CHANGES IN THE SYSTEMIC HEMODYNAMICS AFTER INJECTION OF SYNTHETIC ANGIOTENSIN II INTO DOGS OF DIFFERENT AGES

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The arterial pressure, cardiac output, total peripheral resistance, and heart rate were studied in experiments on puppies aged 18-22 days and 2-3 months and on adult dogs receiving injections of synthetic angiotensin II-amide in a dose of 2 μg/kg body weight/min. Elevation of the arterial pressure in the adult dogs as a result of the action of angiotensin was due to an increase in the total peripheral resistance, but in puppies it was due to an increase both in the total peripheral resistance and in the cardiac output.

KEY WORDS: hemodynamics; cardiac output; angiotensin; age reactivity.

Angiotensin, when injected into the blood stream, is known to increase the total peripheral resistance and the systemic arterial pressure. Most workers have found a reduction in the minute blood volume under these circumstances [2, 10-12]. Meanwhile, if the experiments are carried out with the heart isolated, a direct positive inotropic and chronotropic effect of angiotensin is found on the myocardium [4, 6, 9]. This effect of angiotensin is evidently not manifested in the intact animal because of the development of various adaptive responses to an increase in the vascular resistance.

In the investigation described below the hemodynamic effects of angiotensin were accordingly studied in experiments on animals of different ages in which the mechanisms of regulation of the cardiovascular system are qualitatively different and imperfect.

EXPERIMENTAL METHOD

Experiments were carried out on puppies aged 18-22 days and 2-3 months and on adult dogs (6 animals in each group). Synthetic angiotensin II-amide (a product of the experimental factory of the Institute of Organic Synthesis of the Latvian SSR) was injected through a fluoroplast catheter into the femoral vein in a dose of 2 μg/kg/min. The arterial blood pressure (BP) was recorded in the femoral artery by a mercury manometer. The minute (MV) and systolic (SV) blood volumes were determined by the thermodilution method [3] with synchronous recording of the ECG. All operative manipulations were carried out under local procaine anesthesia. In control experiments (two animals in each age group) the corresponding volume of physiological saline was injected.

EXPERIMENTAL RESULTS AND DISCUSSION

In all animals injection of angiotensin II caused elevation of the BP; the amount of the rise of pressure was a little greater in the puppies aged 18-22 days. Hemodynamic changes in the adult dogs corresponded to those described in the literature and consisted of a marked increase of total peripheral resistance (TPR) and a decrease in MV and SV (Table 1). The minute and stroke work of the left ventricle were reduced correspondingly. The BP returned to normal 5 min after injection of the preparation as a result of a sharp decrease in MV and SV, tachycardia developed, but the TPR remained higher than initially as before.

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TABLE 1. Changes in Systemic Hemodynamics under the Influence of Angiotensin II in Adult Dogs (M ± m)

Index studied	Background	During injection of angiotensin	5 min after injection
VP (in mm Hg)	160,66±4,23	185,00±4,67	158,00±3,67
P		<0,01	>0,5
Heart rate (in beats/min)	104,00±9,34	115,60±9,22	142,50±12,66
P		>0,1	<0,05
MV (in ml/min)	1 812,24±69,95	1 444,44±48,35	1 228,95±130,63
P		<0,01	<0,01
Cardiac index (in liters/m^2 · min)	1,06±0,02	0,89±0,001	0,77±0,04
P		<0,01	<0,001
SV (in ml)	16,06±0,55	12,42±0,68	8,59±0,52
P		<0,01	<0,001
Systolic index (in ml/m^2)	10,05±0,93	8,86±0,67	5,46±0,34
P		>0,1	<0,01
TPR (in dynes · sec · cm^{-5})	7 301,50±124,13	10 200,64±217,82	9 687,76±682,22
P		<0,001	<0,01
Specific TPR (in dynes · sec · m^2 · cm^{-5})	12 329,57±387,33	16 977,73±826,30	17 119,59±890,92
P		<0,001	<0,001
Work index of left ventricle (in kg · m/m^2)	2,33±0,06	2,23±0,09	1,58±0,08
P		>0,1	>0,001
Stroke work index of left ventricle (in g · m/m^2)	22,01±1,58	20,94±1,28	11,31±0,44
P		>0,5	<0,001

TABLE 2. Changes in Systemic Hemodynamics under the Influence of Angiotensin II in Puppies Aged 2-3 Months

