Review Article

Childhood Hypertension

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Introduction

Hypertension is one of the commonest diseases with an estimated worldwide prevalence of 1 billion. Data from the 3rd National Health and Nutritional Assessment Survey reveals that in US, one-third of people were unaware of this problem and another one third had blood pressure control below established goals(1). To add to this is the observation in the 7th Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure report that each increment of 20 mm Hg in systolic or 10 mm Hg diastolic pressure doubles the risk of cardiovascular disease(2). There are no similar data in children. where the age, gender and height need to be taken into account while interpreting blood pressure values.

Essential hypertension has been found to be associated with family history of hypertension, IUGR, oligonephronia, obesity and elevated uric acid levels. According to studies in adult populations, the effective treatment of hypertension reduces the risk of coronary heart disease, stroke, renal disease, and congestive heart failure(3).

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Prevalence of Primary and Secondary Hypertension

The prevalence of hypertension in children is reported to be 1-3%. In recent years, the prevalence of hypertension in school-aged children appears to be increasing, perhaps as a result of the increased prevalence of obesity. School-based blood pressure screening and measurement of height and weight in 5102 children, revealed a prevalence of 4.5%, which is higher than that reported earlier(4). The majority of these children have mild hypertension, most often primary (essential). A small group of children have much higher blood pressures usually due to a secondary cause. The prevalence of persistent secondary hypertension in children is 0.1% and renal disease predominates in this group(5). Education, anticipatory guidance, early detection, accurate diagnosis and effective therapy may help improve the long-term outcomes of children and adolescents with hypertension.

Hypertension—Techniques and Case Definitions

All measurements used in constructing the task force tables were made with a standard mercury sphygmomanometer(6). Despite the availability of electronic monitors, the mercury instrument remains the method of choice. The aneroid sphygmomanometer requires periodic calibration. Automated oscillometric devices are useful but expensive and require maintenance and calibration. However, these automated devices can be very helpful in evaluating infants and small

children in whom resting, quiet, auscultatory readings are difficult to obtain. The cuff should encircle at least 80-100% of the arm and the bladder length should be >40% of the arm circumference(7). Inappropriately small cuffs give aberrantly high readings; inappropriately large cuffs will underestimate the true reading. Measurements should be taken after 3 to 5 minutes of resting. Children should have measurements taken while sitting, with the arm at the level of the heart, and infants should have measurements taken while supine. Ambulatory blood pressure monitoring (ABPM) is based on the principle that repeated measurements of blood pressure through 24-hr provide an approximation of true blood pressure than does a single measurement. Because ABPM values have not been precisely correlated with single or repeated conventional cuff measurements, cuff and ABPM measurements cannot be used interchangeably, either for clinical management or in trials of antihypertension agents; both types of measurements therefore should be evaluated according to respective standard tables(8).

A definition of hypertension ideally is based on a threshold level of blood pressure that divides those at risk for adverse outcomes from those who have no increased risk. The normative values are based on the "The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents"(7), as follows :-

- Hypertension is defined as average systolic and/or diastolic pressure >95th percentile for gender, age and height on >3 occasions.
- Prehypertension is defined as average systolic or diastolic pressures between 90-95th percentile. These children should be observed carefully and evaluated if risk factors like obesity are present; tracking data suggest that this subgroup is more likely to develop overt hypertension over time than normotensive children(9).
- Adolescents with blood pressure levels more than 120/80 mm Hg should be considered prehypertensive.
- A patient with blood pressure levels >95th percentile in a physician's office or clinic, who is normotensive outside a clinical setting, has white-coat hypertension.
- If the blood pressure is >95th percentile, it should be staged. If stage 1 (95th percentile to the 99th percentile plus 5 mm Hg), measurements should be repeated on 2 more occasions. If hypertension is confirmed, evaluation should proceed. If blood pressure is stage 2 (>99th percentile plus 5 mm Hg), prompt referral should be made for evaluation and therapy. If the patient is symptomatic, immediate referral and treatment are indicated.

All children should have yearly blood pressure evaluation beyond 3 years of age. There is an increased risk of hypertension in children with history of hypertension in family members, those who are obese, IUGR or have urinary infections and renal scars.

