

Hypertension in Adolescent

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Abstract

Hypertension in adolescents is, as in other patients, one of the important cardiovascular risk factors, associated with hypertension in adults and with appearance of cardiovascular complications later in life. In recent years it is in increase, in parallel with occurrence of overweight in this age group. There is mostly essential or obesity-related hypertension. It is often asymptomatic, therefore it holds true also for adolescents, that it has to be actively searched, especially in risk groups such as overweight adolescents, adolescents with positive family history or some of the other classical cardiovascular risk factors. If we have normal-weight adolescent with important hypertension or symptomatic adolescent without positive family history, the possibility of secondary hypertension has to be thinking of and extended, on possible cause focused and stepwise diagnostics performed. In this case, the treatment is etiological. Otherwise, the first-line treatment in adolescents comprises nonpharmacological treatment measures. Sometimes, because of poor nonpharmacological treatment compliance and presence of hypertensive-target organ damage, antihypertensive medications have to be introduced. However, preventive actions represent the most important task, in the form of primary and primordial prevention. In this article, diagnostic approach, prevention and treatment strategies in adolescents are shortly presented.

Keywords

Hypertension, Diagnostic Approach, Prevention, Treatment, Adolescent

1. Introduction

Hypertension is one of the most common chronic diseases in children, especially in adolescents [1]. In recent years, it has been increased, mainly due to a rise of obesity, having a significant impact on the level of blood pressure [BP] [2]. Thus, in one study of schoolchildren overweight has been observed in 27.9%, increased BP in 18.4%, and persistently elevated BP in 2.8% of included patients [3]. In American adolescents prehypertension or hypertension were observed in 14%, which is an important part of adolescents at risk [1]. In adolescents with the single measurement of BP in pre-hypertensive range, after two years hypertension was confirmed in 14% of

boys and 12% of girls [4]. It has been assessed that the rate of progression from prehypertension to hypertension in adolescents is 7% annually [4]. In our population of adolescents with essential hypertension, we also found a link with overweight, as 42% of the subjects were overweight and 23% obese, respectively [5]. Many other studies have clearly demonstrated that hypertension also occurs in children, especially in obese, and that it is not rare [6]. Moreover, there is increasing evidence that it is associated with the development of hypertension and the occurrence of cardiovascular complications in adulthood, although we still do not have prospective study that would directly demonstrate the connection between hypertension in childhood and cardiovascular events later in life [7]-[10].

In pediatrics, American recommendations for management of children and adolescents with hypertension have been published in 2004 and European ones in 2009, both needing the revision [11] [12]. They cover both the normative values as well as algorithms for diagnosis and treatment. A few years ago, our recommendations for the diagnostic approach to the child with hypertension have also been published [13]. We must be aware that adolescents with cardiovascular risk, which include adolescents with elevated BP, have to be actively searched, since they are generally asymptomatic. These also often apply to young people who have a significant increase in BP values and most likely secondary hypertension [11]-[13]. At the same time, we have to take the principles of BP measurement into account using the appropriate devices and cuffs, normative values according to gender, age and height of the adolescent, reproducibility of measurements and evidence of sustained hypertension. These has to be followed by the decision about focused etiological diagnostics, and afterwards the determination of traditional cardiovascular risk factors, co-morbidity status, hypertensive target organ damage and total cardiovascular risk score have to be performed in all young hypertensive patients [12] [13]. Based on all these findings the decision about the proper therapy has to be made, which is primarily non-pharmacological. When cardiovascular risk is determined even in adolescents the medications are introduced, mostly angiotensin-converting enzyme (ACE) inhibitors and calcium channel antagonists [14]. At least, as important as treatment, our work in the field of prevention of cardiovascular diseases should start in childhood [15] [16].

