REGULAR REVIEW

Dietary treatment of renal insufficiency

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The kidney has considerable functional reserve. Glomerular filtration rate (GFR) can be reduced to around 50 ml/min/1.73 m² body surface area without producing significant biochemical disturbance or clinical disease. A further 50% reduction, to 25 ml/min/1.73 m² is generally associated with some biochemical disturbances including phosphate retention, renal bone disease, acidosis, and a variable degree of growth retardation. Even this degree of renal insufficiency is often relatively asymptomatic. When GFR declines to 10 ml/min/1.73 m² end stage renal disease is generally reached and some form of renal replacement treatment is required.

Although there are some exceptions, renal insufficiency of whatever aetiology once established tends to progress over a variable period of time to end stage renal failure. This deterioration continues even when the original insult has ended. Furthermore, when the end stage kidney is examined histologically, it is frequently impossible to determine the nature of the original disease because most progressive types of renal injury result in non-specific scarring, fibrosis, and glomerular sclerosis.

There are many factors that have an important role in the progression of kidney disease.¹ These include immunological injury, cytokine and other humoral factors, intraglomerular coagulation, proteinuria, abnormal intraglomerular hydrostatic forces with or without associated systemic hypertension, and renal parenchymal calcification. These in turn may be influenced by diet.

Effects of dietary protein on normal renal function

Dietary protein intake has been shown to have a significant effect on the function of normal kidneys in both adults and children. Alleyne found a significantly reduced GFR in malnourished children that increased after protein feeding.² These findings have been confirmed by others and are independent of dehydration and blood volume changes. Experimental studies have shown that GFR and effective renal plasma flow both decline when normal adults are fed a low protein diet, but increase after high protein feeding.³ A similar increase was observed after the intravenous infusion of amino acids.

Excess dietary protein has been shown to cause pathological changes in the kidneys of otherwise healthy animals,⁴ conversely animals fed a reduced protein diet live longer and have

fewer degenerative diseases than those fed freely.⁵ Both the quantity and quality of dietary protein intake would seem to have important effects on renal function.

Effects of dietary protein intake in renal disease

There are many animal studies demonstrating the adverse effects of dietary protein on the progression of renal disease. Even when 50% of renal function is lost by a uninephrectomy, glomerular sclerosis and proteinuria develop in animals fed high protein diets.⁶ Similar renal lesions have been produced in animals with experimentally induced nephritis. In contrast those fed low protein diets develop less severe renal lesions, less proteinuria, and live longer.⁷ These, and other, studies have renewed interest in the treatment of patients with renal insufficiency by low protein diets. Oldrizzi *et al* examined the effects of low protein diets (0.6 g/kg body weight/day) in adult patients with various renal diseases and compared these results with control groups with similar diseases fed normal diets.⁸ The protein restricted patients had slower rates of progression of their renal diseases than the controls. The rates of progression were faster in those with systemic hypertension or nephrotic syndrome. In contrast another study showed no beneficial effects of low protein diets on the rate of progression of renal diseases,⁹ and others suggest that the beneficial effects were selective as only those with primary glomerular diseases responded to the diet and the rates of decline in renal function were greater in males than females.^{10 11} In two studies in children randomly allocated to low protein diets (0.8-1.1 g/kg body weight/day) the rates of progression of renal disease were shown to be similar at 3 years in the treated group when compared with a control group of children fed normally.^{12 13} This degree of protein restriction had no adverse nutritional effects.

There are two major difficulties surrounding the assessment of the effects of protein restricted diets in children. The first concerns a definition of what constitutes a nutritionally safe low protein diet, and the second the techniques used to measure GFR. In adults a low protein diet of 0.6 g/kg body weight/day has been shown to slow the rate of progression of renal insufficiency without adverse effects upon nutritional status assessed by anthropomorphic measurements, plasma albumin concentrations, and protein metabolic rates.¹⁴

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There are no clear guidelines in children with renal failure as to what constitutes a safe low protein diet. Even the recommendation of what is the normal daily protein requirement in healthy infants and children has been criticised as being too high.¹⁵ It is generally assumed that the protein requirements of normal children are greater than adults because of the effects of anabolism and growth, but a nutritionally safe low protein diet has yet to be defined for children with renal failure.

