Assessment and Management of Hypertension in Children and Adolescents: Part B – Investigations and Management

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Abstract
Once the diagnosis of hypertension has been established in a child or an adolescent, the investigations to be requested need to include a search for the primary cause when secondary hypertension is suspected, the identification of associated and co-morbid conditions and the evaluation of target-organ damage. Instituting therapy should be based on clear indications, the choice of lifestyle and/or pharmacological treatment should be guided by the pathophysiology of the underlying mechanism and based on evidence-based guidelines.

Key words: Adolescent, blood pressure, child, humans, hypertension.

Introduction
After the confirmation of hypertension in a child or an adolescent, selected investigations should be performed according to a carefully planned strategy guided by the initial clinical assessment. When therapy is required, the goals should be well defined and the selection of the appropriate therapeutic measures should follow an evidence-based approach.

Investigations
The objectives of the investigations include a search for the primary cause when secondary hypertension is suspected, the identification of associated and co-morbid conditions and the evaluation of target-organ damage in all cases of hypertension.1

The preferred strategy is to proceed from simple tests that can be performed in an outpatient setting to complex noninvasive tests and finally to invasive tests. Findings from the patient's history and physical examination should dictate the appropriate type and order of tests. In general, severe elevations of blood pressure warrant aggressive evaluation. However, as mild elevations of blood pressure are usually not associated with secondary disease, the initial evaluation is uncomplicated and aims mainly to identify renal disease. If renal disease is not identified, the additional diagnostic tests are usually reserved for patients with higher blood pressure levels.

Initial Evaluation
A complete blood count may indicate anaemia due to chronic renal disease.
Measurement of serum electrolytes, creatinine, urea nitrogen, calcium and uric acid may reveal an increased serum creatinine concentration suggestive of renal disease or hypokalaemia suggestive of hyperaldosteronism. When metabolic syndrome is suspected in an obese child, fasting lipid panels and oral glucose-tolerance tests should be ordered. Urinalysis by dipstick testing, may show the presence of blood and/or protein indicative of
a renal pathology. A urine culture is performed to look for urinary tract infections and pyelonephritis.

Abdominal ultrasonography is a useful screening investigation. It allows the evaluation of the size of the kidneys (small if hypoplastic or scarred, or large in polycystic kidney disease), the presence of cortical scarring, renal calculi, hydronephrosis, duplex system, ureteroceles or thickened bladder wall. Asymmetry in renal size suggests renal dysplasia or renal artery stenosis. Renal or extrarenal masses suggest a Wilms tumor or neuroblastoma, respectively.

**Additional Tests, only as Indicated**

All children with history of urinary tract infection should undergo a 99Tc dimercaptosuccinic acid (DMSA) 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. It can also detect differences in perfusion between the two kidneys. A frusemide DTPA scan is helpful whenever an obstructive uropathy is suspected.

An micturating cystourethrogram (MCUG) is recommended in children under 2 years of age with history of urinary tract infection to diagnose and grade the degree of vesicoureteral reflux and plan further management. When illicit drug use is suspected to be the cause of hypertension, drug screening would identify the offending substances.

Echocardiography is essential in the evaluation of suspected aortic coarctation. Precise anatomic detail of the aortic arch and its branches must be obtained.

Thyroid function testing with measurement of serum T3, T4 and TSH is useful to rule out hyperthyroidism.

A pregnancy test may be useful in a sexually active female who is noted to be hypertensive in view of the possibility of preeclampsia. Plasma and urinary steroids should be measured when an adrenal cause of hypertension is suspected. Peripheral plasma renin activity (with or without captopril) is a useful screening test for both renovascular and renal parenchymal disease. It should be remembered that normal values gradually decrease with age. A suppressed value suggests excess mineralocorticoid effect (hyperaldosteronism, Liddle syndrome), or apparent mineralocorticoid excess. An elevated value is associated with renal or renal vascular hypertension, including coarctation of the aorta. A high plasma aldosterone concentration is diagnostic of hyperaldosteronism. Urinary catecholamines metabolites measurements are useful when pheochromocytoma or neuroblastoma are suspected, with high levels being confirmatory. However, measurement of resting, supine plasma catecholamines by radioenzymatic assay have been shown to be more useful than either 24-hour urinary vanillylmandelic acid (VMA) or metanephrines.