2. Definition of Hypertension in Adolescent

The most important step in the search for adolescents with hypertension is correct measurement of BP [11] [12]. BP devices must be technically approved and the measurements made by protocol [12]. The cuff size has to be adapted to growth and development of adolescents and obesity if present. Therefore, even in individuals of the same age it may be different and should cover two-thirds of upper arm [11]. If measurement using the oscillometric method of BP measurement is performed it must be confirmed with auscultatory one, with calibrated devices [12] [17]. Another problem is the mercury device which is practically no longer produced in Europe, which necessitates the use of oscillometric devices. One important objective is to develop new exact BP devices and devices appropriate normative values [12]. Most reference values for children and adolescents, gained on large samples of included subjects, were carried out using the auscultatory method, and with the increasing use of oscillometric devices the reference values for them are needed. Some of the latter have already been published [18] [19].

Furthermore, it is important to use the reference values according to gender, age and height of the child and adolescent, the definition of hypertension in children and adolescents (**Table 1**) and to confirm persistently elevated BP [11] [12]. Diagnostic criteria for adolescents, as well as for children, are based on percentile curves, obtained by measuring BP of healthy population and define the increased BP as a systolic and/or diastolic BP above the 95th percentile for gender, age and height, measured at least at three different occasions [11]. Because we treat adolescents, it is also necessary to know the definition of hypertension for the adult population. According to the latest recommendations the high-normal BP for adults is in the range of 130 - 139 and/or 85/89 mmHg, and hypertension, which has 3 stages, above the value of 140/90 mmHg. Recommendations also use optimal BP, which is below 120/80 mmHg [20]. The recommendations for children and adolescents also define high normal BP, which is more than 120/80 mmHg, and hypertension with 2 stages (**Table 1**) [12]. In this light it is interesting to look at the results of one of the studies investigating the incidence of hypertension in 18-year old adolescents using adult criteria versus pediatric percentile curves. It was found that in the first case, the hypertension was 9%, and in the second one, 14.7% [21]. **Table 1** shows the frequency of follow-up of adolescents at each hypertension stage [11] [12]. In recent years, 24-hour ambulatory BP measurement has also been increasingly used with reference values for this form of measurement [22] [23]. This is especially useful in

Table 1. Definition of elevated blood pressure (BP) in children and adolescents and recommendation for follow-up measurements and diagnostic approach [11] [12].

BP, hypertension	Percentiles of systolic and/or diastolic BP	Follow-up measurements of BP and diagnostic approach
Normal BP	<90 th percentile	During routine systematic and other pediatric examinations
High-normal BP	≥90 th to <95 th percentile ≥120/80, in adolescents, even if the value of BP is below 90 th percentile	After 6 months
Stage 1 hypertension	Between 95 th and 99 th percentile plus 5 mmHg	After 1 to 2 weeks or before, if the patient is symptomatic; if the BP is persistently elevated, diagnostics has to be performed in 1 month
Stage 2 hypertension	>99 th percentile plus 5 mmHg	Diagnostics and treatment in 1 week or immediately, if the patient is symptomatic

determining white coat hypertension and masked hypertension, to monitor the effectiveness of pharmacological treatment and BP variability as well as in research purposes [22]. There is evidence that it better predicts cardiovascular events and the risk of target organ damage as the standard methods of measurement [24] [25].

