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EFFECTS OF A NEW PHOSPHODIESTERASE 5 INHIBITOR, MIRODENAFIL, ON THE FEMALE RAT BLADDER IN A PARTIAL BLADDER OUTLET OBSTRUCTION MODEL: PHYSIOLOGICAL AND IMMUNOHISTOCHEMICAL ASPECTS

Hypothesis / aims of study

We investigated the effects of mirodenafil, new phosphodiesterase-5 inhibitor developed in Korea, on the female rat bladder in a partial bladder outlet obstruction (BOO) model through cystometry and immunohistochemistry

Study design, materials and methods

Thirty six female Sprague-Dawley rats (body weight, 200-300 g) were divided into 4 groups; the control group (sham-operation), BOO-no medication group (BOO for 2 weeks), BOO-1mg/kg group (mirodenafil medication at 1mg/kg after BOO), BOO-4mg/kg group (mirodenafil medication at 4 mg/kg after BOO). To obtain a partial obstruction of the urethra, we modified the method of Mattiason and Uvelius. The rats of BOO-1mg/kg and BOO-4mg/kg groups were orally fed with mirodenafil once daily for 2 weeks. Two weeks later, the rats of each group underwent cystometry under urethane anesthesia. A PE-50 catheter was inserted into the bladder through the bladder dome and connected to a pressure transducer and a syringe pump for infusing saline using a three-way stopcock. After cystometry, the bladder was excised to perform immunohistochemical staining for connexin 43 and Rho-kinase

Results

The 3 BOO groups induced a significant increase in bladder weight compared to the control group. Baseline pressure, threshold pressure and maximum voiding pressure were not different between the 4 groups. Voiding interval was significantly reduced in the 3 BOO groups compared to the control group ($p<0.05$). The interval was prolonged in the 2 mirodenafil medication groups compared to BOO-no medication group ($p<0.05$) (Table).

On imunohistochemical examination, connexin 43 was localized in the submucosal area. Staining intensity increased in the 3 BOO groups compared with the control group, but decreased in the 2 mirodenafil medication group compared to the BOO-no medication group. The results of Rho-kinase staining were similar to those of connexin 43 staining

Interpretation of results

Mirodenafil can increase the voiding intervals of female rats in a partial BOO model. It also decrease the expression of connexin 43 and Rho-kinase. The decrease of bladder overactivity by mirodenafil may correlate intracellular communication through connexin 43 and PDE-5 inhibitor-induced cGMP might decrease bladder overactivity through Rho/Rho-kinase mechanism.

Concluding message

Mirodenafil could be possible option for the treatment of overactive bladder.

Table. Cystometric parameters in each group

Group	BPr (cmH_2O)	ThPr (cmH_2O)	ThPr-BPr (cmH_2O)	MVP (cmH_2O)	Contraction interval (sec)
Control (n=8)	5.2±4.5	9.6±6.7	4.4±2.7	33.3±5.7	421.6±88.0
BOO-no mx (n=9)	4.3±4.4	8.0±6.1	3.7±2.0	31.4±8.9	92.4±37.6*
BOO-1mg/kg (n=9)	3.8±5.2	8.1±5.6	4.3±1.9	42.7±18.1	151.2±69.7*+
BOO-4mg/kg (n=8)	5.3±4.8	10.0±4.9	4.7±1.2	43.9±24.5	228.4±55.1*+

BPr: baseline pressure, ThPr: threshold pressure, MVP: maximum voiding pressure
*p<0.05 (vs control), +p<0.05 (vs BOO no medication),

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