Review Article

Management of Paediatric Hypertension : An Update

T Jesmin[1], G Muinuddin[2], M H Rahman[3], S S Huque[4]

Introduction

Hypertension is an increasingly common problem in adolescents; the awareness of it among both the medical community and general public has increased in recent years1, leading to greater numbers of hypertensive children coming to medical attention. Increases in the prevalence of hypertension are related to the increased prevalence of childhood obesity[2]. The causes of hypertension in children are diverse. Systemic arterial hypertension in children has traditionally been thought to be secondary in origin. Increased incidence of risk factors like obesity, sedentary life-styles, and faulty dietary habits has led to increased prevalence of the primary arterial hypertension (PAH), particularly in adolescents. Presence of childhood hypertension may cause risk of coronary artery attack in children. Early development of atherosclerosis may be associated with childhood hypertension[3]. The Pediatricians should be keep in mind that they have to know the different types of hypertension, seen in childhood, as well as to have an organized approach for the diagnostic evaluation and treatment of such patients.

Evaluation of the Child with Suspected Hypertension

The evaluation of pediatric children starts correct measurement of BP4 preferable by conventional mercury column or aneroid sphygmomanometer. Although less accurate, an automated, oscillometric device can be used in infants and toddlers who will not cooperate with manual BP determinastion. The bladder of the cuff should encircle 80-100% of the circumference of the upper arm, and its width should be at 40% of the upper arm circumference5. Since too narrow of a cuff will create false reading, children with longer upper arms than others of the same age require a wider cuff. Not to be overlooked is a large adult or thigh cuff for use in obese children. The child should be seated quietly for at least 5 minutes prior to BP determination. The arm should be supported at heart level. Infants' blood pressures should be obtained in the supine position. The disappearance of the 5th heart sound is now preferred for the diastolic reading[6].

Clinical presentation varies depending upon age, the target organ involved, and etiology. Neonates may present with apnea, cyanosis, irritability, and poor feeding[7]. In addition, clinical features may reflect specific etiologies. Older children with long-term hypertension or acute exacerbation of chronic hypertension or sudden severe elevation of blood pressure may present with symptoms related to end organ abnormalities involving the heart, eye, kidney, and brain[8].

If a child has been a persistently elevated BP, the first step is to obtain a thorough history and should focus on whether symptoms of another underlying disorder are present, including symptoms of underlying renal disease (enuresis, gross hematuria, edema, fatigue), heart disease (chest pain, exertional dyspnea, palpitations) etc. The past history should include recent as well as chronic illnesses and neonatal history of umbilical line placement (in infants). A family history of hypertension, diabetes, renal disease and other cardiovascular disease (hyperlipidemia, stroke) should be obtained. Physical examination should focus on discovering specific findings that may provide clues to the etiology and/or degree of hypertension. Common examples of such findings are listed in Table I.

[1]Dr. Tahmina Jesmin
Resident Phase B
Pediatric Nephrology
Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka

[2]Prof. Goalm Muinuddin
Professor and Chairman of
Pediatric Nephrology
Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka

[3]Prof. Md. Habibur Rahman
Professor of Pediatric Nephrology
Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka

[4]Dr. Syed Saimul Huque
Assistant Professor
Pediatric Nephrology
Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbagh, Dhaka

Correspondence :
Dr. Tahmina Jesmin
Resident Phase B
Pediatric Nephrology
Bangabandhu Sheikh Mujib Medical University (BSMMU)
Shahbagh, Dhaka
email: tahmina.jesmin@yahoo.com

Table-I: Physical Exam findings in Childhood Hypertension[9]

