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THE EFFECT OF AN ANGIOTENSIN TYPE I RECEPTOR BLOCKER, OLMESARTAN FOR BLADDER DYSFUNCTION IN THE SPONTANEOUSLY HYPERTENSIVE RAT

Hypothesis / aims of study

Increasing evidence suggests that pelvic ischemia is one of the main risk factors for developing overactive bladder. Spontaneously hypertensive rat (SHR) is a well-established experimental model for the study of bladder dysfunction [1-3]. In this study we investigated the effect of olmesartan and nifedipine on bladder dysfunction in the SHR.

Results

Twelve-week-old male SHRs were six-weeks treated with olmesartan (1 or 3 mg/kg/day p.o.) or nifedipine (30 mg/kg/day p.o.). Wistar rats were used as controls. The effect of olmesartan or nifedipine on urodynamic parameters was measured using metabolic cage and by cystometry. Bladder blood flow (BBF) was measured by hydrogen clearance method. The expressions of nerve growth factor (NGF) and gap junction proteins, connexin (Cx)26, Cx43 and Cx45 in the bladder were analyzed using ELISA and Western blot analysis, respectively.

Interpretation of results

The SHR showed significant increases in blood pressure, micturition frequency, and NGF and Cx26 expressions in the bladder, and decreases in BBF and single voided volume compared to the controls. Although blood pressure in the SHR was significantly decreased by treatment with both doses of olmesartan or nifedipine, only treatment with the high dose of olmesartan significantly ameliorated these parameters except for expressions of Cx26.

TABLE 1. General features in the experimental animals

					Blood Pressure (mmHg)		
Group	Body weight (g)	Bladder weight (mg)	BBR ($10\times^{-4}$)	Heart Rate (bpm)	Systolic	Mean	Diastolic
Cont	445 ± 4	204 ± 21	4.53 ± 0.45	372.4 ± 7.1	123.1 ± 2.8	99.9 ± 2.3	88.5 ± 2.2
SHR	318 ± 5 *	123 ± 8 *	3.85 ± 0.22	330.1 ± 10.4 *	197.3 ± 6.6 *	164.0 ± 6.0 *	147.4 ± 6.0 *
Olm 1	306 ± 6 *	104 ± 6 *	3.40 ± 0.23	319.6 ± 8.4 *	170.1 ± 5.1 * #	141.6 ± 3.5 * #	125.9 ± 4.4 * #
Olm 3	314 ± 7 *	116 ± 6 *	3.71 ± 0.19	317.5 ± 8.0 *	159.5 ± 3.5 * #	130.0 ± 2.9 * # †	115.3 ± 3.4 * #
Nif	303 ± 5 *	113 ± 7 *	3.72 ± 0.21	346.6 ± 13.3	141.9 ± 3.1 * #	119.9 ± 2.2 * # †	109.3 ± 2.6 * #

BBR; Bladder Body Ratio.
Cont; Wistar rats treated with vehicle,p.o.; SHR, SHRs treated with vehicle, p.o.; Olm 1, SHRs treated with olmesartan at a daily dose of 1 mg/kg, p.o. ; Olm 3, SHRs treated with olmesartan at a daily dose of 3 mg/kg, p.o. ; Nif, SHRs treated with nifedipine at a daily dose of 30 mg/kg, p.o. Data are shown as mean ± SEM of eight separate determinations in each group.

