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Comparison of the role of the renin-angiotensin aldosterone system in the genesis of hypertension between two groups of nonhunting dogs and hunting dogs

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Abstract: The role of the renin-angiotensin aldosterone system in the genesis of hypertension between nonhunting dogs and hunting dogs of various breeds was comparatively studied in the city of Tuzla (Bosnia and Herzegovina). Sixty dogs were divided into four subgroups based on different age categories. Hypertension was recorded in 21 dogs or in 35% of examined dogs. Fourteen dogs had mild (23.3%), 5 dogs had moderate (8.3%), and 2 dogs had severe hypertension (3.3%). The most cases of hypertension (n = 9) were recorded in hunting dogs aged from 9 to 12 years. In subgroups of nonhunting and hunting dogs aged from 1 to 3 years, a high correlation was recorded between systolic and diastolic pressures ($P < 0.0001$). A certain degree of correlation was recorded between systolic pressure and renin ($P = 0.037$) and between heart rate and renin ($P = 0.024$). In subgroups of nonhunting and hunting dogs aged from 9 to 12 years, a high correlation was recorded between systolic and diastolic pressures ($P = 0.006$) and between diastolic pressure and heart rate ($P = 0.002$). A certain degree of correlation existed between systolic pressure and heart rate ($P = 0.041$), systolic pressure and aldosterone ($P = 0.035$), and heart rate and renin ($P = 0.038$). Increased values of renin were mostly recorded in dogs with hypertension. This research indicates the importance of routine blood pressure measurement during every examination, which can thus serve as a screening for undertaking further steps in processing the patient.

Key words: Hypertension, nonhunting dogs, hunting dogs, renin-angiotensin aldosterone system

1. Introduction

Essential hypertension is one of the most prevalent diseases of developed Western countries as well as developing countries and is an important risk factor for cardiovascular morbidity and mortality (1). Human essential hypertension is a complex condition and shares many features common to animal hypertension (2). Many etiological factors are responsible for human and animal hypertension, such as excessive salt intake, fatty meals, obesity, hyperactivity of the renin-angiotensin aldosterone system (RAAS), and genetic factors (2). It is universally known that the RAAS is a hormone system that regulates hypertension and fluid balance. The present study examines this focusing on carefully selected groups and subgroups of nonhunting and hunting dogs of various breeds in the city of Tuzla (Bosnia and Herzegovina). Many studies from different parts of the world have estimated the incidence of obesity in dog populations to be between 22% and 40% as a consequence of excessive nutrition or inadequate energy utilization due to limited physical activity (3). Much evidence from animal and genetic studies suggests that salt intake also plays an important role in regulating blood pressure (4). Sodium chloride infusion in normal dogs caused very little change in blood pressure, although it is known that the anionic component of sodium chloride induces significant increase in systolic and diastolic blood pressures (5,6). However, in dogs infused with low doses of angiotensin II, the same sodium chloride infusion caused a large increase in blood pressure (5,7). It is obvious that RAAS suppression has an important role in preventing large increases in blood pressure when salt intake is increased above usual levels (4). Many studies have also suggested that essential hypertension must be related to the RAAS and to an undefined renal dysfunction (8). Furthermore, hypertension can be caused in a normotensive animal by transplantation of a kidney from a hypertensive donor (8). However, some studies have shown that angiotensin II can stimulate oxidative stress, which can activate some vasopressor mechanisms that can cause the vasoconstrictor effect of angiotensin II (1,9). The aim of this study was to compare the role of the RAAS in the genesis of hypertension between nonhunting dogs of various breeds and hunting dogs of various breeds from two age categories, from 1 to 3 years old and from 9 to 12 years old, in Tuzla Canton, Bosnia and Herzegovina.