	Finding	Possible Etiology
Vital Signs	Tachycardia	Hyperthyroidism, Pheochromocytoma, Neuroblastoma, Essential Hypertension
	Decreased LE pulses; drop in BP from UE's to LE's	Aortic Coarctation
Height/weight	Growth retardation	Chronic renal failure
	Obesity	Primary hypertension
	Truncal obesity	Cushing's syndrome
Head & Neck	Moon facies	Cushing's syndrome
	Elfin facies	Williams syndrome
	Webbe d neck	Turner's syndrome
	Thyromegaly	Hyperthyroidism
Skin	Pallor, flushing, diaphoresis	Pheochromocytoma
	Acne, hirsutism, striae	Cushing's syndrome, anabolic steroid Abuse
	Cafe-au-lait spots	Neurofibromatosis
	Adenoma sebaceum	Tuberous sclerosis
	Malar rash	Systemic Lupus Erythematosus
Chest	Widely spaced nipples	Turner's syndrome
	Heart murmur	Coarctation
	Friction rub	Systemic Lupus Erythematosus (pericarditis)
	Apical heave	Left ventricular hypertrophy/chronic Hypertension
Abdomen	Mass	Wilms' tumor, Neuroblastoma, Pheochromocytoma
	Epigastric/flank bruit	Renal artery stenosis
	Palpable kidneys	Polycystic kidney disease, hydronephrosis, Multicystic -dysplastic kidney
Genitalia	Ambiguous/virilization	Adrenal hyperplasia
Extremities	Joint swelling	Systemic Lupus Erythematosus
	Muscle weakness	Hyperaldosteronism, Liddle's syndrome

Many hypertensive children have normal physical examinations, even in the presence of significant underlying renal or other organ system disease. Therefore, laboratory testing is usually necessary in order to complete the child's evaluation. Before starting on laboratory testing, however, the child's age, history, physical exam findings, and degree of blood pressure elevation should be used to decide what are the best studies for the particular child.

Dividing the laboratory evaluation into screening, specific and specialized phases as outlined in Table II is helpful.

Table-II : Laboratory evaluation of the child with hypertension[5, 10, 11]

Phase	Studies
Screening tests	Urinalysis and culture Electrolytes, BUN, creatinine, glucose, calcium, phosphorus, uric acid Lipid panel (cholesterol, triglycerides, etc.) CBC with differential, platelet count
Specific tests	24 hour urine collection for protein excretion & creatinine clearance Urine and serum catecholamines Hormone levels (thyroid, adrenal, etc.) Echocardiogram Renal ultrasound
Specialized studies	Renin profiling (plasma renin & 24 hour urinary sodium excretion) Renal ult rasound with Doppler study of renal arteries Captopril challenge test Renal angiography with renal vein renins Magnetic resonance angiography Captopril renal scan Ambulatory blood pressure monitoring Renal biopsy

All hypertensive children should undergo the screening laboratory tests listed and will usually detect whether significant renal disease or another chronic illness is present. Of the more specific tests, only those indicated by the history, physical examination and screening tests should be obtained. For example, the echocardiogram, which should be obtained in any hypertensive child because left ventricular hypertrophy can be present even in children with mild hypertension[12,13]

On the other hand, renal ultrasounds probably only need to be obtained in preadolescent children with hypertension, and in hypertensive adolescents with abnormal urinalyses or unusually severe hypertension. It may be helpful to consult a specialist with experience in pediatric hypertension at this stage of the evaluation, especially if one or more of the screening studies was abnormal. The specialized studies listed in Table II are typically done at referral centers, or by pediatric subspecialists with extensive experience managing hypertensive children. Several of these are used to investigate the possibility of renal artery stenosis. It is important to note that since renal artery stenosis in children is typically caused by fibromuscular dysplasia[14], angiography is still the gold standard for diagnosis because of its superior ability to detect branch vessel disease, especially in infants and young children[10]. Magnetic resonance angiography, which is finding increased use for evaluation of hypertension in adults may have a role in the adolescent or older child who can cooperate with the procedure. However, if the magnetic resonance angiogram reveals the presence of renal artery stenosis, the child may still need to undergo an angiogram prior to revascularization surgery.