* significantly different from the Cont group. ($P < 0.05$)
# significantly different from the SHR group. ($P < 0.05$)
† significantly different from the Olm 1 group. ($P < 0.05$)

TABLE 2. Voiding behavior studies in the experimental rats

Group	Urine output (ml/24 hr)	Micturition frequency (/24 hr)	Single voided volume (ml)
Cont	19.9 ± 1.9	8.1 ± 1.0	2.70 ± 0.04
SHR	11.4 ± 1.2 *	20.2 ± 1.3 *	0.60 ± 0.06 *
Olm1	10.2 ± 1.2 *	15.7 ± 1.2 *#	0.71 ± 0.04 *
Olm3	11.9 ± 1.0 *	14.0 ± 1.0 *#	0.91 ± 0.09 *#
Nif	11.2 ± 1.0 *	17.4 ± 0.8 *	0.61 ± 0.05 *

Cont; Wistar rats treated with vehicle,p.o.; SHR, SHRs treated with vehicle, p.o.; Olm 1, SHRs treated with olmesartan at a daily dose of 1 mg/kg, p.o. ; Olm 3, SHRs treated with olmesartan at a daily dose of 3 mg/kg, p.o. ; Nif, SHRs treated with nifedipine at a daily dose of 30 mg/kg, p.o. Data are shown as mean ± SEM of eight separate determinations in each group.

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TABLE 3 . The results of cystometric studies in the experimental rats

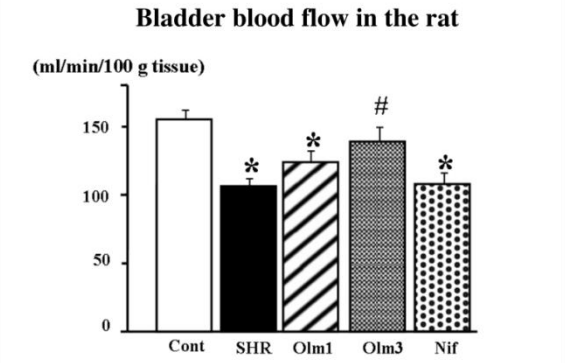
Group	P_{det} (cmH_2O)	Single voided volume (mL)	Post-voiding residual urine (mL)	ICI (sec)	NVC (/micturition)	Bladder compliance (mL/cmH_2O)
Cont	36.0 ± 1.7	0.73 ± 0.09	0.28 ± 0.04	218.1 ± 28.2	1.0 ± 0.4	0.18 ±0.05
SHR	34.8 ± 1.3	0.33 ± 0.04 *	0.19 ± 0.04	99.3 ± 10.7 *	1.9 ± 0.8	0.08 ±0.08 *
Olm1	30.0 ± 2.0	0.25 ± 0.03 *	0.29 ± 0.04	73.7 ± 8.6 *	1.2 ± 0.5	0.07 ±0.02 *
Olm3	30.2 ± 3.6	0.50 ± 0.06 # †	0.30 ± 0.09	146.9 ± 18.8 # †	1.0 ± 0.3	0.10 ±0.03
Nif	28.6 ± 1.6 *#	0.38 ± 0.06 *	0.18 ± 0.09	113.9 ± 17.0 *	1.5 ± 0.5	0.07 ±0.02 *

P_{det}, maximal detrusor pressure, ICI; intercontractile interval, NVC; non-voiding contraction. Cont; Wistar rats treated with vehicle, p.o. ; SHR, SHRs treated with vehicle, p.o. ; Olm 1, SHRs treated with olmesartan at a daily dose of 1 mg/kg, p.o.; Olm 3, SHRs treated with olmesartan at a daily dose of 3 mg/kg, p.o. ; Nif, SHRs treated with nifedipine at a daily dose of 30 mg/kg, p.o. Data are shown as mean ± SEM of eight separate determinations in each group.

* significantly different from the Cont group. ($P < 0.05$)

significantly different from the SHR group. ($P < 0.05$)

† significantly different from the Olm 1 group. ($P < 0.05$)



Concluding message

Our data suggest that olmesartan but not nifedipine might improve the bladder dysfunction in the SHR, and that Cx26 might be involved in hypertension-related bladder dysfunction. In addition, our data suggest that expressions of Cx26 in the bladder may not be a suitable dysfunction

References

1. Exp Physiol 1999; 84: 137-47.
2. Life Sci 2007; 81: 218-22.
3. Life Sci 2009; 85: 334-8.

Disclosures

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