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Antihypertensive Effect of Captopril in Turkeys (41315)

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Abstract. In experiment 1, dietary administration of captopril to turkeys from 6 to 10 weeks of age attenuated the development of elevation of blood pressure and ratio of heart weight to body weight which occurred in untreated turkeys during this 4-week period. In experiment 2, 16 male and 16 female turkeys were fed a control diet until 6 weeks of age. At this time, 8 turkeys of each sex were continued on the control diet and the other 8 of each sex were changed to a diet containing captopril. Four males and four females in each group were sacrificed at 10 weeks of age. The remaining 4 males and 4 females previously fed a control diet were transferred to a diet containing captopril until 14 weeks of age. Similarly, turkeys previously fed captopril were fed a control diet until 14 weeks of age. Captopril attenuated the increase in both blood pressure and ratio of heart weight to body weight that occurred in control turkeys at 10 weeks of age. Removal of captopril from the diet and feeding of the control diet was accompanied by an increase of blood pressure and ratio of heart weight to body weight, but addition of captopril to the diet at 10 weeks of age resulted in reduction of blood pressure and ratio of heart weight to body weight. These results indicate that captopril attenuates the natural development of hypertension in Broad-Breasted White turkeys.

Administration of captopril (SQ14225), a potent inhibitor of angiotensin I converting enzyme, is accompanied by a reduction in blood pressure of both spontaneous and two-kidney renal hypertensive rats (2K-RHR) (1, 2), hypertensive humans (3–5), dogs (6), rabbits (7), and cats (8,9). Captopril prevents the development of hypertension, reverses cardiac hypertrophy (10), and increases water intake in spontaneously hypertensive rats (11).

It is known that the Broad-Breasted White (BBW) turkey has a blood pressure that is greatly elevated in comparison to that of other vertebrates (12). The elevated blood pressure in this spontaneously hypertensive species is, in all probability, responsible for the intimal hyperplasia of the abdominal aorta that develops spontaneously in these turkeys by 6 weeks of age (13). In addition, chronic administration of either propranolol (14) or reserpine (15) to turkeys reduces blood pressure and other hemodynamics and protects them against rupture of aortic dissecting aneurysms. The same two drugs also are effective for the treatment of aneurysms of humans (16). In view of the apparent similarity of the responses of turkeys and humans to these two medicaments, it was decided to determine whether captopril had an antihypertensive effect in Broad-Breasted White (BBW) turkeys.

Materials and Methods. Two experiments were conducted in which BBW turkeys were fed captopril (CA). In the first experiment, five male and five female turkeys were fed a control diet until 10 weeks of age. A similar number of males and females was fed the same diet in which CA was mixed. By determining daily feed intake, it was found that these turkeys consumed about 22 mg CA/kg during a period of 24 hr. Feeding of CA began at 6 weeks of age and continued through 10 weeks of age, at which time all turkeys were sacrificed.

In the second experiment, 16 male and 16 female turkeys were fed the control diet until 6 weeks of age. At this time, 8 males and 8 females were continued on the same diet, and a similar number of males and females were transferred to the control diet containing CA until 10 weeks of age. One-half of the turkeys in each group of eight were sacrificed at 10 weeks of age. The remaining 4 males and 4 females fed the control diet from 6 to 10 weeks of age were transferred to the CA diet, and a similar number of male and female turkeys fed CA from 6 to 10 weeks of age were changed to the control diet until sacrificed at 14 weeks of age.

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Hemodynamic parameters were measured during the course of the two experiments. These measurements were determined prior to the commencement of each experiment, at the conclusion of experiments or at the time of changing of diets (experiment 2). Direct blood pressure and heart rate were measured in unanesthetized birds whose left carotid artery was cannulated following local anesthesia by lidocaine. Both blood pressure and heart rate were measured using a linear core P1000 transducer (Narco Bio-Systems).

Water and food consumption were determined at the conclusion of experiment 1, and also at the time of changing of diets in experiment 2. At the conclusion of each experiment, birds were killed and their hearts removed, cleaned, and weighed.

