EFFECT OF THE α-ADRENOBLOCKER PYRROXAN ON THE SYSTEMIC HEMODYNAMICS IN PUPPIES AND DOGS WITH VASORENAL HYPERTENSION

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Vasorenal hypertension was induced in puppies aged 2-3 months and in adult dogs by constricting both renal arteries. Pyrroxan (1.5 mg/kg) was injected intravenously 3 and 14 days later. Both in the adult dogs and in the puppies the elevated arterial blood pressure was lowered by pyrroxan, and in the latter it fell below normal. The hypotensive effect of the drug in the adult animals was connected with a decrease in the general peripheral vascular resistance, whereas in the puppies in addition the cardiac output was reduced. In all animals injection of pyrroxan was followed by tachycardia, shortening of the phase of isometric contraction, and activation of contractility of the myocardium.

KEY WORDS: renal hypertension; adrenoblockers; hemodynamics; age reactivity.

Many investigations have yielded evidence of the participation of the sympathico-adrenal system in the pathogenesis of vasorenal hypertension [2-6, 8, 9]. However, age differences in the role of α-adrenergic mechanisms in the pathogenesis of vasorenal hypertension have not yet been investigated, especially in the early stages of its formation. In order to study this problem in experiments on dogs and puppies the Soviet drug pyrroxan, which selectively blocks α-adrenoreceptors wherever they are situated [1], was used.

EXPERIMENTAL METHOD

Experiments were carried out on 12 puppies aged 2 months and 12 adult (3-5 years) dogs in which vasorenal hypertension was induced by constriction of both renal arteries [7]. Pyrroxan was injected intravenously in a dose of 1.5 mg/kg into the dogs 3 and 14 days after ischemization of the kidneys and also into intact animals. The mean blood pressure (MBP) in the femoral artery, and the minute and systolic blood volumes (by the thermodilution method) were measured and recorded simultaneously with the electrocardiogram, the phase structure of the cycle of the left ventricle was recorded by polycardiography on the 6-NÉK-3 electrocardiograph, the pressure inside the left ventricle (IVP) was recorded with a VM-101 electromanometer, and the first derivative of the pressure (dp/dt) was recorded through a differential circuit.

The specific peripheral vascular resistance (SPVR), the cardiac and systolic indices, the working index of the left ventricle (WILV), indices of contractility, and the "tension-time index" (TTI) were calculated. In the statistical analysis the probability of significance of the difference (P) was calculated after injection of pyrroxan compared with the previous stage of the investigation, and on the 3rd and 14th days of hypertension compared with the original background.

EXPERIMENTAL RESULTS

The experiments showed that injection of pyrroxan into adult animals 3 days after ischemization of the kidneys lowered the raised arterial pressure through a decrease in the peripheral vascular resistance (Table 1). The cardiac and systolic indices, which were significantly lowered during hypertension, showed little change after injection of pyrroxan. It is important to emphasize that in the intact adult dogs injection of pyrroxan did not affect the blood pressure, for a tendency for SPVR to fall was combined with a tendency for the cardiac index to rise. In the "hypertensive" animals the α-adrenoreceptor blockade was accompanied by a decrease in WILV and in the maximal intraventricular pressure (IVP_{max}), and the index of contractivity

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TABLE 1. Changes in Principal Hemodynamic Parameters under the Influence of Pyrroxan in Adult Dogs with Vasorenal Hypertension

