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CLINICAL STUDY

Ambulatory blood pressure monitoring of healthy schoolchildren with a family history of hypertension

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ABSTRACT

Early detection of primary hypertension (HT) is essential to prevent the development of end organ damage, especially in patients with a family history of HT. Physicians must pay a great attention during the follow-up of these children. Our aim was to investigate whether children with hypertensive parents are under the risk of development of HT or not by using ambulatory blood pressure measurement (ABPM). Seventy-nine healthy children were enrolled in the study: 39 with positive familial history of primary HT (study group) and 40 without familial history of HT (control group). Complete blood count, urinalysis, and biochemical tests were performed in all children in the study group. Children in both groups were examined by casual BP measurement and ABPM. The study group had significantly higher levels of BP ($p < 0.05$) than the controls. In the study group systolic BP and diastolic BP loads were significantly higher than the controls ($p < 0.000$; $p = 0.002$, respectively). In conclusion, parental BP is a strong predictor of the future BP in their children. It is possible that early abnormalities of BP may escape from detection by casual office measurement, and ABPM is recommended especially to detect BP abnormalities before HT becomes clinically overt.

Keywords: ambulatory blood pressure monitoring; familial hypertension; primary hypertension; children

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INTRODUCTION

Prospective studies have shown that risk factors for cardiovascular diseases such as high BP and plasma cholesterol level aggregate in some families.[1] Although it has long been recognized that primary hypertension (HT) has its roots early in life, epidemiologic studies have yielded inconsistent results on the extent and timing of the BP increase in offspring of hypertensive parents.[2,3] However, early recognition of children who are under the risk of development of HT in adulthood has a vital importance for preventing the development of end organ damage. The sensitivity and reproducibility of previous clinical studies may have been compromised by the exclusive use of casual BP measurements. Recently, it has become obvious that early abnormalities of BP may escape from detection by casual office measurement and the specificity of casual readings is severely hampered by the high prevalence of white coat HT in children.[4–6] Ambulatory blood pressure measurement (ABPM) is recommended especially to detect BP abnormalities before HT becomes clinically overt.[4–6]

In this study healthy school children with and without a family history of HT were examined by casual blood pressure measurement and by ABPM. Our aim was to investigate whether children with hypertensive parents are under the risk of development of HT or not by using ABPM.

PATIENTS AND METHODS

Selection of cases

This study was planned as descriptive, cross-sectional study. A questionnaire was administered to the families of 2776 students of elementary and secondary schools in Middle Anatolia region of Turkey. Within the questionnaire there was a section about children's prenatal and postnatal history, including gestational week and birth weight. Child's dietary and exercise habits and life style were also asked in the questionnaire. History

of any chronic illness and medication was also checked carefully. The second section of questionnaire was composed of questions about family members including grandfathers and grandmothers. Familial dietary and exercise habits, presence of obesity, history of cardiovascular disease, renal disease, HT, hyperlipidemia, hypercholesterolemia, and diabetes mellitus were checked in this section. From the results of the questionnaire we found that 39 children had a family member with a history of primary HT (the study group). Forty healthy children with healthy parents were selected as a control group and overall 79 children were invited to outpatient clinic of Pediatric Nephrology Department for detailed examination.

Evaluation of the cases

Body weight and height were measured and body mass index (BMI) was calculated as weight (kg)/height^2 (m^2). Corresponding percentiles of weight and height were recorded using standardized values for Turkish children,[7] whereas percentile of BMI was calculated from CDC growth charts.[8] Blood pressure was measured using a sphygmomanometer (ERKA D-83646 Bad Tölz, Germany) according to standardized protocol with an appropriate cuff placed on non-dominant arm of a sitting subject after a resting period of 15 minutes.[9]

Systemic and renal diseases were excluded through physical examination, serum biochemistry, and urinalysis. Creatinine clearance was calculated with Schwartz formula.[10]

Twenty-four hour ABPMs

ABPM was measured at home using the oscillometric device. An appropriate cuff, chosen out of three available sizes, was attached to the non-dominant arm. Measurements were performed every 20 minutes during daytime and every 30 minutes during the night.

BP load is defined as the percentage of total BP values exceeding the 95th percentile, adjusted for time periods of being awake and being asleep. Depending on age, sex, and height, the BP values ranging from 90th to 95th percentiles are defined as pre-hypertensive, meaning that individuals are in high-risk group for HT; for that reason BP loads are also calculated for the values in 90th percentile. Any BP load greater than 25% was defined as elevated.

