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Ambulatory blood pressure monitoring in children and adolescents: recommendations and standard assessments

As a result of the incidence in obesity in pediatrics becoming a global epidemic, clinicians have seen a steady increase in hypertension in children and adolescents, putting this patient population at risk for end organ damage. In August 2008, the American Heart Association (AHA) released guidelines for recommendations of ambulatory blood pressure monitoring (ABPM) in children and adolescents. Ambulatory blood pressure monitoring is a method by which blood pressure is measured multiple times during a predefined period. This method has been shown to be more accurate and superior to clinic blood pressure monitoring (CBP) because it provides continuous blood pressure readings during daily activities. Additionally, it is beneficial in evaluating white coat hypertension, risk for target organ damage, and drug resistance or symptoms of low blood pressure in patients already receiving drug therapy.

In children ≥ 5 years of age, portable oscillometric monitors are provided and set to record blood pressure readings every 15 to 30 minutes during the day, for a 15-hour period, either from 6 am to 9 pm or 9 am to midnight. Evening and sleep recordings are taken every 20 to 60 minutes for a 9-hour period, either from 9 pm to 6 am or from midnight to 9 am. One valid reading per hour is necessary for appropriate interpretation of the results.

Blood pressure standards in children and adolescents are reported as percentiles based on gender, age, and height. The stages of hypertension and therapy recommendations are listed in table 1.

Table 1. Classification of hypertension in children and adolescents.

	Systolic or diastolic percentile	Therapeutic lifestyle changes	Pharmacologic therapy
Normal	<90th	Healthy diet, sleep, and physical activity	None
Pre-hypertension	90 th to <95 th or if blood pressure >120/80 even if <90 th percentile up to 95 th percentile	Weight management counseling; physical activity and diet management with aid of dietician	None unless compelling indications such as chronic kidney disease, diabetes mellitus, heart failure, or left ventricular heart failure present
Stage 1	95 th to 99 th percentile plus 5 mm Hg		May initiate therapy for presence of symptomatic hypertension, secondary hypertension, hypertensive organ damage, diabetes (type 1 and 2), persistent hypertension despite no pharmacologic measures
Stage 2	>99 th percentile plus 5 mm Hg		Initiate therapy; more than 1 agent may be required

The AHA guidelines provide the following key recommendations for standard assessment of ABPM in children:

- ABPM is useful to differentiate true hypertension from white coat syndrome, blood pressure variability, effectiveness

of blood pressure medications, or hypotensive symptoms in patients receiving pharmacologic therapy

- Suitable ABPM devices that have been validated should be used; appropriate cuff sizes are necessary to ensure valid results
- Standard approaches should be employed including: measurements should be performed by trained personnel; monitors should be applied to the non-dominant arm; devices should be programmed to record blood pressures every 20 to 30 minutes during the day and every 30 to 60 minutes during sleep
- The average of 3 CBP and 3 ABP measurements should be used to calibrate the device
- The results should be interpreted based on a minimum of 1 blood pressure reading per hour, 40 to 50 readings during a 24-hour period, or 65% to 75% of all possible blood pressure readings for a partial day report
- ABPM values should be edited for outliers
- Standard calculations should be used for mean daily blood pressure, blood pressure percentiles, and the percent difference between day and nighttime readings
- Evaluation of ABPM values should be compared with gender, age, and height specific data

Ambulatory blood pressure monitoring is an effective and accurate tool, and provides valuable data for measuring blood pressure in children and adolescents. As this technique becomes more accepted in clinical practice, it is probable that pediatric patients will be appropriately diagnosed with hypertension, thus minimizing the risks of end organ damage as they progress into adulthood.

Clinical practice guidelines for cholesterol screening in children

In July 2008, the American Academy of Pediatrics (AAP) published updated guidelines for lipid screening in pediatric patients. Previous guidelines, first published in 1992 then updated in 1998, focused on 2 primary methods for the management of high cholesterol in children: the population approach and the individualized approach. The population approach was aimed at all children 2 years of age and older, and provided nutrition recommendations to minimize the consumption of saturated fats and dietary cholesterol. The individualized approach recommended cholesterol screening for children with positive family history of premature cardiovascular disease (CVD) or those with a parent with a total cholesterol ≥ 240 mg/dL.

