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ORIGINAL ARTICLE

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Childhood hypertension is not a silent disease

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Abstract Early hypertension has generally been considered to be an asymptomatic condition; however, recent data show that many hypertensive children have evidence of end organ damage. We sought to determine if a spectrum of common symptoms is associated with early hypertension and whether those symptoms resolve with lowered blood pressure. Four hundred and nine consecutive children, 7–18 years old, examined in the Texas Children's Hospital Hypertension Clinic for new-onset high blood pressure (BP) completed a questionnaire, including the self-reporting of 15 symptoms potentially attributed to high blood pressure. Subjects received anti-hypertensive treatment and repeated the questionnaire 4–6 months after initiation of therapy. One-hundred fifty healthy, normotensive children completed the questionnaire as controls. Of hypertensive children, 64% were symptomatic, compared with 26% of normotensive children ($P<0.001$). Fifty-one percent of hypertensive children reported 1–4 symptoms, 14% >4 symptoms. Following treatment only 28% of children remained symptomatic. The three most common symptoms in hypertensive patients, headache, 42%, difficulty initiating sleep, 27%, and daytime tiredness, 26%, were markedly reduced with treatment, to 6.2%, 1.5% and 10%, respectively ($P<0.001$). We conclude that newly diagnosed hypertensive children had a variety of non-specific symptoms, more prevalent than those of normotensive children, and most somatic complaints improved with 4–6 months of anti-hypertensive treatment.

Keywords Hypertension · Children · Adolescents · Clinical research · Retrospective study

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Introduction

Chronic hypertension is traditionally thought of as a silent or symptom-free disease; however, this belief has been recently challenged by the results of studies in elderly patients. The Syst-Eur Trial identified a variety of symptomatic complaints, including headache, palpitations and visual disturbances, which are more prevalent in elderly hypertensive patients [1]. Similar symptoms were noted in the Trial of nonpharmacologic interventions in the elderly (TONE), and treatment resulted in the decreased prevalence of somatic complaints and improved quality of life [2]. Several studies have also revealed that adults with hypertension are more likely to complain of sleep disturbances, particularly difficulty initiating sleep [3–5]. In contrast, little is known about the impact of hypertension on somatic complaints in the pediatric population.

Over the past several years there has been increasing concern about hypertension in childhood. Coincident with the worsening obesity epidemic [6], a recent evaluation of the National Health and Nutrition Examination Survey (NHANES III) indicated that blood pressure among American children of all races has been increasing over the past decade [7]. Several studies have shown that end organ damage is frequently present in hypertensive children and young adults [8], including increased atherosclerosis [9, 10] and carotid intimal thickness [11, 12], left ventricular hypertrophy [13], proteinuria [14] and mildly impaired cognitive function [15].

We retrospectively examined a large and ethnically diverse cohort of children and adolescents with well-characterized hypertension to determine if they had a profile of somatic complaints similar to that observed in

elderly hypertensive patients and whether the symptoms improved with treatment of hypertension.

Materials and methods

Patient population

We evaluated the records of 409 consecutive patients, ages 7 years to 17 years, referred for initial evaluation of elevated blood pressure, to the Hypertension Clinic at Texas Children's Hospital in Houston, between July 2002 and December 2004. Fifty-eight patients were excluded from the analysis because they had been initiated on antihypertensive agents prior to referral. Eight patients with one or more missing data points were also excluded, leaving a total of 343 patients for analysis. The population included patients with white coat, secondary and essential hypertension but did not include children with renal transplants or known chronic or acute kidney disease. All the patients had normal glomerular filtration rate by Schwartz formula assessment. Sixteen patients were diabetic and five had a history of bone marrow transplantation (BMT) more than 5 years prior to evaluation for hypertension. Records were analyzed retrospectively. Control subjects were recruited from the Pediatrics Clinics at Texas Children's Hospital during well-child checks or obesity evaluation and from the Renal Clinic at Texas Children's Hospital and included children referred for the evaluation of uncomplicated microscopic hematuria, uncomplicated urinary tract infections, solitary kidney (without renal insufficiency) or growth delay.

Definition of hypertension

Hypertension was defined in accordance with the Fourth Report on the Diagnosis, Evaluation and Treatment of High Blood Pressure in Children and Adolescents [16]. Children with pre-hypertension [16] or white coat hypertension [17] were considered normotensive.

