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NITRENDIPINE INCREASES SODIUM EXCRETION IN ACUTELY SALINE-LOADED RATS

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Vasodilator substances, e.g. hydralazine and minoxidil, have been widely used in the treatment of hypertension. However, tolerance to their hypotensive action develops with sodium and water retention unless diuretics are added to the therapy (1). With a new class of vasodilators, the calcium antagonists, substances have been introduced that seem not to induce generalized edema during therapy (2).
Recently, we have suggested that calcium antagonists, in contrast to other vasodilators, may improve renal function in addition to their peripheral vasodilating effect (3). To further elucidate the mechanism of hypotensive action of calcium antagonists, the present study investigates the effect of the new calcium antagonist nitrendipine (4) on the elimination of an acute saline load in normotensive and spontaneously hypertensive rats.

Diuresis was induced in female normotensive (Wistar) and spontaneously hypertensive rats (Okamoto) by gavage of 30 ml 0.9 % saline/kg body weight. Controls or treated animals received additionally 5 ml tylose suspension/kg without or with drugs. After treatment, the rats were kept in metabolic cages and total excretion of urine and sodium (analyzed by flame photometry) for six hours was determined. Systolic blood pressure was measured in parallel experiments by means of the tail microphone technique in conscious animals prewarmed to 35°C in thermostatic cages. The maximum decrease in systolic blood pressure during six hours period was used for calculation.

After oral administration of nitrendipine, the excretion of the acute saline load was similarly increased in both normotensive and spontaneously hypertensive rats (Table 1).

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Table 1. Excretion of urinary volume and sodium after acute saline load and systolic blood pressure in normotensive (NR) and spontaneously hypertensive rats (SHR).
Effect of nitrendipine during six hours period (n=6, mean ± S.E.).

Rats and treatment	Dosage mg/kg p.o.	Urine volume ml/kg/6 h	Sodium excretion µmol/kg/6 h	Blood pressure mm Hg
NR controls	0 (NaCl)	23.0 ± 1.4	1524 ± 155	117 ± 1
NR nitren-	1.0	27.3 ± 1.1	1883 ± 222	111 ± 1
dipine	3.15	27.6 ± 0.4	2296 ± 163	108 ± 3
	10.0	28.2 ± 2.2	2308 ± 310	94 ± 2
	31.5	30.2 ± 2.2	2620 ± 222	87 ± 2
SHR controls	0 (NaCl)	26.9 ± 1.7	2137 ± 510	174 ± 3
SHR nitren-	1.0	26.1 ± 2.8	2638 ± 344	156 ± 4
dipine	3.15	25.0 ± 2.8	2265 ± 298	131 ± 4
	10.0	32.2 ± 2.6	2998 ± 201	102 ± 4
	31.5	34.5 ± 2.9	3262 ± 291	94 ± 3

This effect was dose-dependent in normotensives and to a certain degree in hypertensives. Significant differences ($p < 0.05$, analysis of variance) were observed with the higher dosages (with 3.15, 10 and 31.5 mg/kg in normotensives and with 31.5 mg/kg in hypertensives). In these dosages, blood pressure was decreased by 9, 23 or 30 mm Hg in normotensives and by 80 mm Hg in hypertensives respectively. In equihypotensive dosage, hydralazine (10 mg/kg p.o.) decreased sodium excretion in acutely saline loaded rats from 1533 ± 146 to 847 ± 202 µmol/kg in normotensives and from 1838 ± 236 to 1347 ± 328 µmol/kg in hypertensives. Minoxidil in a dosage of 3.15 mg/kg p.o. (blood pressure decrease -10 mm Hg and -67 mm Hg respectively) reduced sodium excretion from 1524 ± 155 to 456 ± 95 µmol/kg in normotensives and from 2137 ± 510 to 446 ± 71 µmol/kg in hypertensives.

The results confirm that calcium antagonists, at least nitrendipine, exert renal effects different from other vasodilators. These new substances seem to enable the kidney to excrete sodium despite a pronounced drop in blood pressure, whereas, according to clinical experience (5) and our findings, vasodilators of a different mechanism of action markedly reduce sodium excretion.

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