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2. Materials and methods

In this study, a total of 60 dogs of various breeds were classified into two groups. Nonhunting dogs as group A were divided by age in two subgroups: A1- dogs aged from 1 to 3 years; A2- dogs aged from 9 to 12 years. Hunting dogs represented the second group, B, which was also divided by age into 2 subgroups: B1- dogs aged from 1 to 3 years; B2- dogs aged from 9 to 12 years. All subgroups contained 15 dogs. Division of dogs into two groups, A (nonhunting dogs) and B (hunting dogs), was done because some breeds of hunting dogs have approximately 10 mmHg higher blood pressure than other breeds (10). In accordance with scientific methodology, the groups of dogs were examined and processed following the principles and schemes of clinical examination: description of the animal, breed, sex, age, color, body marks, name, identification chip or mark, disease history, and the animal's condition at initial presentation (general condition, habitus, body temperature, pulse, breathing, visible mucosa, and lymph nodes). Blood pressure (BP) measurement in dogs was carried out using an oscillometric method without anesthesia with the MEC-1200 Vet device. Before the attempt of measuring BP, dogs were kept for 10 min with their owners in the measurement room. Dogs were carefully restrained and placed in the lateral position. The cuff was placed on the front part of the foot near the carpus (radial artery), and the width of the cuff was from 0.3 to 0.4 the volume of the leg. During the BP measurement dogs were calm and motionless. The first measurement was discarded, the following 3 measurements were recorded, and the obtained average value represented the measured BP. The same technician performed the measurements for all 60 examined dogs.

For examining the rennin and aldosterone levels, blood samples were taken from all dogs following the guidelines for particular diagnostic procedures according to established standards. Blood was taken by venipuncture (*v. brachiocephalica antebrachii*, *v. saphaena*) at the Tuzla Veterinary Station. Careful standardization of preparing the dog and the conditions of taking blood samples were based on strictly established principles. Blood was collected in previously cooled tubes with EDTA as the anticoagulant. Blood samples were kept cool and centrifuged at about $2000 \times g$ (1118×10^{-8}) in order to renew the plasma. Blood samples were kept deep-frozen at –20 °C or below from the beginning of the processing. Prior to the procedure, the blood samples were thoroughly mixed, keeping in mind that the temperature should not exceed 4 °C. It was necessary to avoid cycles of repeated freezing-defreezing of the blood samples. Further procedure followed standard measurement protocols. Classification of BP in mmHg for dogs was determined according to the criteria of the World Veterinary Association (WVA). Thus, the following groups were distinguished: dogs with normal BP, with systolic BP of 118–149 mmHg and diastolic BP of 66–88 mmHg; dogs with mild hypertension (systolic BP 150 and diastolic 95); dogs with moderate hypertension (systolic BP 160 and diastolic BP 100); and dogs with severe hypertension (systolic BP 180 and diastolic BP 120). After obtaining the data of the values of BP, pulse, and age of the examined dogs, measurement of the concentrations of hormones renin and aldosterone were carried out. Analysis of correlations between the measured variables of systolic and diastolic BP, heartbeat rate, and renin and aldosterone concentrations in all four subgroups of nonhunting and hunting dogs was performed by Student's t-test.

3. Results

In subgroup A1 (nonhunting dogs aged from 1 to 3 years), mild hypertension was recorded in one dog (Table 1). In 93% of the dogs in this subgroup (14 dogs), there was no hypertension recorded. The BP for subgroup A1 showed values for systolic pressure in the range of 116–152 mmHg (Table 1). The lowest value of systolic pressure was observed in a dog aged 12 months, while a higher value of systolic pressure was observed in a dog aged 24 months (Table 1). The values of diastolic pressure in this category of nonhunting dogs were in the range of 71–94 mmHg, while the pulse rate was from 79 to 115 heartbeats per minute (Table 1). Increased values of renin were noted only in a dog with mild hypertension (Table 1). Low values of the concentration of renin were accompanied by low arterial BP (Table 1). The concentration of aldosterone was between 0.000 nmol/L and 0.041 nmol/L. In subgroup A2 (nonhunting dogs aged from 9 to 12 years), there were five cases of mild hypertension recorded (Table 1). These cases of mild hypertension were related to the age of the dogs in this subgroup, accompanied by normal or slightly increased pulse rate from 94 to 107 heartbeats per minute (Table 1). Only one case of moderate hypertension, which bordered on severe hypertension, was recorded in this subgroup (Table 1). The dog had the highest arterial BP, which was on the boundary between moderate and severe hypertension. This dog's renin concentration was also the highest (0.388 nmol/L) (Table 1). Borderline values of renin concentration were also measured in five dogs (Table 1). In all five dogs with borderline values of renin, mild hypertension was recorded (Table 1). Increased aldosterone concentration from 1.003 nmol/L was measured only in one dog with mild hypertension (Table 1). In subgroup A2, there were 33% cases of mild hypertension and 7% of moderate hypertension, and in 60% of dogs, hypertension was not recorded (Table 1). In subgroup B1 (hunting dogs aged from 1 to 3 years), mild hypertension was recorded in two dogs (Table 2). Moderate hypertension was recorded in two dogs with BP of 177/115 mmHg and 166/96 mmHg