Results. In the first experiment, there was no significant difference in blood pressure or heart rate among untreated male or female turkeys at the commencement of the trial (6 weeks of age). The average systolic and diastolic blood pressures of untreated male and female turkeys increased by about 50 mm Hg from 6 to 10 weeks of age (Table I). In contrast, among male and female turkeys fed CA for 4 weeks the systolic blood pressure increased from 0 to 11 mm Hg and diastolic blood pressure increased from 21 to 24 mm Hg. Mean heart weight of CA-treated female turkeys was significantly less ($P < 0.01$) than that of untreated controls (Table I).

In experiment 2, male and female turkeys fed a control diet from 6 to 10 weeks of age had an average increase in systolic and diastolic blood pressure of 22 and 23 mm Hg, respectively, during this interval of 4 weeks. However, turkeys fed CA from 6 to 10 weeks of age averaged a decline of 30 and 11 mm Hg in systolic and diastolic blood pressure, respectively, during this period of 4 weeks. Heart rate was unaffected by therapy. The ratio of heart to body weight of both male and female turkeys fed CA was significantly less than that of the control group at necropsy (Table II) at 10 weeks of age.

In experiment 2, turkeys previously fed a control diet from 6 to 10 weeks of age were transferred to a diet containing CA, and

TABLE I. EFFECT OF CHRONIC ADMINISTRATION OF CAPTOPRIL ON CARDIOVASCULAR FUNCTIONS IN TURKEYS (EXPERIMENT 1)

	6-Week data				10-Week data (4 weeks of treatment)				
	Blood pressure (mm Hg)		Mean (mm Hg)	Heart rate (beats/min)	Blood pressure (mm Hg)		Mean (mm Hg)	Heart rate (beats/min)	Heart wt (g/kg body wt)
	Systolic	Diastolic			Systolic	Diastolic			
Male									
Control (5)	170 ± 5[a]	114 ± 7	142 ± 7	358 ± 7	227 ± 6	164 ± 8	196 ± 6	268 ± 10	4.3 ± 0.2
Captopril (5)	164 ± 13	103 ± 10	134 ± 12	342 ± 14	175 ± 17*	127 ± 13*	151 ± 14	294 ± 13	3.4 ± 0.4
Female									
Control (5)	151 ± 7	99 ± 9	125 ± 8	342 ± 14	202 ± 4	160 ± 3	181 ± 3	283 ± 9	4.0 ± 0.2
Captopril (5)	152 ± 4	97 ± 6	125 ± 5	318 ± 7	152 ± 16*	118 ± 12**	135 ± 14*	282 ± 4	2.6 ± 0.2**

[a] 1 SE of mean.
* Significantly different from controls ($P < 0.05$).
** Significantly different from controls ($P < 0.01$).

TABLE II. EFFECT OF CAPTOPRIL ON HEMODYNAMICS, HEART WEIGHTS, AND WATER CONSUMPTION OF TURKEYS (EXPERIMENT 2)

Experimental group	Blood pressure (mm Hg)			Heart rate (beats/min)	Heart wt/body wt (g/kg)	Water consumption (ml/24 hr)
	Systolic	Diastolic	Mean			
			Week 6—Pretreatment			
Male						
Control (16)	153 ± 3[a]	111 ± 5	125 ± 4	323 ± 8		
Female						
Control (16)	153 ± 3	113 ± 4	127 ± 3	310 ± 9		
			Week 10—CA treatment			
Male						
Control (8)	177 ± 7	133 ± 9	149 ± 8	307 ± 15	4.25 ± 0.25	
Captopril treated (8)	121 ± 9**	96 ± 8*	104 ± 8**	323 ± 11	3.09 ± 0.15*	
Female						
Control (8)	171 ± 2	134 ± 3	147 ± 2	313 ± 8	4.33 ± 0.63	
Captopril treated (8)	131 ± 12*	104 ± 10*	114 ± 11*	317 ± 6	3.17 ± 0.29*	
			Week 14—Treatment reversal			
Male						
Control (4)	192 ± 9	137 ± 4	155 ± 6	280 ± 11	3.13 ± 0.22	—
Captopril treated (4)	145 ± 9**	107 ± 16	119 ± 13*	316 ± 15	2.17 ± 0.03*	—
Female						
Control (4)	177 ± 5	133 ± 6	148 ± 5	263 ± 17	2.96 ± 0.14	680 ± 16.17
Captopril treated (4)	167 ± 4	125 ± 15	139 ± 11	333 ± 7**	2.33 ± 0.17*	904 ± 36.95**