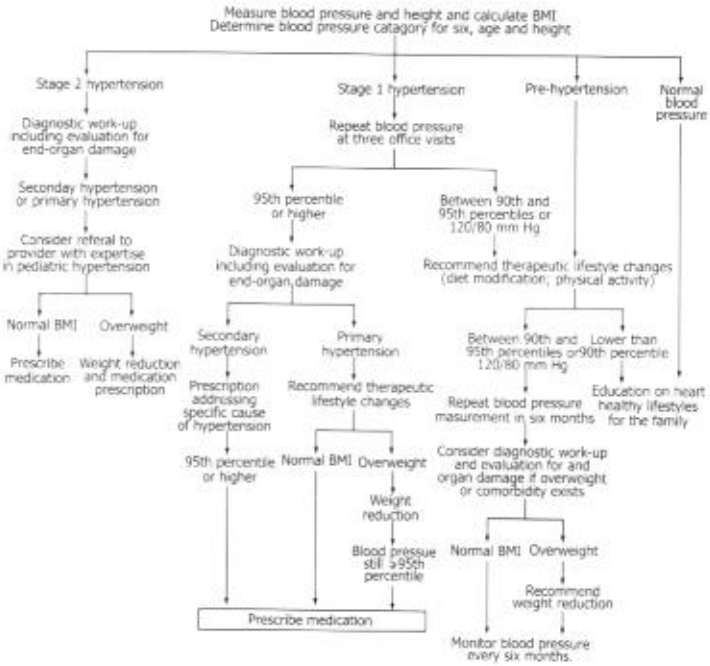
Another diagnostic study that deserves specific mention is ambulatory blood pressure monitoring (ABPM). In this

procedure, the subject wears a blood pressure cuff that takes BP at regular intervals for an entire day. Lightweight devices and a variety of cuff sizes are widely available, making it possible to obtain ABPM studies in young children as well as teenagers[15].

Finally, no diagnostic evaluation of a hypertensive child would be complete without including one or more studies to assess for the presence of end-organ damage[16]. Although hypertension itself is virtually unknown as a cause of chronic renal failure in childhood, both left ventricular hypertrophy and retinal changes are relatively common, even in children with essential hypertension[12].

As will be discussed later, if such abnormalities are present, the child will likely require antihypertensive drug treatment.

Treatment of Childhood hypertension



Algorithm for the management of childhood hypertension

Adapted with permission from National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004; 114 (2 suppl 4th report):571.

A. Pharmacotherapy

Reasons to initiate antihypertensive medication in children and adolescents include symptomatic hypertension, end-organ damage (e.g., LVH, retinopathy, proteinuria), secondary hypertension, stage 1 hypertension that does not respond to lifestyle changes, and stage 2 hypertension. Drug therapy is always an adjunct to nonpharmacologic measures.

Table III : Antihypertensive Medications with FDA Approval for Use in Children[17]

Class	Drug	Initial dosage	Maximum dosage
Angiotensin-converting enzyme inhibitor*†‡	Benazepril (Lotensin)§	0.2 mg per kg per day up to 10 mg per day	0.6 mg per kg per day up to 40 mg per day
	Enalapril (Vasotec)§	0.08 mg per kg per day up to 5 mg per day	0.6 mg per kg per day up to 40 mg per day
	Fosinopril (Monopril)	Children heavier than 50 kg: 5 to 10mg per day	Children heavier than 50 kg: 40 mg per day
	Lisinopril (Zestril)§	0.07 mg per kg per day up to 5 mg per day	0.6 mg per kg per day up to 40 mg per day
Angiotensin-receptor blocker*†‡	Irbesartan (Avapro)	Six to 12 years of age: 75 to 150 mg per day	Same as initial
		13 years of age: 150 to 300 mg per day	Same as initial
	Losartan (Cozaar)§	0.7 mg per kg per day up to 50 mg per day	1.4 mg per kg per day up to 100 mg per day
Beta blocker	Propranolol (Inderal)||	1 to 2 mg per kg per day	4 mg per kg per day up to 640 mg per day
Calcium channel blocker¶	Amlodipine (Norvasc)§	6 to 17 years of age: 2.5 to 5.0 mg per day	10 mg per day
Diuretic**	Hydrochloro thiazide (Hydrodiuril)	1 mg per kg per day up to 50 mg per day	3 mg per kg per day up to 50 mg per day