Radioisotope iodine-131-meta-iodobenzylguanidine (MIBG) scan is used when pheochromocytoma or neuroblastoma are suspected. Doppler ultrasound of renal arteries may demonstrate abnormal arterial and venous blood flow as well as lesions in the main arteries or in the segmental branches. Asymmetry in renal artery blood flow suggests renal artery stenosis. Radionuclide renal imaging (without or with captopril) may suggest renal artery stenosis when it shows asymmetry of uptake. Renal arteriography or digital subtraction arteriography (after pheochromocytoma has been excluded by catecholamines measurements) can demonstrate lesions and change in diameter in the main arteries or in the segmental branches.

Sampling of blood from renal arteries, renal veins, and aorta may reveal differences in plasma renin activity between the kidneys. A renin activity ratio of 3:1 between the kidneys is considered diagnostic of renal vascular hypertension.

Polysomnography helps in identifying sleep disorders associated with hypertension, especially in obese children with a history of snoring, daytime sleepiness, or any sleep difficulties.
Investigations for Associated Risk Factors and Target End Organ Damage

The evaluation of hypertensive children should include assessment for additional risk factors, such as low plasma high-density lipoprotein cholesterol, elevated plasma triglycerides and abnormal glucose tolerance. If there is a strong family history of diabetes, a hemoglobin A1c or glucose tolerance test should also be considered especially in adolescents.

Sustained hypertension results in changes in eyes (hypertensive retinopathy), heart (increased left ventricular mass, diastolic dysfunction), kidneys (albuminuria), brain and blood vessels (increased intimal and medial thickness). Although these changes usually indicate longstanding hypertension, there is evidence that they are common even in patients with stage 1 hypertension if it has been present for a long time. A fundocopic examination and estimation of proteinuria are imperative. An echocardiography is also recommended to evaluate for evidence of left ventricular hypertrophy and to assess left ventricular function. Left ventricular hypertrophy is usually symmetric, with equivalent increases in thickness of both the left ventricular portion of the ventricular septum and the left ventricular posterior wall, and its presence confirms the chronicity of the hypertension and is an absolute indication for starting or intensifying treatment.

Management

Persistent elevation of blood pressure above the 95th percentile for age, gender and height, requires treatment.

Goal of Treatment

The target blood pressure goal for children with uncomplicated primary hypertension and in the absence of hypertensive target-organ damage, should be less than the 95th percentile for gender, age and height, in order to decrease the short- and long-term risks of cardiovascular and end-organ disease. However, reducing the blood pressure alone is insufficient for this objective and therefore obesity, hyperlipidaemia, smoking and glucose intolerance must also be addressed.

For children with chronic renal disease, diabetes, or hypertensive target-organ damage, the goal should be instead a blood pressure less than the 90th percentile for gender, age and height.

Principles of Treatment

Whenever possible, treatment of hypertension should address the primary cause and correct it. Both non-pharmacologic and pharmacologic approaches to treatment are used in managing children with elevated blood pressure.

Medications are not recommended for all affected children, in view of the undesirable effects of many antihypertensive drugs and since there are no long-term pediatric data on their benefits or adverse effects on growth and development. The initial management for children with essential hypertension usually always begins with lifestyle modifications, as discussed later.

Most children with sustained secondary hypertension require treatment with antihypertensive agents. While data on the short-term efficacy and tolerability of antihypertensive agents in children and adolescents exist, there are no studies of sufficient duration to answer the long-term questions.

Pre-Hypertension

Affected children are primarily managed by lifestyle modifications and revaluated after a period of 6 months. Medications are not required unless the child has comorbid conditions such as chronic kidney disease, diabetes mellitus or dyslipidaemia, or has evidence of target organ damage.

Essential Hypertension

In view of the undesirable effects of many antihypertensive drugs, patients with essential hypertension are also initially managed with lifestyle modifications. It must be remembered that adolescents, who are notoriously poorly compliant with changes in lifestyle, are also unlikely to be compliant with a long-term drug therapy. Pharmacological therapy is initiated if there is either a comorbid condition such as chronic kidney disease, diabetes mellitus,
dyslipidaemia, target organ damage or in case of failure of blood pressure to decline below the 95th percentile despite a 6-month period of lifestyle modifications. In addition, adolescents should always be counseled about the adverse effects of tobacco and alcohol on blood pressure.