To calculate the individual nocturnal BP decreases, the nocturnal mean BP was compared with the daytime mean BP in each subject and the difference expressed as percentage of the daytime mean BP. A dipper is a person with a BP decrement by at least 10% during sleep. HT was defined as mean systolic BP (SBP) or diastolic BP (DBP) higher than 95th percentile, adjusted for gender and height, according to "The forth report on the diagnosis, evaluation and treatment of high BP in children and adolescents".[11]

Statistical methods

The ABPM profiles were analyzed using the ABPM-Fit program, which performs conventional linear analyses (calculation of BP mean, SD, load, highest and lowest readings) for user-defined day and night periods. Data are given as mean ± SD. Student's t-test, χ^2-test, and univariate analyses were used to test the difference between the study group and the control subjects. Possible correlations were tested by Pearson bivariate analysis. Statistical significance was defined as $p < 0.05$.

RESULTS

The questionnaire of 2776 children revealed that 39 (1.4%) children had at least one hypertensive relative. Mothers of 8.3%, fathers of 4.5%, brothers/sisters of 0.4% of cases were found to be hypertensive. The history of HT was quite high in grandmothers and grandfathers, 44.5% and 19.4%, respectively.

Forty children without any relative with HT were selected randomly as a control group. The groups were matched for ages and sexes. Both groups were also identical in terms of weight, height, BMI, socioeconomic status, life style, and diet and exercise habits. All children in both groups have normal physical examination, without any history of illness or drugs that will affect BP. Demographic data of the study group and controls are given in Table 1. Mean age, sex distribution, and birth weights were identical in both groups. Though the difference was not significant, 13 children (33.3%) in study group and 8 children (20%) in control group were found to have a BMI higher than 85% ($p > 0.05$) (Table 1). Estimated glomerular filtration rate as well as serum biochemical analysis and urinalysis was normal in both groups (Table 2).

Casual blood pressure measurements did not reveal any significant difference between the groups. However, 24-hour ABPM revealed higher mean SBP and DBP in the study group than controls ($p < 0.05$). Daytime and nighttime BP measurements were also found to be higher in the study group ($p < 0.05$) (Table 3, Figures 1–3).

Blood pressure load was found to be significantly higher in the study group, with BP load defined as whether the percentage of total BP values exceeds the 90th or 95th percentile ($p < 0.05$) (Table 4). The number of subjects having BP load higher than 25% was also significantly higher than controls (Table 4, Figure 3) ($p < 0.05$). SBP load higher than 25% was found in 15 subjects (38.46%) and DBP load in 2 (5.12%)

TABLE 1. Demographic data of the study and the control groups.

	Study group, $n = 39$	Controls, $n = 40$	p-Value
Female/male (n)	15/24	17/23	NS
Age (year)	14.02 ± 1.88	13.77 ± 2.45	NS
Birth weight (g)	3327.43 ± 443.70	3353.87 ± 453.08	NS
Current weight (kg)	54.55 ± 17.56	49.22 ± 12.64	0.06
Height (cm)	160.11 ± 11.51	158.10 ± 13.32	NS
BMI > 85%	13/39	8/40	NS
Pulse rate	75.53 ± 6.02	74.25 ± 5.38	0.3
Casual systolic BP (mmHg)	113.15 ± 9.74	106.87 ± 11.58	0.055
Casual diastolic BP (mmHg)	69.69 ± 6.19	67.02 ± 7.26	0.08

Note: BMI, body mass index.

TABLE 2. Biochemical analysis of the study and control groups.

Laboratory	Study group, $n = 39$	Controls, $n = 40$	p-Value
Hemoglobin (g/dL)	13.75 ± 1.15	13.34 ± 1.04	0.10
Hematocrit (%)	41.16 ± 3.16	39.74 ± 3.00	0.05
WBC (×1000/μL)	7.05 ± 1.83	6.60 ± 1.43	0.23
Thrombocyte (×1000/μL)	295.31 ± 70.60	281.00 ± 67.27	0.36
Creatinine (mg/dL)	0.76 ± 0.17	0.70 ± 0.14	0.11
Serum Na (mmol/L)	139.23 ± 2.44	138.79 ± 2.14	0.40
T. cholesterol (mg/dL)	160.48 ± 40.08	151.71 ± 40.08	0.27
HDL-cholesterol (mg/dL)	51.03 ± 9.34	51.07 ± 15.92	0.99
LDL-cholesterol (mg/dL)	87.62 ± 35.22	75.48 ± 24.62	0.08
VLDL-cholesterol (mg/dL)	18.69 ± 9.11	18.69 ± 9.72	0.58
Triglyceride (mg/dL)	98.92 ± 44.93	91.10 ± 91.10	0.47
Creatinine clearance (mL/min/1.73m^2)	121.98 ± 23.31	126.24 ± 21.00	0.40

Note: Na, sodium; HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein; WBC, white blood count.

subjects in the study group. In the control group only two subjects (5.0%) had SBP load higher than 25%. No subject in the control group had DBP load higher than 25%. The BP differences between the genders were not found to be significant.

