The Assessment and Management of Hypertensive Emergencies and Urgencies in Children

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Abstract: Although the prevalence of hypertension in the pediatric population is estimated at only 1% to 2%, hypertensive urgencies and emergencies may be encountered in the emergency department. Efficient management of these children is of utmost importance to avoid some of the life-threatening complications associated with hypertension and its treatment. This article serves to review some of the important aspects of pediatric hypertensive emergencies, including diagnosis, emergency department investigations, and pharmacologic management.

Key Words: hypertension, hypertensive urgencies, hypertensive emergencies

TARGET AUDIENCE

This CME activity is intended for physicians, nurses, physician assistants, and nurse practicioners who care for children in an office, urgent care or emergency department setting. Emergency and critical care physicians caring for children will find the information contained in this article particularly useful.

LEARNING OBJECTIVES

After completion of this article, the reader will be able to:

1. Recall the key elements necessary for the diagnosis and investigation of hypertension.
2. Discuss the differential diagnosis of hypertension by age group.
3. Discuss the various pharmacologic treatment options for the management of hypertensive urgencies and emergencies.

The prevalence of hypertension in the pediatric population is estimated at 1% to 2% according to most studies. Although the overall prevalence has remained constant for the past decade, there has been a notable increase in the incidence of primary hypertension in children, likely due to the rising trend toward childhood obesity.[1]

The role of the emergency physician is to recognize potentially harmful blood pressures in children and ensure they are adequately treated, so as to avoid life-threatening complications. A hypertensive *emergency* is a severely elevated blood pressure with evidence of target organ injury. Most commonly, organ injury secondary to hypertension involves damage to the central nervous system, kidneys, or cardiovascular system. A hypertensive *urgency* is a severely elevated blood pressure with no current evidence of secondary organ damage, although if left untreated, target organ injury may result imminently.

DEFINING HYPERTENSION IN THE PEDIATRIC POPULATION

Significant variability exists over how hypertension is defined in the pediatric population. In its 1987 report, the Second Task Force on Blood Pressure Control in Children stated that by clinical experience and consensus alone, average systolic and/or diastolic blood pressures persistently above the 95th percentile should be considered hypertensive.[2] Severe hypertension was defined as blood pressures above the 99th percentile for age and sex. The 2004 report on high blood pressure in children and adolescents reiterates these definitions, but states that children with blood pressures greater than 5 mm Hg above the 99th percentile require prompt treatment.[3]

BLOOD PRESSURE MEASUREMENT

Accurate blood pressure measurement requires using adequate equipment and proper technique. Blood pressure

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Dr. Constantine and Dr. Linakis have disclosed that they have no significant relationships with or financial interests in any commercial companies that pertain to this educational activity.

Wolters Kluwer Health has identified and resolved all faculty conflicts of interest regarding this educational activity.

Drs. Constantine and Linakis have disclosed that labetalol, nicardipine, nifedipine, and enalaprilat have not been approved by the US Food and Drug Administration for use in the treatment of hypertension in children. Please consult product labeling for the approved usage of these drugs.

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ISSN: 0749-5161/05/2106-0391

measurements should be taken with the patient in a seated position, using the child's right arm placed at the level of the heart. The right arm should be used for ease of comparison to standardized tables. In the emergency department in particular, abnormally high blood pressures should be repeated after a few moments of quiet rest.

Blood pressure cuff size is critical in measuring blood pressure accurately, as a cuff that is too small will produce blood pressure measurements that are artificially high. Similarly, a cuff that is too large will produce measurements that are artificially low. If, however, the size of a child's arm falls between two cuff sizes, the larger of the two should be used. The width of the inflatable bladder should be at least 40% of the arm circumference at a point midway between the acromion process and the olecranon.[3] Using commercial blood pressure cuffs that are available, this will usually produce a bladder length that encircles 80% to 100% of the circumference of the arm.[4]

In the emergency department setting, use of an automated oscillometric device for measuring blood pressures is common. Although this is useful in young infants and in the noisy environment of the emergency department, care must be taken to ensure that the machine is calibrated for accuracy on a regular basis. It is recommended that abnormal blood pressures be verified by auscultation using a sphygmomanometer.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of hypertension in the pediatric population depends largely on the age of the child. Typically, the higher the blood pressure, the more likely it is that a secondary cause for the hypertension exists.

