Alpha1D-Adrenergic Antagonists Inhibits TRPM8 Receptor Related Cold Stress-Induced Detrusor Overactivity in Ovariectomized Rats

Introduction and Objective: Lower urinary tract symptoms (LUTS) of postmenopausal women are developed with cold stress including a sudden drop of temperature or serious cold sensation. However, the mechanisms are not well known. We determined if alpha1D-adrenergic receptor antagonists inhibited the cold stress-induced detrusor overactivity in ovariectomized rats, and the cold responses were related with TRPM8 receptors expressing on skin.
Materials and Methods: Five weeks prior to cystometric investigation, 12 female Sprague-Dawley rats (30W, SD) were received bilateral ovariectomy (OVX), and then divided into saline-administration and naftopidil-administration groups (n=6 in each). Six SD rats were received sham operation. The cystometric investigation was performed in conscious and free-moving condition. They were placed at room temperature (28±2ºC). The ovariectomized rats were intravenously administrated with 1mg/kg naftopidil or saline, and then transferred to low temperature (4±2ºC). During the cystometric investigations, their micturition parameters were recorded. After the cystometric investigation, expression level of TRPM8 mRNA of the lump skin was measured.
Results: In room temperature, voiding interval (VI) and bladder capacity (BC) of the ovariectomized rats were significantly lower than these of the sham rats (Table 1). The VI and BP of the sham and saline-administrated OVX rats transferred into low temperature decreased. However, the VI and BC of naftopidil-administrated OVX rats were not decreased, and the both values were significantly higher than those of the saline-administrated OVX rats (Table 1). The TRPM8 mRNA expression level of the ovariectomized rats (2.36±0.61) was significantly higher than that of the sham operated rats (0.83±0.12, P<0.01).
Conclusion: The VI and BC of the ovariectomized rats significantly decreased under room temperature condition. The TRPM8 mRNA expression level of the ovariectomized rats significantly increased. Alpha 1D- adrenergic receptor antagonists partially inhibited the TRPM8 related cold stress-induced detrusor overactivity.

Table 1. Voiding interval and bladder capacity in each group and temperature condition.

	Room temperature	Low temperature
Voiding Interval (min)		
Sham	4.86±0.54	2.97±0.56
Saline-administrated OVX	3.11±0.43*	1.99±0.37
Naftopidil-administrated OVX		4.70±0.91§§
Bladder Capacity (ml)		
Sham	1.10±0.09	0.73±0.11
Saline-administrated OVX	0.54±0.06**	0.39±0.07
Naftopidil-administrated OVX		0.83±0.15§

*P<0.05, **P<0.01; compared to sham operated rats in room temperature.

§P<0.05, §§P<0.01; compared to saline-administrated OVX rats in low temperature.