Non-Pharmacologic Measures. Lifestyle Modifications

Non-pharmacologic approaches to hypertension include dietary changes, increased physical activity and weight loss in the obese child. Although difficult to apply successfully in practice, there is evidence supporting their efficacy in children and adolescents and they remain a cornerstone of recent recommendations. Interventions should focus on the risk factors and approaches based on daily routines are more likely to be successful. In addition, studies in adults have demonstrated that successful lifestyle modification measures enhance the efficacy of antihypertensive drug therapy.

Obesity and hypertension are closely correlated, particularly in adolescents. Weight reduction, although often difficult to achieve, should be a goal in overweight children with hypertension. Reduction of weight reduces sensitivity of blood pressure to salt and attenuates cardiovascular risk factors such as dyslipidaemia and insulin resistance. Reduction of BMI by 10% has been shown to lead to 8-12 mm Hg fall in systemic blood pressure. This effect is more marked in obese adolescents. In addition, prevention of excess weight gain has another long-term protective role as it will also limit future increases in blood pressure.

In the absence of controlled trials in children and adolescents, dietary modifications are recommended following extrapolations from studies on adults. Salt restriction seems to benefit only a subgroup of patients with hypertension, particularly African American patients, who may have a defect in the cellular handling of sodium. In the past a daily sodium intake of only 1.2 g/day for 4- to 8-year-olds and 1.5 g/day for older children used to be recommended. However, recent studies have shown that a ‘no added salt diet’ or a daily sodium intake ranging between 1-1.5 g (45-65 mEq sodium, 2.6-3.8 g salt) are associated with small reductions (approximately 4%) in blood pressure. It is important to remind the children and their families that they also must avoid food products high in sodium, such as processed and canned foods and meals prepared in fast food shops including pizzas, pickles and salted potato chips. A low-fat diet is also recommended as patients with elevated fat content have been reported to have low levels of adipokine, a substance the absence of which, is known to cause an elevation of blood pressure. Although increasing dietary potassium intake, through vegetables and fruits, is associated with modest reduction of systolic and diastolic blood pressure in adults with essential hypertension, this effect on children with hypertension remains unknown. Nevertheless, avoiding potassium depletion from diuretic therapy and prescribing a potassium-rich diet in patients without renal insufficiency is indicated. Potassium intake should however be restricted in children with chronic kidney disease with glomerular filtration rate (GFR) below 30 mL/ min/1.73 m², adrenal insufficiency, severe heart failure, or those receiving treatment with angiotensin converting enzyme inhibitors (ACEI), non-steroidal anti-inflammatory agents and potassium sparing diuretics. An increased intake of fresh vegetables and fruits, whole grains and non-fat dairy is recommended, as they are low in sodium and saturated fat and rich in minerals (potassium, calcium, magnesium) and fiber, despite limited evidence regarding their effectiveness.

Exercise is helpful in reducing weight, as well as reducing both systolic and diastolic blood pressure levels. However, to have lasting benefit, it must be undertaken on a continuing basis. The degree of physical fitness has been shown to be inversely related to blood pressure in grade-school children. Obese adolescents also show significant reductions in
blood pressure with weight loss, especially when exercise is incorporated into the weight-loss programme. A minimum of 30-60 minutes or more of daily physical activity involving a variety of activities is encouraged. Both aerobic and isotonic exercises should be included in such a programme. Paediatricians are frequently asked about hypertensive adolescents’ participation in organized sports. There is no evidence to suggest that mild or moderate hypertension increases the risk of cardiovascular events while participating in these sports, and furthermore, the occurrence of sudden cardiac death is not associated with hypertension in young athletes. As fitness contributes to blood-pressure control, exercise should be encouraged, except for those with untreated severe hypertension or identified cardiac abnormalities. Participation in aerobic, isotonic exercises and competitive sports should be avoided in patients with stage 2 hypertension, severe uncontrolled hypertension, or target organ damage until blood pressure is well controlled. Strength training (isometric) exercises (e.g., weight lifting, gymnastics, karate and judo) should be avoided in such children.

When performed on a regular basis, stress-reducing activities (e.g., meditation, yoga, biofeedback) can reduce BP but this effect is lost when the activity is discontinued.

