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ALPHA-1 ADRENOCEPTOR ANTAGONIST IMPROVES IRRITATIVE SYMPTOMS; VIA CENTRAL PATHWAY? IN VIVO ANIMAL MODEL

Hypothesis / aims of study

Although it is reported that alpha-1 adrenoceptor (AR) antagonist, including tamsulosin, improves not only voiding symptoms but also storage symptoms, the mechanism of alpha-1 AR antagonists to improve OAB remains controversial. The crucial aspect for tamsulosin is its ability to cross the blood-brain barrier (1,2). The present study is to investigate the effects of tamsulosin on urinary bladder functions and central micturition reflex by cystometric variables and c-Fos, nitric oxide synthase (NOS) expression in the medial preoptic area (MPA), ventrolateral periaqueductal gray (vlPAG), pontine micturition center (PMC) and spinal cord following cyclophosphamide-induced OAB rat model.

Study design, materials and methods

Female Sprague-Dawley rats (250 ~300 gm) were divided into 5 groups (n = 8, each group): the normal control group (Group I), the cyclophspamide (cp)-injection disease control group (Group II), the cp-injection and 0.01 mg/kg tamsulosin-treated group (Group III), the cp-injection and 0.1 mg/kg tamsulosin-treated group (Group IV), the cp-injection and 1 mg/kg tamsulosin-treated group (Group V). Cystometrography was performed and the pattern of non-voiding bladder contraction (NVC) was monitored. After cystometry, the animal was sacrificed immediately. Then the brain and spinal cord (L4-L5) were dissected for the pathologic examination. To assess c-Fos and NOS expression in the MPA, PMC, vlPAG, spinal cord (L4-L5) regions, immunohistochemistry was done. The data was analyzed by one-way ANOVA followed by Duncan's post-hoc test.

Results

Cyclophsphamide enhanced NVC pressure and duration in Group II compared to Group I. In treatment groups (Group III-V) it was significantly suppressed. This suppression was reversely proportional to the dose of tamsulosin (Table). The expression of c-Fos and NOS in all the CNS region was significantly enhanced in Group II compared to Group I. In treatment groups (Group III-V) it was significantly suppressed in all the CNS regions. This suppression was also reversely proportional to the dose of tamsulosin as the pattern of NVC (Table).

Interpretation of results

Alpha-1 AR antagonist, tamsulosin, improved cyclophospamide-induced NVC pattern. This might be caused by the suppression of central afferent/efferent activation on the lower urinary tract.

Concluding message

The present results demonstrated that symptoms of OAB could be alleviated by alpha-1 AR antagonist, tamsulosin through the suppression of the central activation. This might be considered as a one of the possible central mechanisms of alpha-1 AR antagonist, tamsulosin to improve OAB.

Table. Changes in cystometric parameters and c-Fos, NOS expression in micturition centers

Group	NVC pressure (cmH_2O)	NVC duration (sec)	spinal cord	MPA	*vlPAG*	*PMC*
			(number of c-Fos positive cells/section)			
			(number of NADPH-d positive cells/section)			
Group I	**3.40±0.27**	**20.80±0.87**	**9.30±1.48**	**73.12±7.53**	**26.46±2.59**	**15.60±1.70**
			3.04±1.62		**19.72±2.45**	**11.63±2.16**
Group II	**9.12±0.62**	**29.74±0.96**	**30.00±1.48**	**142.00±8.17**	**61.07±3.60**	**49.84±5.59**
			47.70±5.02		**87.75±6.15**	**70.52±6.13**
Group III	**4.13±0.02**	**16.92±0.40**	**16.62±1.81**	**93.75±18.22**	**28.42±3.20**	**26.71±2.15**
			20.05±1.72		**38.04±2.45**	**29.75±2.87**
Group IV	**5.40±0.43**	**16.98±0.02**	**22.84±1.70**	**115.33±11.9**	**39.68±2.36**	**37.23±2.43**
			36.75±1.50	**8**	**51.28±2.87**	**48.62±2.17**
Group V	**6.20±1.61**	**18.79±0.56**	**24.4±1.97**	**136.75±10.7**	**44.26±3.27**	**36.00±2.12**
			35.80±1.80	**9**	**62.75±3.34**	**49.03±2.15**

NVC: non-voiding bladder contraction; MPA: medial preoptic area; vlPAG: ventrolateral periaqueductal gray; PMC: pontine micturition center

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Specify source of funding or grant	**No**
Is this a clinical trial?	**No**
What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
Name of ethics committee	**Animal Care Committee of KyungHee University School of Medicine**