In the first year of life, renovascular disease, renal parenchymal disease (including congenital anomalies of the kidney), and coarctation of the aorta should be considered. In early childhood, renal parenchymal disease is among the more common causes of hypertension. Renovascular disease and coarctation of the aorta should also be considered in this age group. In school-aged children, essential hypertension becomes increasingly common, although less so than renal parenchymal and renovascular causes. Beyond 12 years, essential hypertension is the most common cause of hypertension, although this less frequently results in a hypertensive urgency or emergency compared with other causes. Endocrine causes of hypertension, such as pheochromocytoma and Cushing disease, should be considered in all age groups, although these remain uncommon causes of hypertension in the pediatric population. Elevated intracranial pressure, medications, and drugs of abuse such as cocaine and amphetamines may also result in moderate to severe hypertension. Table 1 outlines the common causes of hypertension by age group.[5,6]

CLINICAL ASSESSMENT

History

The history of the presenting complaint should focus on determining causes of hypertension and assessing whether target organ system damage has occurred. Prior history of hypertension and treatment of hypertension is particularly important, as abrupt withdrawal of some hypertensive medications may be detrimental to the patient.[7] Symptoms of visual changes, central nervous system disturbance, renal disease, and cardiovascular compromise should be elicited. Flushing, tachycardia, and weight changes may provide clues to an endocrine cause of hypertension. History of umbilical vessel catheterization, genitourinary abnormalities, or recent head injury is also important, as is the use of medications that may cause elevations in blood pressure, such as oral contraceptive pills and steroids. A social history detailing the use of any substances of abuse is often helpful. Finally, a family history of essential hypertension or endocrinopathies can provide useful clues to the etiology of the child's hypertension.

Physical Examination

Physical examination should begin with a full set of vital signs, including 4-limb blood pressures, respiratory rate, heart rate, and oxygen saturation. An accurate weight, and if possible, height, should be determined. Funduscopic examination, and a full neurologic examination including mental status evaluation, should be conducted, when possible, to assess for hypertensive encephalopathy. Evidence of an acute head injury is usually obvious, but the possibility of an occult head injury, as seen in child abuse, should be considered, particularly in younger children. Cardiovascular

TABLE 1. Common Causes of Hypertension in Children*

Age Group	Cause
Newborns	Renal vessel thrombosis
	Renal artery stenosis
	Congenital renal anomalies
	Coarctation of the aorta
Early childhood (Infancy to 6 years)	Renal parenchymal disease
	Renovascular disease
	Coarctation of the aorta
School age (6–10 years)	Renal parenchymal disease
	Renovascular disease
	Essential hypertension
Adolescence	Essential hypertension
	Renal parenchymal disease
	Renovascular disease

*Although significantly less common, endocrine causes of hypertension, such as pheochromocytoma and Cushing disease, should be considered in all age groups.

examination should focus on signs of ventricular hypertrophy or cardiac failure, including pulmonary edema, hepatomegaly, additional heart sounds on auscultation, tachycardia, or a displaced apical impulse. Femoral pulses should be evaluated to exclude coarctation of the aorta. Renal artery bruits, edema, or growth failure may point to an underlying renal cause for the hypertension.

Ancillary Investigations

Diagnostic testing for hypertensive urgencies and emergencies in the emergency department should be limited to the simplest of investigations, as the primary goal in the emergency department is to acutely lower the blood pressure. Initial investigations in the emergency department depend on findings from the history and physical examination.

Most children should have a chest x-ray and an electrocardiogram to evaluate for signs of cardiac involvement secondary to the hypertension. A CT of the head may be indicated if the patient has any abnormal neurologic findings. Urinalysis and serum BUN and creatinine determinations are helpful in determining baseline renal function. A complete blood count should also be performed to rule out evidence of a microangiopathic hemolytic anemia, as would be seen in hemolytic-uremic syndrome. Anemia may also be encountered in renal failure or glomerulonephritis.

