Chronic Kidney Disease

:Lecturer

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TUCOM

Objecties:

- Defintion of CKD.
- Etiology of CKD.
- Pathogenesis of CKD.
- Pathophysiology of CKD.
- Clinical manifestations of CKD.
- Laboratory findings in patient with CKD.
- Treatment of CKD.

:DEFINITION

Chronic kidney disease (CKD) is defined as either renal injury (proteinuria) and/or a glomerular filtration rate <60 mL/.min/1.73 m2 for <3 mo

The prevalence of CKD in the pediatric population is approximately 18 per 1 million. The prognosis for the infant, child, or adolescent with CKD has improved dramatically over the past 4 decades because of improvements in medical management (aggressive nutritional support, recombinant erythropoietin, recombinant growth hormone), dialysis techniques, and renal transplantation

ETIOLOGY

.Etiology is closely correlated to the age
CKD in children younger than 5 yr is most commonly a result of congenital abnormalities such as renal hypoplasia, dysplasia, and/or obstructive uropathy. Additional causes include congenital nephrotic syndrome, prune belly syndrome, cortical necrosis, focal segmental glomerulosclerosis, polycystic kidney disease, renal vein thrombosis, and hemolytic uremic syndrome

After 5 yr of age, acquired diseases (various forms of glomerulonephritis including lupus nephritis) and inherited disorders (familial juvenile nephronophthisis, Alport .syndrome) predominate

CKD related to metabolic disorders (cystinosis, hyperoxaluria) and certain inherited disorders (polycystic kidney disease) may present throughout the childhood years

PATHOGENESIS

In addition to progressive injury with ongoing structural/ metabolic genetic diseases, renal injury may progress .despite removal of the original insult

Hyperfiltration injury may be an important final common pathway of glomerular destruction, independent of the underlying cause of renal injury. As nephrons are lost, the remaining nephrons undergo structural and functional hypertrophy characterized by an increase in glomerular .blood flow and hyperfiltration injury

Proteinuria itself may contribute to renal functional decline, as evidenced by studies that have shown a .beneficial effect of reduction in proteinuria

Uncontrolled hypertension may exacerbate disease progression by causing arteriolar nephrosclerosis .as well as by increasing the hyperfiltration injury

Hyperphosphatemia may increase progression of disease by leading to calcium-phosphate deposition .in the renal interstitium and blood vessels

Hyperlipidemia, a common condition in CKD patients, may adversely affect glomerular function .through oxidant-mediated injury

Pathophysiology of Chronic Kidney Disease

:Accumulation of nitrogenous waste products due to

Decrease in glomerular filtration rate-

Decreased ammonia synthesis -

:Acidosisdue to

Decreased net acid excretion -

Impaired bicarbonate reabsorption-

:Sodium retention due to

Excessive renin production-

Oliguria-

:wasting Sodium due to

Solute diuresis

Tubular damage

Urinary concentrating defect due to

Solute diuresis

Tubular damage

:Hyperkalemia due to

Decrease in glomerular filtration rate

Metabolic acidosis

Excessive potassium intake

Hyporeninemic hypoaldosteronism

:Renal osteodystrophy due to

Impaired renal production of 1, 25-dihydroxycholecalciferol
Hyperphosphatemia
Hypocalcemia
Secondary hyperparathyroidism

:Growth retardation due to

Inadequate caloric intake
Renal osteodystrophy
Metabolic acidosis
Anemia
Growth hormone resistance

:Anemia due to

Decreased erythropoietin production
Iron deficiency
Folate deficiency
Vitamin B12 deficiency
Decreased erythrocyte survival

:Bleeding tendency Infection due to

Defective platelet function
Defective granulocyte function
Impaired cellular immune functions
Indwelling dialysis catheters

Gastrointestinal symptoms (feeding intolerance, abdominal :pain) due to

Gastroesophageal reflux

Decreased gastrointestinal motility

:Hypertension due to

Volume overload

Excessive renin production

:Hyperlipidemia due to

Decreased plasma lipoprotein lipase activity

:Pericarditis/cardiomyopathy due to

Hypertension

Fluid overload

:Glucose intolerance due to

Tissue insulin resistance

CLINICAL MANIFESTATIONS

The clinical presentation of CKD is quite varied and dependent on the .underlying renal disease

Children and adolescents with CKD from chronic glomerulonephritis (membranoproliferative glomerulonephritis) may present with edema, .hypertension, hematuria, and proteinuria

Infants and children with congenital disorders such as renal dysplasia and obstructive uropathy may present in the neonatal period with failure to thrive, polyuria dehydration, urinary tract infection. Many infants with congenital kidney

disease are identified with prenatal ultrasonography, allowing early .diagnostic and therapeutic intervention

Other nonspecific complaints such as headache, fatigue, lethargy, anorexia, vomiting, polydipsia, polyuria, and growth failure over a .number of years

