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Bonita Falkner
Pediatrics and Medicine, Thomas Jefferson University, Bonita.Falkner@jefferson.edu

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EDUCATIONAL REVIEW

Hypertension in children and adolescents: epidemiology and natural history

Bonita Falkner

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Abstract Primary hypertension is detectable in children and adolescents and, as in adults, is associated with a positive family history of hypertension, obesity, and life-style factors. Owing to the well-established childhood obesity epidemic, the population prevalence of high blood pressure (BP) in the young is increasing. Hypertension in childhood is commonly associated with other cardiovascular risk factors as well as obesity. Although death and cardiovascular disability do not occur in hypertensive children, intermediate markers of target organ damage, such as left ventricular hypertrophy, thickening of the carotid vessel wall, retinal vascular changes, and even subtle cognitive changes, are detectable in children and adolescents with high BP. Considering the rates of verified hypertension (>3%) and pre-hypertension (>3%) in asymptomatic children and adolescents, high BP should be considered a common long-term health problem in childhood.

Keywords Blood pressure · Hypertension · Pre-hypertension · Childhood · Adolescence

Introduction

Hypertension is a major long-term health condition and is the leading cause of premature death among adults throughout the world, including both developed, developing, and lesser developed countries [1]. Primary hypertension emerges from a complex inter-play of genetic, environmental, and behavioral factors. Owing to the hereditary component of hypertension, the disorder is considered to have its origins in the young [2]. It is now established that hypertension is detectable in children and adolescents and is not uncommon. Population changes in health-related behaviors, including the childhood obesity epidemic, indicate that the rates of hypertension in the young are increasing [3]. Several challenges regarding hypertension now confront clinicians who care for children and adolescents and include detecting hypertension, distinguishing secondary hypertension from primary hypertension, examining patients for hypertension-related risk factors and target organ damage, applying interventions to control blood pressure (BP), and encouraging preventive lifestyles. This review discusses the epidemiology and natural history of primary hypertension in children and adolescents.

Normative blood pressure data

The definition of hypertension in adults is based on the approximate level of BP that marks an increase in cardiovascular events and death. Several expert panels have defined hypertension in adults as systolic pressure ≥ 140 mmHg or diastolic pressure ≥ 90 mmHg [4–6]. These are the approximate BP levels above which the risks for morbid events is significantly heightened and the benefits of treatment are established. However, it is now recognized that the risk for cardiovascular events attributable to BP level in adults does not begin at 140/90 mmHg but is linear, and that the risk begins to rise at BP levels below 140/90 mmHg. For BP levels greater than 115/75 mmHg, the risk for hypertension-related events doubles with each 20 mmHg increase in systolic pressure or each 10 mmHg increase in

B. Falkner (✉)
Pediatrics and Medicine, Thomas Jefferson University,
833 Chestnut Street, Suite 700,
Philadelphia, PA 19107, USA
e-mail: Bonita.Falkner@jefferson.edu

diastolic BP [7]. Based on these findings in adults, pre-hypertension is defined in adults as systolic BP between 120 mmHg and 139 mmHg or diastolic BP between 80 mmHg and 89 mmHg, and lifestyle changes to prevent or delay progression to hypertension are recommended [1].

The definition of hypertension in adults is based on, and supported by, outcome data. Similar data to define hypertension in childhood that are based on risk for events in adult years are not available. Master et al. [8] published a report in 1950 that challenged the use of a single number to define hypertension in adults. They contended that an increase in BP was a reflection of aging and that hypertension was over-diagnosed in the elderly. Because BP, like most human characteristics, demonstrates a frequency distribution that yields a fairly normal curve, they proposed that BP that reached a level that was two standard deviations beyond the statistical mean, or greater than the 95th percentile, should be considered abnormal. Using a statistical method to define the normal range of BP, they described the normal range of systolic BP in young men to be 105–135 mmHg at age 16 years, rising progressively with age to reach 115–170 mmHg at age 60–65 years. They also noted a gender difference in the normal range of BP, with lower levels in younger women than in younger men. A large body of subsequent epidemiological and clinical investigations on hypertension in adults has clearly dismissed the conclusion by Master et al. that hypertension should be statistically defined in adults. However, their report was the earliest to show that the normal range of BP is lower in persons aged 16–19 years than that in early adulthood, and gender differences were also identified. Of most significance is that their report provided a statistical method to define the normal BP range, and abnormal BP could be defined in the absence of mortality or morbidity end points.

