

Persistent Hypertension in Thai Children: Etiologies and Outcome

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A retrospective study was done in 66 children (0.21% of all admitted children) below the age of 18 years with persistent hypertension diagnosed at the Department of Pediatrics, Faculty of Medicine Siriraj Hospital from Jan 1999 to Dec 2003. Male to female ratio was 1.4:1 with 54.5% aged between 6-12 years old and 9.1% aged less than 1 year.

Hypertension was found to be severe (BP more than the 99th percentile for age, sex and height) in 79.1% but most (78.6%) of the patients did not have symptoms related to hypertension. Chronic headaches were found in 10%, hypertensive encephalopathy in 8.6%, epistaxis in 1.4% and visual disturbance in 1.4%. The most common cause of hypertension was renal parenchymal diseases (62.7%) mainly lupus nephritis (26.9%), idiopathic nephrotic syndrome (16.4%) and chronic renal failure (16.4%). Other causes of hypertension included renovascular diseases (7.5%), drug-induced (7.5%), essential (7.5%), tumors (4.5%), coarctation of aorta (3.0%), bronchopulmonary dysplasia (3.0%), and pheochromocytoma (1.5%). Obesity and overweight (body mass index, BMI more than 25) was found in only 10 patients (15.1%). The proportion of children with BMI more than 25 was not different between essential and secondary hypertension ($p = 0.15$). Left ventricular hypertrophy was noted in 7.5%, hypertensive retinopathy in 3.0%, and hypertensive encephalopathy in 9.0%. One-third of the patients had normal BP within 1 month and another 47.0% had normal BP within 6 months of diagnosis. One-fifth of the patients also needed surgical intervention for specific underlying diseases.

The authors suggest that since a large number of children with hypertension have secondary hypertension, intensive investigation and prompt management should be done in all. Obesity and overweight is not reliable in the differentiation between primary and secondary hypertension. Short term outcome of hypertension is good with medications and surgery in selected cases but long term outcome is still unknown.

Keywords: Childhood hypertension, Renal disease, Obesity, Left ventricular hypertrophy

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Hypertension during childhood is not rare. Often under diagnosed, an estimated prevalence is 1%-2% compared to 25%-35% in adults. Hypertension may be a sign of underlying disease (secondary hypertension) or an early onset of essential hypertension. Most adult hypertension is essential hypertension but secondary hypertension is more prevalent in children. The underlying causes are renal parenchymal (60-70%),

renovascular (5-25%), cardiovascular and endocrine diseases⁽¹⁾. At present, there are not much data on hypertension in Thai children. The present study showed etiologies of childhood hypertension and outcome of treatment in a tertiary care hospital.

Material and Method

Medical records of all children less than 18 years old diagnosed as persistent hypertension at the Department of Pediatrics, Faculty of Medicine, Siriraj Hospital from Jan 1999 to Dec 2003 were reviewed. Persistent hypertension was defined as BP measurements persistently higher than the 95th percentile for age, sex,

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and height more than 3 months. Demographic data on age, sex, weight, height, sign and symptoms at diagnosis were recorded. Underlying diseases, complications and the time when BP returned to normal were also recorded. Statistical analysis was done using Fisher's exact test and p value less than 0.5 was considered significant.

Results

From Jan 1999 to Dec 2003, 66 children (0.21% of all admitted children at the same period) were diagnosed as having persistent hypertension. Male to female ratio was 1.4:1 with peak age (54.5%) between 6-12 years old and 9.1% aged less than 1 year.