Index	Initial background	Injection of pyrroxan	3rd day of renal ischemia	Injection of pyrroxan	14th day of renal ischemia	Injection of pyrroxan
MBP, mm Hg	145,4±2.17	143,5±2,84	157,6±3,18*	142,4±1,90*	174,6±2,74*	150.0±3.51*
Heart rate, beats/min	120,0±4,48	128,3±9,59	154,4±7,72*	164.0±5.06	126,5±6,15	166,4±8,31*
Cardiac index, liters/m²	1,11±0.02	1,15±0,03	0,92±0,03*	0.88±0.04	0,97±0,03*	1.11±0.04*
Systolic index, ml/m²	9,46±0,47	9,23±0,65	6,37±0,49*	5,41±0,27	6,82±0,27*	6,83±0,22
SPVR, dynes·sec·cm⁻⁵·m²	10 634±367	9 995±206	13 803±336*	12 029±208*	14 798±298*	11 187±912*
WILV, kg·m/m²	2,22±0.03	2,24±0,05	1,93±0,08*	1,69±0,07*	2,30±0,09	2,35±0,11
IVP_{max}, mm Hg	167,7±2,32	174,2±2,77	174,2±1,54*	163,9±2,97*	184,6±2,26*	179,7±2,28
Index of contractility	13,56±0.71	15,52±0,47*	13,88±0,38	14,32±0.22	14,52±0,34	16.15±0,72
dp/dt, mm Hg/sec	2 275±112,77	2 704±64,65*	2 425±87,71	2 407±39,79	2 650±75,18*	2 895±88,96
TTI, mm Hg·sec	2 972±104,74	2 751±152,11	3 449±82,08*	3 673±179,27	3 739±50,74*	3 427±82,05*
Contraction time, sec	0,075±0,02	0,071±0,0009	0,085±0,001*	0,080±0,001*	0,085±0,003*	0,078±0,002
Phase of asynchronous contraction, sec	0,039±0,001	0,039±0,005	0,041±0,0008	0.042±0,001	0,037±0,002	0,047±0,002*
Phase of isometric contraction, sec	0,036±0,002	0,032±0,001	0,045±0,001*	0.037±0,001*	0,048±0,002*	0,031±0,002*
Expulsion time, sec	0,110±0,004	0,097±0,005	0,087±0,005*	0.086±0,003	0,105±0,004	0,084±0,004*

*P < 0.05.

TABLE 2. Changes in Principal Hemodynamic Parameters under the Influence of Pyrroxan in Puppies Aged 2-3 Months with Vasorenal Hypertension

Index	Initial background	Injection of pyrroxan	3rd day of renal ischemia	Injection of pyrroxan	14th day of renal ischemia	Injection of pyrroxan
MBP, mm Hg	117,0±2,24	91,0±4,29*	144,3±2,43*	103,3±3,74*	166,1±2,52*	127,6±3,18*
Heart rate, beats/min	127,6±2,05	135,6±2,43*	150,6±2,74*	168,6±4,11*	131,0±2,43	148,0±2,24*
Cardiac index, liters/m²	1,70±0,02	1,56±0,05*	2,28±0,04*	1,89±0,04*	1,57±0,03*	1,78±0,05*
Systolic index, ml/m²	13,36±0,36	11,56±0,47*	15,17±0,41*	11,26±0,42*	12,02±0,33*	12,03±0,30
SPVR, dynes·sec·cm⁻⁵·m²	5503±164	4655±184*	5068±126	4383±224*	8443±239*	5756±168*
WILV, kg·m/m²	2,71±0,04	1,97±0,06*	4,48±0,07*	2,65±0,09*	3,56±0,05*	3,09±0,13*
IVP_{max}, mm Hg	130,2±1,03	115,0±1,50*	165,6±1,63*	118,6±1,64*	183,4±2,89*	133,6±2,52*
Index of contractility	12,01±0,38	14,82±0,57	13,68±0,29*	17,43±0,45*	8,14±0,45*	12,36±0,47*
dp/dt, mm Hg/sec	1541±76,28	1704±52,93	2258±80,95*	2066±51,37*	1495±95,73	1587±91,06
TTI, mm Hg·sec	2177±31,22	1710±65,94*	3511±67,11*	2638±84,68*	3522±104,63*	2572±32,29*
Contraction time, sec	0,06±0,001	0,051±0,001*	0,057±0,002	0,054±0,002	0,069±0,001*	0,061±0,0009*
Phase of asynchronous contraction,	0,029±0,0007	0,028±0,001	0,029±0,001	0,032±0,001*	0,036±0,0009*	0,033±0,0006*
Phase of isometric contraction, sec	0,031±0,0008	0,023±0,0006*	0,026±0,001*	0,022±0,001*	0,033±0,0007	0,028±0,0006*
Expulsion time, sec	0,099±0,0007	0,086±0,002*	0,119±0,0007*	0,109±0,0009*	0,118±0,003*	0,106±0,00*