Measurement of blood pressure

Blood pressure measurements were made by trained personnel using aneroid blood pressure (BP) monitors. Cuff size was selected in accordance with Task Force recommendations [16], and, once selected, the same cuff and monitor were used for a patient's subsequent visit(s). Each BP datum point was the mean of four upper extremity measurements, performed on seated children who had been relaxing in a quiet examination room for more than 10 min. Twenty-four-hour ambulatory blood pressure monitoring was performed on children whose clinic BP fell into the pre-hypertensive or stage 1 hypertension range, using Space Labs 90217 monitors as previously described [18]. Ambulatory blood pressure monitoring (ABPM) was not performed on children presenting with stage 2 hypertension, to avoid delayed initiation of therapy.

Clinical evaluation of hypertension

The initial examination of all children in the hypertension clinic was directed toward confirmation of hypertension, distinguishing essential from secondary hypertension, and directing therapy and has been described previously [18, 19].

Treatment of hypertension

The choice of treatment was made by the provider. All children received counseling on dietary modification, weight loss or maintenance, and exercise. The frequency of treatment modalities was: solely non-pharmacological therapy 44, single drug therapy 156, two-drug therapy 36, three-drug therapy 11, four-drug therapy 2, five-drug therapy 1, surgery or angioplasty only 9. The treated blood pressure values correspond to the visit on which the follow-up symptom data were collected, 4 months to 6 months after initiation of therapy.

Acquisition of symptom data

Upon arrival for a first visit to the Hypertension Clinic at Texas Children's Hospital, all children and families were administered a questionnaire regarding medical and family history. Within the questionnaire was a section for children to check from a list of symptoms. The children were instructed to complete the symptom questionnaire without parental input and to mark only those symptoms that bothered them more frequently than once a week. Positive responses were further investigated during a verbal interview; however, only the symptoms marked by the children on the questionnaire were scored. The symptom checklist was administered at each follow-up visit to the Hypertension Clinic without reference to early responses. Responses to the symptom checklist were recorded in the patient's electronic medical record. For children undergoing treatment, the initial symptom data were compared with checklist data 4 months to 6 months following the initiation of therapy. The analysis was performed on an intent-to-treat basis, without taking into account success of therapy or treatment modality. Pre-hypertensive and white coat hypertension patients typically returned after approximately 6 months for re-assessment. In contrast to the children who had confirmed hypertension, all of whom were still followed at 6 months, there was a 15% loss to follow-up among the white coat hypertension group (13 of 84). Control subjects completed the same questionnaire, to avoid any bias introduced by any difference in the appearance of the forms.

Statistical analysis

Comparisons between the means of continuous data points were performed by analysis of variance (ANOVA) and two-tailed *t*-test. Non-parametric symptom data were compared between the diagnostic groups and before and after treatment by Kruskal–Wallis ANOVA. Correlation analysis of non-parametric variables was performed with the Spearman rank order test. *P* values <0.05 were considered significant. Odds ratios and 95th percent confidence intervals were calculated by standard means using 2×2 tables. Results were considered statistically significant if 95th percent confidence intervals did not contain an odds ratio of 1.0. Statistical analysis was performed with Statistica 7 Software, StatSoft, Tulsa, Okla., USA.

Results

Patient population

Table 1 compared the hypertensive and normotensive populations evaluated in this study. The populations are extremely similar, with no statistically significant differences in age, gender, ethnic make up and physical body parameters. When the hypertensive population is separated into essential and secondary hypertension, however, differences in body weight are apparent. As has been previously reported, children with essential hypertension tend to be more overweight [body mass index (BMI) percentile 88±14 vs 68±33, *P*=0.012) and older (14.5±2.4 years vs 10.6±5.4 years, *P*=0.02] than children with secondary hypertension [18]. The inclusion of children being investigated for obesity in the control population makes them more comparable to the hypertensive popu-

Table 1 Characteristics of the patient population. Group comparisons by ANOVA were made between all hypertension vs all normal blood pressure, subgroups of hypertension (essential and secondary) vs all normal blood pressure and subgroups of normal blood pressure (white coat and pre-hypertension, controls) vs all hypertension (*SBP* systolic blood pressure, *DBP* diastolic blood pressure)

