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Abstract Reproduction Form B-1

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Title (type in
CAPITAL
LETTERS)PERIPHERAL AND SPINAL EFFECTS OF α_1 & α_2 ADRENOCEPTOR
ANTAGONISTS ON MICTURITION REFLEX IN RATS

Aims of Study This study elucidate the effects of α_1 and α_2 adrenoceptor antagonists in the micturition reflex (MR) which is induced by bladder distension in normal anesthetized rat at peripheral and spinal level.

Methods 80 female SD rats were anesthetized with urethane. Continuous cystometry was done (saline infusion rate of 0.5 ml./min). For the intraarterial (i.a) or intrathecal (i.t) injection of drugs, PE-10 catheter was inserted into the femoral artery or subarachnoid space at the level of L6-S1 spinal cord segments. Changes of basal pressure (BP), micturition pressure (MP), bladder capacity (BC), micturition volume (MV), frequency were analyzed before and after the drug injections.

Results Phentolamine (PT, i.t.) raised BP and abolished MR followed by overflow incontinence. After i.a. injection, decreases in MP ($p < 0.05$) were noted. Only i.a. injections of prazosin (PZ), doxazosin (DZ) and tamsulosin (TS) decreased MP ($p < 0.05$). DZ (i.a.) increased BC and voiding interval ($p < 0.05$, $p < 0.01$). TS (i.t.) decreased frequency and increased BC ($p < 0.05$). MP was more significantly inhibited after DZ than PZ or TS (i.a.). Clonidine (CLO, i.a.) increased only frequency ($p < 0.05$). CLO (i.t.) markedly increased BP and frequency; whereas MV and BC were significantly decreased. Yohimbine (YOH, i.t. 10^{-3} M) abolished the MR. Similar cystometric results were noted after i.a. YOH injections.

Table 1 Changes of cystometric parameters after intrathecal administrations of α -adrenoceptor blockers

		BP	MP	MV	Frequency	BC	RV
Phentolamine (10^{-6} M)	† Before	2.62 ± 0.27	35.42 ± 5.36	0.54 ± 0.21	0.32 ± 0.12	0.63 ± 0.14	0.35 ± 0.19
	After	3.59 ± 1.21	7.38 ± 1.16**	0.28 ± 0.10	0.30 ± 0.13	0.73 ± 0.15	0.33 ± 0.05
	† Before	3.25 ± 1.01	37.28 ± 8.59	0.45 ± 0.15	0.36 ± 0.11	0.76 ± 0.12	0.27 ± 0.12
	After	3.40 ± 0.84	34.75 ± 3.75	0.18 ± 0.08	0.92 ± 0.19*	0.21 ± 0.10**	0.33 ± 0.09
Prazosin (10^{-6} M)	Before	2.97 ± 0.46	30.43 ± 1.75	0.53 ± 0.02	0.29 ± 0.04	0.65 ± 0.09	0.32 ± 0.03
	After	3.54 ± 0.98	27.57 ± 2.75	0.66 ± 0.05**	0.19 ± 0.05	0.83 ± 0.16	0.20 ± 0.12
Doxazosin (10^{-6} M)	Before	4.80 ± 0.87	30.44 ± 2.17	0.21 ± 0.05	0.42 ± 0.07	1.20 ± 0.24	0.96 ± 0.27
	After	4.48 ± 0.83	26.28 ± 1.30	0.46 ± 0.12	0.24 ± 0.04	1.37 ± 0.20	0.91 ± 0.32
Tamsulosin (10^{-6} M)	Before	3.04 ± 0.32	31.68 ± 4.46	0.32 ± 0.02	0.49 ± 0.11	0.65 ± 0.03	0.45 ± 0.07
	After	3.86 ± 0.47	26.82 ± 2.57	0.34 ± 0.38	0.39 ± 0.07*	0.71 ± 0.04*	0.37 ± 0.12

† overflow incontinence

‡ urinary retention

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Table 2 Changes of cystometric parameters after intraarterial administrations of α -adrenoceptor blockers