Table 1. The values of measured variables in nonhunting dogs.

Nonhunting dogs aged from 1 to 3 years, A1 subgroup							
Ordinal number of dog	Age in months	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)	Type of hypertension	Heart rate (per minute)	Renin (nmol/L)	Aldosterone (nmol/L)
1	24	136	88	-	115	0.306	0.008
2	30	132	82	-	108	0.240	0.001
3	18	129	79	-	103	0.210	0.001
4	24	125	71	-	102	0.302	0.010
5	24	144	87	-	105	0.202	0.010
6	24	119	82	-	79	0.302	0.023
7	24	143	84	-	103	0.189	0.000
8	12	116	94	-	81	0.293	0.001
9	24	152	91	Mild hypertension	101	0.309	0.001
10	24	134	84	-	113	1.490	0.001
11	20	136	79	-	107	0.022	0.002
12	12	134	73	-	110	1.460	0.001
13	24	130	91	-	103	0.004	0.013
14	12	141	93	-	103	0.010	0.003
15	24	140	87	-	81	0.300	0.041
Nonhunting dogs aged from 9 to 12 years, A2 subgroup							
1	108	119	67	-	99	0.001	1.312
2	108	121	85	-	78	0.001	0.235
3	114	121	80	-	87	0.002	0.698
4	120	146	88	-	98	0.122	0.001
5	132	143	79	-	81	0.118	0.001
6	132	143	93	-	93	0.001	0.186
7	108	140	92	-	90	0.110	0.003
8	120	155	97	Mild hypertension	94	0.307	0.001
9	132	152	99	Mild hypertension	103	0.302	0.004
10	120	152	107	Mild hypertension	107	0.303	1.003
11	120	132	111	-	90	0.240	0.008
12	120	152	96	Mild hypertension	100	0.304	0.002
13	108	179	94	Moderate hypertension	99	0.388	0.005
14	108	152	100	Mild hypertension	101	0.307	0.004
15	120	141	100	-	102	0.005	0.022

Table 2. The values of measured variables in hunting dogs.