[a] One standard error of mean.
* Significantly different from simultaneous control group ($P < 0.05$).
** Significantly different from simultaneous control group ($P < 0.01$).

those fed CA from 6 to 10 weeks of age and having reduced blood pressures were changed to the control diet (Table II). All turkeys were sacrificed at 14 weeks of age. The average systolic blood pressure of the former group declined by 18 mm Hg and the diastolic blood pressure declined by 20 mm Hg at 14 weeks of age when compared to pressures at 10 weeks of age; heart rate increased significantly only in females. The average systolic blood pressure of the latter group increased by 64 mm Hg and the average diastolic blood pressure increased by 42 mm Hg at 14 weeks of age when compared to pressures at 10 weeks of age; heart rate decreased. Water consumption was greater and the ratio of heart weight per kilogram body weight at 14 weeks of age was lower in turkeys transferred from a control diet to a diet with CA, as compared to turkeys transferred from the CA diet to a control diet at 10 weeks of age (Table II).

Discussion. The mature BBW turkey has a blood pressure that is extremely high in comparison to other vertebrates (12). The factors involved in such an elevated blood pressure have not been ascertained, but it is probable that genetic selection has contributed since the native, or wild turkey is reported to have a blood pressure lower than that of the BBW turkey (17).

One objective of this study was to determine whether chronic administration of the angiotensin I converting enzyme inhibitor, captopril, would affect the blood pressure of the BBW turkey. Previous studies with such BBW turkeys provided indirect evidence that the converting enzyme was present (18); this was essential information since the presence of the angiotensin I converting enzyme had not been reported previously in turkeys. Thus, administration of either 6.0 or 12.0 μg of angiotensin I/kg body weight, iv was accompanied by sig-

nificant increases in both systolic and diastolic blood pressures. However, 6 to 10 min following blockade with CA (35 mg/kg), blood pressure failed to increase when the same doses of angiotensin I were administered. Pressor responsiveness to administration of either angiotensin II or norepinephrine was maintained, however.

The present studies show that mean blood pressure of BBW turkeys increased approximately 50 mm Hg from week 6 to week 10 of age (Table I), and that both sexes responded similarly to CA. Heart rate was not consistently affected. Treatment for 4 weeks provided significant protection against hypertension (Table I). Further evidence that CA protected against hypertension is evident from the lowering of the ratio of heart weight to body weight. The development of systemic hypertension is generally accompanied by hypertrophy of the left heart and a thicker cardiac wall to pump against an increased peripheral resistance. Treatment with CA not only protected against elevation of blood pressure to the level of untreated controls, but also prevented cardiac hypertrophy (Tables I, II). The possibility that the renin–angiotensin system contributes to the naturally occurring elevation of blood pressure remains for further testing.

The antihypertensive activity of CA has been reported for several species of animals, including humans, dogs, cats, and rats (19). The turkey can now be added to this list. Additional similarities have been noted in the responses of turkeys and certain mammals to the administration of CA; for example, an increased water intake accompanied chronic administration of CA to turkeys (Table II), as has been reported for rats (20, 21). The similarities of responsiveness of both the turkey and the mammalian species listed above to treatment with CA provide further evidence that the BBW turkey may be a useful model in which to evaluate drugs that may be beneficial in the treatment of hypertension in humans.

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