Pediatrics – Dr. Bakr – Lecture 6 – Chronic Renal Failure

CHRONIC RENAL FAILURE or CHRONIC KIDNEY DISEASE

Definition:

old: irreversible renal injury.

new: is defined as either renal injury and/or a glomerular filtration rate less than 60 ml/min/1.73 m2 for more than 3 months.

Glomerulofilteration rate can be determined by the following formula

GFR(mL/min/1.73 m2)= K x height (cm)/ serum creatinine (mg/dL)

Etiology:

The causes may be congenital,inherited,acquired or metabolic.

In children below 5 years is most commonly result of congenital abnormalities like:

-renal hypoplasia.

-renal dysplasia.

-Obstructive uropathy.

Other causes like congenital nephrotic syndrome, prune belly syndrome,corticalnecrosis,focalsegmentalglomeruloseclerosis, polycystic kidney disease, renal vein thrombosis, hemolytic uremic syndrome.

After the age of 5 years acquired and inherited diseases predominate like:

1-Glomerulonephritis .

2- Lupus nephritis.

3-Alport syndrome.

4-Cystenosis.

5-hyperoxal uria.

6-polysystic kidney disease.

Pathogenesis: in patients with CKD progressive renal injury occur through the following mechanism:

-hyper filtration injury.

-proteinuria.

-hypertension.

-hyperphosphatemia.

Stages of chronic kidney disease:

1. Stage 1:kidney damage with normal or increased GFR >90
2. Stage 2:kidney damage with mild decrease GFR 60-89
3. Stage 3:moderate decrease GFR30-59
4. Stage 4:severe decrease in GFR 15-30
5. Stage 5: kidney failure GFR< 15

Clinical manifestations:

-varied depend on the underlying cause

Neonate and infants with congenital disorder like dysplasia,obstructive uropathy may presents with:

1-failure to thrive.

2-polyuria dehydration.

3-UTI

4-urin retention.

5- abdominal mass.

Children may presents with:

1-non specific complain like headache,fatigue,lethargy,anorexia,vomiting,polydipsia,polyuria,growth failure.

2-pallor

3-short stature bony abnormalities of renal oseodystrophy.

4-edema hypertension.

LABORATORY FINDING

1-elivated blood urea and creatinine.

2-hyperkalemia,hyperphophatemia,hyperurecimia.

3-hyponatremia,hypocalcimia,hypoalbumenimia.

4-Elevated serum cholesterol and triglyceride.

5-Acidosis.

6-Normochromic normocytic anemia.

7-hematuria,protein uria,in parient with dysplastic lesion GUE shows low specific gravity and minimal abnormalities.

TREATMENT

The aim of treatment of patient with CKD is :

1-replacing diminished or absent renal function.

2-slowing the progression of renal dysfunction.

Children with CKD should be treated in a medical center capable of providing multidisciplinary services, including medical,nursing,social service,nutritional,and psychosocial support.

FLUID AND ELECTROLYTE:

-most children with CKD maintain normal sodium and water balance with sodium intake derived from appropriate diet.

-infant and children with renal dysplasia may be polyuric with significant sodium losses. These children may benefit from high voume,low caloric density feeding with sodium supplementation.

-Children with hypertension ,edema or heart failure may require sodium restriction and diuretic therapy.

-Fluid restriction is rarely required in patient with CKD until require dialysis.

HYPERKALEMIA

-In most patient with CKD potassium balance is maintained until renal function deteriorate and require dialysis, but some patient with moderate renal dysfunction may develop hyperkalemia and require treatment.

ACIDOSIS:

Acidosis develops in almost all patient with with CKD as a result of decreased net acid excretion by the kidney they require treatment with sodium citrate or sodium bicarbonate to maintain bicarbonate above 22mEq/L.

NUTRITION:

-patient with CKD require progressive restriction of various dietary component as there renal function decline.

-diatey phosphorus,potassium,and sodium should be restricted according to the laboratory results.

-In infant formula with reduced amount of phosphate(similac PM 60/40) are commonly used.

-The caloric intake should be at least the recommended dietary allowance of caloric intake for age.

-protein intake should be (2.5gm/kg/day) and should consist of protein of high biological value that are metabolized primarily to usable amino acid. The protein of high biological value are those of eggs,milk,meat,fish and fowl.

-If oral caloric intake remain inadequate and or weight gain and growth velocity suboptimal ,enteral tube feeding should be considered.

-Children with CKD may become deficient in water-soluble vitamins either because of inadequate intake or dialysis. These should be routinely provide using preparation like NEPHROCAPE.Supplimentation with fat-soluble vitamins is usually not require.

GROWTH

Short stature is a significant long-term sequela of childhood CKD.

-Children with CKD have growth hormone resistant with elevated level of GH but decreased level of insulin-like growth factor 1.