3. Diagnostic Evaluation of Hypertension in Adolescent

Since the recommendations for BP measurements from the third year of age as a part of the routine preventive management of all children, it is possible to actively search for children at risk and thus adolescents, which are often, with significant hypertension, completely asymptomatic [11] [12]. When in adolescent persistently elevated BP is confirmed, he is classified, according to the clinical features, into one of two groups of patients. Most young people belong to the group of patients with mildly elevated BP, who are mostly asymptomatic, without changes in hypertensive target organs and the possible cardiovascular complications later in life [13]. These are adolescents with essential hypertension or obesity-related hypertension. Sometimes, even in this group a clinical suspicion of one of the secondary forms of hypertension is made, especially if we are dealing with a normally nourished, symptomatic adolescent with significant hypertension and a negative family history of cardiovascular diseases. The most common causes of elevated BP in adolescent patients are essential hypertension, and obesity-related hypertension, but iatrogenic causes, consumption of certain food supplements and drugs, renal parenchymal disease, renal vascular disease, endocrine causes and coarctation of the aorta can be diagnosed as well [11]-[13]. Most of them should be suspected with accurate history and good clinical examination [26]. Diagnostics must be stepwise [26]. Most adolescents need only investigations of Step 1, which are performed in all patients (routine tests) (Figure 1) [12]. They are needed for hypertensive target organ damage and traditional cardiovascular risk factors determination. Consideration should be given to concomitant diseases and the cardiovascular risk evaluation [12] [13]. Hypertensive target organ damage status is one of the important parts of the diagnostics, as it gives us insight into the initial effects of hypertension in adolescents, but also serves as an intermediate objective of successful treatment monitoring [12] [27]. Investigations of recent years show that the initial damage of target organs is present more often than it has been thought, even in adolescents with mildly elevated BP, and is, at least in the early stages, reversible [28] [29]. In recent years intensive research has been performed investigating the importance of the earliest indicators of target organ damage, which includes measurement of intima media thickness of the carotid artery, pulse wave velocity measurement of vessels, microalbuminuria [29]-[31]. Further research is needed in the field of early indicators of damage of target organs and early markers of cardiovascular risks, especially in the area of potential genetic factors [32].

4. Prevention of Hypertension in Adolescent

Without a doubt, the most important part of management of adolescents in terms of cardiovascular health is prevention. The measures of primary prevention are used to prevent the occurrence of cardiovascular disease through the reduction of known cardiovascular risk factors. Secondary prevention includes measures for the

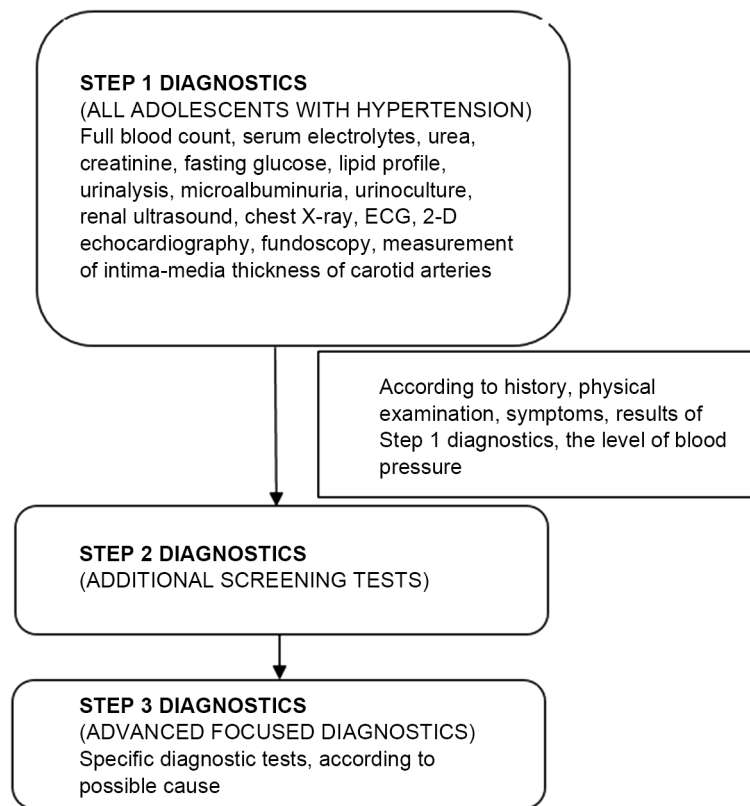


Figure 1. Diagnostics of adolescents with elevated blood pressure [12] [13].