Based on levels of low-density lipoprotein (LDL) cholesterol, children's levels were categorized as acceptable (< 110 mg/dL), borderline (110 to 129 mg/dL), or high (≥ 130 mg/dL). Children classified as acceptable were recommended to

be given nutrition education and have a repeat cholesterol screen in 5 years. For those with borderline LDL levels, the Step-One diet was recommended. Children with high LDL were recommended to start the Step-One diet for at least 3 months, followed by the Step-Two diet if LDL did not decrease. The Step-Two diet is a stricter version of the Step-One diet and requires the assistance of a dietician. Drug therapy was recommended only in children older than 10 years of age with LDL cholesterol ≥ 190 mg/dL, or ≥ 160 mg/dL with a positive family history, after failing a 6 to 12 month trial of diet therapy. The only recommended agents were the bile acid sequestrants, cholestyramine and colestipol.

The 2008 update to the AAP guidelines recommends significant changes from the previous version and aggressive management of high cholesterol. The overall theme is the same, with a focus on diet and physical activity as the primary intervention. However the guidelines suggest a more restrictive diet and consideration of pharmacologic treatment at an earlier age and in a wider group of children. Similar to the previous guidelines, there is a focus on 2 strategies: the population approach and the individual approach.

Additional guidance regarding cholesterol screening in children and adolescents is provided by the new guidelines. While the same selective screening process is still recommended, which includes screening those with a positive family history of hyperlipidemia or premature CVD, the new guidelines also recommend screening patients with unknown family history and those with other CVD risk factors. They define these risk factors as diabetes, smoking, hypertension ($\geq 95^{\text{th}}$ percentile), and overweight or obese ($\geq 85^{\text{th}}$ percentile). Direction is also given as to when screening should occur. It is recommended that the first screening occur after 2 years of age, but before the age of 10 years in these high-risk patients. The same categories of acceptable, borderline, and elevated are used for classifying cholesterol levels, but the new guidelines also include total cholesterol levels (in addition to LDL) into the categories. Acceptable levels consist of total cholesterol < 170 mg/dL and LDL < 110 mg/dL. Borderline is considered total cholesterol 170 to 199 mg/dL and LDL 110 to 129 mg/dL. Elevated levels are total cholesterol > 200 mg/dL and LDL > 130 mg/dL.

The population approach focuses on diet and physical activity, as it did previously. Following release of the United States Department of Agriculture (USDA) dietary recommendations, a new diet is suggested. The AAP has endorsed the American Heart Association (AHA) diet for children and adolescents, which is based on the new USDA recommendations. The AHA diet varies by age and focuses on increased intake of fruits, vegetables, whole grains, and low-fat dairy products. As before, the population approach is recommended only in children older than 2 years of age, though it is noted that diet strategies have been shown to be safe in children under the age of 2 years as well.

The individual approach targets the high-risk children

and adolescents. The primary intervention for this group is a strict diet of <7% of total calories from saturated fats and dietary cholesterol <200 mg/day. The assistance of a dietician is highly advised, as is involvement of the entire family in the process. Additional non-pharmacologic recommendations include increased intake of soluble fiber, plant sterols and stanols, and increased physical activity.

Pharmacologic treatment is now suggested in children as young as 8 years of age, instead of at the age of 10 years as in the previous guidelines. Drug therapy is indicated for 3 categories of patients, based on LDL levels and risk factors. The first category is for those with serum LDL >190 mg/dL despite diet therapy and no other CVD risk factors. The second category includes those with LDL >160 mg/dL despite diet therapy with other risk factors, as noted previously. The final category is for children with diabetes mellitus; drug therapy is advised when LDL \geq 130 mg/dL. Several medications are recommended, including the bile acid-binding resins, 3-hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins), cholesterol-absorption inhibitors, and possibly fibrates.

Specific recommendations as to which agents are first-line therapies or when to use certain agents in particular situations are not given, though a few suggestions are proposed. The guidelines note that the adverse effects of the bile acid-binding resins may limit their use in children and result in low compliance. Due to adverse effects, niacin is not recommended for routine use. Statins, the most widely used cholesterol-lowering agents in adults, have now been studied in children and adolescents. One agent, pravastatin, has received approval by the Food and Drug Administration (FDA) for use in children 8 years of age and older. The cholesterol-absorption inhibitor, ezetimibe, is suggested as a potential first-line therapy due to its good tolerability; however, there are only limited studies of the drug in children. The fibrates are suggested for treatment of high triglycerides, though the lack of data for their use in children and their adverse effects profile warrants caution in this population.