White Coat Hypertension

These children have isolated office hypertension in that their blood pressure is normal when measured at home, at work, or by ABPM(10). These patients have a relatively benign outcome compared to those with sustained hypertension. They may be at increased risk for eventual sustained hypertension and cardiovascular disease, although the risk of cardiovascular complications appears low as long as the ambulatory pressure remains normal.

Etiology

Hypertension is usually described as primary (essential) or secondary due to a definable cause.

The younger the patient and more severe the hypertension, the more likely that a secondary cause will be found.

Most acute hypertension in childhood is due to glomerulonephritis. Chronic hypertension is commonly associated with renal parenchymal disease and only a small proportion have renovascular hypertension, pheochromocytoma or coarctation of the aorta (*Table I*). Late in the first decade and into the second decade of life, primary hypertension begins to predominate(11). Coarctation of the aorta accounts for one third cases of hypertension in neonatal period and infancy. Renovascular causes are amongst the curable forms of hypertension(12). In Asia, aorto-arteritis is common and accounts for most patients with malignant hypertension(13).

Comorbid Factors

Children with blood pressure who are in higher percentiles tend to track in those percentiles in adulthood. Obesity is a common cofactor in the development of essential hypertension. Obesity contributes to blood pressure control through high sodium intake and insulin resistance. The "syndrome X" of hypertension, obesity, hyperlipidemia and diabetes mellitus is a major cause of long-term cardiovascular morbidity and mortality. Sleep disorders including sleep apnea are associated with hypertension; approximately 15% of children snore, and 1-3% have sleep-disordered breathing. Repetitive loud snoring followed by silent periods of apnea usually represents the syndrome of obstructive sleep apnea. Because of the associations of hypertension with sleep disorders, particularly among overweight children, a history of sleeping patterns should be obtained(7).

Clinical Presentation

Young infants may present in acute distress with signs and symptoms of congestive heart failure. In contrast, after infancy hypertension is usually silent. Patients with severe hypertension may have headache, vision changes, nosebleeds, or nausea and should be treated immediately. Presence of edema, oliguria, hematuria suggests rapidly progressive renal failure. Presence of joint pains, rash and systemic symptoms suggests connective tissue disorders. Hypertensive emergencies are defined as the presence of severe hypertension associated with life-threatening or organ-threatening complications, including encephalopathy (seizures, stroke, focal deficits), acute heart failure, pulmonary edema, dissecting aortic aneurysm or acute renal failure.

Attention should to be paid on physical examination to anthropometric measurements, height, weight and body mass index. It

TABLE I–*Common Causes of Hypertension in Different Age Groups*

Age group	Common causes
Newborns	Renal artery thrombosis, renal artery stenosis, congenital malformation, coarctation of aorta, bronchopulmonary dysplasia
Infancy-6 yr	Renal parenchymal disease, coarctation of aorta, renal artery stenosis
6-10 yr	Essential hypertension, renal artery stenosis, renal parenchymal disease.
Adolescence	Essential hypertension, renal parenchymal disease.

may also show features of the specific cause, e.g. weak pulses or blood pressure difference between the upper and lower limbs in coarctation of the aorta, café-au-lait patches or features of neurofibromatosis with renal artery disease and abdominal masses in polycystic kidney disease. Signs and symptoms of cardiomegaly, hypertensive retinopathy or neurological involvement are important, since they indicate longstanding hypertension.

Evaluation

The extent of the evaluation depends on the age of the child, the severity of the hypertension, the extent of end-organ damage, and the long-term risk factors for the individual patient. Children with blood pressure levels >90th percentile have 2.4 times the risk of hypertension in adulthood, compared to those with levels <90th percentile(14).

(1) *Initial evaluation*

This needs to be performed by the general pediatrician. A thorough personal and family history and physical examination is followed by urine dipstick exam and baseline chemistry (*Table II*). An abdominal ultrasound is a useful screening investigation, which evaluates the size of the kidneys, detects tumors of the adrenal gland and the kidneys and is valuable in the diagnosis of cystic renal diseases, renal calculi, dilatation of the collecting system, or of duplex system, ureterocele, and thickened bladder wall.