The early efforts to describe the normal range BP according to age throughout childhood reported markedly different results [9]. In a recent analysis, Din-Dzietham et al. [10] applied the 95th percentile definition of high BP, based on the most current BP percentile tables, published in 2004 [2], to the data from the early surveys on children's BP. As shown in their report, in using the current BP level for the 95th percentile (by age and gender), they found that the rates of high BP in the earlier surveys were astonishingly high. According to current BP levels for the 95th percentile, the overall estimated prevalence of high BP among children in the 1963–1970 survey would have been 37.2%; in the 1971–1975 survey it decreased to 16.9%; in the 1976–1980 it decreased to 11.1%. By 1982–1984 the prevalence was 4.7%, and the lowest was 2.7% in the 1988–1994 survey. The earliest childhood BP surveys were, in general, based on a single BP measurement, and a standardized method for BP measurement was not uniformly applied. It is unlikely that the prevalence of high BP was so high in 1963 and that the prevalence would have changed so drastically from 1963 to 1994. What changed was the body of normative BP data from which the BP percentiles were derived [11]. The need to obtain a larger body of data on BP in the young within the context of childhood growth was recognized by the National Heart, Lung, and Blood Institute (NHLBI) in the 1970s. The NHLBI subsequently supported several epidemiological studies that prospectively investigated BP and growth in children and adolescents. These projects were conducted at several sites and enrolled representative samples of children and adolescents. Rigorous detail was applied to the methodology of BP measurement. Growth and development measures were obtained, and BP level was examined relative to physiological development. This collective body of children's BP data provided the data on BP distribution reported in the second Task Force on Blood Pressure in Children and Adolescents [12]. Subsequently, there was little shift in the distribution of children's BP [13] until the recent upward trend attributed to the rising rates of childhood obesity [3, 10].

Rather than a single BP level, the top portion of the distribution of BP specific to age, gender, and height continues to be used to define high BP throughout childhood. Hypertension in childhood is defined as systolic and/or diastolic BP that is ≥95th percentile for age, gender, and height. Previously, children with BP levels ≥90th percentile but <95th percentile were termed high normal. To be consistent with adult terms, and the concept that BP risks are linear rather than categorical, this term been changed to pre-hypertension. Therefore, pre-hypertension is defined as systolic and/or diastolic BP that is >90th percentile (for age, gender, and height) but <95th percentile. However, this designation remains arbitrary and without supportive childhood evidence. Moreover, in adolescence, the 90th percentile is often higher than the adult threshold for pre-hypertension of 120/80 mmHg. Therefore, beginning for children aged 12 years, pre-hypertension is defined as BP levels in the range of 120/80 mmHg to the 95th percentile. The rationale for this definition is based on the findings that the risk for events in adults begins to rise at a BP level above 115/75 mmHg, and that, for clinical purposes, adolescents could benefit from preventive lifestyle interventions as well as adults. BP levels that are consistently above the 95th percentile are staged for severity. Stage 1 hypertension is defined as an average BP level from the 95th percentile to 5 mmHg above the 99th percentile. Stage 2 hypertension is defined as an average BP that exceeds 5 mmHg above the 99th percentile. Owing to BP variability within individual patients, in clinical practice the diagnoses of hypertension and pre-hypertension require repeated measurements [2]. In adults the diagnosis of hypertension is verified by BP ≥140/90 mmHg on two separate visits. To avoid over-diagnosis of hypertension in a child with a single elevated BP, three separate visits for BP measurement are recommended, with an average BP ≥95th percentile required for diagnosis of hypertension. An exception to the necessity for repeated BP measurement would be stage 2 hypertension or a child with symptomatic hypertension.

In other countries the BP percentile level that is used to define high BP in children varies somewhat from the US definitions described above. High BP in the UK is defined as BP above the 98th percentile for age [14]. BP reference values have also been reported in Northern Europe [15] and Asia [16]. These reports describe a slightly higher BP level at the 95th percentile. However, all epidemiological reports on normative childhood BP data demonstrate a consistent and significant relationship of BP with age, height, and body weight throughout childhood.

Prevalence of childhood hypertension

The prevalence of pediatric hypertension worldwide is not known, due to regional differences in the definition of high BP, the distribution of reference BP data, and the BP measurement methodology. Based on the use of ≥95th percentile to define hypertension, it would be expected that the prevalence of hypertension would be approximately 5%. However, due to the effects of accommodation and regression to the mean with repeated measures, the prevalence of hypertension is lower than 5% and had been expected to be from 1–3% following the recommended three separate measurements in children with an initial BP measurement ≥95th percentile.