The physical examination in patients with CKD may reveal -
.pallor and a sallow appearance

Patients with long-standing untreated CKD may have short-
.stature and the bony abnormalities of renal osteodystrophy

Children with CKD due to chronic glomerulonephritis (or-
children with advanced renal failure from any cause) may
have edema, hypertension, and other signs of extracellular
.fluid volume overload

Laboratory findings

Include elevations in blood urea nitrogen and serum-
creatinine, hyperkalemia, hyponatremia (if volume
overloaded), acidosis, hypocalcemia, hyperphosphatemia,
.and an elevation in uric acid
.Patients with heavy proteinuria may have hypoalbuminemia-
A complete blood cell count usually shows a -
.normochromic, normocytic anemia
Serum cholesterol and triglyceride levels are usually-
.elevated
In children with CKD caused by glomerulonephritis, the -
.urinalysis shows hematuria and proteinuria
In children with CKD from con-genital lesions such as renal-
.dysplasia, the urinalysis usually has a low specific gravity

TREATMENT

The treatment of CKD is aimed at
replacing absent/diminished renal functions, which) 1(
progressively deteriorate in parallel with the progressive
.loss of GFR
.slowing the progression of renal dysfunction) 2(

Children with CKD should be treated at a medical center capable of supplying multiservices, including medical, nursing, social service, nutritional, and psychological .support
The management of CKD requires close monitoring of a .patient's clinical and laboratory status

FLUID AND ELECTROLYTE MANAGEMENT

- Most children with CKD maintain normal sodium and water balance with the sodium intake derived from an appropriate diet.
- Polyuric infants with significant urinary sodium losses may benefit from high volume, low caloric density feedings with sodium supplementation.
- Children with high blood pressure, edema, or heart failure may require sodium restriction and diuretic therapy.
- Fluid restriction is rarely necessary in children with CKD until the development of end-stage renal disease (ESRD) requires the initiation of dialysis.
- In most children with CKD, potassium balance is maintained until renal function deteriorates to the level at which dialysis is initiated.
- Hyperkalemia may develop and may be treated by restriction of dietary potassium intake, administration of oral alkalinizing agents, and/or treatment with Kayexalate.

ACIDOSIS

Metabolic acidosis develops in almost all children with CKD as a result of decreased net acid excretion .by the failing kidneys
Either Bicitra (1 mEq sodium citrate/mL) or sodium bicarbonate tablets (650 mg equals 8 mEq of base) may be used to maintain the serum bicarbonate .level >22 mEq/L

NUTRITION

- Dietary phosphorus, potassium, and sodium should be restricted according to the individual patient's laboratory studies and fluid balance.
- In infants with CKD, formulas containing a reduced amount of phosphate are commonly employed.
- The optimal caloric intake in patients with CKD is unknown, but it is recommended to provide at least the recommended dietary allowance of caloric intake for age.
- Protein intake should be 2.5 g/kg/24 hr and should consist of proteins of high biologic value that are metabolized primarily to usable amino acids rather than to nitrogenous wastes. The proteins of highest biologic value are those of eggs and milk, followed by meat, fish, and fowl.
- Children with CKD may become deficient in water-soluble vitamins (not fat-soluble vitamins) either because of inadequate dietary intake or dialysis losses. These should be routinely supplied (Zinc and iron supplements should be added only if deficiencies are confirmed).

GROWTH

Short stature is a significant long-term sequela of childhood CKD. Children with CKD have an apparent growth hormone (GH)-resistant state with elevated GH levels but decreased insulin-like growth factor 1 levels and major abnormalities of .insulin-like growth factor–binding proteins

Children with CKD who remain less than -2 SD for height despite optimal medical support (adequate caloric intake and effective treatment of renal osteodystrophy, anemia, and metabolic acidosis) may benefit from treatment with .pharmacologic doses of recombinant human GH (rHuGH)

RENAL OSTEODYSTROPHY

The term renal osteodystrophy is used to indicate a spectrum of bone disorders seen in patients with CKD. The most common condition seen in children is high-turnover bone disease caused by secondary .hyperparathyroidism

:The pathophysiology of renal osteodystrophy is
Impaired renal production of 1, 25-dihydroxycholecalciferol-
Hyperphosphatemia-
Hypocalcemia -
Secondary hyperparathyroidism -

Clinical manifestations of renal osteodystrophy include muscle weakness, bone pain, and fractures with minor trauma. In growing children varus and valgus deformities of the long bones, and slipped .capital femoral epiphyses may be seen

Laboratory studies may demonstrate a decreased serum calcium level, increased serum phosphorus level, increased alkaline phosphatase, and .a normal PTH level

Radiographs of the hands, wrists, and knees show subperiosteal .resorption of bone with widening of the metaphysis