(2) *Additional evaluation*

All children with hypertension need a nephrology consult for additional evaluation as by definition, essential hypertension is a diagnosis of exclusion. All children with history of UTI should undergo a ^{99}Tc-dimercaptosuccinic acid static scan. This is more sensitive than conventional intravenous urography, requires less exposure to radiation and is considered the gold standard for diagnosis of renal scarring. A frusemide DTPA scan is helpful when an obstructive uropathy is suspected (*Table II*). An MCU is recommended in children under 2 years of age with history of UTI to diagnose and stage the degree of reflux and plan further management.

(3) *Target end organ damage*

The evaluation of hypertensive children should include assessment for additional risk factors. These risk factors include low plasma high-density lipoprotein cholesterol, elevated plasma triglyceride and abnormal glucose tolerance. If there is a strong family history of diabetes, a hemoglobin A1c or glucose tolerance test may be considered especially in adolescents. An echocardiography is recommended to evaluate for evidence of LVH(7).

TABLE II–*Evaluation of Child with Hypertension*

Level I (Initial evaluation)
Full blood count
Serum electrolytes, uric acid, renal function tests, lipid profile
Urinalysis, culture.
Renal ultrasound
Level II (Additional tests as indicated)
Echocardiography
Nuclear scans - DMSA, captopril renography, DTPA diuretic scan
Doppler ultrasound of renal arteries
Serum T3, T4, TSH
Urinary catecholamines
Plasma aldosterone and plasma renin activity, urine steroids
MIBG scan
Renal arteriography/DSA (after urinary catecholamines exclude pheochromocytoma)

Management of Pediatric Hypertension

The goal of treatment is to decrease the short- and long-term risks of cardiovascular diseases and end-organ disease. Reducing the blood pressure alone is insufficient for this objective; the issues of obesity, hyperlipidemia, smoking and glucose intolerance must also be addressed.

Most nephrologists agree that therapy is warranted in children who have persistent elevation of blood pressure above the 99th percentile. In young adults who were being followed up in the Bogalusa Heart Study but who died from accidental injuries, an autopsy series revealed significant and independent correlations between childhood hypertension and hypercholesterolemia and the early development of aortic and coronary atherosclerosis(15). Studies in adult patients have shown that the treatment of mild to moderate hypertension decreases the risk of stroke and coronary heart disease(16).

Nonpharmacologic- Life style modifications

Currently the initial treatment for hypertension involves weight reduction, exercise and dietary intervention. Weight reduction has been shown to be an effective therapy for obese children with hypertension(17). However, weight reduction in children, as in adults, is a goal that is extremely difficult to achieve. Exercise is helpful in reducing weight and both systolic and diastolic blood pressure levels. It must be undertaken on a continuing basis to have lasting benefit in the treatment of hypertension. Combinations of aerobic and static exercise should be followed. Dietary salt restriction has a very important place in the control of blood pressure. The current recommendation for adequate daily sodium intake is only 1.2 g/day for 4- to 8-year-olds and 1.5 g/day for older children(6).

Pharmacologic

Although conservative measures clearly can reduce blood pressure, these options are often insufficient for the treatment of hypertension because of patient and family compliance problems.

The indications for antihypertensive therapy are (*i*) symptomatic hypertension, (*ii*) secondary hypertension, (*iii*) hypertensive target-organ damage, (*iv*) diabetes and (*v*) persistent hypertension despite non-pharmacologic measures.

No particular class of antihypertensive drugs has been shown to be superior to another class in terms of their effects in children. The choice of antihypertensive agent depends on the underlying cause *e.g* in post streptococcal glomerulonephritis, diuretics are the preferred agents, since hypertension is secondary to salt and water retention. When choosing the available therapies, the clinician must also consider efficacy, dosing availability and frequency, adverse effects and cost(17). It is easier to dose amlodepin in children, as it is water soluble and stable as a suspension as opposed to nifedipine. Angiotensin converting enzyme inhibitors (ACEI) and angiotensin receptor blockers have assumed increasing popularity in recent times in view of their advantages of reducing proteinuria and retarding the progression of renal disease, an effect independent of their antihypertensive effect. Common medications used to treat hypertension are shown in *Table III.*

The target blood pressure goal for children with uncomplicated primary hypertension and no hypertensive target-organ damage, should be <95th percentile for gender, age and height. For children with chronic renal disease, diabetes, or hypertensive target-organ damage, the goal BP should be <90th

percentile for gender, age and height.