Hunting dogs aged from 1 to 3 years, B1 subgroup							
Ordinal number of dog	Age in months	Systolic blood pressure(mmHg)	Diastolic blood pressure (mmHg)	Type of hypertension	Heart rate (per minute)	Renin (nmol/L)	Aldosterone (nmol/L)
1	36	137	81	-	104	0.001	1.034
2	20	151	87	Mild hypertension	123	0.308	0.002
3	12	155	105	Mild hypertension	106	0.309	0.003
4	30	177	115	Moderate hypertension	94	0.312	0.004
5	30	137	88	-	125	0.001	0.217
6	36	136	91	-	121	0.024	0.002
7	24	129	97	-	98	0.002	0.035
8	36	134	97	-	101	0.005	0.022
9	24	137	88	-	96	0.004	0.230
10	36	127	100	-	99	0.004	0.341
11	36	137	95	-	101	0.003	0.005
12	24	205	109	Severe hypertension	103	1.510	0.008
13	36	141	91	-	96	0.003	0.050
14	36	166	96	Moderate hypertension	99	0.312	0.006
15	36	125	91	-	99	0.309	0.210
Hunting dogs aged from 9 to 12 years, B2 subgroup							
1	108	151	127	Mild hypertension	125	0.303	0.003
2	108	158	111	Mild hypertension	106	0.302	0.004
3	108	136	87	-	89	0.004	0.148
4	120	182	98	Severe hypertension	106	0.313	0.007
5	108	153	134	Mild hypertension	120	0.302	0.004
6	120	151	110	Mild hypertension	106	0.304	0.003
7	108	132	84	-	109	1.470	0.004
8	120	167	113	Moderate hypertension	105	0.307	0.004
9	108	152	92	Mild hypertension	108	0.301	0.001
10	132	156	99	Mild hypertension	98	0.303	0.002
11	108	132	78	-	114	0.303	0.001
12	120	139	97	-	105	0.001	0.007
13	108	139	97	-	85	0.305	1.650
14	120	147	97	-	98	0.002	0.002
15	108	166	99	Moderate hypertension	101	0.308	0.005

(Table 2). The severe type of hypertension was recorded in one dog, whose BP was 205/109 mmHg. In all five dogs with increased BP, increased values of renin from 0.308 to 1.510 nmol/L were recorded (Table 2). The ratio between the renin concentration level and BP for subgroup B1 indicates that dog with severe hypertension had the highest measured values of renin (Table 2). In eight dogs higher aldosterone values were recorded (Table 2). In subgroup B1, moderate and mild hypertension were recorded in 13% of the cases, while severe hypertension was recorded in 7% of the cases. In 67% of the cases there was no hypertension recorded. In hunting dogs from subgroup B2 (dogs aged from 9 to 12 years), hypertension was recorded in 9 dogs (Table 2). Mild hypertension is a typical feature of this subgroup, considering its age structure, and it was recorded 6 times (Table 2). Moderate hypertension was recorded in two dogs, while severe hypertension was seen in only one dog accompanied by slight increase in pulse rate (Table 2). An increased level of renin concentration of 0.313 nmol/L was recorded in a dog whose arterial pressure was 182/98 mmHg, which matches severe hypertension (Table 2). This was the oldest dog in this subgroup, aged 120 months (Table 2). In most dogs in this subgroup, the values of aldosterone concentration corresponded to the normal level, except two dogs with 0.148 and 1.650 nmol/L (Table 2). In subgroup B2, there were 40% cases of mild hypertension, 13% cases of moderate hypertension, and 7% cases of severe hypertension. In 40% of the examined dogs, there was no type of hypertension recorded (Table 2). In subgroups A1 and B1, there was high correlation between systolic and diastolic pressure ($P < 0.0001$), and a certain degree of correlation between systolic pressure and renin ($P = 0.037$) and pulse rate and renin ($P = 0.024$). Other observed parameters did not exhibit significant correlation. In subgroups A2 and B2, there were high correlations between the following variables: systolic and diastolic pressure ($P = 0.006$), and diastolic pressure and pulse rate ($P = 0.002$). There was, to a certain degree, correlation between systolic pressure and pulse rate ($P = 0.041$), systolic pressure and aldosterone ($P = 0.035$), and pulse rate and renin ($P = 0.038$). Other observed parameters did not exhibit significant correlation. In subgroup A1, there was a certain degree of correlation between age and pulse rate ($P = 0.041$) and pulse rate and renin ($P = 0.045$). Other observed parameters did not exhibit significant correlation. In subgroup A2, there was a high correlation between systolic pressure and renin ($P < 0.0001$) and a certain degree of correlation between diastolic pressure and renin ($P = 0.018$). Other observed parameters did not exhibit significant correlation. The overall results presented in this study clearly indicate the difference in the values of renin and aldosterone levels in both groups of dogs, nonhunting and hunting.