**Pharmacologic Measures**

Most antihypertensive agents have not been fully tested in children, and the risks of using them might be higher in children, in view of the longer duration of administration, especially during a time of rapid growth and development. It should also be remembered that it is still not known whether starting antihypertensive medications earlier in life reduces the risk of later cardiovascular disease.

**Indications for Antihypertensive Therapy**

- stage 2 hypertension
- stage 1 hypertension that persists despite 6-months’ of lifestyle modifications
- symptomatic hypertension
- secondary hypertension
- acute or chronic complications of hypertension, including evidence of hypertensive target organ damage
- pre-hypertension or stage 1 hypertension with comorbid conditions such as diabetes, chronic kidney disease or dyslipidaemia
- diabetes
- persistent hypertension despite non-pharmacologic measures.

**General Principles of Pharmacological Therapy**

- Blood pressure is considered controlled when it is less than the 95th percentile in children with uncomplicated primary hypertension. When patients have chronic renal disease, diabetes, or hypertensive target-organ damage, the goal should be less than the 90th percentile.
- Medications with a longer duration of action (once or twice daily dosing) are preferred to ensure better compliance.
- A low dose of one drug should be started first.
- If unsuccessful, the dose should be increased.
- Dose adjustment of antihypertensive medications should not be made more frequently than every few days.

If there are side effects a drug from a different class should be substituted.

If blood pressure is not controlled with one medication at an adequate dosage, and if poor compliance is not at fault, a drug from another class should be added and a stepped-care approach should be followed. The basic principle of combination antihypertensive therapy is the co-administration of drugs with different sites or mechanisms of action. Combinations minimize the side effects by allowing administration of lower dosage of different agents. In addition, by combining drugs with complementary mechanism of
action such as angiotensin converting enzyme inhibitors, or angiotensin receptor blocker with a calcium channel blocker or a thiazide diuretic, or vasodilator with diuretic or β-blocker, the synergism might be more successful in controlling the blood pressure. However caution must be exercised with combination therapy in view of side effects, such as the long term combination therapy of thiazides with β-blockers found to be associated with an increased incidence of glucose intolerance. Stepped-care allows for the individualization of therapy according to the needs of the child and also facilitates the identification of adverse effects as drug doses are increased or new agents added. The stepped-care approach has been recommended by many paediatric working groups as an appropriate approach to the use of antihypertensive drugs in children and adolescents. Because compliance may become a problem, the drug regimen should be as simple as possible and should take advantage of longer acting agents that can be administered once or twice daily, when available. Drug calendars, parental supervision, and close patient-physician communication also help ensure compliance.

If control is not achieved with 2 drugs, reconsider the possibility of secondary hypertension before adding a third drug, following the same stepped-care approach.

The appropriate duration of treatment for a child or adolescent is not exactly known. While some children 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. The drug step-down approach attempts a gradual reduction of the medication after 8-12 months of satisfactory blood pressure control. Children must maintain a healthy lifestyle and blood pressure should be checked regularly, such as every 3 months, after cessation of therapy. Step-down of drug therapy might also be possible in patients in whom a specific intervention has ameliorated the underlying cause for hypertension, such as following resection of pheochromocytoma or balloon dilatation for renovascular disease. It is essential that blood pressure is monitored carefully on follow up, since a significant proportion of patients may become hypertensive again in the future.

**Commonly Used Antihypertensive Medications**

Calcium channel blockers such as nifedipine and amlodipine are effective in children. The availability of long acting preparations permits once or twice daily dosing. Sustained release preparations of nifedipine should be swallowed whole, and not crushed or chewed. Calcium-channel blockers are recommended essentially for children with hypertension and migraine headaches.

Angiotensin converting enzyme inhibitors such as captopril are mainly used in young infants and require dosing every 6-8 hr. Beyond infancy, enalapril (in 1-2 daily doses) is preferred as it has a longer duration of action. Newer products such as lisinopril or ramipril are drawing interest as they require once daily dosing and have fewer side effects. Angiotensin converting enzyme inhibitors have been recommended only for children with diabetes and microalbuminuria or proteinuric renal disease.