early detection and treatment of preclinical changes and with that appropriately control the progression of the disease [15] [16]. In addition to primary and secondary prevention in recent times the importance of so-called primordial prevention has been increasingly recognized as a new important mechanism for improving cardiovascular health. The term refers to the way of maintaining normal levels of known cardiovascular risk factors, including the BP, from childhood to adulthood [15]. It is derived from the principles of a healthy lifestyle, which does not allow the occurrence of cardiovascular risk factors and as such represents the best way to lower cardiovascular risk [16]. Few recent research studies have shown that individuals who maintain an ideal profile of cardiovascular risk factors from youth to middle age, have significantly reduced risk of all cardiovascular events and a better quality of life in later life [33]. In addition to focus on maintaining good health, it is necessary to search for individuals with increased cardiovascular risks, which have, due to inappropriate lifestyle, genetic predisposition or diseases, a greater likelihood of early cardiovascular aging [34]. These clearly include adolescents with hypertension, especially adipose ones. After identification of adolescents at risk there is urgent need to initiate appropriate treatment and to follow-up them regularly. Better detection of young hypertensive patients is undoubtedly enabled by regular measurements of BP from the third year onwards, as well as by search for potential patients through regular visits to personal pediatricians, including adipose adolescents and those with a positive family history of cardiovascular disease [34]. It has to be stressed that cardiovascular prevention and active search for adolescents at risk are not only the task of health workers, but of the entire state and civil society [35]. Healthy lifestyle and self-care are the duties of each individual, but we must encourage them at all levels, in families, schools, local communities, relevant ministries, with the support of the public media [35]. Moreover, there is a need for a global approach to the problem of cardiovascular health with long-term goal to limit the cardiovascular disease epidemic [36]. Recently recommendations on the preservation of cardiovascular health by age and developmental pediatric groups have also been published [37].

5. Treatment of Hypertension in Adolescent

The main goal of the treatment of hypertension in adolescence is to reduce the cardiovascular risk associated

with persistently elevated BP [38]. Rarely, emergency treatment is required due to very high values of BP and symptomatology. In this case, the use of short-acting intravenous antihypertensive agents is needed, with careful monitoring of the cardiovascular system, preferably in an intensive care unit [39] [40]. The basis of treatment represent non-pharmacological treatment measures, introduced in all patients, including those who require pharmacological treatment. Lifestyle change and a healthy lifestyle promotion with a healthy diet, improved quality of sleep, regular physical activity and limited sedentary activities represent the first line therapy [41] [42]. Dietary changes include a reduction in fat and cholesterol, especially saturated fat, reduction of the intake of soft drinks and fast food, increased intake of fresh fruits, vegetables and whole grains, quantitative restrictions of meals and drinks, limitation of discharging meals. Thus, randomized study DASH (Dietary Approaches to Stop Hypertension) in a group of adolescents with hypertension has shown, that the increase in fruit and vegetable intake and limitation of the fat intake was associated with a clear BP reduction [43]. The best results were achieved by a combination of modified diet and regular physical activity. It has also been shown that a moderate reduction in salt intake lowers the level of BP [44]. Further significant reduction of BP has been achieved by physical activity [45] [46]. At least 60 minutes of moderate to intensive physical activity daily are recommended as well as limitation of sedentary activities to less than two hours per day [37] [42].

In adolescents, the basis of treatment as a rule is non-pharmacological treatment. Indications for the introduction of drugs are symptomatic hypertension, presence of hypertensive target organ damage, secondary hypertension, hypertension of stage 2, presence of diabetes, persistent hypertension despite non-pharmacological measures [12]. Treatment algorithm is shown in **Figure 2** [12]. At this point it should be noted that long-term consequences of untreated hypertension in otherwise healthy and asymptomatic adolescents are not known [47]. It is also not clear if there are some long-term effects of antihypertensive drugs on growth and development [11]. On the other hand, it has been proven that with the effective treatment hypertensive end-organ damage is reversible [48]. In recent years, quite a lot clinical research was performed also in children and adolescents on the efficacy and safety of antihypertensive drugs, as well as comparisons between different groups of antihypertensive medications [49]-[53]. Anyway, we still have the problem of the indications for use in small children [54] [55]. Drug classes with individual representatives, initial doses and maximum doses, are shown in **Table 2** [12] [38] [56]. Among them, the most commonly used medications are those in the first five groups, in particular ACE inhibitors and calcium channel antagonists [14]. Dosage for adults should not be overcome [38] [56]. In some clinical situations, depending on the pathophysiological mechanism, a certain class of antihypertensive agent is preferably recommended (**Table 3**) [12]. The target value of BP also depends on the clinical condition (**Table 4**), although additional studies to confirm these values are needed [12]. Sometimes for BP regulation in adolescents more antihypertensive drugs are needed, while we prefer a combination with complementary mechanisms of action. In our hypertensive adolescents more drugs have been introduced in 15.8% of all patients, treated pharmacologically. The drugs were introduced in one third of investigated patients [57]. In overweight adolescents with