The second methodological difficulty concerns the measurement of GFR. Most studies in humans have determined the rate of progression of renal disease by measurement of the plasma creatinine concentration. But its correlation with the measured GFR is imprecise, particularly when renal function is diminished.¹⁶ Furthermore, the plasma creatinine concentration is influenced by changes in the volume of total body water, which tend to increase in patients with renal failure (personal observations). This will result in an increased plasma volume and thus a lower plasma creatinine concentration than might be expected for the degree of renal failure. Finally, the rate of creatinine production is determined by muscle mass which will be effected by growth and nutrition. Both of which are impaired in children with advanced renal insufficiency and malnutrition.

What is the mechanism by which a low protein diet might influence the progression of renal failure? As renal function declines, the function of the remaining nephrons increases. This is accompanied by an increase in glomerular intracapillary hydrostatic pressure (glomerular hyperfiltration) which is harmful to the glomerular capillary, eventually leading to glomerular sclerosis. Experimental studies by Nath *et al* have demonstrated that the preservation of renal function in animals with established renal insufficiency fed low protein diets is associated with the reduction of glomerular capillary hydrostatic pressure.¹⁷ GFR is preserved because glomerular ultrafiltration increases despite the reduction of intracapillary pressure.

A variety of other hormone factors may also be involved in the regulation of the renal response to a dietary protein load. Glucagon is released by the pancreas after a protein meal or amino acid infusion and has been proposed to be the most likely candidate responsible for the hyperfiltration syndrome. Glucagon infusion increases GFR and renal plasma flow in man. In dogs infusion of glucagon into the portal vein is a potent stimulus of glomerulopressin, which is a glucuronide of low molecular weight that enhances GFR by reducing the tone of the glomerular afferent arteriole.¹⁸ Prostaglandins may also be involved as the increase in GFR after an intravenous infusion of amino acids can be blocked by the administration of indomethacin.

Effects of dietary energy intake

A relationship between energy metabolism, specifically basal metabolic rate, and protein metabolism has been recognised for many years

and it is likely that the ratio of energy intake to protein intake will prove to be an important factor in the dietary management of renal failure.

Uraemia is associated with abnormal glucose metabolism. A high plasma insulin concentration and a blunted glucose response to the administration of insulin both support the presence of insulin resistance in uraemia.¹⁹ Studies of the epididymal adipose tissue of normal rats have shown that the insulin stimulated transport and metabolism of glucose were both inhibited by the serum of uraemic patients without alteration of insulin binding. Furthermore, inhibition was markedly reduced in the serum after patients had undergone haemodialysis treatment suggesting the presence of a circulating insulin resistance factor in uraemia. Further studies have suggested the insulin resistant factor in uraemic serum is a small molecular weight peptide.²⁰

Hyperparathyroidism and vitamin D deficiency may inhibit insulin secretion in uraemia leading to glucose intolerance.²¹ The impaired peripheral utilisation of glucose and reduced cellular energy supply may contribute to the increased protein catabolism and growth impairment that are frequent findings in children with renal insufficiency.

But one study of children with renal insufficiency has failed to show an acceleration in growth velocities after energy supplementation²² and, in a second, slow improvement in growth was observed in 50% of the children who presented with renal insufficiency before the age of 2 years.²³

It is generally accepted that dietary energy supplementation aiming to bring the intake at least to the recommended daily allowance is necessary, but the true energy requirements of children with renal insufficiency have yet to be defined.

Effects of dietary phosphate on renal function

In 1972 Slatopolsky *et al* demonstrated that if the dietary phosphate was progressively reduced as GFR declined, then the development of secondary hyperparathyroidism in chronic renal failure could be prevented.²⁴ Studies feeding low phosphate diets to rats with various experimental renal diseases have shown that progression of renal insufficiency was prevented and that the proteinuria, histological damage, and renal parenchymal calcification found in the control animals fed freely did not occur.²⁵ In clinical practice the beneficial effects of a low phosphate diet on the development of renal bone disease have been confirmed and the combined dietary restriction of protein and phosphate in patients with chronic renal failure has been shown both to prevent renal osteodystrophy and to slow the progression of renal functional deterioration.²⁶