Angiotensin receptor blockers are another class of antihypertensive drugs used in children and include losartan, valsartan and irbesartan. These drugs have been recommended only for children with diabetes and microalbuminuria or proteinuric renal disease.

Cardioselective β-blockers (atenolol, metoprolol) are effective agents, requiring once or twice daily dosing and have few side effects. The use of propranolol is limited in view of the need for multiple daily doses and side effects. Labetalol, an α- and β-blocker, is useful in patients refractory to other medications. Beta-blockers have been recommended for
children with hypertension and migraine headaches.\(^5\)

There is no single recommended regimen for children, and medications commonly prescribed for adults have been successfully used in children.\(^{12,24}\) It must be emphasised that paediatric clinical trials have focused on the ability of each drug to lower blood pressure, but the effects of these drugs on clinical endpoints have not been compared. No particular class of antihypertensive drugs has been shown to be superior to another class in terms of their effects in children. Starting with a class of antihypertensive medication appropriate for each specific patient is recommended.\(^5\) When choosing an antihypertensive drug, the paediatrician must also consider efficacy, dosing availability and frequency, adverse effects and cost.\(^{10}\)

In children with primary or essential hypertension, controversy persists regarding the choice of the initial agent. In adults, a thiazide diuretic is usually chosen, based upon evidence of the superiority of this class in reducing cardiovascular morbidity and mortality in large-scale trials.\(^{25}\) Given the lack of comparable studies in the young, the choice of initial agent in children with primary hypertension remains therefore arbitrary and paediatricians are advised to prescribe only those agents that have established pediatric indications and/or labeling information.\(^5\) Fortunately, the number of such agents has greatly recently increased with increased availability of information on their efficacy in hypertensive children and adolescents.\(^8\) Initial therapy with a diuretic or a β-blocking agent is commonly used in affected children. Calcium channel blockers or angiotensin converting enzyme inhibitors can also be prescribed, and if they cannot be tolerated, β-blockers can be used.\(^{23}\)

In secondary hypertension, the cause of the hypertension and the associated complications dictate the choice of medication. Drugs with different sites and mechanisms of action are available so that therapy can be tailored to the specific pathologic condition.

In acute post-streptococcal glomerulonephritis with circulatory congestion, hypertension and edema, fluid and sodium restriction with judicious use of loop diuretics are indicated since hypertension is of short duration and is caused mainly by salt and water retention.

In children with chronic kidney disease, the target blood pressure is under the 90th percentile. In chronic kidney disease stage I-III (GFR >30 mL/min/1.73 m\(^2\)) therapy should be initiated with angiotensin converting enzyme inhibitors, since these agents also reduce proteinuria and retard progression of renal damage.\(^{26}\) Monitoring of serum potassium and creatinine is necessary, initially at 7-14 days and then every 1-3 months. The dose of angiotensin converting enzyme inhibitor or angiotensin receptor blocker is reduced if serum creatinine exceeds 30-35% from the baseline, or in case of hyperkalaemia. Treatment with these agents should be avoided in patients with advanced chronic kidney disease (stage IV-V; GFR <30 mL/min/1.73 m\(^2\)) where either calcium channel blockers or β-blockers should be used. Management of children with chronic kidney disease also includes restriction of sodium intake between 1-1.5 g (45-65 mEq sodium, 2.6-3.8 g salt), co-administration of thiazide diuretics to reduce sodium and volume overload, appreciating that they are only effective when the GFR exceeds 30 mL/min/1.73 m\(^2\). Caution should be exercised in children with chronic kidney disease as the dosage of some medications such as atenolol will need adjustment in function of the GFR.

In patients with a high probability of, or confirmed renovascular disease, therapy should be initiated with a calcium channel blocker and/or a β-blocker. Additional agents include prazosin, labetalol, clonidine, hydralazine and/or minoxidil. It must be remembered that therapy with angiotensin converting enzyme inhibitors or angiotensin receptor blockers is avoided in patients with bilateral renovascular disease, but they might be used very cautiously in unilateral renovascular hypertension.
Excessive activity of the renin-angiotensin-aldosterone system may be treated effectively with either β-blockers, such as propranolol, to suppress renin secretion, or an angiotensin converting enzyme inhibitor such as captopril or enalapril, or, rarely, an aldosterone antagonist such as spironolactone.