Index studied	Background	During injection of angiotensin	5 min after injection
VP (in mm Hg)	98,86±4,18	125,66±2,49	96,66±3,36
P		<0,001	>0,5
Heart rate (in beats/min)	147,43±1,79	159,42±2,88	159,50±1,98
P		<0,01	<0,01
MV (in ml/min)	384,36±14,54	487,43±24,78	415,13±19,17
P		<0,01	>0,2
Cardiac index (in liters/m^2 · min)	1,78±0,05	2,24±0,03	1,86±0,08
P		<0,001	>0,3
SV (in ml)	2,63±0,07	3,09±0,08	2,61±0,07
P		<0,01	>0,8
Systolic index (in ml/m^2)	12,40±0,29	14,47±0,47	11,76±0,61
P		<0,01	>0,3
TPR (in dynes · sec · cm^{-5})	20 217,75±215,46	21 498,96±500,57	19 495,71±517,53
P		<0,05	>0,2
Specific TPR (in dynes · sec · m^2 · cm^{-5})	4 203,43±72,39	4 857,80±127,98	3 815,45±213,25
P		<0,01	>0,1
Work index of left ventricle (in kg · m/m^2)	2,44±0,11	3,73±0,11	2,53±0,07
P		<0,001	>0,4
Stroke work index of left ventricle (in g · m/m^2)	16,70±0,76	24,22±0,94	15,93±0,29
P		<0,001	<0,3

Changes in the hemodynamics in puppies aged 2-3 months and 18-22 days (Tables 2 and 3) were largely similar in type and consisted not only of an increase in TPR, but also of the appearance of tachycardia and an increase in MV and in the minute work of the heart. Meanwhile in the puppies aged 2-3 months, an increase in SV and the stroke work of the heart was found, whereas in puppies aged 18-22 days SV was reduced. In the puppies of both groups 5 min after injection of angiotensin TPR and MV were reduced but the tachycardia still remained. Injection of physiological saline had virtually no effect on the hemodynamic indices in the control animals.

The age differences in the changes in the hemodynamics after injection of synthetic angiotensin II can be interpreted as follows. Angiotensin is known to cause liberation of the adrenergic mediator from sympathetic endings [5, 7] and the adrenals [8], and its hemodynamic effects are partly due to the action of catecholamines [4, 7]. In particular, the positive inotropic and chronotropic action of angiotensin on the

TABLE 3. Changes in Systemic Hemodynamics under the Influence of Angiotensin II in Puppies Aged 18-22 Days

Index studied	Background	During injection angiotensin	5 min after injection
VP (in mm Hg)	87,00±2,52	117,00±3,62	91,33±2,37
P		<0,001	>0,2
Heart rate (in beats/min)	182,66±3,80	238,66±3,36	239,66±1,81
P		<0,001	<0,001
MV (in ml/min)	141,42±3,85	159,49±6,04	145,37±3,31
P		<0,05	>0,3
Cardiac index (in liters/m^2 · min)	1,93±0,02	2,13±0,03	1,85±0,05
P		<0,001	>0,1
SV (in ml)	0,77±0,01	0,63±0,02	0,57±0,02
P		<0,001	<0,001
Systolic index (in ml/m^2)	10,86±0,1	8,62±0,11	7,73±0,16
P		<0,001	<0,001
TPR (in dynes · sec · cm^{-5})	49 747,49±749,39	61 412,40±3146,91	5 1687,61±779,01
P		<0,01	>0,1
Specific TPR (in dynes · sec · m^2 · cm^{-5})	3 592,54±69,71	4 478,46±136,00	3 847,90±82,36
P		<0,001	<0,05
Work index of left ventricle (in kg · m/m^2)	2,27±0,08	3,47±0,09	2,41±0,09
P		<0,001	>0,2
Stroke work index of left ventricle (in g · m/m^2)	12,48±0,42	13,74±0,51	9,68±0,44
P		>0,05	<0,01

heart is linked with liberation of these last substances. In puppies, unlike in adult dogs, the heart is predominantly under the influence of sympathico-adrenal regulation [1], and this also leads to manifestation of the positive inotropic and chronotropic effects of angiotensin. At the age of 18-22 days activation of sympathico-adrenal influences evidently does not yet give rise to any marked inotropic effect, and for that reason the increase in MV in puppies of this age is attributable only to the tachycardia associated with the reduced SV. In adult dogs, with more perfect regulatory responses, elevation of BP leads to a decrease in MV and SV. After the end of the pressor action of angiotensin the reflex influences on the heart evidently disappear; the tachycardia thus produced could be the result of the direct action of angiotensin.

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