Effects of hyperlipidaemia on renal function

Disorders of lipid metabolism are well described in a variety of renal diseases including

nephrotic syndrome, diabetic nephropathy, and chronic renal insufficiency. In contrast, children with deficiency of the enzyme lecithin cholesterol acyltransferase have hyperlipidaemia at an early age and develop glomerular disease with nephrotic syndrome.²⁷ There is also experimental evidence which shows animals fed high cholesterol diets are more likely to develop focal segmental glomerular sclerosis than controls fed normal diets.²⁸ Furthermore, the incidence of focal segmental glomerular sclerosis is reduced by treatment with lipid lowering drugs. The beneficial effects of these drugs occur independent of the normal compensatory increase in glomerular capillary pressure, suggesting that hyperlipidaemia has a specific adverse effect on renal function. The development of cholesterol lowering drugs, such as the 3-hydroxide, 3-methylglutaryl coenzyme A reductase inhibitors may enable us to examine the beneficial effects of reducing circulating cholesterol in steroid resistant nephrotic syndrome as well as renal insufficiency.

Miscellaneous dietary factors

(1) ACIDOSIS

When a low protein diet is prescribed a number of metabolic adjustments take place. These include a reduction in protein turnover largely due to a reduction in proteinolysis. Studies have shown that this adaptive response is impaired in the presence of metabolic acidosis which increases muscle protein breakdown and decreases nitrogen utilisation.²⁹ Metabolic acidosis overrides the adaptive responses to a low protein diet diminishing the efficacy of the diet and accelerating the loss of lean body mass. Correction of the acidosis decrease skeletal muscle catabolism.

(2) SODIUM AND POTASSIUM

As GFR falls, the kidney's ability to excrete a dietary sodium load is increasingly impaired. Salt and water retention become manifest as oedema, hypervolaemia, and hypertension. In these situations, a reduced dietary sodium and fluid intake is required to maintain balance. Conversely in some types of progressive renal disease, such as renal dysplasia or the nephropathy after resection of urethral valves, inappropriately high urinary sodium losses occur.

Studies have shown that normal rats fed salt deficient diets have a reduced rate of gain in both weight and length and that this is associated with a diminished nitrogen balance, muscle protein synthesis, and decreased muscle RNA concentrations. These changes were rapidly reversed by sodium supplementation.³⁰ Careful attention to the sodium balance of children with renal disease is important so that optimum growth rates may be achieved.

Hyperkalaemia is a frequent problem in children with progressive renal disease. Only 2% of total body potassium is in the extracellular fluid space, but its concentrations is critically important. The concentration of

potassium in the plasma depends upon the ratio of intracellular to extracellular potassium and the rate of excretion by the kidney. The normal kidney is extremely efficient in excreting large loads of potassium within a few hours, but this is impaired in renal failure when potassium restricted diets are necessary.

(3) VITAMINS

Bone disease occurs even in patients with mild to moderate renal impairment. This is due to the reduced serum concentration of 1,25 dihydroxycholecalciferol and the diminished effects of vitamin D on the bone and the gut. Early treatment with 1,25 dihydroxy vitamin D has been shown to produce a significant fall in the alkaline phosphatase concentration and histological evidence of bone healing.³¹ This occurs without deterioration of renal function provided plasma phosphorus concentrations are controlled.

Practical issues of dietary treatment

In mild renal insufficiency dietary management seldom poses major practical problems but as renal function declines (GFR less than 25 ml/min/1.73 m²) and uraemia increases adequate dietary intakes are compromised by anorexia, altered taste perception, multiple drug administration, and behavioural disorders. Vomiting due to gastro-oesophageal reflux, delayed gastric emptying, and uncoordinated gastric electrical activity may add to these difficulties.³² At this stage the involvement of a skilled paediatric dietitian who is experienced in the management of children with renal insufficiency and the associated physiological, biochemical, and psychological factors effecting appetite is essential.

Protein and energy intakes

It is usual to restrict dietary protein intakes, however the minimal amount of protein required for growth must be provided and this should be adjusted as the child gains weight. Although nutritionally safe low protein diets have yet to be established in uraemia, it is usual to recommend protein intakes of 1.8 g/kg/day for infants under 1 year of age, 1.0–1.5 g/kg/day for infants aged 1 to 2 years, and 1 g/kg/day for children aged 2 to 16 years.