Characteristic	All normal BP	All hypertension	Normal BP subgroups		Hypertension subgroups	
			Controls	White coat and pre-hypertension	Essential hypertension	Secondary hypertension
Number	234	259	150	84	139	120
Age (years)	12.6±4.1	12.7±4.5	13.6±5.2	10.7±4.8[a]	14.5±2.4[a]	10.6±5.4[a]
Male (%)	60	62	59	61	70[a]	58
Height (cm)	148±35	154±27	153±22	140±30[a]	165±14[a]	138±33[a]
Weight (kg)	61.2±28	69.0±34[b]	65.5±31	54±30[a]	84.7±28[a]	49.5±32[a]
BMI (kg/m^2)	26.6±9.2	27.0±8.6	26.2±7.1	24.2±8.3	30.8±7.9	22.2±7.5[a]
BMI percentile	75±24	79±28	74±22	75±30	88±14[a]	68±33
Ethnicity						
African–American (%)	31	30	32	30	34	25
Caucasian (%)	42	43	41	45	44	41
Hispanic (%)	25	24	27	24	19	31[a]
BP before treatment						
SBP	112±8	140±16[c]	111±12[c]	114±13[c]	144±10	134±19
SBP index	0.90±0.08	1.12±0.12[b]	0.81±0.08[c]	0.93±0.07[b]	1.11±0.08	1.13±0.14
DBP	65±7.3	82±14[c]	65±6[c]	65±8.3[c]	81±10	82±16
DBP index	0.81±0.10	1.04±0.17[b]	0.79±0.10	0.84±0.09[b]	0.98±0.13	1.07±0.20
After treatment						
SBP	N/A	120±12	N/A	112±8[d]	124±9[a]	115±13[a]
SBP index	N/A	0.95±0.06	N/A	0.88±0.06[d]	0.95±0.05	0.94±0.07
DBP	N/A	67±10	N/A	66±7[d]	67±12	66±8
DBP index	N/A	0.85±0.12	N/A	0.81±0.07[d]	0.85±0.13	0.85±0.11
BMI (kg/m^2)	N/A	26.5±9.1[e]	N/A	25.1±8.6[d,e]	30.5±8.1[e]	22.9±7.4[e]

[a] *P* between 0.01 and 0.05
[b] *P* between 0.001 and 0.01
[c] *P*<0.001
[d] Follow-up blood pressures after 4–6 months were obtained for 71 of the 84 subjects with white coat and pre-hypertension. None of these patients were prescribed anti-hypertensive medications
[e] BMI after the treatment period was compared with BMI prior treatment for the same group (hypertension to hypertension after treatment, essential hypertension to essential hypertension after treatment, etc.). There were no statistically significant changes in BMI

lation but perhaps less representative of the general pediatric population.

Blood pressures and the effects of treatment

The blood pressures of the subjects and controls are reported in Table 1. Because of the variation in age and height in the population, the ratio of the measured blood pressure to the 95th percentile blood pressure for the subject (blood pressure index) has also been reported. The importance of this is demonstrated by the pretreatment systolic blood pressure. Children with essential hypertension have higher pressures than those with secondary hypertension (mean 144±10 mmHg vs 134±19 mmHg, P=0.02); however, because the children with secondary hypertension are younger and shorter, the degree of hypertension is essentially the same (SBP index 1.11±0.14 vs 1.13±0.07, P=0.67). Treatment of hypertension led to a marked reduction in systolic (mean decrease of 20 mmHg) and diastolic (mean decrease of 15 mmHg). There was no significant change in BMI during the treatment period. Children with white coat and pre-hypertension (71 of 84, 85%) returned to the Hypertension Program after 6 months and showed no significant change in mean blood pressure.

Symptoms associated with hypertension

The children with confirmed hypertension reported a variety of non-specific complaints (Table 2). Of newly diagnosed hypertensive children, 64% reported that at least one of the symptoms occurred more frequently than once a week. Thirteen percent of newly diagnosed hypertensive children complained of five or more symptoms, each occurring more than once a week. In contrast, only 26% of normotensive children reported one or more symptoms, with 2.2% complaining of five or more symptoms (Fig. 1). The number of symptoms did not correlate with degree to which blood pressure was elevated (r=0.0064, P=0.87). The most common symptoms among hypertensive children were headache (42%), difficulty falling asleep (27%), daytime fatigue (26%) and chest pain (14.2%). Of 259 hypertensive patients 127 (49%) reported one or more somatic pain complaint (headache, abdominal pain or chest pain) more frequently than once a week at the time of initial evaluation, in contrast to 16.9% of normotensive individuals (P<0.001). Similarly, 102 of 259 (39.4%) of hypertensive children reported one or more types of sleep disturbance (trouble falling asleep, frequent awakening or daytime fatigue) compared with only 12.6% of normotensive children (P<0.001) (Table 2).