α-adrenergic blocking agents such as phentolamine or phenoxybenzamine are beneficial in hypertensive urgencies or emergencies. They may occur, for example, in children with acute glomerulonephritis, necessary. They may occur as a result of an acute illness, such as post-infectious glomerulonephritis or acute renal failure. These children require hospitalization for monitoring and supportive care.

Hypertensive crisis consists of either hypertensive urgencies or hypertensive emergencies. Urgencies differ from emergencies in having no evidence of acute target organ damage. As most children with hypertensive crisis have chronic or acute renal disease, management of blood pressure also requires careful attention to fluid balance, as well as diuresis with intravenous frusemide, which is usually effective, even though glomerular filtration may be impaired.

Hypertensive Urgencies

Hypertensive urgencies are not associated with hypertensive acute target organ damage, the immediate risk of complications is less, but prompt institution of drug therapy and reduction of blood pressure over 24 hours is necessary. They may occur, for example, in children with acute glomerulonephritis, accelerated hypertension or hypertension following kidney transplantation. Controlled reduction of blood pressure, using oral medications, over several hours is desirable. Children with longstanding hypertension should have a 20-30% reduction in their mean arterial pressure over 60-90 minutes. The onset of action of nifedipine (0.25 mg/kg, maximum 10 mg) administered orally is within 5-10 minutes, peaks at 30-60 minutes and lasts for 2-6 hours. However, as the action of oral nifedipine is short-lived, additional longer-acting medications are required. Oral administration of clonidine (0.05-0.1 mg) is also effective, although the onset of action (30-60 minutes) and peak effect (2-4 hours) is delayed. Sedation and orthostatic hypotension occur in many patients. Sublingual or oral administration of captopril (6.25-25 mg) also shows a rapid onset (10-30 minutes), peaks (1-2 hours) and has a relatively prolonged duration of action (4-8 hours). Despite the overall efficacy of the above agents, a predictable reduction of blood pressure is often not possible. Patients with hypertensive urgencies should be observed closely, since use of IV medications might be required.

Hypertensive Emergencies

Hypertensive emergencies are situations associated with hypertensive acute target organ damage and where blood pressure must be lowered within one hour. They may occur as a result of an acute illness, such as post-infectious glomerulonephritis or acute renal failure, or as an exacerbation of stage 2 hypertension. They may present with acute, life threatening target organ damage, which may involve the central nervous system (severe headaches, cerebral oedema, encephalopathy, seizures), heart failure (pulmonary oedema) or kidneys (acute renal failure). These children require hospitalization for monitoring and supportive care. Blood pressure levels are usually 5-15 mm above the 99th percentile, and should be slowly reduced to safe levels. It is important to select an agent with a rapid and predictable onset of action and to monitor blood pressure carefully while it is
be reduced. Although intravenous administration of labetalol or sodium nitroprusside is often preferred so that the fall in blood pressure can be carefully titrated, oral nifedipine has also been used successfully. As rapid reduction of blood pressure might, compromise blood flow and result in ischemic complications in the brain, retina, spinal cord and kidneys, blood pressure reduction must be regulated in order to prevent end organ damage to these organs.\textsuperscript{28} The difference between the observed and desired (95th percentile) blood pressure is estimated and the aim is to have 25-30\% of the desired reduction occurring in the first 3-6 hours, another 25-30\% in the next 24 hours, and then to the desired level over the next 2 days. Because hypertensive encephalopathy is a possible complication of hypertensive emergencies, antihypertensive agents with minimal central nervous system side effects should be chosen to avoid confusion between symptoms of disease and adverse effects of the drug.

\textbf{Medications Currently Used}

Oral or sublingual nifedipine is widely used in asymptomatic children, but for rapid absorption the drug must first be removed from the capsule or the patient must bite through the capsule.\textsuperscript{7} Although the drug has often been placed in the sublingual space to achieve rapid absorption, gastrointestinal absorption is also sufficiently rapid to be effective in a hypertensive crisis. The onset of action of nifedipine (0.25 mg/kg, maximum 10 mg) administered orally is within 5-10 min, peaks at 30-60 min and lasts for 2-6 hr. However, the action of oral nifedipine is short-lived, and additional longer-acting medications are required.\textsuperscript{27} Its use in hypertensive hospitalized children was shown to be safe and efficacious with minimal side effects.\textsuperscript{29} Children may show reflex tachycardia, but serious complications are rare.\textsuperscript{27} The occurrence of arrhythmias, syncope, cerebrovascular accidents and myocardial infarction following sudden reduction of blood pressure in adults have very rarely been reported in children in whom it has been used safely and effectively for hypertensive emergencies.\textsuperscript{30} These risks are very rare if the dose is kept between 0.1-0.25 mg/kg.\textsuperscript{29}

