

Hypertension in children with chronic Renal failure

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Systemic hypertension (HTN) is one of the major problems associated with chronic renal failure (CRF). HTN is a symptom and complication of CRF. The prevalence of HTN varies with the cause of CRF. The incidence of HTN increased up to 90% with progressive deterioration of the glomerular filtration rate (GFR). HTN is the major risk factor for decline in renal function and progression of CRF. It is the most important risk factor for cardiovascular diseases and morbidity and mortality in patients with CRF and end-stage renal disease (ESRD) on dialysis. The target blood pressure for hypertensive children with CRF should be under the 95th percentile for sex and age. The therapeutic approach in CRF is directed at reducing volume expansion and sodium retention, and decreasing peripheral vascular resistance. Diuretics are first-line therapy for HTN in patients with CRF with sodium and water retention. ACE inhibitors are the first-class drugs because of their renoprotective effect in preventing deterioration of kidney function. Calcium channel blockers are excellent first-line antihypertensive drugs. Recently angiotensin II receptor blockers and ACE inhibitors have been efficiently used together for the treatment of HTN and to prevent further decline in renal function.

Key words: hypertension, chronic renal failure, children, treatment.

Introduction

Hypertension (HTN) is both a cause and a complication of chronic kidney disease (CKD)¹. HTN in patients with CKD is associated with: faster decline of kidney function, progression of kidney disease, risk of development of kidney failure, cardiovascular disease (CVD) and higher mortality¹⁻⁵. Patients on dialysis who have HTN are prone to higher risk of morbidity and mortality due to CVD. After renal transplantation (RTR), HTN is responsible for more rapid development of graft failure¹. The appropriate evaluation and management of HTN remains a major component of the care of patients with CKD⁶. Blood pressure (BP) should be closely monitored in all children with CKD⁷.

Prevalence of HTN

Chronic parenchymal renal diseases are the most frequent cause of secondary HTN. Approximately 60% to 80% of secondary HTN cases in childhood are caused by renal parenchymal disease⁸, and they represent about

5% of all cases of HTN. The incidence of HTN in children with CKD is reported as 38 to 78%⁹. HTN is infrequent in congenital renal disease, but it is almost universal in primary glomerular disease and renal injury caused by systemic diseases⁷. HTN presents in 27% of children before the onset of chronic renal failure (CRF), in 57% with the development of CRF, and in 85-90% of the patients with end-stage renal disease (ESRD) before they enter the dialysis program^{10,11}.

The most important pathogenetic mechanisms of high blood pressure in CKD are listed in Table I¹².

Normal blood pressure in children, according to the definition of The Report of the Second Task Force on Blood Pressure Control in Children 1987¹³, should be <90th percentile for sex age and height⁶. Children with blood pressure between the 90th and 95th percentile are delineated as having normal high blood pressure. HTN is found in cases of systolic and diastolic blood pressure values above 95th percentile for age, sex and height. Significant

Table I. Pathogenetic Mechanisms of High Blood Pressure in Chronic Kidney Disease

Pre-existing essential hypertension
Extracellular fluid volume expansion
Renin-angiotensin aldosterone system stimulation
Increased sympathetic activity
Endogenous digitalis-like factors
Prostaglandins/bradykinins
Alteration in endothelium-derived factors (nitric oxide/endothelin)
Increased body weight
Erythropoietin administration
Parathyroid hormone secretion/increased intracellular calcium/hypercalcemia
Calcified arterial tree
Renal vascular disease and renal arterial stenosis
Chronic allograft dysfunction
Cadaver allografts, especially from a donor with a family history of hypertension
Cyclosporine, tacrolimus, other immunosuppressive and corticosteroid therapy

HTN indicates children with blood pressure in a range of 95th-98th percentile with no target organ damage, and blood pressure >99th percentile is considered severe HTN.

Goals of therapy of HTN in CKD are to prevent or slow down a further decline in renal function, and to prevent atherosclerosis, stroke, and CVD. Usual pediatric goal blood pressure is based on weight, sex and age^{1,14}.

Treatment of HTN in CKD should include: specification of target blood pressure levels, non-pharmacological therapy and specific antihypertensive agents for the prevention of progression of CKD and development of CVD^{1,6,10,15}. Blood pressure should vary through childhood and should be maintained within two standard deviations of the mean for normal children of the same height and sex¹⁶. It is recommended that the systolic blood pressure during pre-terminal CRF, peritoneal dialysis (PD) and hemodialysis (HD) should be maintained at <90th percentile for age, gender and height^{9,14}. Appropriate equipment for measurement of blood pressure should be at home and it should be measured on the days between dialyses, as this may be more representative of overall control than the pre-dialysis blood pressure.

Non-pharmacologic therapy should include: control of extracellular fluid volume and maintenance of "dry weight"; reduction in fluid intake and ultra filtration in HD and PD patients; dietary salt reduction; protein, phosphorus, cholesterol restriction with increase of calcium in the diet. Moderate physical activity is recommended^{10,17,18}.

Antihypertensive medications are indicated in cases of significant HTN, defined as diastolic blood pressure >90 mmHg in adolescents, >86 mmHg in children and >80 mmHg for infants and in cases with signs of end-organ damage and symptoms related to HTN^{16,19}.

