HYPOTENSIVE AND DIURETIC EFFECTS OF A VASODEPRESSOR LIPID OF RENAL ORIGIN

L. I. Somova

UDC 615.361.611:[615.225.2+615.154.1

A vasodepressor lipid, which was an unsaturated hydroxybutyric acid belonging to the prostaglandin group, was isolated from the renal medulla of rabbits. This vasodepressor lipid has a hypotensive and diuretic action on animals, most marked at the beginning of development of experimental hypertension. Under its influence the blood pressure and the electrolyte levels in the serum, urine, and tissues of rats with hypertension tend toward normal.

Besides the important role of disturbances of the CNS in the pathogenesis of hypertension, the work of Parin and Shenderov [2] and others has demonstrated the importance of the renal factor, and it is clear that the role of the kidneys in the pathogenesis of hypertension is not confined to the pressor mechanism [4]. During the last few years a vasodepressor lipid (VDL) has been isolated from the renal medulla [5]. A more detailed study of the chemical structure of this lipid by Daniels et al. [3] has shown that in all probability it is prostaglandin E_2 (PGE_2). Further investigations have been undertaken to ascertain the role of prostaglandins in hypertension [6].

The experiments described below were carried out to study the hypotensive and diuretic effects of the VDL of renal origin.

EXPERIMENTAL METHOD

To study the mechanism of action of VDL at different stages of experimental renal hypertension experiments were carried out on 170 Wistar albina rats weighing 240-260 g. To obtain experimental renal hypertension, the method of Page [7] was used. The arterial pressure was measured by Kogan's bloodless plethysmometric method in the tail. The VDL was extracted from rabbit kidneys and purified by Hickler's method [5]. All the experiments were carried out with the pure lipid which, as spectral analysis showed, was an unsaturated hydroxybutyric acid belonging to the prostaglandin group (PGE_2). To study the excretory function of the kidneys the blood urea and the uric acid, creatinine, and protein in the urine were determined by the usual micromethods. The hemoglobin concentration and red and white cell counts also were determined. The electrolyte concentrations were determined in the serum, urine, and tissues by means of Opton's flame photometer. Aldosterone in the urine was determined by Neher's method.

EXPERIMENTAL RESULTS

In the 56 control animals with experimental hypertension characteristic disturbances of the arterial pressure (Table 1), the excretory function of the kidneys, and the ECG as well as morphological changes were observed. The discovery of changes in the electrolyte concentrations in the blood serum, urine, and tissues was particularly important (Table 2). The aldosterone concentration in the urine 20 days after the onset of hypertension was increased by 204%, and after 1 month it was increased by 250%.

The hypotensive action of VDL on the animals with hypertension (34) was clearly defined (Table 1). The arterial pressure was lowered during the first days after administration of VDL and it remained low

Hypertension Group, Medical Department, Bulgarian Academy of Sciences, Sofia. (Presented by Academician of the Academy of Medical Sciences of the USSR A. M. Chernukh.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 75, No. 1, pp. 36-40, January, 1973. Original article submitted November 3, 1971.

TABLE 1. Arterial Pressure of Control Rats and Rats with Experimental Hypertension

Time of investigation	Control rats with hypertension		Rats with hypertension receiving renal cortical extract			Rats with hypertension receiving VDL		
	arterial pressure (in mm Hg) x ± S	P	arterial pressure (in mm Hg) x ± S	decrease in arterial pressure, n ± m_n*	P	arterial pressure (in mm Hg) x ± S	decrease in arterial pressure, n ± m_n*	P
Before experiment	93,2±7,7		96,0±5,3			100,0±5,8		
After procedure:								
14 days after hypertension:	149,4±14,9	<0,001	149,0±12,9	11,6±5,7	>0,05	115,2±20,2	73,1±7,7	<0,01
30 " "	143,9±12,3	<0,001	139,8±14,3	27,0±17,9	>0,1	104,0±10,2	92,9±4,4	<0,001
45 " "	136,9±12,7	<0,001	138,4±13,1	29,3±10,4	<0,01	102,4±8,6	96,7±3,6	<0,001
60 " "	132,7±17,2	<0,001	140,8±12,2	25,3±9,9	<0,02	111,2±8,4	80,2±8,4	<0,01
75 " "	134,5±11,0	<0,001	142,4±5,5	22,6±14,6	>0,1	105,7±11,5	90,0±9,4	<0,001
90 " "	136,3±10,1	<0,001	139,8±7,0	27,0±15,6	>0,1	113,1±12,0	76,8±13,3	<0,05

*n denotes decrease in arterial pressure in %; m_n denotes mean error.