More specialized testing, based on the results of initial investigations, may be indicated once the child's blood pressure is more controlled. This may include further radiologic investigations and hormonal studies.

MANAGEMENT

Usually, the patient with a persistent mild to moderate blood pressure elevation in the emergency department can be discharged with close follow up to institute outpatient evaluation and management. Management of severely elevated blood pressure, on the other hand, should focus on lowering the blood pressure in a safe and timely manner, and treating any secondary complications that the hypertension may have caused.

It is recommended that blood pressure be reduced by no more than 25% in the first 2 hours, then reduced gradually to normal over the next 3 to 4 days. This is because in long-standing hypertension, cerebral vascular autoregulatory mechanisms are frequently overwhelmed and can no longer compensate for rapid changes in pressure. Rapid lowering of blood pressure in such cases can result in serious neurologic sequelae.[8]

Medications used to treat hypertension should be chosen according to their side-effect profile, availability, and physician familiarity with the drug. The intravenous route for medication administration is preferred for most hypertensive emergencies, because it allows for easier titration and more predictable absorption.[9] As with many pharmacologic agents used in pediatrics, many of the drugs presented here have not been specifically studied in children; rather, their use has been extrapolated from the adult literature.

Sodium Nitroprusside

Sodium nitroprusside is an arterial and venous vasodilator that is among the more commonly used agents for the treatment of hypertensive urgencies and emergencies. It does not have significant inotropic or chronotropic effects on the heart.[10]

Sodium nitroprusside has an extremely short half-life and requires administration by continuous infusion. Although the short half-life causes a nearly immediate return of blood pressure to pretreatment levels upon discontinuation of the drip, it is a drug that can easily be titrated to effect owing to its rapid onset and termination of action. Dosing recommendations start at 0.3 to 0.5 μg/kg/min, to a maximum of 8 μg/kg/min. Most patients will respond to rates of approximately 3 μg/kg/min.[11]

Nitroprusside is metabolized by erythrocytes to cyanide, which is subsequently converted to thiocyanate in the liver and excreted by the kidneys. As a result, extreme caution should be exercised when using this drug in patients with impaired hepatic or renal function. Moreover, use of the drug for longer than 24 to 48 hours can lead to an accumulation of cyanide and thiocyanate in the blood, causing signs and symptoms of toxicity. Signs of cyanide toxicity include metabolic acidosis, tachycardia, altered level of consciousness, decreased reflexes, and methemoglobinemia. Thiocyanate toxicity may also cause an alteration in mental status, as well as nausea, seizures, anorexia, and coma. Because of these potential toxicities, cyanide and thiocyanate levels should be obtained when used in patients with hepatic or renal impairments, for infusions lasting more than 24 hours, or when used at doses higher than 3 μg/kg/min. Cyanide toxicity may be treated with amyl nitrite, sodium nitrate, and sodium thiosulfate. Sodium thiosulfate may also be used to prevent thiocyanate toxicity.[12,13]

Sodium nitroprusside has been shown in adults to cause an increase in intracranial pressure, although it is believed that the accompanying drop in blood pressure blocks the rise in cerebral blood flow. Consequently, nitroprusside is still recommended, in the adult literature, for use in patients with cerebrovascular accidents and hypertensive encephalopathy.[14,15] It should not be used in the pregnant patient due to adverse outcomes demonstrated in animal studies.[16] The drug should be protected from light to prevent its degradation.