-Children with CKD who remain 2SD less than mean for height may benefit from GH therapy.

-Treatment with GH continue until the patient:

1-reaches the 50th percentile for parental height.

2-achieves a final adult height.

3-undergoes renal transplantation.

RENAL OSTEODYSTROPHY

It is a spectrum of bone disorder seen in patient with CKD.

PATHOLOGY: Early in the course of CKD ,when GFR decline to 50% of normal there is decreased activity of one Alfa –hydroxylase activity ,with decreased production of activated vitamin D which leads to hypocalcaemia and increased parathyroid gland activity. Excessive parathyroid hormone secretion attempts to correct the hypocalcaemia by increasing bone resorption.

Later when the GFR decline to 20-25% of normal compensatory mechanism to enhance phosphate excretion become inadequate resulting in hyperphosphatemia which further promotes hypocalcaemia and increased PTH secretion.

The pathologic finding is osteitis fibrosa cystica.

CLINICAL MANIFESTATION:

-muscle weakness,bone pain ,and fractures with minor trauma.In growing children rachitic changes,varus and valgus deformities of the long bones , and slipped capital femoral epiphyses may be seen.

LABORATORY FINDING:

-hypocalcemia,hyperphosphatemia,increased alkaline phosphatase , and a normal PTH.

-Radiographs of the hand ,wrist ,and knee show subperiosteal resorption of bone with widening of the metaphyses.

TREATMENT:

-Children and adolescents should follow a low phosphorus diet and infants should be provided with low phosphorus formula like similac PM 60/40.

-Phosphate binder can be use to enhance fecal excretion of phosphate like calcium carbonate. Calcium citrate, non calcium based binder such as sevelamer in patient prone to hypercalcimia can be use.

- The corner stone of treatment is vitamin D.

ANEMIA

In patient with CKD anemia is common and it is usually normocytic anemia occur at stage 3-4 of the renal failure causes are:

1-main cause is inadequate erythropoietin production by the kidney.

2-iron ,B12 folic acid deficiency.

3-decreased RBC survival.

4-blood loss.

5-bone marrow suppression by uremia.

TRETMENT: is erythropoietin indicated when hemoglobin is below 10gm/dL.All patient receive erythropoietin should receive oral or IV iron.

HYPERTENTION

-Children with CKD may have sustained hypertension with volume overload these patient should be treated by sodium restriction with diuretic like thiazide or furosemide.

- Patient with CKD and protein urea the best drug for treatment of hypertension is angiotensin-converting enzyme inhibitors like enlapril,lisinopril because they slow the progression to ESRD.

-Calcium channel blocker ,B-blocker,centrally acting anti hypertensive can be use as adjuvant therapy in patient not responding to salt restriction, diuretic and ACE inhibitor.

DRUG THERAPY IN PATIENT WITH CKD

-because many drugs are excreted by the kidneys ,their dosing may need to be adjusted in patient with CKD.

SLOWING THE RATE OF PROGRESSION OF RENAL DYSFUNCTION

Because there is no definitive treatment in patient with CKD there are many strategies to decrease the rate of renal dysfunction:

1-optimal control of hypertension. ACE inhibitor or angiotensin blocker should be antihypertensive of choice.

2-serum phosphorus should be maintained within normal range for age. Calcium – phosphorus product should be <55.

3-promt treatment of infection and dehydration episode.

4-treatment of anemia .

5-controlof hyperlipidemia.

6-avoidance of cigarette and obesity.

7-minimization use of nonsteroidial anti-inflammatory medication.

END –STAGE RENAL DISEASE

-ESRD is the stage 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 renal transplantation because it provide the most normal life style.

-plans for renal replacement therapy should be initiated when a child reaches stage 4 CKD.

-children with CKD require period of dialysis before transplantation.

The optimal time to initiate dialysis is based on a combinations of a clinical and biochemical characteristics of the patient including:

-Refractory fluid overload.

-Electrolyte imbalance.

-Acidosis.

-Growth failure.

-Uremic symptoms.

TYPES OF DIALYSIS:

1-peritonial dialysis: is a technique that employs the patients peritoneal membrane as a dialyzer. Access to peritoneal cavity is achieved by surgically placed catheter. The dialysate which is a high glucose concentration fluid is inserted through the catheter to the peritoneal cavity, excessive body fluid is removed by an osmotic gradiant, wastes are removed by diffusion from the peritoneal capillaries into the dialysate.

Peritoneal dialysis is mainly used in children below the age of (5) years, it can be provided either as continuous ambulatory or cyclical peritoneal dialysis.

2-Hemodialysis : in this type of dialysis access to the child circulation is achieved by a surgically created arteriovenous fistula,graft,indwelling subclavian or internal jugular catheter. Commonly use for children above the age of (5) years. Unlike peritoneal dialysis is performed in a hospital setting .patient require 3-4 sessions per week.