FDA = U.S. Food and Drug Administration.
*—Contraindicated during pregnancy; females of childbearing age should be counseled to use contraception.
†—Check serum potassium and creatinine periodically to monitor for hyperkalemia or azotemia.
‡—FDA approval is limited to children six years of age or older with creatinine clearance of at least 30 ml per min per 1.73 m2.
§—Can be prepared as a suspension.
||—Contraindicated in asthma and heart failure. Heart rate is dose-limiting. May impair athletic performance. Should not be used in insulindependent patients with diabetes. A sustained-release, once-daily formulation is available.
¶— May cause tachycardia.
**—All patients treated with diuretic medications should have electrolytes monitored shortly after initiation of therapy and periodically thereafter.
Useful as add-on therapy in patients being treated with drugs from other drug classes.
Adapted with permission from National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents.The fourth report on the diagnosis, evaluation, and treatment of high blood pressure in children and adolescents. Pediatrics 2004;114(2 suppl 4th report):568-9.

Table IV : Selected Combinations of Drug Products

Combination	Some Available Preparations
ACEi plus CCB	
Benazepril/Amlodipine	10 mg/2.5 mg; 10 mg/ 5 mg; 20 mg/5 mg
ACEi plus Diuretic	
Benazepril/Hydrochlorothiazide	5 mg/6.25 mg; 10 mg/12.5 mg; 20 mg/12.5 mg
Captopril/Hydrochlorothiazide	25 mg/15 mg; 25 mg/25 mg
Enalapril/Hydrochlorothiazide	5 mg/12.5 mg; 10 mg/25 mg
Lisinopril/Hydrochlorothiazide	10 mg/12.5 mg; 20 mg/12.5 mg
ARB plus Diuretic	
Losartan/Hydrochlorothiazide	50 mg/12.5 mg; 100 mg/12.5 mg
Irbesartan/Hydrochlorothiazide	150 mg/12.5 mg; 300 mg/12.5 mg

ACEi_angiotensin-converting enzyme inhibitor, CCB_calcium channel blocker, ARB_angiotensin receptor blocker

*Check pediatric labeling and safety information on all agents. These drug combinations do not have specific pediatric testing or indications but are recommended on the basis of clinical experience in adolescents and young adults.[1]

Special Treatment Issues[18]

Essential Hypertension: The decision to treat a patient who has essential hypertension often is controversial. Initially conservative management including dietary modifications and exercise programs are appropriate as long as there is no evidence of end-organ damage. If medication need, it is important to maximize compliance and minimize adverse metabolic side effects. The most commonly used drugs are long-acting calcium channel blockers and ACEIs.

Hypertensive Athletes: For the pediatric athlete, ACEIs and calcium channel blockers are often excellent pharmacologic options because they do not suppress cardiovascular function. Diuretics are banned by many sports organizations and should be avoided because of the additional adverse effects of enhanced volume contraction.

Neonatal Hypertension: In the neonatae group, the most common causes of hypertension include congenital renal diseases, renal ischemic events, and a combination of cardiopulmonary disease and multiple drug regimens. There are very few data regarding long-term use and safety of antihypertensive drugs ACEIs work well in renin mediated hypertension due to renal ischemia or congenital obstructions. The clinician should be aware for abnormal renal development in the very preterm infant in whom nephrogenesis is incomplete. Each infant's special problems should be considered individually prior to choosing of drugs.

Hypertensive Emergencies: The goal of treatment of hypertensive urgencies is to reduce the blood pressure over a 24-hour period. Oral or sublingual nifedipine is effective but short-lived, and additional, longer-acting medications should be added or increased. The addition of intravenous medications should be considered if oral options do not produce the desired results quickly. In hypertensive emergency that involves acute, life threatening cardiovascular or cerebrovascular complications, intravenous medications and intra-arterial monitoring are mandatory. Oral or sublingual nifedipine are helpful in the initial stages of treatment, but continuous intravenous infusions with sodium nitroprusside, nicardipine, or labetalol should be initiated as rapidly as possible.