Labetalol

Labetalol is both an α and β sympathetic blocker. Its mechanism of action is through reduction of peripheral

vascular resistance. Its plasma half-life is 3 to 5 hours, making it more difficult to titrate than sodium nitroprusside.[11]

Labetalol may be administered by continuous infusion or bolus dosing. Dosing recommendations vary considerably in the literature. For continuous infusions, recommendations range from 0.2 to 3 mg/kg/h. Labetalol may also be administered by intermittent boluses of 0.2 to 1 mg/kg, or by an initial bolus of 0.2 to 1 mg/kg followed by a continuous infusion of 0.25 to 1.5 mg/kg/h.[11]

As with many β-blockers, labetalol is contraindicated in patients with asthma and chronic lung disease as it may precipitate bronchospasm. It is also contraindicated in patients with congestive heart failure due to its negative inotropic and dromotropic effects. Labetalol may also mask signs and symptoms of hypoglycemia, and should be used with caution in children with diabetes.[10]

Nicardipine

Nicardipine is a dihydropyridine calcium channel blocker, the first of its class approved for intravenous administration. It works by blocking the movement of calcium across vascular smooth muscle cells, thereby preventing contraction and decreasing total vascular resistance. Unlike other calcium channel blockers, nicardipine has limited effects on chronotropic, inotropic, and dromotropic function of the heart.

Although nicardipine has been extensively studied in adults, experience in children is mostly limited to case reports. Most reports highlight use of the drug in cases where sodium nitroprusside or intravenous labetalol may be contraindicated, such as in hepatic or renal failure, and in patients with asthma or lung disease.[17,18]

The recommended starting dose of nicardipine is 0.5 to 1 μg/kg/min, to a maximum of 3 μg/kg/min. The rate of infusion should be increased every 15 to 30 minutes until the desired effect is achieved. Some authors recommend a starting dose of 5 μg/kg/min followed by 1 to 3 μg/kg/min once the desired mean arterial pressure is achieved. Its onset of action is within a few minutes, and half-life is 10 to 15 minutes.[19]

Adverse effects of nicardipine include increased intracranial pressure. As a result, caution should be exercised in children with space-occupying lesions. Other side effects include headache, nausea, and hypotension.[18]

Esmolol

Esmolol is a cardioselective β-adrenergic blocking agent. Some authors suggest it is of particular use in the management of hypertensive crises associated with the repair of congenital heart disease.[11] When given as in intravenous infusion, a loading dose of 100 to 500 μg/kg followed by a continuous infusion of 50 to 300 μg/kg/min should be administered. Side effects are similar to those of any other beta-blocking agents; these may include bronchospasm, bradycardia, and congestive heart failure.[3,7]

Hydralazine

Hydralazine is a potent arterial vasodilator that is used to reduce systemic blood pressure. Its onset of action is 5 to 30 minutes with a duration of action lasting 4 to 12 hours. Although it remains one of the oldest antihypertensive agents available, it has largely been replaced by faster acting, more effective drugs.[11]

The drug is administered by the intravenous route, usually every 4 to 6 hours. The recommended dose of hydralazine is 0.1 to 0.5 mg/kg/dose to a maximum dose of 20 mg. Adverse effects include flushing, tachycardia, hypotension, and lupus-like syndrome.[7,12]

Fenoldopam

Fenoldopam is a selective dopamine agonist causing vasodilation of the renal, coronary, cerebral, and splanchnic vasculature, thus resulting in a decrease in mean arterial pressure. The use of fenoldopam in pediatrics has increased in recent years. Case reports have demonstrated success with its use for controlled hypotension during spinal instrumentation, and in the intensive care setting when conventional therapy was unsuccessful.[20,21]

In adults, peak effects of fenoldopam have been observed in 5 to 15 minutes, with steady-state serum levels achieved in 30 to 60 minutes. Infusion rates of 0.1 to 2 μg/kg/min have been reported for use in children. Side effects include reflex tachycardia, increased intracranial pressure, and increased intraocular pressure. Although pediatric experience with fenoldopam is limited, it appears to be a reasonable alternative to other more conventional therapies.