Hypertensive Emergencies

Hypertensive emergencies are situations where BP must be lowered within 1 hour as in children with seizures, severe headaches, eye changes or cardiac failure. Oral or sublingual nifedipine are helpful in the initial stages of treatment, during establishment of access and delivery of other medications. Intravenous treatment should be started with IV sodium nitroprusside or labetolol infusion if available. Bolus doses of IV hydralazine can be given initially where an infusion is unavailable. It is recommended that children with longstanding hypertension have a 20-30% reduction in their mean arterial pressure over 60-90 minutes. The goal of treatment of hypertensive urgencies is to reduce the blood pressure over a 24-hr period; it can be attempted with any of the previously listed oral medications. In many instances, dose increases in the patient's current medications may be sufficient. Despite concerns in adults, short-acting nifedipine in hypertensive, hospitalized children appears to be a safe and efficacious medication with minimal side effects(19). However, as its action is short-lived, additional, longer-acting medications are required(20).

Hypertensive urgencies are situations where in the immediate risk of complications is less but prompt institution of drug therapy

TABLE III–*Antihypertensive Drugs.*

Drug	Dose initial	Maximum
Hypertensive emergencies		
Nifedipine	0.25 mg/kg	0.5 mg/kg
Sodium nitroprusside	0.5 µg/kg/min IV	8 µg/kg/min IV
Labetalol	1 mg/kg/hr IV, can be given as bolus or steady infusion	3 mg/kg/hr IV
Long-term therapy		
Captopril		
neonates	0.03 mg/kg/d	2 mg/kg/d
children	1.5 mg/kg/d	6 mg/kg/d
Enalapril	0.15 mg/kg/d	0.6 mg/kg/d
Losartan	0.7 mg/kg/d	1.4 mg/kg/d
Extended-release nifedipine	0.25 mg/kg/d	3 mg/kg/d
Amlodipine	0.1 mg/kg/dose	0.6 mg/kg/d (maximum 20 mg/d)
Propranolol	1 mg/kg/d	8 mg/kg/d
Atenolol	1 mg/kg/d	8 mg/kg/d
Prazosin	0.05-0.1 mg/kg/d	0.5 mg/kg/d
Minoxidil	0.1-0.2 mg/kg/d	1 mg/kg/d
Hydrochlorothiazide	1 mg/kg/d	2-3 mg/kg/d
Furosemide	1 mg/kg/d	12 mg/kg/d

and reduction of blood pressure over 24 hr is appropriate. This is true for patients with acute glomerulo-nephritis, accelerated hypertension or that following kidney transplantation.

Surgery

Correction of renal artery stenosis by balloon angioplasty or operative bypass procedures is needed to correct hypertension and preserve the function of the affected kidney(12). Similarly, in cases of segmental renal infarct, unilateral renal hypoplasia with diminished function, or chronic obstruction, partial or complete nephrectomy can be considered. To maximize the potential for complete resolution of hypertension, the affected and contralateral kidney should be evaluated carefully, including assessment of renal vein renin prior to surgical intervention. The other major role for surgical intervention is in cases of pheochromocytoma.

Length of Therapy

The appropriate duration of treatment for a child or adolescent is unknown. Some patients require lifelong therapy; others may experience improvement or even resolution of hypertension. For these reasons, if blood pressure is under excellent control and no organ system damage is present, medications can be tapered and discontinued under careful observation if the underlying cause is corrected (*i.e.*, renovascular hypertension, drug induced hypertension, adrenal tumors). Blood pressure should be monitored carefully on follow up, since a significant proportion of patients become hypertensive in the future.

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