Dipping status was not found to be significantly different between the groups.

Univariate analysis revealed that the family history of primary HT affects SBP and DBP in offspring independent of BMI ($R = 0.25$, $p < 0.05$ and $R = 0.23$, $p < 0.05$, respectively).

DISCUSSION

Genetic factors are known to play an important role in the etiology of primary HT. Cardiovascular risk factors including high BP are known to aggregate in some families.[1,12] Associations between parental HT and BP in children have been reported in some studies from Britain, USA, Denmark, and Australia.[13–17] It was claimed that presence of HT in one of the family members leads to exaggerated pressure response to stress in the offspring.[18,19] However, more recently Bond et al. observed normal exercise BP response in women with parental history of HT.[20] Thus, prospective studies with large groups of patients are needed to explain the genetic and environmental factors lying behind the etiology of HT.

In this study we found that actual parental BP is a strong determinant of the natural history of BP in their offspring. Similarly Alpay et al.,[21] in their very recent publication, claimed that parental history of HT was independently correlated with increase of daytime mean arterial BP standard deviation score (SDS). However, Van Hooft et al. found no difference in BP according to parental HT among Dutch children.[3] It should be emphasized that all studies apart from Alpay et al.'s[13] in this field were based on casual blood pressure measurements and the sensitivity and reproducibility of those clinical studies may have been compromised by the exclusive use of casual BP measurements. ABPM measures BP multiple times during a predefined time period, more accurately reflecting the continuous nature of BP. ABPM also allows measurement of BP in the patient's normal environment during both awake and sleep periods.[4] Recent studies have also shown how ABPM can be used to evaluate BP abnormalities in specific pediatric patient populations known to be at risk for HT and its complications. It was demonstrated that ABPM allows early and sensitive identification of abnormalities in BP and circadian BP patterns in high-risk children that may allow

TABLE 3. Mean, minimum, and maximum values of total, daytime, and nighttime systolic, diastolic, and mean arterial BP of the groups.

	Mean	Study group (n = 39) Mean ± SD	Control group (n = 40) Mean ± SD	p-Value
24-hour BP	SBP	115.71 ± 8.84	101.22 ± 16.87	0.000
	DBP	65.64 ± 6.85	58.90 ± 5.51	0.000
	MABP	82.33 ± 6.91	74.22 ± 6.01	0.000
Daytime BP	SBP	118.74 ± 9.44	106.72 ± 8.42	0.000
	DBP	68.41 ± 7.77	61.62 ± 5.40	0.000
	MABP	85.05 ± 7.74	77.00 ± 5.86	0.000
Nighttime BP	SBP	107.20 ± 7.37	96.30 ± 8.28	0.000
	DBP	57.82 ± 5.49	51.60 ± 5.81	0.000
	MABP	72.36 ± 10.81	66.62 ± 6.42	0.005

Note: SBP, systolic blood pressure; DBP, diastolic blood pressure; MABP, mean arterial blood pressure.

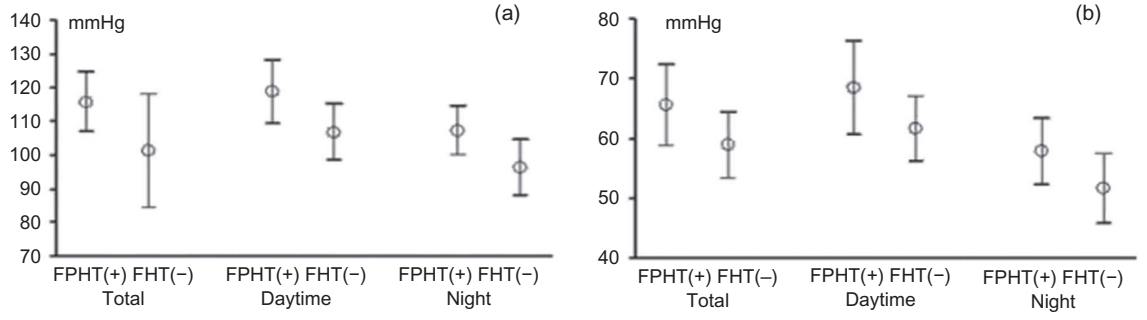

FIGURE 1. The total, daytime, and nighttime systolic (a) and diastolic (b) BP values of the study and control groups. Note: FPHT(+): The group which has primary HT in family; FHT(-): The group which does not have HT in family.