Nifedipine

Much controversy has arisen in the literature over the use of nifedipine in the pediatric population.[22–24] In adults, reports of adverse cardiac and neurologic sequelae secondary to hypotension from the use of nifedipine have led to a moratorium on its use in the treatment of adult hypertension. This has led many to question its use in children. Similar sequelae related to hypotension have not been observed in children, however. Instead, case reports have been published detailing rebound hypertension causing adverse neurologic events associated with the use of short-acting nifedipine.[25]

Nevertheless, many nephrologists continue to use nifedipine for the treatment of moderate to severe hypertension. Blaszak et al[26] published a retrospective study of 117 children treated with nifedipine, determining that the drug is safe and effective provided the initial dose is no greater than 0.25 mg/kg. No clinically significant side effects were observed during the study.

Nifedipine can be administered sublingually or orally. For enhanced absorption, the liquid-filled capsule may be bitten and swallowed. Because the smallest dose available is a 10-mg capsule, the liquid within the capsule is often aspirated with a small needle for smaller dosing requirements.

Due to the unpredictable nature of the orally administered drug, it is recommended that use of nifedipine be limited to hypertensive urgencies alone. Intravenous medications are better suited to hypertensive emergencies.

Other Agents

Several other agents have been used in pediatrics to treat hypertension in more specific situations. Phentolamine has been used with success in the treatment of hypertensive crises secondary to pheochromocytoma or increased plasma catecholamines, as seen in cocaine and amphetamine overdose. Enalaprilat, the intravenous formulation of enalapril, has been used for hypertension associated with high renin states. Details of these drugs are outlined in Table 2.[11,12]

CONCLUSIONS

Although relatively uncommon in the emergency department, pediatric hypertensive urgencies and emergencies must be recognized and treated promptly. Treatment goals are to lower the blood pressure in a safe and effective manner, and to recognize and treat any secondary sequelae which may result from the hypertensive crisis. The medication chosen to accomplish adequate blood pressure reduction should depend on its side effect profile and physician familiarity with the drug. Although the underlying cause of hypertension is important in determining which medication

TABLE 2. Drugs Commonly Used for the Treatment of Hypertensive Emergencies in Children*

Drug	Dose	Onset of Action	Duration of Action	Mechanism of Action	Comments
Sodium nitroprusside	0.3–8.0 μg/kg/min IV infusion	Seconds	During infusion only	Vasodilation of arterioles and veins	May increase ICP. Risk of cyanide and thiocyanate toxicity
Labetalol	0.4–3.0 mg/kg/h IV infusion *or* 0.2–1 mg/kg initial bolus, then 0.25–1.5 mg/kg/h infusion *or* 0.2–1 mg/kg/dose maximum 20 mg	2–5 min	2–6 hr	β- and α_1-adrenergic blockade	Contraindicated in asthma, chronic lung disease, and heart failure. May mask symptoms of hypoglycemia
Nicardipine	0.5–3.0 μg/kg/min IV infusion	2–5 min	30 min–4 hr (duration of action increases with time of infusion)	Calcium channel blockade	May cause increased ICP
Esmolol	100–500 μg/kg loading dose then 50–300 μg/kg/min	Immediate	10–30 min	β-adrenergic blockade	May cause bronchospasm and congestive heart failure
Hydralazine	0.1–0.5 mg/kg/dose, maximum 20 mg/dose	5–30 min	4–12 hr	Direct arteriolar vasodilator	Less potent than other agents
Fenoldopam	0.1–2 μg/kg/min	5–40 min	60 min	Vasodilation of renal, coronary, cerebral, and splanchnic vasculature	Limited experience in children
Nifedipine	0.25–0.5 mg/kg/dose maximum 10 mg	5–15 min	6 hr	Calcium channel blocker—decreases peripheral vascular resistance	Difficult to administer exact dosages. Risk of hypotension and rebound hypertension
Enalaprilat	5–10 μg/kg/dose	Up to 60 min	4–6 hr	Calcium channel blocker	Particularly useful for high renin states
Phentolamine	0.1 mg/kg IV bolus, max 5 mg	Seconds	15–30 min	α-adrenergic blocker	Used primarily for hypertension secondary to excessive circulating plasma catecholamines

GI indicates gastrointestinal; ICP, intracranial pressure; ICU, intensive care unit; IV, intravenous; PO, orally.
*Because several of these medications have not been extensively tested in children, existing pharmacokinetic data are frequently based on studies in adults.

to use, often in the emergency department, the cause of the hypertension is unknown.