Children and adolescents should follow a *low phosphorus diet*, and infants should be provided with a *low-phosphorus formula* such as .Similac PM 60/40

Because it is impossible to fully restrict phosphorus intake, *phosphate .binders* are used to enhance fecal phosphate excretion

The cornerstone of therapy for renal osteodystrophy is *vitamin D :administration*. Vitamin D therapy is indicated in patients with hydroxy-vitamin D levels below the established goal range for his-25) 1 (or her particular stage of CKD or
.PTH levels above the established goal range for CKD stage) 2 (

ANEMIA

:Anemia in patients with CKD is primarily the result of
Inadequate erythropoietin production by the failing kidneys- 1
.Iron deficiency, folic acid or vitamin B12 deficiency- 2
.Decreased erythrocyte survival- 3

Recombinant human erythropoietin (rHuEPO) therapy has decreased the need for transfusion in patients with CKD. Erythropoietin is usually initiated when the patient's hemoglobin concentration falls below 10 g/dL, at a dose of 50–150 mg/kg/dose subcutaneously 1-3 times weekly. The dose is adjusted to maintain the hemoglobin concentration between 12 .and 13 g/dL

An alternative option is darbopoeitin alfa (Aranesp), a longer-acting agent administered at a dose of 0.45 µg/kg/wk. The chief advantage to this agent is that it may be dosed once weekly to once monthly because .of its extended duration of action

HYPERTENSION

:Children with CKD may have sustained hypertension related to
Volume overload and/or *
.Excessive renin production related to glomerular disease *

Hypertensive children with suspected volume overload should follow a-salt-restricted diet (2–3 g/24 hr) and may benefit from diuretic therapy. Thiazide diuretics (hydrochlorothiazide 2 mg/kg/24 hr divided bid) are the initial diuretic class of choice for children with mild renal dysfunction (CKD stages 1-3). However, when a patient's estimated GFR falls into stage 4 CKD, thiazides are less effective and loop diuretics (furosemide .1–2 mg/kg/dose bid or tid) become the diuretic class of choice

Angiotensin-converting enzyme (ACE) inhibitors (enalapril, -lisinopril) and angiotensin II blockers (losartan) are the antihypertensive medications of choice in all children with proteinuric renal disease because of their potential ability to .slow the progression to ESRD

Calcium channel blockers (amlodipine), β blockers -(propranolol, atenolol), and centrally acting agents (clonidine) may be useful as adjunctive agents in children with CKD whose blood pressure cannot be controlled using .dietary sodium restriction, diuretics, and ACE inhibitors

IMMUNIZATIONS

Children with CKD should receive all standard - immunizations according to the schedule used for healthy children excep live vaccines for children with CKD related to glomerulonephritis during treatment with .immunosuppressive medications

It is critical, however, to administer live virus vaccines- [MMR (mumps, measles, rubella), varicella] before renal transplantation because these vaccines are not advised for .use in immunosuppressed patients

All children with CKD should receive a yearly influenza- .vaccine

:End-Stage Renal Disease

ESRD represents the state in which a patient's renal dysfunction has progressed to the point at which homeostasis and survival can no longer be sustained with native kidney function and maximal medical management. At this point, renal replacement therapy (dialysis or renal transplantation) becomes necessary. The ultimate goal for children with ESRD is successful kidney transplantation because it provides the most .normal lifestyle and possibility for rehabilitation for the child and family

It is recommended that plans for renal replacement therapy be initiated when a child reaches stage 4 CKD. The optimal time to actually initiate dialysis, however, is based on a combination of the biochemical and clinical characteristics of the patient including refractory fluid overload, electrolyte imbalance, acidosis, growth failure, or uremic symptoms, .including fatigue, nausea, and impaired school performance

In general, most nephrologists attempt to initiate dialysis early enough to prevent the development of severe fluid and electrolyte abnormalities, .malnutrition, and uremic symptoms

The selection of dialysis modality must be individualized to fit the needs of each child. Age is a defining factor in dialysis modality selection: 88% of infants and children from birth to 5 yr of age are treated with peritoneal dialysis, whereas 54% of children older than 12 yr of age are treated with .hemodialysis

Peritoneal dialysis is a technique that employs the patient's peritoneal membrane as a dialyzer. Excess body water is removed by an osmotic gradient created by the high dextrose concentration in the dialysate; wastes are removed by diffusion from the peritoneal capillaries into the dialysate. Access to the peritoneal cavity is achieved by a surgically .inserted, tunneled Tenckhoff catheter

Hemodialysis, unlike peritoneal dialysis, is usually performed in a hospital setting. Children and adolescents typically have three 3- to 4-hr sessions per week during which fluid and solute wastes are removed. Access to the child's circulation is achieved by a surgically created arteriovenous fistula, graft, or indwelling subclavian or .internal jugular catheter