*P < 0.05.

showed a tendency to rise. The first derivative of the intraventricular pressure was virtually unchanged, but under the influence of pyrroxan the original duration of isometric contraction was restored in the phase structure of the cycle of the left ventricle. The results are evidence that by the 3rd day of experimental vasorenal hypertension the increased vascular tone was due not only to the direct constrictor effect of angiotensin, but also to activation of α-adrenergic influences. The hypokinetic character of the hypertension arising in the adult dogs 3 days after ischemization of the kidneys was evidently not entirely due to increased resistance to the expulsion of blood.

Injection of pyrroxan into the dogs 14 days after renal ischemia also lowered the raised blood pressure through a decrease in SPVR. However, by contrast with the previous time of investigation, features of activation of the cardiac contracting mechanism were now observed: an increase in the cardiac index and in the power of the left ventricle, a decrease in TTI and the phase of isometric contraction, and a tendency for the index of contractility and dp/dt to rise. On the 14th day also, vasorenal hypertension was thus characterized by activation of α-adrenergic influences.

α-Adrenoreceptor blockade in puppies 3 days after ischemia of the kidneys thus caused the blood pressure to fall below normal through a decrease in both SPVR and the cardiac index (Table 2). The systolic index, IVP, and TTI also fell under these circumstances. Shortening of the phase of isometric contraction and the expulsion time also was observed in the phase structure of the cardiac cycle. It must be emphasized that injection of pyrroxan into intact puppies led to similar, but less marked changes in the hemodynamics. The fall in the peripheral vascular resistance under the influence of pyrroxan was mainly connected with the peripheral α-adrenoblocking action of the drug, whereas the decrease in the cardiac output in both the "hypertensive" and the intact puppies must be regarded as the result of blockade of α-adrenergic structures in the posterior hypothalamus [1]. Since the hemodynamic changes under the influence of pyrroxan were more marked in the "hypertensive" puppies it can be concluded that in young animals the early phases of vasorenal hypertension are characterized by a higher level of central and peripheral α-adrenergic activity. During α-adrenoreceptor blockade, despite the weakening of adrenergic stimulation of the heart and the reduction in the cardiac output, the intrinsic inotropic properties of the myocardium evidently increase, and this is reflected in an increase in the index of contractility.

Even more marked changes in the hemodynamic parameters were produced by pyrroxan 14 days after ischemization of the kidneys compared with 3 days after ischemization.

The data described above indicate that central and peripheral α-adrenergic influences play a role in the genesis of the hemodynamic changes in the initial period of formation of vasorenal hypertension.

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CHANGES IN FAST UTERINE MUSCLE POTENTIALS IN RABBITS EXPOSED TO CHRONIC HYPOXIA

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Changes in high-frequency myometrial electrical activity after separate and simultaneous division of the uterine and ovarian vessels were studied in 137 chronic experiments on 18 nonpregnant parous rabbits. The deepest and longest (up to 45 days) depression of the amplitude and frequency of fast myometrial potentials was shown to take place after simultaneous division of the uterine and ovarian arteries and veins. Both the amplitude and frequency of the potentials were gradually restored during compensation of the circulation along collateral vessels.

KEY WORDS: spike potentials; circulatory hypoxia; myometrium; uterine and ovarian vessels.

Ligation of the principal uterine vessels in cases of atonic uterine bleeding in the early puerperium is an effective emergency treatment of this pathology [2, 12, 15].

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