Once treatment is instituted in the emergency department, the patient should be admitted for close monitoring, often in the intensive care setting. Frequently, further diagnostic testing will be necessary at that time. Adjustment of treatment regimens and definitive treatment of the underlying cause can then take place.

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CME EXAM

Instructions for the *Pediatric Emergency Care* CME Program Examination

To earn CME credit, you must read the designated article and complete the examination below, answering at least 80% of the questions correctly. Mail a photocopy of the completed answer sheet to the Office of Continuing Education, Wolters Kluwer Health, 530 Walnut Street, 8th Floor East, Philadelphia, PA 19106. Only the first answer form will be considered for credit and must be received by Wolters Kluwer Health by August 15, 2005. Answer sheets will be graded and certificates will be mailed to each participant within six to eight weeks after WKH receipt. The answers for this examination will appear in the September 2005 issue of *Pediatric Emergency Care*.

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CME EXAMINATION
June 2005

Please mark your answers on the ANSWER SHEET.

The Assessment and Management of Hypertensive Emergencies and Urgencies in Children, *Constantine and Linakis*

1. A three-year old child presents to the emergency department with a blood pressure of 125/90. All of the following are possible explanations for her elevated blood pressure *except*:
   a) The child was crying at the time of blood pressure measurement.
   b) The cuff chosen for blood pressure measurement was too large.
   c) She has underlying kidney disease.
   d) She recently ingested her older brother's methylphenidate.
   e) The oscillometric device used for blood pressure measurement was poorly calibrated.
2. An 18 month-old child with no significant past medical history presents to the emergency department with a blood pressure of 180/95. Of the following, the *most likely* cause for her hypertension is:
   a) Coarctation of the aorta.
   b) Pheochromocytoma.
   c) Essential hypertension.
   d) Renal parenchymal disease.
   e) Renovascular disease.
3. A 12-year-old boy arrives in the emergency department for treatment of a laceration to his hand. His blood pressure upon arrival is 141/90, and repeat measurements after a period of rest are unchanged. Which of the following is an appropriate action:
   a) Refer the child to his pediatrician for outpatient workup and management of his hypertension.
   b) Administer an appropriate dose of sublingual nifedipine.
   c) Start an infusion of sodium nitroprusside.
   d) Consult nephrology.
   e) No further action is necessary.
4. Work-up of severe hypertension in the emergency department should routinely include all of the following *except*:
   a) A chest x-ray.
   b) An EKG.
   c) Serum BUN and creatinine.
   d) A urinalysis.
   e) Plasma catecholamines.
5. Regarding the pharmacologic management of hypertensive urgencies and emergencies, all of the following are true *except*:
   a) A higher risk of thiocyanate toxicity exists with the use of sodium nitroprusside in children with renal failure.
   b) Labetalol is contraindicated in children with a history of asthma.
   c) Nifedipine is no longer recommended for use in children because of its propensity to induce severe hypotension.
   d) Phentolamine is recommended for the treatment of hypertensive urgencies and emergencies related to pheochromocytoma.
   e) Nicardipine may increase intracranial pressure.

ANSWER SHEET FOR THE *PEDIATRIC EMERGENCY CARE* CME PROGRAM EXAM

June 2005

Please answer the questions on page 397 by filling in the appropriate circles on the answer sheet below. Please mark the one best answer and fill in the circle until the letter is no longer visible. To process your exam, you must also provide the following information:

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CME EXAM ANSWERS

Answers for the Pediatric Emergency Care CME Program Exam

Below you will find the answers to the examination covering the review article in the March 2005 issue. All participants whose examinations were postmarked by May 15, 2005 and who achieved a score of 80% or greater will receive a certificate from Wolters Kluwer Health.

EXAM ANSWERS

March 2005

1. TRUE
2. A
3. B
4. FALSE
5. E
6. C