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CYSTOMETRIC ANALYSIS OF EFFECTS ON BLADDER FUNCTION OF ALPHA ADRENOCEPTOR ANTAGONIST OR CHOLINESTERASE INHIBITOR IN A NOVEL ANIMAL MODEL OF UNDERACTIVE BLADDER

Hypothesis / aims of study

Only a few underactive bladder/detrusor underactivity (UAB) models have been reported, and partial decentralization models would probably be more useful than complete decentralization models for elucidation of the pathophysiology and evaluation of the therapeutic implications of a specific drug. In clinical settings, pharmacological management for UAB with high level of evidence has not been reported 1). Empirically, alpha adrenoceptor antagonist or cholinesterase inhibitor has been often used in UAB patients. Recently, a rat lumbar canal stenosis (LCS) model as one of the UAB model was reported 2). The LCS rats showed a significant increase in residual urine rate (RUR) and a significant decrease in maximum intravesical pressure during voiding (Pmax). To explore possibilities of that model, we examined the lower urinary tract function of the rat LCS model with in vivo cystometry before and after taking alpha adrenoceptor antagonist or cholinesterase inhibitor.

Study design, materials and methods

Wistar rats (180 to 190 g) were employed in the present study. One small hole drilled at fifth lumbar vertebral arch (Sham group), and a rectangular piece of silicone rubber (0.5×3.5×5.0 mm) was then placed into the L5 to L6 epidural space (LCS group). After surgery, rats underwent bladder expression at least twice a day in order to avoid bladder overdistension. Awake cystometry (CMG) was performed 2 weeks after surgery, with vehicle, tamusulosin (TAM, 0.03 and 0.1 mg/kg) or distigmine (DIS, 0.3 and 1 mg/kg) being orally administered. The following cystometric parameters were investigated: baseline intravesical pressure (Pbase), threshold intravesical pressure (Pth), Pmax, frequency of non-voiding contraction (NVC), maximal cystometric capacity (MCC), voided volume (VV), postvoid residual urine volume (PVR), and RUR. We compared these parameters between pre- and post-drug administration.

Results

As shown in table, the LCS rats showed large MCC and high PUR with low Pmax. TAM and DIS significantly decreased Pth, MCC and PVR. RUR was also significantly decreased by TAM and DIS except TAM 0.1mg/kg. DIS significantly increased NVC. Pmax did not show a significant difference even after administration of DIS.

Interpretation of results

The LCS rats had salient characteristics of severe infra-sacral neuropathic bladder dysfunctions. TAM and DIS decreased PVR. However, this decrease was not accompanied with increased Pmax, nor increased VV. Rather, decreased MCC was a possible contributing factor. Moreover, increased NVC after administration of DIS might participate in decreased MCC. Therefore, in this model, TAM and DIS might affect afferent system in the lower urinary tract.

Concluding message

Both Alpha adrenoceptor antagonist and cholinesterase inhibitor is effective for decreasing RUR in a rat LCS model. It is expected that this novel model will be useful in studying the pharmacotherapy of UAB. TAM and DIS decrease RUR without increase in Pmax. Therefore, urethral functional studies are needed to answer whether decrease in urethral resistance is associated with improvement of RUR.

Table: Cystometric parameters in LCS rats before and after drug administration ☐

	Pbase (mmHg)	Pth (mmHg)	Pmax (mmHg)	NVC (/min)	MCC (mL)	VV (mL)	PVR (mL)	RUR (%)
Vehicle (n=10)								
Pre	2.4±0.14	6.6±0.62	11.0±1.19	0.1±0.02	2.5±0.14	0.1±0.02	2.4±0.12	94.6±0.64
Post	2.5±0.17	6.2±0.66	11.0±1.44	0.2±0.02	2.3±0.21	0.1±0.02	2.1±0.22	94.0±1.20
p	ns	ns	ns	ns	ns	ns	ns	ns
TAM 0.03mg/kg (n=11)								
Pre	4.0±0.95	7.5±1.12	10.3±1.14	0.0±0.01	2.2±0.13	0.1±0.02	2.1±0.14	95.1±1.29
Post	3.6±0.89	6.0±1.07	9.0±1.13	0.1±0.02	1.6±0.24	0.3±0.09	1.3±0.30	73.8±8.40
p	ns	<0.05	ns	ns	<0.05	ns	<0.01	<0.05
TAM 0.1mg/kg (n=10)								
Pre	3.5±0.75	7.2±0.85	10.0±1.00	0.1±0.03	2.3±0.12	0.1±0.01	2.2±0.11	96.5±0.41
Post	3.5±0.78	5.7±0.86	9.2±1.14	0.1±0.02	1.6±0.24	0.2±0.07	1.4±0.27	83.5±6.85
p	ns	<0.01	ns	ns	<0.01	ns	<0.01	ns
DIS 0.3mg/kg (n=11)								
Pre	2.1±0.23	5.3±0.24	8.3±0.41	0.1±0.01	2.4±0.15	0.2±0.04	2.2±0.16	91.7±2.00
Post	2.1±0.22	4.3±0.35	8.5±0.61	0.2±0.02	1.6±0.22	0.3±0.08	1.3±0.21	81.2±4.54
p	ns	<0.05	ns	<0.001	<0.001	ns	<0.001	<0.05
DIS 1.0mg/kg								
Pre	2.7±0.18	6.5±0.40	9.1±0.73	0.1±0.02	2.4±0.13	0.2±0.02	2.2±0.14	93.0±1.29
Post	3.1±0.24	5.2±0.38	9.7±1.15	0.2±0.05	1.1±0.22	0.2±0.06	0.8±0.21	71.6±3.72
p	ns	<0.05	ns	<0.05	<0.001	ns	<0.0001	<0.001

Mean±SE, baseline intravesical pressure (Pbase), threshold intravesical pressure (Pth), maximum intravesical pressure during voiding (Pmax), frequency of non-voiding contraction (NCV), maximal cystometric capacity (MCC), voided volume (VV), postvoid residual urine volume (PVR), and residual urine rate (RUR). ☐

References

1. BJU 99: 749, 2007
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Disclosures

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