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FUNCTION OF THE LOWER URINARY TRACT IN MICE LACKING A1D-ADRENOCEPTOR

Hypothesis / aims of study

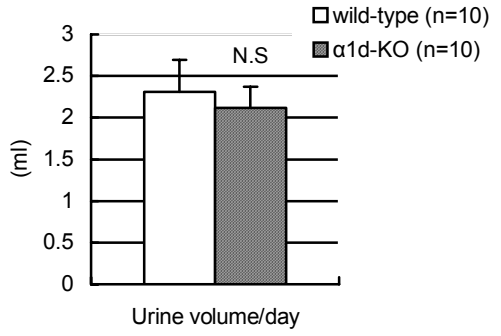
α_1 -adrenoceptor blockers are well known to relieve storage symptoms as well as voiding symptoms in elderly men. However, its exact pharmacological mechanism remains unclear. Recently, several investigations have suggested that an α_{1d} -adrenoceptor subtype plays a significant role in regulating the detrusor contractility. In this study, we investigated the function of the lower urinary tract in α_{1d}-adrenoceptor knockout (α_{1d}-KO) and its wild-type mice using frequency/volume analysis and filling-cystometry.

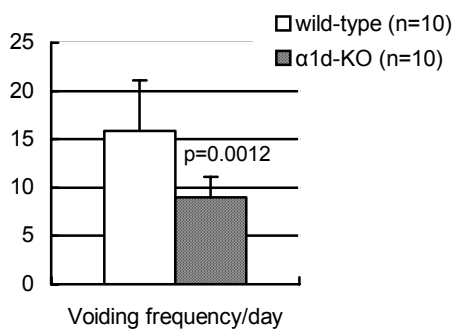
Study design, materials and methods

Twelve weeks of age female α_{1d}-KO (n=10, weighing 23.6±0.5 gm) and its wild-type mice (n=10, weighing 24.3±0.9 gm) were used (J Clin Invest 109: 765, 2002). The mouse was put into a metabolic cage connected with digital scale and PC. After being acclimatized for 2 days in the cage, a 48-hour voiding frequency/volume pattern was recorded. The mouse 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 α_{1d}-KO (n=4) and its wild-type mice (n=4) under the anesthesia. Two days later, filling-cystometry was performed in awake condition. Histological investigation of the bladder and urethra removed was carried out.

Results

Figure 1: 48-hour frequency/volume analysis in the wild-type and α_{1d}-KO mice.





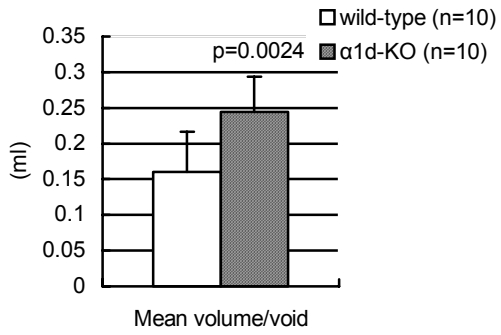


Table 1: Cystometric analysis in the wild-type and α_{1d} -KO mice.

	Bladder capacity (ml)	Voided volume (ml)	Residual volume (ml)	Maximum pressure at void (mmHg)
wild-type (n=4)	0.15±0.01	0.13±0.01	0.02±0.01	34.9±1.6
α_{1d}-KO (n=4)	0.21±0.01**	0.19±0.02*	0.02±0.01	33.5±1.5

* p□0.01, ** p□0.001

Interpretation of results

Voiding frequency/day in the α_{1d} -KO mice was 9.0±2.1, significantly lower than 15.9±5.2 in the wild-type mice (p=0.0012). Mean volume/void in the α_{1d} -KO mice (0.24±0.02 ml) was significantly larger, compared with 0.16±0.03 ml in the wild-type mice (p=0.0024). Similarly, the cystometric analysis demonstrated larger bladder capacity (140%, p<0.001) and voided volume (146%, p<0.01) in the α_{1d} -KO mice, compared with those in the wild-type mice. No significant difference in the residual volume and maximum pressure at void was observed between the two groups. No apparent difference of the histological structure in the bladder and urethra was identified.

Concluding message

The results suggest that the α_{1d}-adrenoceptor subtype plays an important role in regulating the bladder function. It is likely that α_1-blockers having a significant affinity for α_{1d}-adrenoceptor, such as naftopidil and tamsulosin are effective for overactive bladder symptoms associated with benign prostatic obstruction.