Hypertension was found to be severe (BP more than the 99th percentile for age, sex and height) in 79.1% but most (78.6%) of the patients did not have symptoms related to hypertension at presentation. Chronic headaches were found in 10%, hypertensive encephalopathy in 8.6%, epistaxis 1.4% and visual disturbance in 1.4%. Most common causes of hypertension were renal parenchymal diseases (62.7%) mainly lupus nephritis (26.9%), idiopathic nephrotic syndrome (16.4%) and chronic renal failure (16.4%). Other causes of hypertension included renovascular diseases (7.5%), drug-induced (7.5%), essential (7.5%), tumors (4.5%), coarctation of aorta (3.0%), bronchopulmonary dysplasia (3.0%), and pheochromocytoma (1.5%). All patients with essential hypertension notably had severe hypertension. One patient was diagnosed as hypertension due to left renal artery stenosis at the age of 9 years. He received balloon dilatation via femoral catheterization and his BP returned to normal for 4 years. He developed hypertension with abdominal pain again at the age of 13 and CT scan revealed enlarged adrenal gland with increased urine catecholamine. Tumor removal was performed and pathological result confirmed pheochromocytoma. His hypertension resolved shortly after operation. Causes of hypertension (67 episodes in 66 patients) according to age are shown in Table 1.

Obesity and overweight (Body mass index more than 25) were found in 10 patients (15.1%) and not different between essential and secondary hypertension ($p = 0.15$). Left ventricular hypertrophy was noted in 7.5%, hypertensive retinopathy in 3.0%, and hypertensive encephalopathy in 9.0%.

Medications used for hypertension varied according to attending physicians. One-fifth of the patients also needed surgical intervention for specific underlying diseases such as coarctation of aorta, pheochromocytoma, neuroblastoma and renal artery steno-

sis. Renal transplantation was performed successfully in six patients with chronic renal failure. Neither mortality nor neurological sequelae due to disease and/or treatment were noted. One-third of the patients had normal BP within 1 month and another 47.0% had normal BP within 6 months of diagnosis.

Discussion

Studies in the field of childhood hypertension have been increasing in recent years, resulting in important new findings in the epidemiology, diagnosis and treatment of hypertension in children. New data from the National Health and Nutrition Examination Survey has been added and the revised childhood BP tables now include the 50th, 90th, 95th, and 99th percentiles for sex, age, and height⁽²⁾. Hypertension in childhood is defined as an average systolic or diastolic BP greater than 95th percentile for age, sex and height on at least three separate occasions. Accurate BP measurement is the basis for diagnosis and the proper technique of BP measurement in childhood has been published. The mercury sphygmomanometer is the gold standard for BP measurement but oscillometric devices provide a reasonable approximation, are easy to use and minimize observer error, especially in newborn and young children.

After confirmation of hypertension, a thorough history and physical examination are essential. Investigations are usually needed to search for an underlying cause of hypertension, look for target organ damage and estimate the cardiovascular risk for the patient. Appropriate investigation tailored to the age, severity, history and physical examination has been proposed⁽³⁾.

Renal parenchymal diseases such as reflux nephropathy, congenital renal anomalies and chronic glomerulonephritis are the most common causes of hypertension in children. Renovascular hypertension is the second most common cause. Cardiovascular diseases such as coarctation of the aorta are also found. Other rarer causes include endocrine diseases such as hyperthyroidism, Cushing's syndrome and pheochromocytoma. No identifiable cause is found in a large proportion of older children and is considered essential hypertension. Risks for essential hypertension include genetic predisposition, obesity, dietary sodium, potassium and calcium. Obesity has become an increasingly important medical problem in children and adolescents. Obese children are reported to have approximately a 3-fold higher risk of hypertension than non-obese children. Once considered rare, primary