Bolus doses of intravenous or intramuscular hydralazine can be given initially when an intravenous infusion of labetalol or sodium nitroprusside is not immediately available. The usual recommended parenteral dosage is 1.7-3.5 mg/kg daily, divided into four to six doses. The average maximal decrease in blood pressure usually occurs 10-80 minutes after intravenous administration. An advantage of hydralazine is that it can be administered intramuscularly, which can be useful in situations when there is an immediate need to lower blood pressure but the child does not yet have intravenous access established.

Intravenous sodium nitroprusside is the agent with the longest track record, readily available and the least expensive of all parenteral drugs. It can be used in most hospital settings having facilities for monitoring blood pressure. It has a rapid onset of action, 1-2 minutes, and a plasma half-life of less than 10 minutes. The infusion is started at a rate of 0.3-0.8 mg/kg per minute, then the rate may be increased in increments of 0.1-0.2 mg/kg per minute, every 15 minutes until the desired reduction in blood pressure has been achieved. Blood pressure should be monitored at least every 15 minutes, as well as pupillary reflexes, visual acuity and level of consciousness. It is recommended to have two intravenous lines placed, one for drug infusion and the other for saline infusion if the blood pressure falls suddenly. Loss of pupillary reflex to light is an early indicator of retinal vascular ischemia, requiring immediate infusion of normal saline. Patients receiving doses exceeding 2-3 mg/kg per minute for longer than 48 hr are at risk of cyanide toxicity, and even earlier in case of hepatic or renal dysfunction.

Intravenous labetalol blocks both $\alpha$- and $\beta$-adrenergic receptors. A single intravenous bolus dose of 0.2-1.0 mg/kg per dose (up to 40 mg/dose dose) is followed by continuous infusion of 0.25-3.0 mg/kg per hour to control a progressive reduction of the blood pressure. The hypotensive effect of a single dose of
intravenous labetalol appears within 2–5 minutes after administration, peaks at 5–15 minutes, and lasts up to 2–4 hours.

As volume depletion is common in children with severe hypertension, we must caution against the use of an intravenous administration of a loop diuretic together with a potent anti-hypertensive agent as this might lead to a dangerously rapid drop in blood pressure.

**Follow up**

Close monitoring of children with hypertension is required, particularly during the initial phase of therapy. After initiation of antihypertensive drug therapy, follow-up visits should be scheduled frequently (every 2–4 weeks) until blood pressure control has been achieved, and then less frequently (every 3–4 months) thereafter.

The frequency of visits is dictated by various factors, including degree of control, extent of understanding of the disease and its treatment by both the parents and/or caregivers and the child, adherence to non-pharmacologic and pharmacologic treatments, ability to properly monitor blood pressure at home, likelihood of drug adverse effects, need to monitor for complications of hypertension, need to monitor for weight loss.

Serum biochemistry should be checked after therapy with angiotensin converting enzyme inhibitors or an angiotensin II receptor blockers has been initiated or the dosage increased.

Home blood pressure monitoring and assessment for medication side-effects are important components of treatment and should be reviewed at each follow-up visit.

Patients and their families should receive counseling for cardiovascular risk factors and dyslipidaemia and continued emphasis should be placed on lifestyle modifications.

Screening for end organ damage and renal dysfunction (proteinuria, serum creatinine) and surveillance for side effects of drugs is required annually.

**Conclusion**

When and how to investigate a child with hypertension relies principally on the initial thorough clinical assessment. The therapeutic plan should rely on a sound pathophysiological approach to the likely underlying mechanism of hypertension. Lifestyle modifications should always be the cornerstone of the treatment and, when necessary, pharmacological therapy should be added in a stepwise fashion following a logical and evidence-based approach. A long-term follow up with clear objectives remains an integral part of the management of hypertension in children and adolescents.

**References**


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