Recent reports have provided a more precise estimate of the prevalence of hypertension verified by separate measurements. In a recent study Hansen et al. [17] applied the above criteria for hypertension and pre-hypertension to electronic medical record data from well-child care visits in a cohort of over 14,000 primary care patients. With the advantage of having data on repeat BP measurements on separate visits, these investigators determined the prevalence of hypertension to be 3.6% and the prevalence of pre-hypertension to be 3.4% in children and adolescents between the ages of 3 years and 18 years. In a cross-sectional study limited to the adolescence age, the prevalence of pre-hypertension and hypertension was determined in a cohort of 6,790 high school students (11–17 years). Using the recommended repeated BP measurements on those with an elevated initial BP measurement, the authors found that the prevalence of hypertension was 3.2% and the prevalence of pre-hypertension was 15.7% in adolescence [18]. In both reports the presence of obesity was associated with higher rates of high BP. In the study on high school students by McNiece et al. [18] the prevalence of hypertension and pre-hypertension combined was over 30% in obese boys and from 23–30% in obese girls, depending on ethnicity.

The current childhood obesity epidemic [19] and the strong relationship of BP with body weight indicate that the population prevalence of high BP in the young will increase. The epidemiologic evidence to support an adverse impact of childhood obesity on child BP levels has been questioned because, as discussed previously, the earlier population data on children's BP (from the 1963–1984) described considerably higher BP values than in the data obtained after 1984 [20]. When the entirety of the data from the children's BP survey from 1963 to 1994 is compared, it would appear that children's BP levels are decreasing, despite an increase in child obesity within the past decade. However, the variable methods used in the earlier BP surveys limit the ability for us to define a longitudinal trend in children's BP over several decades. An analysis of the trends in childhood BP from two more recent studies by the National Health and Nutrition Examination Surveys (NHANES) group, which were sequential, national and cross-sectional, identified a significant increase in both systolic and diastolic BPs. The BP increase is most striking among minority groups that also have the highest rates of childhood obesity [3]. Another analysis of the same two data cohorts demonstrated an overall increase in the prevalence of hypertension, from 2.7% in the 1988–1994 survey to 3.7% in the 1999–2002 survey [10]. Both analyses verified that the population increase in BP among children and adolescents was largely due to the increase in obesity.

Incidence of hypertension in childhood

Among adults, the prevalence of hypertension increases with age, indicating that new cases of hypertension in adults are diagnosed each year. Although primary hypertension is more commonly identified in adolescence than earlier in childhood, there is little information about the incident rates of hypertension in childhood. Within the National Childhood Blood Pressure database, a segment of adolescents underwent BP measurement at intervals of 2 years and 4 years. An analysis of these data found that, among adolescents with pre-hypertension, 14% had developed hypertension 2 years later, which yielded an approximate incidence rate of 7% per year. A limitation of these data is that they were based on only a single blood pressure measurement for BP classification. Despite this limitation, the serial data indicate that those with high BP continue to have high BP. Among adolescents with high risk BP values, including those designated from a single measurement as having pre-hypertension and hypertension combined, 68% of boys and 43% of girls had developed pre-hypertension or hypertension 2 years later [21].

Despite the well-known variability in serial BP measurements in children, there is now substantial evidence that BP measured in childhood predicts future BP. Those with BP levels in the higher portions of the distribution curve tend to maintain that position over time which is indicative of BP tracking [22]. For example, a community study of 1,505 children aged 5–14 years demonstrated tracking of systolic and diastolic BPs over 15 years, with statistically significant correlation coefficients between childhood BP and later BP levels. Of 116 young adult participants who had developed hypertension, 48% and 41% had suffered elevated childhood systolic and diastolic BPs, respectively [23]. The patterns may vary by race, but weight does not seem to affect population tracking data significantly [24, 25].

A recent systematic review and analysis of 50 cohort studies that examined BP tracking documented significant BP tracking correlation coefficients from childhood into adulthood. The strength of the tracking increased with baseline age and decreased with length of follow-up period. The analysis concluded that data from diverse populations show that the evidence for BP tracking from childhood into adulthood is strong and that early intervention is important [26]. In another study Sun et al. [27] examined serial data from participants in the Fels Longitudinal Study and derived age- and gender-specific BP levels in childhood that predicted hypertension in adulthood. Using random-effects models they found that the earliest significant difference in childhood systolic BP values among adults with and without hypertension occurred at age 5 years for boys and 8 years for girls. The interesting finding from this study was the level of childhood BP that was predictive of subsequent hypertension in adults. The age- and gender-specific values for childhood systolic BP among adults with hypertension were below the 50th percentile for systolic BP in children of median height, based on data in the Fourth report on diagnosis, evaluation, and treatment of high blood pressure in children and adolescents [2]. Therefore, the childhood systolic BP values in the Fels Longitudinal Study that were predictive of future hypertension in adults were well below childhood BP levels that are presently considered to be high risk. These results raise the question of whether the 95th percentile or the 90th percentile for BP in childhood adequately captures high risk BP.