Table 1. Causes of hypertension according to age groups

Age	Cause	No. of patient (%)
Newborn -1 year	Coarctation of aorta	1 (16.7)
	Bronchopulmonary dysplasia	2 (33.3)
	Lupus nephritis	1 (16.7)
	Wilm's tumor	1 (16.7)
	Unknown*	1 (16.7)
	Total	6 (100)
1-6 years	Idiopathic nephrotic syndrome	8 (72.7)
	Neuroblastoma	2 (18.2)
	Drug-induced	1 (9.1)
	Total	11 (100)
6-12 years	Lupus nephritis	13 (36.1)
	Chronic renal failure	8 (22.2)
	Idiopathic nephrotic syndrome	2 (5.6)
	IgA Nephropathy	1 (2.8)
	Renovascular disease	5 (13.9)
	Drug-induced	4 (11.1)
	Coarctation of aorta	1 (2.8)
	Essential hypertension	1 (2.8)
	Unknown	1 (2.8)
	Total	36 (100)
12-18 years	Lupus nephritis	4 (28.6)
	Chronic renal failure	2 (14.3)
	Idiopathic nephrotic syndrome	1 (7.1)
	Henoch-Sch nlein nephritis	1 (7.1)
	Chronic glomerulonephritis	1 (7.1)
	Pheochromocytoma	1 (7.1)
	Essential hypertension	4 (28.6)
	Total	14 (100)

* with history of umbilical vein catheterization

hypertension in children has become increasingly common in association with obesity and other risk factors, including family history of hypertension⁽⁴⁾. The present study showed only 15.5% of patients were overweight/obese and there was no difference between the proportions of overweight/obese children in the primary and secondary hypertension groups. In all age groups, essential hypertension was found in 7.5% but the proportion increased markedly to 28.6% in the 12-18 year group. The prevalence in the present study may be underestimated as patients with essential hypertension usually have mild hypertension and, therefore, may not be referred to the hospital.

A study in a tertiary care hospital in India showed the most common cause of childhood hypertension to be renal parenchymal diseases i.e. chronic

glomerulonephritis 49.2%, obstructive uropathy 15.8%, reflux nephropathy 12.2%, thrombotic microangiopathy 6.1%, hypoplastic and dysplastic kidney 2%, and nephronophthisis 2%. Other causes were renovascular diseases 5.8%, coarctation of the aorta 3.7%, endocrine cause 1.3% and essential hypertension 1.7%. Takayasu's disease was the most common cause of renovascular hypertension and coarctation of the aorta was the most common cause in infancy⁽⁵⁾. The present study in Thai children revealed similar findings except for a higher incidence of lupus nephritis and no Takayasu's disease was found.

The most common complications of severe hypertension are hypertensive encephalopathy, cerebral infarction and hemorrhage, facial palsy, visual symptoms, cardiac failure and renal failure. Early but

gradual reduction of BP is associated with a lower risk of neurological damage.

Nonpharmacological treatments of hypertension can delay or prevent the need for antihypertensive agents. These include dietary salt restriction, mineral supplementation, weight control, regular exercise, and lifestyle modification (alcohol, cigarettes, and stress reduction). Antihypertensive drugs are usually needed in patients with secondary hypertension or target organ involvement. Angiotensin-converting enzyme inhibitors and calcium channel antagonists are commonly prescribed antihypertensive medications in children. Beta-adrenoreceptor antagonists, alpha-adrenoreceptor antagonists, alpha-adrenoreceptor agonists and direct vasodilators are less commonly used because of adverse effects. Diuretics are usually adjunct therapy.

Antihypertensive drugs for hypertensive emergencies in children include hydralazine, labetalol, nicardipine and sodium nitroprusside. Clonidine, enalaprilat, fenoldopam, isradipine and minoxidil may also be useful. Specific uses in neonatal, essential hypertension and various underlying diseases are described^(2,6-8). Some underlying causes of hypertension e.g. pheochromocytoma can be surgically curable and antihypertensive drugs may be discontinued soon afterward. Monitor for the side effects if the child is on antihypertensive agents, an explanation of the disease and the need for treatment as well as education of patients and their parents about healthy lifestyle measures are essential in the management of childhood hypertension.

After many years, untreated elevated BP causes target organ damages including the blood vessels, brain, eyes, kidneys and heart. All children with hypertension need regular long term follow up with special attention paid to target organ injury and underlying diseases. Echocardiography is recommended for evaluating target organ abnormalities. Left ventricular hypertrophy can be an indication for initiating or intensifying drug therapy to lower BP⁽¹⁻³⁾. Left ventricular hypertrophy was reported in as high as 34-38% of children and adolescent with mild, untreated hypertension^(9,10). The 7.5% left ventricular hypertrophy noted in the present study may be an under estimate since not all patients had echocardiography. Few data are available on childhood hypertensive retinopathy and

the present study revealed a probable underestimated incidence of 3.0%.