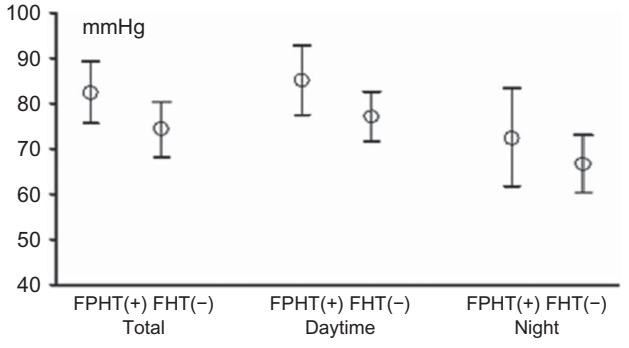

FIGURE 2. The total, daytime, and nighttime mean arterial BP values of study and control groups.

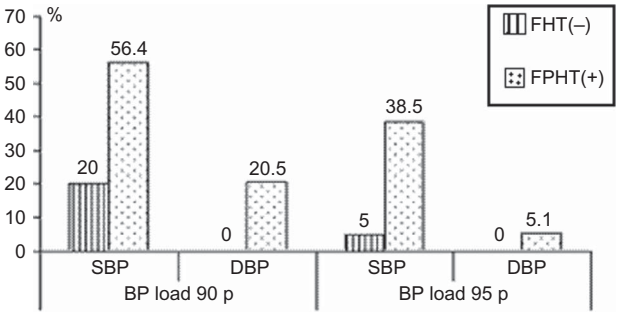

FIGURE 3. BP loads of the study and control groups.

intervention prior to the onset of hypertensive sequelae.[4–6]

Burke et al. have shown that reported paternal HT significantly predicts SBP in sons and daughters as young as 9 years old.[14] They claimed that reported maternal HT was not a significant predictor of SBP in offspring. They suggest that a family history of HT should be examined separately according to the sex of the child and sex of the patient.[14] However, some authors claimed that maternal, rather than paternal, HT has an important role as a predictor of BP in

TABLE 4. BP loads of the groups.

	Study group (n = 39) Mean ± SD, median (min–max)		Control group (n = 40) Mean ± SD, median (min–max)		p-Value
90 p ↑ (%)					
SBPL	32.83 ± 25.03	26 (2–100)	12.28 ± 17.65	5.5 (0–76)	0.000
DBPL	15.18 ± 14.55	10 (0–71)	5.95 ± 6.29	4 (0–22)	0.000
95 p ↑ (%)					
SBPL	24.61 ± 22.47	16 (0–95)	7.82 ± 14.35	2 (0–72)	0.000
DBPL	9.45 ± 12.56	5 (0–71)	2.57 ± 3.49	0 (0–11)	0.002

Note: SBPL, systolic BP load; DBPL, diastolic BP load; SD, standard deviation.

offspring.[22,23] In our study, the affect of maternal or paternal BP on offspring was found to be similar.

Previously it was shown that obesity is one of the major factors that was influencing BP. Pela et al. have shown that SBP is higher in obese children.[24] Though the number of obese children was also higher in the study group, the difference was not statistically significant. Moreover, univariate analysis revealed that the affect of the history of primary HT in family members on offspring's BP was independent of BMI.

Non-dipping is an important independent risk factor for cardiac and cerebrovascular morbidity in adults.[25,26] The physiological nocturnal BP drop matures during childhood.[27] However, Sorof et al. have claimed that non-dipping status is not a risk factor predicting end organ damage.[28] In our study, as well as in Alpay et al.,[21] we did not find any significant difference in terms of dipping status between the groups. Blood pressure load is the other important risk factor predicting end organ damage and we found a significantly higher SBP load in the study group.

The major limitation of our study is the method of categorization of family members as hypertensive or normotensive. Though the information about family histories of HT was obtained by a detailed questionnaire administered to the participants in consultation with their parents, the categorization of family members as hypertensive or normotensive might have been inaccurate. Blood pressures of parents were not measured and parents' medical records were not used for validation. Unfortunately, most of the studies in this field also failed to select hypertensive parents by medical records, or physical examination, may be because of the technical difficulties of this procedure. Maldoon et al. have pointed out that failure to confirm reported hypertensive or normotensive status is a problem in as many as two-thirds of the family history studies they reviewed.[14,29] The second limitation of our study is the usage of "the forth report on the diagnosis, evaluation and treatment of high BP in children and adolescents"[11] data to define HT, rather than Wühl et al.'s[6] or Soergel et al.'s[30] data.

In conclusion, the results of this study indicate that parental BP is a strong predictor of BP in their children. Children with positive family history of HT have an increased risk of development of HT. Thus, interventions should be aimed at early life risk factors in these families, such as quitting smoking during pregnancy, breast feeding, and prevention of obesity in all family members. Follow-up of these children by ABPM will help to detect HT at early ages.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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