Table 2 Prevalence of symptoms

Symptom	Confirmed hypertension before treatment	Confirmed hypertension after treatment	All normal blood pressure	Normal BP subgroups		
				Controls	White coat hypertension, initial	White coat hypertension, follow-up
Pain and Discomfort						
Abdominal pain	10.4%	3.9%[a]	3.0%[b]	2.7%	4.8%[a]	3.6%
Chest pain	14.2%	3.4%[b]	4.7%[b]	4.0%	7.1%[a]	5.9%
Headaches	42%	6.2%[c]	10.3%[b]	6.8%	15.5%[b]	16.6%
Nausea or vomiting	4.2%	1.1%	1.3%	0.7%	2.3%	2.3%
Palpitations	6.5%	3.1%	1.7%[b]	0%	5.9%	4.8%
Sleep disturbances						
Difficulty initiating sleep	27%	1.5%[c]	6.0%[b]	2.7%	11.9%[b]	11.9%
Difficulty maintaining sleep	7.7%	2.3%[a]	1.3%[b]	0%	4.7%	3.5%
Daytime tiredness	26%	10%[c]	5.5%[c]	5.3%	8.3%[c]	5.9%
Respiratory complaints						
Shortness of breath	4.6%	2.3%	1.7%[a]	0%	4.8%	4.8%
Exercise intolerance	3.4%	1.5%	1.3%	0%	4.8%	3.6%
Neurosensory complaints						
Concentration problems	9.6%	8.8%	4.5%[a]	4%	5.6%[a]	5.6%
School failure	10%	9.3%	3.8%[b]	4%	3.6%[b]	3.6%
Dizziness	1.5%	1.9%	0.9%	0.7%	1.2%	1.2%
Hearing problems	1.1%	1.9%	1.9%	2.9%	0%	0%
Vision problems	3.9%	3.9%	2.5%	1.3%	4.7%	4.7%

The data in columns "Confirmed hypertension after treatment", "All normal blood pressure" and "White coat hypertension, initial", were compared with "Confirmed hypertension before treatment", using Kruskal–Wallis ANOVA for non-parametric variables with the following P values:
[a] P between 0.01 and 0.05
[b] P between 0.001 and 0.01
[c] P<0.001
The data in the "White coat hypertension, follow-up" column were compared with those in "White coat hypertension, initial," column by Kruskal–Wallis ANOVA. There were no statistically significant differences

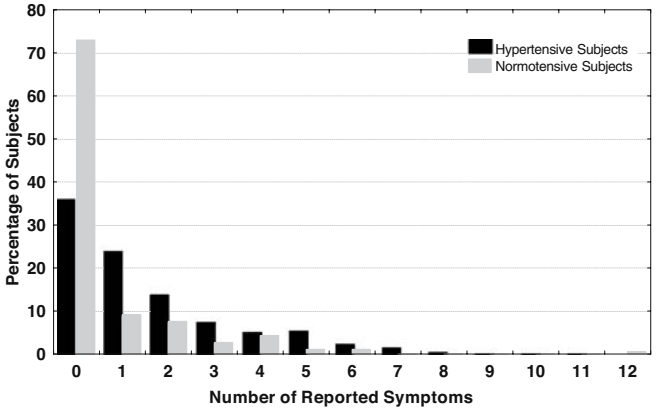

Fig. 1 The number of symptom complaints among hypertensive and normotensive children. The number of symptoms reported at the time of initial evaluation is plotted against the percentage of children making the complaints. The hypertensive (*open bars*) and normotensive populations are plotted separately

Treatment of hypertension resulted in a reduced prevalence of reported symptoms. Headache, abdominal pain, chest pain, delayed initiation of sleep, frequent awakening and daytime tiredness were all less common 4–6 months after initiation of therapy. In contrast, there was no detectable improvement in respiratory or neurosensory complaints after this duration of therapy. To address the possibility that re-administration of the checklist biased the results, we compared the initial complaints for the children with white coat or pre-hypertension with their complaints at 6-month follow-up visits (Table 2). There were no significant differences in the symptom prevalence associated with follow up, suggesting that the observed changes may be due to treatment of confirmed hypertension. There were also no significant changes in BMI before and after treatment (Table 2).