STEM CELLS : Stem cells are the most primary cells in the human body. When the stem cells are transfused into human body through veins, the kidney lesions will set some signals to attract stem cells. The stem cells will produce a large number of daughter cells. These daughter cells will continue to develop into various cells, tissues and renal vessels the kidney needs.

It can improve renal local microcirculation, lower the high pressure in the glomerulus, remit renal ischemia and anoxia and recover and remove general blood circulation. The active factors released by stem cells will activate the kidney cells to secrete erythropoietin, and the erythropoietin can promote the formation of red blood cells thus easing the state of anemia.

Besides, stem cells can restrain immune activity, differentiate into immune cells and regulate the function of immune system so as to achieve the purpose of repairing the kidney. These are the systematic function of stem cells. The stem cells can make different repair according to different disease condition.

RENAL TUBULAR ACIDOSIS

These are heterogeneous group of disorders, all of which are characterized by a normal anion gap metabolic acidosis and tubular dysfunction, but usually not by renal insufficiency. Both inherited and acquired primary and secondary forms exist.

There are three main forms of RTA :

1-Proximal type ll RTA.

2-Distal type l RTA.

3-Hyperkalemic type lV RTA.

4-Type lll RTA which involve a mixed lesions of type l and type ll has been designated by some auther.

Distal Renal tubular Acidosis (Type I)

Is characterized by failure of the distal renal tubules to secrete the 1-3 mEq /kg/day of dietary acid (hydrogen ion) necessary to maintain acid-base homeostasis.

The urine cannot be maximally acidified (urine PH can not be reduced below 5.5) despite of severe metabolic acidosis and new bicarbonate cannot be generated.

Chronic positive hydrogen ion imbalance results in buffering by bone. This leads to increased skeletal calcium resorption, hypercalciuria, and increased risk of nephrocalcinosis and stones.

CAUSES OF DISTAL RTA

1-Primary sporadic or inherited.

2- secondary to:

1. -interstitial nephritis.
2. -obstructive uropathy.
3. -pyelonephritis.
4. -vesicoureteral reflux.
5. -lupus nephritis.
6. -drugs like Amphotericin B ,Lithium.

Proximal Renal Tubular Acidosis (Type II)

Is characterized by decreased proximal tubular reabsorption of bicarbonate. A reduction in the normally variable renal threshold of bicarbonate causes a marked bicarbonate leak, which disappears when serum bicarbonate falls below the threshold level (e.g. to 15mEq/L). The defect may be isolated or may occur with other proximal tubular abnormalities, such as glycosuria, aminoaciduria, phosphaturia . Diffuse proximal tubular dysfunction is termed Fanconi's syndrome.

Causes of proximal RTA

1-isolated which could be hereditary or sporadic.

2-Fanconi syndrome: which can be:

-primary either sporadic or hereditary like: cystenosis,lowe syndrome,Galactosemia,Tyrosenemia,Wilson disease.

-Fanconi syndrome can be secondary to: heavy metals, outdate tetracycline,gentamycine.

Type IV renal tubular acidosis

Includes a group of disorders, all of which are characterized by impaired aldosterone production or impaired renal responsiveness to aldosterone leading to hyperchloremic metabolic acidosis and hyperkalemia.

Causes of type IV RTA

1-Primary which could be hereditary or sporadic.

2-Secondary to : hypoaldostronism,Addison disease,CAH,DM,pyelonephritis,obstructive nephropathy,Drugs

CLINICAL MANIFESTATIONS OF RTA

-there is normal anion gap metabolic acidosis.

-Growth failure in the first year of life.

-Polyuria and dehydration.

-Anorxia,vomiting ,constipation , hypotonia.

-Rickets.

-Features of the underlying causes.

-Patient with distal RTA may present with hypercalciuria and nephrocalcinosis.

DIAGNOSIS OF RTA

1-the first step in evaluation of patient with suspected RTA is to confirm the presence of a normal anion gap metabolic acidosis by this equation(Na_Cl +HCO3),value <12 demonstrate the absence of an anion gap.

2-Serum electrolytes, blood urea nitrogen,calcium,phosphorus, and createnine with blood PH should be by venous puncture.

3-Urine PH can differentiated between proximal and distal RTA because urine PH <5.5 with metabolic acidosis indicate proximal RTA,while in patient with distal RTA urine PH will be >6 despite severe metabolic acidosis.

4- Urine analysis should be done.

5- Renal ultrasound is necessary to detect structural abnormalities.

TREATMENT

-The main step of treatment is bicarbonate replacement. Patient with proximal RTA require large quantities of bicarbonate.

-patient with Fanconi syndrome require phosphate replacement.

-patient with nephrocalcinosis and hypercalciuria needs treatment with thiazide diuretics.

- Patient with hyperkalemic RTA needs chronic treatment for hyperkalemia.