4. Discussion

In dogs, limited data exist about naturally occurring hypertension, probably because of inadequate equipment for measurements of BP in veterinary clinics (11). Few cases of primary hypertension have been reported (11). The major source of information is from studies using the dog as an experimental model (11). The animal models of hypertension share many features common to human hypertension and because of that some studies on experimental hypertension were carried out in dogs (2). Physiological values of BP in dogs vary from 118 to 149 mmHg for systolic pressure and 66 to 88 mmHg for diastolic pressure according to the WVA. During this study in the Tuzla municipality, hypertension was recorded in 35% of dogs. In the A1 subgroup of nonhunting dogs of different breeds from 1 to 3 years of age, only one dog had BP of 152/91 mmHg, while in the B1 subgroup of hunting dogs of the same ages, five cases of hypertension were recorded. One dog from this subgroup, aged 24 months, had BP of 205/109 mmHg and renin concentration of 1.510 nmol/L. This hypertension cannot be attributed to the age of dog, because this was not the oldest dog in this subgroup. BP increases with age from 1 to 3 mmHg per year (12). Furthermore, males have 10 mmHg higher BP than females, and hunting dogs have slightly higher BPs than other breeds of nonhunting dogs (10). In this subgroup (B1) of hunting dogs hypertension was seen in 33%. All dogs with high BP also had elevated concentrations of renin. In the subgroup (B2) of hunting dogs aged from 9 to 12 years, hypertension was seen in 60%. The dog with the greatest BP of 182/98 mmHg had the highest concentration of renin of 0.3113 nmol/L, whereas in the nonhunting group of dogs aged from 9 to 12 years hypertension was seen in 40%, which was related to the age of the dogs. Similar results were also reported by Watkins et al. (13). The reason for this high BP probably lies in a disorder of the RAAS or kidney disease. Hypertension in dogs occurs in a high percentage of cases as a consequence of kidney disease (14). Renal hypertension is mostly caused by renal artery constriction, which activates the peripheral RAAS and the sympathetic nervous system (15). In this study in the Tuzla municipality, mostly a high renin level was recorded in dogs with mild, moderate, or severe hypertension. Similar results were obtained in studies in the United States (16). Renin is secreted from the kidneys when sympathetic activity is increased (2). Renin also converts angiotensinogen to angiotensin II, which is a potent vasoconstrictor and increases the BP (2). In our study hypertension was established in 21 dogs. The results of our study are very similar to the results reported by Syme et al. (17), who confirmed that excessive activity of the RAAS affects the occurrence of hypertension. However, in some dogs with mild hypertension, a slight

increase in heart rate was recorded, which could be related to reduced vasodilatory control, because the value of the heart rate does not follow the elevated BP. The occurrence of hypertension in dogs is affected by many factors such as obesity, chronic renal dysfunction, diabetes mellitus, and cardiovascular disease (14,18,19). However, in order to be absolutely sure and to exclude these diseases, information should be available about weight, glucose, blood urine nitrogen or creatinine levels, and ECG results, as well as scanning of the renal artery, which would significantly increase the scope of this study. In addition to life expectancy, BP itself varies with breed. This variation is thought to have a genetic basis, because both racing and show greyhounds have high BP, suggesting that these do not result from feeding or exercise levels (20). Some studies showed that exercise may have a large impact on the value of BP. When examined within breeds, one group demonstrated that dogs that exercised heavily had lower resting BPs than those that did not (20). In lean dogs, left atrial pressure decreased as a response to exercise, while in obese dogs it increased dramatically (21). A number of studies based their position on the assumption that in dogs, just like in humans, age increases hypertension prevalence. However, it was proven that in dogs age alone is not the only exclusive hypertension factor, but that it is also a primary disease causing hypertension, which is largely in line with our results. Namely, hypertension prevalence in the population of dogs in Bosnia and Herzegovina is quite low, which was confirmed by our study, in which a total of 60 dogs were examined, with 21 cases of hypertension detected (35%). However, this study, like many other previous studies, suggests that the RAAS has great importance in the occurrence and detection of high BP whether it is primary or secondary hypertension.