		BP	MP	MV	Frequency	BC	RV
Phentolamine (10^{-6} M)	Before	9.49 \pm 2.00	53.34 \pm 5.48	0.10 \pm 0.03	0.46 \pm 0.14	0.22 \pm 0.09	0.11 \pm 0.08
	After	9.51 \pm 2.02	45.58 \pm 8.17*	0.17 \pm 0.10	0.43 \pm 0.11*	0.38 \pm 0.16	0.21 \pm 0.22
Prazosin (10^{-6} M)	Before	8.42 \pm 1.40	53.01 \pm 5.17	0.12 \pm 0.05	0.43 \pm 0.12	0.24 \pm 0.07	0.11 \pm 0.08
	After	9.61 \pm 1.61	46.34 \pm 4.04*	0.17 \pm 0.05	0.34 \pm 0.08	0.51 \pm 0.27	0.34 \pm 0.28
Doxazosin (10^{-8} M)	Before	10.83 \pm 1.28	54.73 \pm 4.20	0.23 \pm 0.08	0.41 \pm 0.11	0.27 \pm 0.07	0.06 \pm 0.02
	After	13.44 \pm 2.24	37.70 \pm 6.16**	0.45 \pm 0.12*	0.14 \pm 0.03*	0.59 \pm 0.11**	0.12 \pm 0.02*
Tamsulosin (10^{-6} M)	Before	5.60 \pm 3.16	47.60 \pm 3.96	0.07 \pm 0.02	0.76 \pm 0.22	0.15 \pm 0.06	0.08 \pm 0.04
	After	7.28 \pm 2.37	39.76 \pm 0.79*	0.12 \pm 0.04	0.53 \pm 0.37*	0.31 \pm 0.20	0.19 \pm 0.15

Table 3 Changes of cystometric parameters after intraarterial administrations of clonidine and yohimbine

		BP	MP	MV	Frequency	BC	RV
Clonidine (10^{-4} M)	Before	7.35 \pm 4.24	34.49 \pm 4.73	0.20 \pm 0.08	0.58 \pm 0.39	0.57 \pm 0.01	0.36 \pm 0.08
	After	9.09 \pm 3.49	35.65 \pm 3.85	0.14 \pm 0.08	1.00 \pm 0.49*	0.75 \pm 0.23	0.60 \pm 0.18
Yohimbine (10^{-6} M)	Before	3.99 \pm 1.50	30.77 \pm 7.06	0.25 \pm 0.07	0.38 \pm 0.09	1.04 \pm 0.22	0.78 \pm 0.23
	After	5.60 \pm 1.08	34.03 \pm 5.96	0.45 \pm 0.07**	0.26 \pm 0.14	1.14 \pm 0.48	0.54 \pm 0.24

Table 4 Changes of cystometric parameters after intrathecal administrations of clonidine and yohimbine

		BP	MP	MV	Frequency	BC	RV
Clonidine (10^{-3} M)	Before	3.00 \pm 0.67	26.51 \pm 7.60	0.24 \pm 0.03	0.28 \pm 0.11	0.81 \pm 0.07	0.55 \pm 0.05
	After	5.96 \pm 7.60**	28.04 \pm 1.56	0.14 \pm 0.02**	0.71 \pm 0.08**	0.69 \pm 0.06*	0.64 \pm 0.08
Yohimbine (10^{-3} M)	Before	6.76 \pm 3.07	30.54 \pm 3.88	0.16 \pm 0.04	1.26 \pm 0.73	0.57 \pm 0.04	0.41 \pm 0.01
	After	4.75 \pm 2.46	26.90 \pm 5.39	0.38 \pm 0.08**	0.51 \pm 0.42	0.68 \pm 0.04*	0.29 \pm 0.04**

* $P < 0.05$ ** $P < 0.01$ BP: basal pressure (cmH₂O), MP: micturition pressure (cmH₂O), BC: bladder capacity(ml), MV: micturition volume(ml), Frequency (cycles/min.), RV: residual volume(ml)

Conclusions At spinal level, antagonism of MR evoked by bladder distension was more prominent by PT or YOH. Inhibition of MR with α_1 adrenoceptor blockers were greater peripherally. It is suggested that both α_1 and α_2 adrenoceptor are involved in MR by volume-induced bladder distention in normal rat.