In conclusion, hypertension in children is not rare and may be asymptomatic. Most childhood hypertension is found to have underlying etiology, so all children with persistent hypertension should undergo screening investigations and definitive investigations accordingly. A significant number of underlying conditions are curable and antihypertensive agents may be discontinued afterward but others may need medication for life. Data on long term outcome of childhood hypertension is needed.

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สาเหตุและผลการรักษาความดันโลหิตสูงในเด็กไทย

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การศึกษาย้อนหลังในผู้ป่วยอายุน้อยกว่า 18 ปี ซึ่งได้รับการวินิจฉัยว่าเป็นความดันโลหิตสูงเรื้อรังที่ภาควิชากุมารเวชศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล ตั้งแต่ มกราคม พ.ศ. 2542 - ธันวาคม พ.ศ. 2546 พบมีผู้ป่วย 66 ราย ชาย:หญิง = 1.4:1 ร้อยละ 54.5 มีอายุ 6-12 ปี และร้อยละ 9.1 อายุน้อยกว่า 1 ปี

พบภาวะความดันโลหิตสูงเป็นชนิดรุนแรงร้อยละ 79.1 ส่วนใหญ่ (78.6%) ไม่มีอาการ อาการปวดศีรษะเรื้อรัง, hypertensive encephalopathy, เลือดกำเดาไหล และการมองเห็นผิดปกติ พบได้ร้อยละ 10, 8.6, 1.4 และ 1.4 ตามลำดับ สาเหตุของความดันโลหิตสูงที่พบบ่อยที่สุดคือโรคของเนื้อไต (62.7%) ซึ่งได้แก่ lupus nephritis (26.9%), โรคไตเนโฟรติก (16.4%) และภาวะไตวายเรื้อรัง (16.4%) ภาวะอ้วนและน้ำหนักเกิน (body mass index, BMI มากกว่า 25) พบได้เพียง 10 ราย (15.1%) อัตราส่วนของเด็กที่มี BMI มากกว่า 25 ไม่แตกต่างกันระหว่างผู้ป่วยความดันโลหิตสูงชนิดปฐมภูมิและชนิดที่มีสาเหตุ ($p = 0.15$) ภาวะแทรกซ้อนจากความดันโลหิตสูง ได้แก่ left ventricular hypertrophy, hypertensive retinopathy และ hypertensive encephalopathy พบได้ร้อยละ 7.5, 3.0 และ 9 ตามลำดับ 1 ใน 3 ของผู้ป่วยสามารถกลับมามีความดันโลหิตปกติภายใน 1 เดือน และอีกร้อยละ 47 มีความดันโลหิตปกติภายใน 6 เดือนหลังได้รับการวินิจฉัย 1 ใน 5 ของผู้ป่วยต้องได้รับการผ่าตัด/หัตถการจำเพาะเพื่อรักษาโรคที่เป็นสาเหตุของความดันโลหิตสูง

ผู้ทำการศึกษาเสนอว่า ความดันโลหิตสูงในผู้ป่วยเด็กส่วนใหญ่เป็นชนิดที่มีสาเหตุ จึงควรทำการสืบค้นและตรวจทางห้องปฏิบัติการเพิ่มเติมทุกรายเพื่อการรักษาอย่างถูกต้องเหมาะสม ภาวะอ้วนและน้ำหนักเกินไม่สามารถใช้แยกผู้ป่วยที่มีความดันโลหิตสูงชนิดปฐมภูมิและทุติยภูมิได้ การรักษาความดันโลหิตสูงด้วยยาและพิจารณาการผ่าตัด/หัตถการในรายที่จำเป็น พบว่าได้ผลดีในระยะสั้น แต่ผลระยะยาวยังไม่ทราบ