Outcomes of childhood onset hypertension

There are presently no long-term data to connect a level of childhood BP with cardiovascular events in later adulthood. Despite the absence of such longitudinal data to assess outcome risk among adolescents with high BP, data on surrogate markers of vascular injury indicate that vascular abnormality does occur even in the young. Left ventricular hypertrophy (LVH) occurs commonly in children and adolescents with high BP [28–31]. Among children and adolescents with primary hypertension, the presence of obesity was associated with marked LVH [28]. Structural changes in forearm vessels of obese adolescents with high BP were detected by Rocchini et al. [32], who observed a significant correlation between peripheral vascular resistance at maximum vasodilation and measures of insulin resistance. Carotid artery intimal medial thickness (cIMT), assessed by ultrasound, has been found to be greater in young adults who had had multiple risk factors since childhood [33–35]. In a smaller cross-sectional study an increase in cIMT was already detectable in adolescents with high BP [36]. Microalbuminuria predicts progressive deterioration of renal function and an increased risk of cardiovascular (CV) events/death in adults. Recently, Assadi demonstrated that, in children with essential hypertension, the treatment of microalbuminuria by renoprotective therapy (angiotensin-converting enzyme inhibitors or angiotensin-receptor blockers) was associated with LVH regression [37]. The Pathologic Determinants of Atherosclerosis in Youth study, based on autopsies of individuals that had suffered accidental death, demonstrated that quantifiable vessel injury is detectable in adolescents and young adults; and there is a relationship, even in youth, between early atherosclerotic lesions and cardiovascular risk factors, including high BP, altered lipids, and smoking exposure [38, 39]. In a recent study by Mitchell et al. [40] digital retinal photographs were used to measure retinal arteriolar caliber in children. The investigators observed that children in the highest quartile of BP had significantly narrower retinal arterioles than those with lower BP, suggesting that higher BP in childhood is associated with alteration in the microvasculature. There is even emerging evidence that cognitive function is adversely affected by elevated blood pressure in childhood [41, 42].

Summary

It is well established that high BP can be identified in children and adolescents [2], and is increasing in prevalence [3, 10]. However, the definition of hypertension continues to be based on the upper segment of the normal BP distribution and not on outcome data. It is quite possible that the percentiles currently used to define hypertension and pre-hypertension in childhood underestimate the longitudinal risk; and future evidence may warrant a lower level to define high risk BP. Despite the meticulous precision in the BP tables, which adjust for gender, age, and height, the percentile method for the evaluation of BP in children is cumbersome and difficult to use in clinical practice. It would be an extremely useful clinical practice advancement if a few numerical levels could be reliably used for the evaluation of children's BP. However, for one to be certain of what BP value is abnormal, there needs to be clear evidence on where the abnormality begins. What is clear is that more BP measurements on an individual child provide a better definition of the BP phenotype. Ambulatory BP monitoring (ABPM) has become a useful tool for evaluating BP patterns in children, and some normative ABPM data are now available. Because ABPM is performed over 24 hours and requires special instrumentation, its use has been generally limited to hypertension specialists. Recommendations on the use of ABPM in clinical practice and interpretation of the results have been published recently in a scientific statement from the American Heart Association [43].

Data from clinical studies on high BP in childhood show that primary hypertension in childhood is commonly associated with other cardiovascular risk factors as well as obesity. It is also apparent that intermediate markers of target organ damage, such as LVH, increased cIMT, retinal vascular changes, and even subtle cognitive changes, are detectable in children and adolescents with high BP. Considering the rates of verified hypertension (>3%) and pre-hypertension (>3%) in asymptomatic children and adolescents, we should consider high BP as a common long-term health problem in childhood. For both clinical and public health benefit, identification, examination, and treatment of children with high risk BP is an important step in reducing the excessive burden of cardiovascular disease.

Questions

(Answers appear following the reference list)

1. Hypertension is defined in adolescents as:
   a. Average BP ≥ 140/90 mmHg
   b. Average BP ≥ 120/80 mmHg
   c. Average BP ≥ 95th percentile
   d. Average BP ≥ 90th percentile
2. The definition of hypertension in children and adolescents is based on:
   a. The top portion of the normal distribution of BP levels in healthy children
   b. Outcome data
   c. Evidence of target organ damage
   d. Two additional cardiovascular risk factors
3. A single BP measurement of 136/74 mmHg in an asymptomatic 12 year old boy indicates:
   a. Essential hypertension
   b. Need for repeat BP measurement
   c. Probable secondary hypertension
   d. Risk for cardiovascular disease
4. The prevalence of hypertension in asymptomatic children and adolescents is approximately:
   a. <1%
   b. 3.5%
   c. 5%
   d. 10%
5. A recent increase in prevalence of childhood hypertension is most related to:
   a. Improved methods of BP measurement
   b. Changes in diet and food supply
   c. Ethnic shifts in the population
   d. Childhood obesity

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Answers

1. c.
2. a.
3. b.
4. b.
5. d.