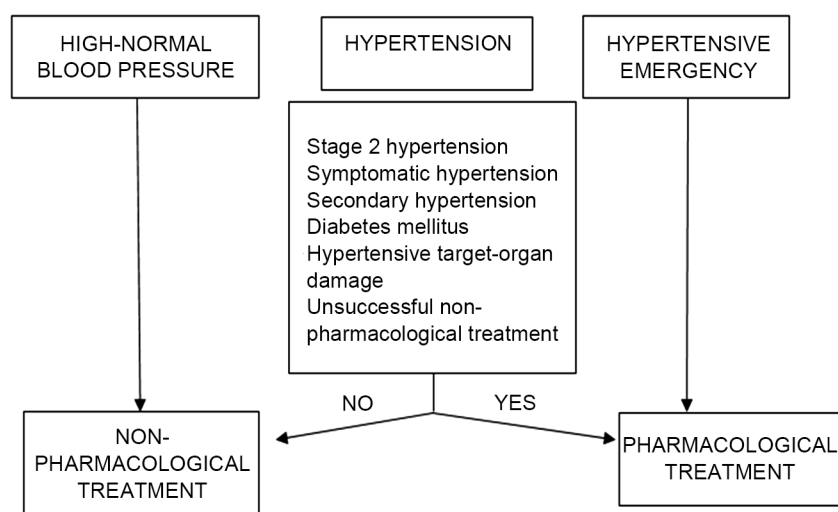


Figure 2. Treatment of child and adolescent with elevated blood pressure (adapted according to ref. [12]).

Table 2. Classes and representatives of antihypertensive medications and doses for children and adolescents, according to weight, with maximum doses (adapted according to ref. [12] [38] and [56]).

Class	Medication	Dose	Interval	Maximum dose
Diuretics	Amiloride	0.4 - 0.6 mg/kg/day	q.d.	20 mg/day
	Chlorthalidone	0.3 mg/kg/day	q.d.	50 mg/day
	Furosemide	0.5 - 2.0 mg/kg/dose	q.d.-b.d.	6 mg/kg/day
	Hydrochloro-thiazide	0.5 - 1.0 mg/kg/day	q.d.-b.d.	50 mg/day
Beta-adrenergic blockers	Chlorothiazide	10 mg/kg/day	b.d.	1 g/day
	Atenolol	0.5 - 1.0 mg/kg/day	q.d.-b.d.	100 mg/day
	Metoprolol	0.5 - 1.0 mg/kg/day	q.d.	200 mg/day
	Propranolol	1.0 mg/kg/day	b.d.-t.d.	320 mg/day
Calcium channel antagonists	Bisoprolol	0.2 mg/kg/day	q.d.	10 mg/day
	Amlodipine	0.06 - 0.3 mg/kg/day	q.d.	10 mg/day
	Felodipine	2.5 mg/day	q.d.	10 mg/day
Angiotensin-converting enzyme inhibitors	Nifedipine (ER)	0.25 - 0.50 mg/kg/day	q.d.-b.d.	120 mg/day
	Captopril	0.3 - 0.5 mg/kg/day	b.d.-t.d.	450 mg/day
	Enalapril	0.08 - 0.60 mg/kg/day	q.d.	40 mg/day
	Fosinopril	0.1 - 0.6 mg/kg/day	q.d.	40 mg/day
	Lisinopril	0.08 - 0.60 mg/kg/day	q.d.	40 mg/day
Angiotensin-receptor blockers	Ramipril	2.5 mg/day	q.d.	20 mg/day
	Candesartan	0.16 - 0.50 mg/kg/day	q.d.	32 mg/day
	Irbesartan	75 - 150 mg/day	q.d.	300 mg/day
	Losartan	0.75 - 1.44 mg/kg/day	q.d.	100 mg/day
Alpha- and beta-adrenergic blockers	Valsartan	2 mg/kg/day	q.d.	320 mg/day
	Labetalol	2 - 3 mg/kg/day	b.d.	1.2 g/day
Aldosterone-receptor blockers	Carvedilol	0.1 mg/kg/dose	b.d.	50 mg/day
	Eplerenone	25 - 50 mg/day	q.d.-b.d.	100 mg/day
Central alpha-agonists	Spironolactone	1 mg/kg/day	q.d.-b.d.	100 mg/day
	Clonidine	5 - 10 µg/kg/day	b.d.-t.d.	0.9 mg/day
Peripheral alpha-adrenergic blockers	Methyldopa	5 mg/kg/day	b.d.-f.d.	3 g/day
	Doxazosin	1 mg/day	f.d.	4 mg/day
	Prazosin	0.05 - 0.1 mg/kg/day	t.d.	0.5 mg/kg/day
Vasodilators	Terazosin	1 mg/day	q.d.	20 mg/day
	Hydralazine	0.25 mg/kg/dose	t.d.-f.d.	200 mg/day
	Minoxidil	0.1 - 0.2 mg/kg/day	b.d.-t.d.	50 mg/day