Table 3 shows the odds ratios and 95th percent confidence intervals for the seven most common complaints. The symptom profiles are compared for children with hypertension versus children without hypertension, for children with hypertension versus the same children after treatment, and for the treated hypertensive children versus the children without hypertension. There is little difference in symptoms between children with treated hypertension and those with confirmed normal blood pressure. Hypertensive children are three-to-six times more likely to have headache, trouble initiating sleep, fatigue, abdominal pain chest pain and self-reported school failure and nearly twice as likely to report trouble concentrating. Treatment of the hypertension improves the pain complaints and sleep disturbances but not the subjective school and attention difficulties (Table 3).

Discussion

In this study we investigated the symptomatic impact of hypertension in a large, ethnically diverse, pediatric population. We found that a majority of hypertensive children are not symptom free. Hypertensive children report a variety of non-specific somatic complaints, including headache, insomnia, fatigue and chest or abdominal pain. Of the hypertensive patients, 49% reported pain complaints more than once a week, compared with only 16.9% of normotensive children. There were 39% of hypertensive children that reported significant sleep disturbance, compared with 13.6% of normotensive children. While it is difficult to attribute causality of the non-specific symptoms directly to the elevation of blood pressure, most symptomatic children had a significant improvement in their symptoms within 4–6 months of treatment, regardless of the treatment modality. The improvement in symptoms was only seen with a concomitant improvement in blood pressure, as there was no change in symptom frequency in children with white coat hypertension who all received non-pharmacological therapy.

As this was a retrospective study, a definitive causal link between reduced blood pressure and improved symptoms cannot be concluded. Either repeated physician visits or repeated administration of a questionnaire could be associated with a change in symptom reporting and account for some improvement. However, such improvement was not seen in the normotensive children. Another possible confounder in the symptom data is that the control subjects completed the questionnaire in the context of a research study, while the hypertensive patients completed the questionnaire for clinical purposes. If the control subjects systematically under-reported symptoms, this would have exaggerated the difference in symptom prevalence between hypertensive and normotensive subjects. This cannot, however, explain the change in symptom complaints seen with treatment.

Obesity is unlikely to account for the observed symptoms, in spite of their non-specific nature, for two reasons.

Table 3 Odds ratios of the seven most commonly reported symptoms, with 95th percent confidence intervals in parentheses

Symptom	Hypertension vs normal BP	Hypertension vs treated hypertension	Treated hypertension vs normal BP
Headache	6.36 (3.90–10.4)	11.0 (6.29–19.4)	0.58 (0.46–.70)
Trouble falling asleep	5.81 (2.88–11.0)	23.6 (8.47–65.4)	0.25 (0.08–1.12)
Tiredness	5.93 (3.19–10.7)	3.13 (1.91–5.10)	1.89 (0.95–3.78)
Chest pain	3.37 (1.66–6.75)	4.63 (2.18–9.78)	0.73 (0.30–1.80)
Abdominal pain	3.77 (1.60–8.76)	2.90 (1.36–6.11)	1.30 (0.49–3.45)
School failure	2.79 (1.42–5.99)	1.09 (0.61–1.95)	2.55 (1.17–5.58)
Poor concentration	2.16 (1.04–4.48)	1.09 (0.60–1.97)	1.97 (0.94–4.06)

First, the control and hypertensive populations are similarly overweight and yet the prevalence of symptoms is different. Second, there was no difference in symptom frequency or profile between the children with essential and secondary hypertension, despite the prevalence of obesity in the former and the lack of obesity in the latter. Third, the improvement in symptoms was associated with treatment of hypertension and improvement in both systolic and diastolic blood pressure but, despite dietary and exercise counseling, there was no statistically significant change in BMI, in either hypertensive or normotensive children during the study period.

A potential shortcoming of this study is that the population was referral based. This could have selected for a more symptomatic population than would be expected if patients were obtained through community screening. This weakness, however, does not obviate the importance of the resolution of symptoms with treatment, and the observation that treated hypertensive children have a symptom profile that does not significantly differ from that of the normotensive population (Tables 2 and 3). Even if the prevalence of symptomatic complaints in a screening population is lower than that seen in referred patients [20], these data suggest that anti-hypertensive treatment, regardless of modality, ameliorates those symptoms.

The results of this study suggest that the presence or degree of symptoms should be factored into the therapeutic plan of hypertensive children. This does not mean that all hypertensive children require anti-hypertensive medications, as some children with essential hypertension were effectively controlled with lifestyle modification alone, and this resulted in an improvement in their symptoms. The high prevalence of symptoms among hypertensive children, and their responsiveness to treatment, however, indicates that insufficient blood pressure screening of children, or delay in the evaluation of hypertension, may leave children unnecessarily uncomfortable and symptomatic.

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