SPECIAL ARTICLE

Conservative Treatment of Chronic Renal Failure (CRF)

by

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I. Prevention of Decline in Kidney Function

The infant, child and adolescent who has irreversible impairment of renal function, regardless of the specific etiology, invariably experiences a progressive decline in glomerular filtration rate (GFR) over time. This decline in GFR can be attributed to an unremitting attack on the remaining unaffected nephrons by the primary disease process such as in a patient with acquired immune complex disease, but the reasons for the progressive decline in GFR in patients with congenital diseases are more difficult to identify.

Currently the hypothesis attributing the decline in GFR to damage to the remaining intact nephrons resulting from hyperperfusion is receiving increasing attention. Creation of CRF in the rat model by 7/8 nephrectomy leads to a rapid decline in GFR and focal glomerulosclerosis (FGS) in the previously normal glomeruli. This lesion of FGS is presumably a result of hyperperfusion of the remaining normal nephrons in order to compensate for the reduction in functioning renal mass.

In this animal model intervention with a low protein diet has markedly reduced the rapidly in decline in GFR, presumably because the reduced protein load affected a reduction in the magnitude of the hyperfusion. This concept has been utilized in man and uncontrolled studies have demonstrated a reduction in the rapidity of decline in GFR in patients given a low protein diet. These initial studies are short-term and no data are available indicating that ESRD can be prevented by a low-protein diet.

No data are available regarding the salutary effect of a low protein diet on preventing the decline in GFR in pediatric patients. Before such studies are undertaken it will be necessary to delineate the precise amount of protein intake that could facilitate the beneficial effect on the hyperpefusion process without adversely affecting statural growth in these patients. Until such precise information is available, it is logical to reduce the protein intake in infants, children and adolescents with CRF to the Recommended Daily Allowances for age in an attempt to thwart the inevitable decline in GFR.

A reduction in GFR is associated with decreased phosphorus excretion and resultant hyperphosphatemia. If the serum calcium level is maintained in the normal range, dystrophic calcification can occur and when the kidneys are involved nephrocalcinosis results. The development of progressive nephrocalcinosis can adversely affect the remaining functioning nephrons in patients with CRF.

Almost a decade ago studies in an animal model validated that hyperphosphatemia led to nephrocalcinosis and a decline in GFR in rats with CRF. Intervention with a low phosphorus diet prevented the nephrocalcinosis and the decline in GFR. Consequently, it would seem propitious to reduce phosphorus intake to the extent that the serum phosphate level is maintained within the normal range in infants, children and adolescents with CRF. As with a low protein diet there are no data to indicate that ESRD can be totally avoided by a low phosphorus diet.

Hypertension alone is associated with nephrosclerosis which can ultimately lead to a decrease in CRF and may progress to ESRD. Therefore, it is easy to comprehend that concomitant hypertension in patients with CRF can add to the rapidity of decline in GFR. Therefore, assiduous attention should be given to both avoiding and treating hypertension in infants, children and adolescents with CRF in order to reduce the potential adverse consequences of an elevated blood pressure on GFR.

Lastly, a significant number of pediatric patients with CRF due to congential lesions are unable to reabsorb sodium. These "salt wasters" can manifest a reversible decline in GFR which is attributable to hypoperfusion secondary to hypovolemia. Supplemental sodium intake is beneficial in maintaining the GFR in this situation. Identification of such "salt wasters" and introduction of appropriate preventive treatment, especially at times of stress, can prevent wide fluctuations in the GFR.

II. Symptomatic Treatment

A. Hyperkalemia

The primary clinical manifestation of hyperkalemia is a disturbance of cardiac rhythm; therefore measures should be taken to maintain the serum potassium level at < 6.0 meq/L during the course of CRF. The principle approach to maintain normokalemia is to limit the dietary intake of potassium. This can be accomplished with the assistance of a renal dietition. If episodes of hyperkalemia (serum potassium level > 6.0 meq/L) ensue despite dietary limitation, the use of either oral or rectal ion-exchange resin (kayexalate) in the dose of 1 mg/kg will lower the serum potassium level 1 meq/L. In addition, the use of a loop diuretic (furosemide) 1 mg/kg/day can be adjunctive by enhancing urinary potassium excretion.

B. Acidosis

The presence of acidosis can potentiate the development of hyperkalemia and adversely affect increases in statural growth in infants, children and adolescents with CRF. The acidosis arises both from an inability of the diseased kidney to excrete an acid load as well as from bicarbonate loss in the urine. Treatment is with oral alkali therapy with the dosage titrated to

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maintain the serum carbon dioxide content within the normal range.

C. Hyponatremia

Renal salt wasting is a frequent occurrence in pediatric patients with congenital renal disease. Such salt wasting can lead to hypovolemia and a further reduction in GFR. The latter can be exacerbated at times of stress. Treatment is with oral sodium chloride supplementation to maintain the serum sodium level within normal limits.

