometry was carried out in awake condition.

### Results

Table1: Micturition characteristics of the rats after tamsulosin administrations

		Urine vol. (ml/day)	Frequency (/day)	vol./micturition (ml)
Control group (n=5, each)				
Saline		14.1 $\pm$ 4.2	26.5 $\pm$ 2.2	0.5 $\pm$ 0.1
Tamsulosin	2 $\mu\text{g}/\text{h}/\text{kg}$	15.3 $\pm$ 5.4	23.7 $\pm$ 2.0	0.6 $\pm$ 0.2
	4	15.6 $\pm$ 1.2	23.0 $\pm$ 3.0	0.7 $\pm$ 0.0
	8	19.6 $\pm$ 6.2	18.0 $\pm$ 1.2 *	1.1 $\pm$ 0.3 *
	16	16.3 $\pm$ 1.5	17.5 $\pm$ 2.1*	0.9 $\pm$ 0.0 *
BOO group (n=5, each)				
Saline		21.2 $\pm$ 2.2	25.7 $\pm$ 1.6	0.7 $\pm$ 0.4
Tamsulosin	2 $\mu\text{g}/\text{h}/\text{kg}$	22.4 $\pm$ 3.2	27.5 $\pm$ 2.3	0.9 $\pm$ 0.4
	4	23.4 $\pm$ 4.1	21.3 $\pm$ 4.1	1.1 $\pm$ 0.3
	8	24.4 $\pm$ 3.4	14.3 $\pm$ 3.2 **	1.7 $\pm$ 0.4 **
	16	26.9 $\pm$ 4.4	12.5 $\pm$ 3.8 **	2.1 $\pm$ 0.6 **

\*  $p \leq 0.05$ ; \*\*  $p \leq 0.01$

Table2: Cystometric analysis of the rats after 8  $\mu\text{g}/\text{h}/\text{kg}$  of tamsulosin administration

	Bladder capacity (ml)	Voided vol. (ml)	Residual (ml)	Pressure at void (mmHg)
Control group (n=5)				
Saline	0.7 $\pm$ 0.1	0.6 $\pm$ 0.2	0.1 $\pm$ 0.0	25.4 $\pm$ 1.7
Tamsulosin	1.0 $\pm$ 0.2 **	0.9 $\pm$ 0.2**	0.1 $\pm$ 0.1	23.2 $\pm$ 2.2
BOO group (n=5)				
Saline	2.6 $\pm$ 0.6	2.0 $\pm$ 0.5	0.4 $\pm$ 0.1	24.3 $\pm$ 1.1
Tamsulosin	3.1 $\pm$ 0.4 *	2.5 $\pm$ 0.4 **	0.5 $\pm$ 0.2 *	19.6 $\pm$ 1.7 *

\*  $p \leq 0.05$ ; \*\*  $p \leq 0.01$

### **Interpretation of results**

After 8 and 16  $\mu\text{g}/\text{h}/\text{kg}$  of the tamsulosin administrations, the urinary frequency significantly decreased in the both control and BOO groups. However, a more prominent change was noticed in the BOO group (44% decrease at 8 $\mu\text{g}/\text{h}/\text{kg}$ , and 51% at 16 $\mu\text{g}/\text{h}/\text{kg}$ ,  $p<0.01$ , both), compared with the control group (32% decrease at 8 $\mu\text{g}/\text{h}/\text{kg}$ , and 34% at 16 $\mu\text{g}/\text{h}/\text{kg}$ ,  $p<0.05$ , both). Similarly, voided volume /micturition significantly increased after the 8,16  $\mu\text{g}/\text{h}/\text{kg}$  administrations in the both groups, and more gain was observed in the BOO group (143% increase at 8 $\mu\text{g}/\text{h}/\text{kg}$ , and 200% at 16 $\mu\text{g}/\text{h}/\text{kg}$ ,  $p<0.01$ , both) than in the control group (120% increase at 8 $\mu\text{g}/\text{h}/\text{kg}$ , and 80% at 16 $\mu\text{g}/\text{h}/\text{kg}$ ,  $p<0.05$ , both). Although the cystometric analysis demonstrated the similar trends in changes of the bladder capacity and voided volume, it revealed significant increase and decrease of the residual volume and pressure at void in the BOO group, respectively.

### **Concluding message**

The results suggest that  $\alpha_1$ -adrenoceptors play a significant role in regulating the bladder function in both the normal and outlet-obstructive conditions. It is likely that BOO enhances the importance of these receptors, and an  $\alpha_1$ -blocker; tamsulosin is effective for OAB symptoms associated with BOO.