The aim of the treatment is to lower the blood pressure under the 95th percentile, optimally to the 50th percentile. All classes of antihypertensive agents are effective¹⁵. Any medication that controls blood pressure protects the renal lesions. There is a series of drugs that are especially indicated in CRF, mainly when glomerular lesions are present¹⁰.

Selected Antihypertensive Drugs for Patients with CRF^{17,19}:

Diuretics

ACE inhibitors (ACEIs)

Calcium channel blockers (CCBs)

Angiotensin II receptor blockers (ARBs)

Beta-blockers

Vasodilators

Central sympatholytics

The possible and recommended drug combinations used in patients with CKD are summarized in Table II.

Treatment of HTN in patients with ESRD on HD and PD includes^{14,21}:

Table II. Drug Combinations in Hypertension in Chronic Renal Failure^{2,10,20}

ACEI+ diuretics
ACEI+ calcium antagonists (CCB)
ACEI+ angiotensin II receptor antagonists (ARBs)
ARBs+ diuretics
Beta-blockers+ diuretics
ACEI+ Beta blocker+ CCB+ Diuretic+ ARBs

ACEI: ACE inhibitors.

CCB: calcium channel blockers.

- Control of extracellular fluid volume
- Maintenance of “dry weight” through dietary salt reduction
- Reduction in fluid intake and ultra filtration
- Definition of the optimal and target blood pressure for antihypertensive therapy to reduce the risk of CVD outcomes.

Furthermore,

- Optimal blood pressure in dialysis patients is not different from recommendations for the general population.
- Antihypertensive medications alone do not effectively control blood pressure in patients with ESRD.
- All classes of antihypertensive agents are effective, with the exception of diuretics.
- Antihypertensive doses may be withheld or reduced on hemodialysis days.
- Short-hours daily HD reduced blood pressure, left ventricular hypertrophy and blood volume expansion when compared to three times weekly conventional treatment.

Treatment of HTN in patients with renal transplantation (RTR)

More than 50% of patients with RTR are hypertensive. HTN after RTR is associated with high risk of graft failure. HTN after RTR is of multifactorial origin: pre-transplant HTN, renal artery stenosis, chronic allograft nephropathy, immunosuppressive therapy and native kidney. All antihypertensive drugs are useful in RTR, but the most commonly used are CCBs and ACEIs [2,10,11,22]. CCB and ACEI could be used together in uncontrolled HTN. Before ACEI therapy is started, renal artery stenosis should be excluded [22]. The choice of drug could depend on the presence of proteinuria. ACEI should be given to children with CKD,

especially those with glomerular diseases presenting with HTN and proteinuria. The combined therapy with ARBs would probably be more efficient in prevention of progressive loss of kidney function, but the data are still very scarce and we need further prospective studies before this combination is strongly recommended²³.

Recently ARBs (Losartan) have been used to control post-transplant HTN.

In renin-dependent uncontrolled HTN, bilateral native kidney nephrectomy could be considered.

The goal of treatment in a hypertensive emergency is a prompt but gradual reduction of blood pressure within a few hours^{4,8,20,24}. Blood pressure should be reduced up to 5-10% above 95th percentile (or 125/75 mmHg for infants and 140/90 mmHg for older children). Careful observation is critical because end-organ ischemia or infarction can occur when pressure is reduced too rapidly^{5,8,24}. Intravenous (IV) treatment should be started with sodium nitroprusside or labetalol infusion if available. Bolus doses of clonidine or hydralazine can be given initially where an infusion is unavailable.

For the treatment of hypertensive crisis in newborns and infants, the recommended drugs are²⁰:

- 1) dihydralazine
- 2) nifedipine sublingual (sl)
- 3) sodium nitroprusside

Contraindication: nifedipine IV

After RTR (<3 months)

- 1) Beta-blockers
- 2) CCBs
- 3) Diuretics

Contraindications: ACEIs, ARBs

Maintenance oral therapy is usually initiated with either an ACEI or CCB because of their efficacy and fewer side effects. Diuretic therapy should be considered in patients with renal disease who are salt- and water-overloaded. Beta-blockers are available if multiple medications are required for control of the HTN or the tachycardia produced by CCB. Centrally acting drugs are also used^{8,10,20,24}.

Angiotensin II receptor blockers and ACEIs produced similar antihypertensive and antiproteinuric effects in patients with essential HTN or CKD. Their combination has a more pronounced renoprotective effect in reducing proteinuria and deterioration of kidney function.

Aggressive treatment of hypertensive emergencies and chronic HTN in children with CRF is indicated to prevent end-organ damage as well as progressive loss of kidney function⁸. At the moment, the most efficient and safest drugs available are ACEIs and ARBs. Well-controlled blood pressure is required to prevent morbidity and mortality in patients with moderate and severe CRF and ESRD from CVD. After kidney transplantation, well-controlled HTN is one of the guarantees for increasing graft survival rate. In uncontrolled HTN in children with CRF, combined therapy might be necessary^{8,10,20}.

Conclusion

Effective control of blood pressure is required to protect the kidneys and heart. It plays an important role in the delay of chronic renal failure, and may arrest its progression.

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