The 2008 update to the AAP guidelines on lipid screening and cardiovascular health in childhood represents a more aggressive approach to the prevention of the development of atherosclerosis and CVD. As the leading cause of death in the United States, CVD is a significant public health issue. Early intervention and prevention of CVD presents a great opportunity to reduce the burden associated with the disease. Research has shown that early cholesterol-lowering intervention slows the process of atherosclerosis and leads to reduced risk of CVD, though the optimal age at which to start this prevention is not clear. In children and adolescents, the primary preventative measures consist of a focus on diet and physical activity. For high-risk children, cholesterol screening is recommended to target those who may benefit from intervention. If strict dietary modifications are unable to control cholesterol levels, pharmacologic therapy should be considered in children aged 8 years and older. The choice of drug therapy will depend on patient characteristics and adverse effects, but several medication

classes are now available for use in children. The AAP guidelines represent a significant change to current practice and reinforce the importance of early intervention in all children to improve long-term cardiovascular health.

Clinical practice guidelines for the long-term management of the child with simple febrile seizures

In June 2008, the American Academy of Pediatrics (AAP) updated the 1999 practice guidelines for the management of simple febrile seizures. The guidelines weigh the risks and benefits of continuous and intermittent anticonvulsant therapy and the use of antipyretics in children who are otherwise neurologically normal and experience simple febrile seizures. These guidelines were produced to help physicians make individualized treatment decisions. The major change is the inclusion of evidence for the use of primidone as continuous treatment to prevent recurrent seizures.

The purpose of the practice guidelines is 4-fold: 1) to give practitioner's a better understanding of the scientific basis for treatments of simple febrile seizures; 2) to discourage treatments which have a high risk of side effects and little benefit; 3) to lower costs by avoiding ineffective therapies; 4) to help educate caregivers that simple febrile seizures have low risks for recurrence. The guidelines provide a rationale for the possible therapies that can be considered for these patients. Recently published evidence for proposed treatments of simple febrile seizures was systematically graded according to quality and strength in order to draw conclusions about the treatments. The AAP Subcommittee on Febrile Seizures, with the help of the University of Kentucky, reviewed 65 evidence-based articles published since 1998 that evaluated the long-term use of intermittent and continuous anticonvulsant therapy to prevent recurrent simple febrile seizures.

Phenobarbital, primidone, valproic acid, carbamazepine and phenytoin have been investigated for their use as long-term continuous anticonvulsant therapy to prevent recurrent simple febrile seizures. Phenobarbital is effective in preventing recurrence if given daily and maintained in therapeutic range, but noncompliance tends to be high because of adverse effects such as lethargy and behavioral effects. Primidone can reduce recurrence in doses 15 to 20 mg/kg/day, but adverse effects include behavioral disturbance, irritability and sleep disturbance. Valproic acid is as effective as phenobarbital, but carries the rare risk of fatal hepatotoxicity in children less than 2 years of age (although no reports yet in cases of febrile seizures), thrombocytopenia, weight loss/gain, gastrointestinal disturbances, and pancreatitis. Carbamazepine and phenytoin are not effective for preventing recurrent febrile seizures.

When evaluating the evidence for the use of intermittent anticonvulsant therapy to prevent recurrent febrile seizures, the committee noted that when given at the

onset of fever, diazepam can reduce the risk of recurrent seizures. Treatment failures occurred in children who were non-compliant. However, a febrile seizure could occur before the fever is noticed which makes this approach questionable. Diazepam has the following side effects: lethargy, drowsiness, ataxia, and may mask infections of the central nervous system. A simple febrile seizure that lasts less than 5 minutes may be treated and interrupted with rectal diazepam and with intranasal or buccal midazolam. The committee also evaluated the use of intermittent antipyretics for the prevention of recurrent seizures and found that there is no evidence to support their efficacy in reducing the risk of recurrence without concurrent use of anticonvulsants. Antipyretics have no effect on outcome except to improve the comfort level of the patient.

The 2008 AAP guidelines were based on evidence that consisted of randomized, controlled trials, and diagnostic studies with minor limitations. The benefit of long-term continuous and intermittent anticonvulsant therapy is to prevent recurrent febrile seizures. The harm of long-term continuous and intermittent anticonvulsant therapy is serious adverse events from treatment such as thrombocytopenia, rare hepatotoxicity, gastrointestinal disturbances, and lethargy. Therefore, the AAP committee concludes that the benefits of these treatments do not outweigh the risks; therefore, neither continuous nor intermittent anticonvulsant long-term therapy is recommended for children with 1 or more simple febrile seizures.

P&T Committee Formulary Action

Additions

Pravastatin
Atorvastatin 80mg tablet

Deletions

Edetate disodium
Ezetimibe
Ezetimibe/simvastatin

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