References

1. Romero JE, Reckelhoff JF. Role of angiotensin and oxidative stress in essential hypertension. Hypertension 1999; 34: 943-949.
2. Badyal DK, Lata H, Dadhich CH AP. Animal models of hypertension and effect of drugs. Indian J Pharmacol 2003; 35: 349-362.
3. German AJ. The growing problem of obesity in dogs and cats. J Nutr 2006; 136: 1940-1946.
4. Feng JH, MacGregor GA. Salt, blood pressure and the renin-angiotensin system. J Renin-Angio-Aldo S 2003; 4: 11-16.
5. DeClue JW, Guyton AC, Cowley AW, Coleman TG, Norman RA, McCaa REE. Subpressor angiotensin infusion, renal sodium handling, and salt-induced hypertension in the dog. Circ Res 1978; 43: 503-512.
6. Kurtz TW, Al-Bander HA, Morris RC Jr. Salt-sensitive essential hypertension in men. Is the sodium ion alone important? N Engl J Med 1987; 317: 1043-1048.
7. Hall JE, Guyton AC, Smith MJ Jr, Coleman TG. Blood pressure and renal function during chronic changes in sodium intake: role of angiotensin. Am J Physiol 1980; 239: 271-280.
8. DeWardener H. The primary role of the kidney and salt intake in the aetiology of essential hypertension. Clin Sci 1990; 79: 193-200.
9. Rajagopalan S, Kurz S, Munzel T, Tarpey M, Freeman BA, Griendling KK, Harrison DG. Angiotensin II-mediated hypertension in the rat increases vascular superoxide production via membrane NADH/NADPH oxidase activation: contribution to alterations of vasomotor tone. J Clin Invest 1996; 97: 1916-1923.
10. Brown S, Atkins C, Bagley R, Carr A, Cowgill L, Davidson M, Egner B, Elliott J, Henik R, Labato M et al. Guidelines for the identification, evaluation and management of systematic hypertension in dogs and cats. J Vet Intern Med 2007; 21: 542-558.
11. Tippett FE, Padgett AG, Eyster G, Blanchard G, Bell T. Primary hypertension a colony of dog. Hypertension 1987; 9: 49-58.
12. Bodey AR, Michell AR. Epidemiological study of blood pressure in domestic dogs. J Small Anim Pract 1996; 37: 116-125.
13. Watkins L Jr, Burton JA, Haber E, Cant JR, Smith FW, Barger AC. The renin angiotensin aldosterone system in congestive failure in conscious dogs. J Clinical Inv 1976; 57: 1606-1617.
14. Hall JE. The kidney, hypertension and obesity. Hypertension 2003; 41: 625-633.
15. Mok JSL, Kong ML, Hutchinson JS. Cardiovascular effects of central and peripheral administration of dopamine in hypertensive and normotensive rats. Indian J Pharmacol 1985; 17: 192-196.
16. DePaula BR, Da Silva AA, Hall EJ. Aldosterone antagonism attenuates obesity-induced hypertension and glomerular hyperfiltration. Hypertension 2004; 43: 41-47.
17. Syme HM, Fletcher MGR, Bailey SR, Elliott J. Measurement of aldosterone in feline, canine and human urine. J Small Anim Pract 2007; 48: 202-208.
18. Kobayashi DL, Peterson ME, Graves TK, Lesser M, Nichols CE. Hypertension in cats with chronic renal failure or hyperthyroidism. J Vet Intern Med 1990; 4: 58-62.
19. Cortadellas O, Del Palacio MJF, Bayón A, Albert A, Talavera J. Systematic hypertension in dogs with leishmaniasis: prevalence and clinical consequences. J Vet Intern Med 2006; 20: 941-947.
20. Montoya JA, Morris JP, Bautista I, Juste CM, Suarez L, Pena C, Hackett RM, Rawlings J. Hypertension: a risk factor associated with weight status in dogs. J Nutr 2006; 136: 2011-2013.
21. Joles JA. Obesity in dogs: effects on renal function, blood pressure and renal disease. Vet Quart 1998; 20: 117-120.