q.d.—once daily, b.d.—twice daily, t.d.—three times daily, f.d.—four times daily, ER—extended release.

Table 3. First choice of antihypertensive medication in adolescent with specific disease and hypertension [12].

Clinical condition	First choice of antihypertensive medication
Without any other disease	Drug from any class
Chronic kidney disease	ACEI/ARB
Migraine	Beta blockers, calcium channel antagonists
Obesity	ACEI
Coarctation of aorta	Beta blockers
Diabetes mellitus	ACEI/ARB
Chronic kidney failure	Diuretics
Hyperaldosteronism	Diuretics
Congestive heart failure	Beta blockers, ACEI/ARB, loop-acting diuretics
Kidney transplantation	Calcium channel antagonists

ACEI—angiotensin-converting enzyme inhibitors, ARB—angiotensin-receptor blockers.

Table 4. Blood pressure targets in different groups of patients [12].

Patients	Blood pressure target
Uncomplicated essential hypertension	<95 th percentile for sex, age and height
Secondary hypertension, diabetes mellitus, hypertensive target-organ damage	<90 th percentile for sex, age and height
Chronic kidney disease without proteinuria	<75 th percentile for sex, age and height
Chronic kidney disease with proteinuria	<50 th percentile for sex, age and height

successful non-pharmacological treatment withdrawal of medications is possible (“step-down” treatment). At that time the reversibility of changes in hypertensive target organ damage has to be taken into account [12]. Furthermore, it has been found out that improved therapies in children have potential for preventing or ameliorating early cardiovascular disease [58].

At the end, the problem of poor treatment compliance of some young people has to be mentioned, especially for non-pharmacological treatments. Even medications are often omitted [59] [60]. Therefore, in adolescents follow-up is of utmost importance, with continuous education, interpretation of the nature of the disease, its long-term consequences, the necessity of treatment [61]. They need to be motivated for treatment, continuously educated and promoted for a healthy lifestyle. It is important to work with the entire family.

6. Conclusion

Hypertension, one of the major cardiovascular risk factors, often also occurs in adolescents. With the introduction of routine measurement of BP of healthy children in pediatric healthcare and the active search for high-risk groups, patients with asymptomatic disease can be detected and appropriately diagnosed and treated, which has a long-term positive effects on cardiovascular health. The preventive action is equally important, in particular with the ever-increasing occurrence of obesity and related diseases. Treatment of adolescents is primarily non-pharmacological, but sometimes also requires the introduction of drugs.

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