D. Renal osteodystrophy (ROD)

Hyperphosphatemia, hypocalcemia, reduction in 1.25 dihydroxycholecalciferol production by the diseased kidney and compensatory increase in the parathormone level all contribute to the osseous lesions of osteomalacia and osteitis fibrosa. The latter are pathologic entities that have radiographic correlates. Clinically, ROD is manifested by severe osseous deformities (primary valgus deformities of the long bones) slipped epiphysis (primarily slipped capital femoral epihysis), rachitic lesions and metastatic calcification. The severity of the clinical manifestations are generally related to the duration of the CRF. When severe the deformities can inhibit adequate ambulation. In addition, ROD may contribute to the growth failure of CRF. Therefore, assidious attempts should be made to prevent the development of ROD.

Prevention of ROD is directed toward: (1) maintaining a normal serum phosphate level with use of phosphate binders and limitation of phosphate intake. Since the relationship between aluminum toxicity (dialysis dementia syndrome, aluminum bone disease and aluminum related anemia) and aluminum containing antacids has been identified, it would seem prudent to avoid aluminum containing antacids as the primary phosphate binders. Fortunately, calcium carbonate is an adequate phosphate binder and is the current binder of choice for infants, children and adolescents with CRF; (2) increasing calcium absorption. This can be accomplished with a supplemental vitamin D preparation such as calcitriol which is a synthetic preparation of 1.25 dihydroxy vitamin D_3. The dosage of the latter requires titration to maintain a normal to slightly elevated serum calcium level while decreasing the serum PTH level toward normal values. Serial assessment of the alkaline phosphatase level is valuable in determining the degree of healing of ROD.

E. Hypertension

Persistent hypertension not only has an adverse affect on renal function, but also can compromise cardiac function and lead to cerebrovascular complications. Therefore, maintenance of a normal blood pressure in infants, children and adolescents with CRF is mandatory.

Treatment of hypertension is undertaken in the following sequence: (1) Dietary restriction of sodium and fluid intake. This is effective in mild hypertension, but is usually only adjunctive in severe hypertension; (2) The use of diuretics, primarily a loop diuretic (furosemide) facilitates sodium and water loss by the kidney and is an effective treatment of mild hypertension; (3) With significant hypertension antihypertensive medications are required. Renin mediated hypertension is frequently present in pediatric patients with CRF. In this situation an angiotensin converting enzyme inhibitor (captopril/enalopril) is quite effective as a primary anti-hypertensive agent in patients with CRF. With severe hypertension a peripheral vasodilator (minoxidil) may be required. As indicated previously, control of hypertension

is imperative, especially for the potential protective effect on the decline in renal function.

F. Dietary Restrictions

The availability of a sympathetic dietitian is of paramount importance when caring for an infant with CRF. A diet must be formulated which is palatable, yet is effective in reducing the intake of potentially toxic constituents. A diet must be developed which potentially limits the following: (1) Sodium, if hypertension is present; (2) Potassium, if the patient has the tendency toward hyperkalemia; (3) Phosphorus to reduce the need for phosphate binders and the potential development of ROD and (4) Protein intake to potentially preserve the rapidity of decline in renal function.

G. Dietary Supplements

In addition to dietary limitations, the renal dietitian must assure adequate nutritional intake. Primarily, adequate calorie intake is important because of the potential adverse impact on growth. In addition, if the diet is limited, adequate vitamin intake must be ensured.

H. Anemia

Symptomatic anemia usually requires blood transfusions. If the serum ferritin level is low, oral iron supplementation is required. The recent availability of synthetic human erythropoietin may limit the requirements for blood transfusions and the risk of hepatitis or AIDS in the future.

I. Growth

Growth retardation is a uniform problem in infants, children and adolescents with CRF. The precise etiology is unknown and multiple factors have been implicated: (1) age at onset of CRF; (2) primary renal disease; (3) adequate calorie intake; (4) renal osteodystrophy; (5) acidosis; and (6) reduced somatomedin activity.
Unfortunately, improved growth velocity rarely results from correction of those factors which can be avoided or improved. The results of a preliminary study using human growth hormone in children with CRF will be presented.

III. Indications for Initiating Dialysis in Children with CRF

In general, plans for insertion of a peritoneal or vascular access should be entertained once the GFR approaches 5 ml/min/1.73m^2 in an infant, child or adolescent with CRF.

Unequivocal indications for initiating dialysis are as follows: (1) episodes of congestive heart failure, either secondary to unremitting hypertension and/or persistent fluid overload; (2) pericarditis; (3) progressive ROD despite appropriate therapy; (4) uremic encephalopathy; and (5) failure to engage in the routine activities of daily living as a manifestation of uremia. The additional indications to initiate dialysis in infants have been detailed previously.

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