The majority of the protein (approximately 70%) should be of high biological value with an optimal amino acid profile. In infants this can be achieved by recommending breast milk or a low solute whey based formula. The protein requirement is met by the appropriate volume of infant formula diluted with water to the required volume. This is then supplemented with a carbohydrate polymer and/or fat emulsion to achieve the recommended energy intake for the child's age. Breast fed infants should be demand fed and their energy intakes supplemented by juice or water containing a glucose polymer. The tolerance of energy supplements varies and to avoid gastrointestinal symptoms they should be introduced and

increased slowly. Infants with a gastro-oesophageal reflux often tolerate carbohydrate polymers better than fat emulsions which may delay gastric emptying.

Weaning foods can be introduced at 3 months of age. Low protein foods such as baby rice and pureed fruit are usually given first, this avoids parental anxiety if protein containing foods are refused. One gram protein exchanges are gradually introduced as the solid foods are accepted. The decrease in dietary protein contribution derived from reducing milk intake should be taken into consideration. Once the infant is fully weaned care should be taken to ensure that sufficient protein of high biological value is given.

Because infant formula milks contain significantly less protein, sodium, potassium, and phosphate concentrations compared with cows' milk, these milks are often recommended for the first two years of life. Older children find cows' milk more palatable, but only limited quantities are allowed.

Infants and children with chronic renal insufficiency are assumed to have normal energy requirements and at all ages the estimated average requirement for energy³³ should be met. Growth should be assessed on an individual basis and appropriate adjustments to energy intake made. Small frequent intakes are often more successful at tempting poor appetites and energy intakes can be enhanced using high energy foods, for example butter and cream, and commercial low electrolyte energy supplements. Unfortunately, high energy low protein products are seldom accepted by children.

Sodium and fluid intakes

It is normal practice to restrict the sodium content of the diets of most infants and children with chronic renal insufficiency except in those where there is a high urinary sodium loss. These children may also have an obligate high urine loss and require increased fluid intake, but in most cases fluid requirements are usually normal. Towards end stage renal failure fluid restrictions may be necessary.

Potassium and phosphate intakes

Restriction of dietary potassium and phosphate as renal failure progresses imposes further constraints on an already restricted diet. The serum phosphate should be maintained, ideally towards the lower end of the normal range by dietary restriction and the use of phosphate binders such as calcium carbonate. Aluminium hydroxide is not recommended for children because of the increased risk of aluminium toxicity.

Vitamin and mineral intakes

There are no specific vitamin or mineral requirements. Dietary assessment will identify nutritional inadequacy, allowing supplementation to be given on an individual basis. Special attention should be given to infants on protein

reduced infant formula as the vitamin and mineral content of the milk will also be reduced. 1,25 Dihydroxy vitamin D is prescribed and the dose adjusted to maintain the plasma calcium concentration between 2.5–2.7 mmol/l.

Dietary non-compliance is a major problem, especially in adolescents when peer group pressure becomes a factor. Dietary restrictions severely compromise the variety in the diet. Popular foods are often excluded, for example cheese which is high in protein, sodium, and phosphate and chocolate, crisps, and chips which are high in potassium. Skilled dietetic advice will help to ensure maximum dietary variety.

When faced with a child who is refusing to eat, and as a result is failing to thrive, many parents become extremely anxious and require psychological support.

Over the past decade the realisation that many children with renal insufficiency are failing to achieve an adequate dietary intake has prompted a more aggressive approach to feeding methods. Feeding via fine bore nasogastric tubes and gastrostomy routes have become popular. When renal insufficiency starts in infancy growth may be significantly impaired,³⁴ and children under 2 years of age may particularly benefit from these feeding techniques. Aggressive nutritional treatment in the first two years of life can lead to dramatic catch-up growth.²³ As nutritional support may be long term, gastrostomy feeding is often the preferred method.

Enteral feeds should be tailored to suit the child's requirements by complementing their oral intake. If the protein requirement is met orally a feed containing only energy (carbohydrate polymer and fat emulsion) is used. If protein is added to the feed, infant formula, a nutritionally complete supplement, or a protein module may be used. Short chain peptide, elemental feeds can be advantageous if there is poor gastric emptying, however, care must be taken that they do not provide an excessive protein or electrolyte load. Feeds are best tolerated if they are administered by a slow overnight continuous infusion permitting the encouragement of oral intake during the day. Dietary intake and growth should be assessed regularly and feeds adjusted accordingly. Vitamin and mineral supplementation must always be assessed on an individual basis.

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