until the end of the experiment. In some animals of this group the duration of action of VDL after a single injection was studied. The arterial pressure was lowered a few hours after injection of VDL and it remained low for 24 h, after which it rose slowly back to its initial level. In the doses used (corresponding to 2 g of renal medulla per rat) VDL was tolerated well by the animals and caused no side effects. All the remaining indices (except the arterial pressure), which were characteristic of the control animals with experimental hypertension, returned to normal. The results of investigation of the electrolytes were particularly interesting. They showed that their level was indistinguishable from that found in the healthy control animals (see Table 2). On the 26th day after injection of VDL the aldosterone concentration in the urine was lowered by 50%. This is evidence that under the experimental conditions used VDL acts in the opposite direction to renin on the electrolyte concentrations in the blood serum, urine, and tissues, i.e., it is possible that electrolytes are the common link in the complex chain of regulation of vascular tone on which both renin and VDL act. On the basis of Parin and Shenderov's hypothesis that the antihypertensive function of the kidneys is effected by their action on electrolyte metabolism in the opposite direction to the action of renin, it can be postulated that the antihypertensive function of the kidneys is determined by VDL secreted by (or accumulating in) their medulla.

The results of the experiments on animals with hypertension receiving an extract of renal cortex (32 animals), or extract of the lung, liver, and heart (12 animals each) showed that all the indices for these animals were indistinguishable from the control group. This result suggests that VDL is not present in the renal cortex or in the other organs (at least in an active state). The persistent hypotensive effect obtained in the animals with experimental hypertension is specific only for VDL from the renal medulla. It was also noted that VDL had no effect on 12 animals with a normal arterial pressure.

LITERATURE CITED

1. A. Kh. Kogan, Byull. Éksperim. Biol. i Med., No. 10, 109 (1959).
2. V. V. Parin and S. M. Shenderov, Cor et Vasa (Prague), 4, 1 (1962).
3. E. Daniels, J. Hinman, B. Leach, et al., Nature, 215, 1298 (1967).
4. A. Grollman, Canad. Med. Ass. J., 90, 299 (1964).
5. R. Hickler, Canad. Med. Ass. J., 90, 280 (1964).

TABLE 2. Dynamics of Indices Studied in Control and Experimental Rats

		Indices studied	In serum		In urine	
			$\bar{x} \pm S$	P	$\bar{x} \pm S$	P
Control animals	Healthy rats	Blood urea (in mg %)	45,0±11,4			
		Creatinine (in mg %)	2,5±0,5			
		Uric acid (in mg %)	2,8±1,3			
		Sodium (in meq/liter)	152,6±20,4			
		Potassium (in meq/liter)	6,2±1,0			
		Chloride (in meq/liter)	102,0±17,1			
		Hemoglobin (in %)	82,5±11,4			
		Red cell count (millions)	5,68±0,97			
		White cell count	11 000±1952			
	Rats with hypertension	Blood urea (in mg %)	83,5±16,5	<0,001		
		Creatinine (in mg %)	2,8±0,4	<0,001		
		Uric acid (in mg %)	4,0±2,1	<0,001		
		Sodium (in meq/liter)	164,0±27,2	>0,05	118,2±24,6	<0,001
		Potassium (in meq/liter)	4,5±2,9	>0,05	69,9±17,1	<0,001
		Chloride (in meq/liter)	122,7±22,5	<0,001	90,5±22,0	<0,001
		Hemoglobin (in %)	69,0±14,9	<0,001		
		Red cell count (millions)	4,88±1,06	<0,001		
		White cell count	11 900±3086	0,05<P<0,1		
Experimental animals	Rats with hypertension receiving renal cortical extract	Blood urea (in mg %)	76,2±10,4	<0,001		
		Creatinine (in mg %)	2,9±0,6	<0,001		
		Uric acid (in mg %)	4,3±0,8	<0,001		
		Sodium (in meq/liter)	162,4±17,0	>0,05	102,4±13,3	<0,001
		Potassium (in meq/liter)	4,6±1,9	>0,05	77,3±13,4	<0,001
		Chloride (in meq/liter)	158,2±26,4	<0,001	86,1±17,6	<0,001
		Hemoglobin (in %)	72,3±7,8	<0,001		
		Red cell count (millions)	4,14±0,68	<0,001		
		White cell count	10 440±1604	0,05<P<0,1		
Experimental animals	Rats with hypertension receiving VDL	Blood urea (in mg %)	76,9±11,5	<0,001		
		Creatinine (in mg %)	3,2±0,5	<0,001		
		Uric acid (in mg %)	4,5±0,8	<0,001		
		Sodium (in meq/liter)	144,6±29,0	0,1<P<0,2	168,8±28,3	0,05<P<0,1
		Potassium (in meq/liter)	5,8±0,9	0,05<P<0,1	89,9±13,7	0,2<P<0,5
		Chloride (in meq/liter)	94,0±11,5	0,1<P<0,2	123,8±18,3	0,2<P<0,5
		Hemoglobin (in %)	63,5±6,6	<0,001		
		Red cell count (millions)	3,85±0,58	<0,001		
		White cell count	10 700±2014	0,05<P<0,1		

6. J. Hinman, Postgrad. Med. J., 46, 562 (1970).
7. I. Page, Science, 89, 273 (1939).