B. Non-pharmacological treatment:

For pediatric patients with pre-hypertension and stage 1 hypertension cases, therapeutic lifestyle changes are usually recommended that includes weight control, exercise (especially cycling and swimming), low-fat and low-sodium diet (such as atkin diet) etc.

Conclusion

The issue of hypertension in childhood is an emerging topic. Well-designed epidemiologic studies have shown that the prevalence of hypertension is increasing among children. Further, hypertension in children is not a benign condition, and it is associated with end-organ damage. Common causes of childhood hypertension include renal and cardiac disease. It may even result in adult hypertension.

The role of the pediatrician, the pediatric nephrologists, and the others caring for children is important in terms of identification of children at risk for hypertension, initiation of preventive measurements, and management of patients with established high blood pressure. Newer imaging modalities, specific management protocol, modern antihypertensive drugs etc have enriched the management of pediatric hypertension.

References

1. Flynn, JT, Falkner, BE. Obesity Hypertension in Adolescents: Epidemiology, Evaluation, and Management. The Journal of Clinical Hypertension 2011; 13(05): 323-331
2. J. Sorof and S. Daniels, "Obesity hypertension in children: a problem of epidemic proportions," Hypertension, vol. 40, no. 4, pp. 441-447, 2002.
3. Berenson GS, Srinivasan SR, Bao W, Newman WP 3rd, Tracy RE, Wattigney WA. Association between multiple cardiovascular risk factors and atherosclerosis in children and young adults. The Bogalusa Heart Study. N Engl J Med. 1998;338:1650-6.
4. Task force on Blood Pressure Control in Children. Report of the second task force on blood pressure control in children - 1987. Pediatrics 1987; 79:1-25.
5. National High Blood Pressure Education Program Working Group. Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents: A working group report from the National High Blood Pressure Education Program. Pediatrics 1996; 98:649-58.
6. Ingelfinger JR. Monogenic and polygenic genetic contributions to hypertension. In: Portman RJ, Sorof JM, Ingelfinger JR, eds. Pediatric Hypertension. Totowa, NJ: Humana Press; 2004: 225-240
7. J. T. Flynn, "Neonatal hypertension: diagnosis and management," Pediatric Nephrology, vol. 14, no. 4, pp. 332-341, 2000.
8. M. M. Mitsnefes, "Hypertension in children and adolescents," Pediatric Clinics of North America, vol. 53, no. 3, pp. 493-512, 2006.
9. Boneparth A, Flynn JT. Evaluation and treatment of hypertension in general pediatric practice. Clin Pediatr (Phila). 2009; 48(1):44-49
10. Prince MR. Renal MR angiography: a comprehensive approach. J Magn Reson Imaging 1998; 8:511-6.
11. Flynn JT. Pediatric use of antihypertensive medications: much more to learn. In press, Curr Ther Res.
12. Laird WP, Fixler DE. Left ventricular hypertrophy in adolescents with elevated blood pressure: Assessment by chest roentgenography, electrocardiography and echocardiography. Pediatrics 1981; 67:255-9.
13. Zahka KG, Neill CA, Kidd L, Cutilletta MA, Cutilletta AF. Cardiac involvement in adolescent hypertension: Echocardiographic determination of myocardial hypertrophy. Hypertension 1981; 3:664-8.
14. Deal JE, Snell MF, Barratt TM, Dillon MJ. Renovascular disease in childhood. J Pediatr 1992; 121:378-84.
15. Sorof JM, Portman RJ. Ambulatory blood pressure monitoring in the pediatric patient. J Pediatr 2000; 136:578-86.
16. Falkner B, Tannenbaum J. Decision-making in childhood hypertension. In: Bühler FR, Laragh JH, eds. Handbook of Hypertension, Vol. 13: The management of hypertension. Elsevier Science Publishers, 1990:495-508.
17. Feld LG, Corey H. Hypertension in Childhood. Pediatrics in Review 2007; 28: 283-292
18. Norwood VF. Hypertension. Pediatrics in Review 2002;23;197-208