Growth and Nutrition of Children with Chronic Renal Failure

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It has long been recognized that chronic renal failure (CRF) in children is associated with growth delay [1]. Still In our days growth retardation remains a major impediment to full rehabilitation of children with CRF [2]. The reduction of height velocity frequently results in diminished final adult height [3]. Psychosocial consequences of short stature, such as difficulties in peer relationships and self-esteem, have been well documented [4, 5]. The children with both CRF and short stature might be particularly vulnerable in these problems [6].

Growth failure was associated in a recent study with a more-complicated clinical course and increased risk of death for children with kidney failure. At the same study a higher proportion of deaths in children with growth failure was found and were attributed to infectious causes [14].

Several factors have been identified as contributors to impaired linear growth and they include protein and calorie malnutrition, metabolic acidosis, salt wasting, anemia, and renal osteodystrophy [7]. In addition there is evidence for a correlation between solute clearance and growth, with residual renal function exerting a significant influence on that outcome [15]. Despite vigorous treatment of these factors, patients with CRF continued to grow poorly. It was hoped that, with modern dialysis and transplantation, these patients would have normal growth or even catch-up growth. Although normal growth may be seen after transplantation, catch-up growth is rare [7].

In the early 90's a significant improvement of growth rate of children with recombinant human growth hormone (rhGH) has been documented in various multicenter studies in children on conservative treatment, dialysis and after renal transplantation [8, 9, 10, 11, 12]. After more than a decade of experience the safety and efficacy of long-term treatment with recombinant human growth hormone (rhGH) in children on peritoneal dialysis has been established [13].

Assessment and interpretation of growth and nutritional status.

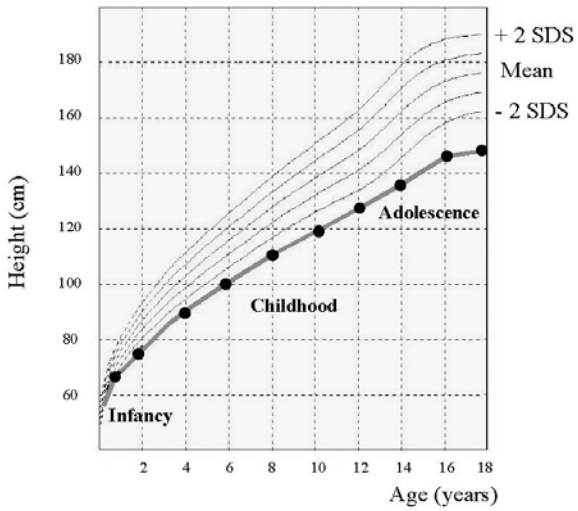
The reliable assessment of growth and nutritional status growth of children with CRF requires staff who have received training in the use of appropriate measuring techniques and equipment. Weight, height (or supine length for patients up to 2-3 years or age) and head circumference (for children up to 2 years of age) should be measured and plotted so that growth velocity can be calculated. The growth in height is divided by mathematical modelling in three phases: infancy, childhood and puberty. There are differences in growth regulation during these phases.

a. During the first two years of life nutrition is the most important factor for growth. Proximately 30% (40 cm) of the total postnatal statural growth occurs in this period [18].

b. During childhood the role of the somatotropic hormone axis becomes more important and thyroid hormone and nutrition have a role of lesser importance. Height velocity is decelerating in this period (figure 2) to an almost constant rate approximately of 5 cm/year.

c. In puberty the gonadotropic hormone axis plays a major role. In average the growth rate doubles during puberty. The growth spurt is lasting between 2.5 and 3 years, and is starting in girls at approximately 11 years and in boys about two years later. The average gain in height during the growth spurt is 25 cm in girls and 28 cm in boys. This pattern of pubertal growth was recently confirmed in a control group of ESRD patients followed in the late 1990s who were not treated with recombinant GH [19].

Figure 1. Height curve of a boy with CRF from infancy



The extent of growth retardation depends on the period that CRF was manifested. Onset of CRF in utero or during infancy is associated with significantly diminished final height. Growth of children with CRF during the first two years of life was affected in 50% of them. It was also found that height SDS was already reduced at birth, decreased further during the first 3 postnatal months. Then after a transient stabilization of growth rates, a further loss in relative height apparently occurs between 9th and 18th month of age [18]. During childhood these patients usually have a growth pattern parallel to the percentile curves (figure 1). However

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significant decrease of growth velocity might occur in these patients when there is not appropriate management of the contributing factors of the development of growth failure. Finally pubertal height gain of CRF patients is only 50% of that observed in healthy children. In addition on average, the onset of puberty in these children is delayed by 2 years.

Clinical assessment of children should be combined with regular dietary assessments which can be with three-day dietary diaries or by dietary recall in clinic by an experienced dietician. Nutrient intakes should be computer analysed and reference made to national guidelines.

Methods for assessment of body composition are usually based on a two or three component model and use several different measurement techniques. Two component models divide the body into fat mass or fat-free mass (the remainder after fat is subtracted). The three-component model divides the body into fat mass and two components of fat-free mass (bone mineral and lean tissue). A two-component criterion model typically uses hydrodensitometry (hydrostatic weighing) measurement technique as a gold standard and in clinical practice anthropometric measurements and bioelectric impedance (BIA) are used. The three-component model uses dual-energy x-ray absorptiometry (DEXA) measurements. With carefully applied skinfold [16] or BIA methods, it is possible to estimate relative body fat percentage with an error of 3% to 4%. However when poor measurement techniques are applied or if the measurement equipment is poorly maintained and calibrated, the errors associated with the body composition estimate will be much larger.

Serum albumin has been identified as a reliable marker for nutritional status. In addition it has become increasingly clear that there is an inverse relationship between serum albumin and mortality rates in adults maintained on chronic dialysis. While dietary protein intake and dialysis adequacy are important variables determining nutritional status, there is increasing evidence linking chronic inflammation in uremia and nutritional status. Such a finding could be consistent with chronic inflammation playing a role in determining the albumin concentration in addition to nutritional status.

Nutrition and growth

Children with CRF on conservative treatment or on dialysis are often anorectic. In the past malnutrition was considered as the main cause of growth retardation in these patients. The negative effect of malnutrition on growth during the first two year of life is well established [19]. However no correlation was found between energy intake and growth rate in older children [20]. A minimum of energy intake of more than 70% of the recommended daily allowance (RDA) is generally accepted as a prerequisite for normal growth velocity. Attempts to improve growth in older children with high-energy diets were generally disappointing [21]. In a recent multicenter study was found that energy intake was less than 70% in 20% of children. It was of interest that only 4% of patients lost weight in relation to height during a mean follow-up of 2.1 years. Therefore it is reasonable to assume that the majority of these patients had adequate energy intake and poor growth [22]. In all children with growth failure before rhGH treatment aggressive nutritional intervention should be started when their weight for height standard deviation score is not acceptable (< -2) in the absence of oedema.

An increase in resting energy expenditure has been described in children treated with rhGH possibly related to increased protein turnover [23]. Therefore meticulous nutritional care should also be provided at the period of rhGH treatment in order to achieve an energy intake of 100% of recommended daily allowances (RDA) and administer the appropriate amount of protein. There is evidence that there is a positive effect of rhGH treatment on protein metabolism. An improvement in nitrogen balance as evidenced by a falling of blood urea nitrogen and urea nitrogen appearance with a constant protein intake was noticed in nine prepubertal patients on peritoneal dialysis treated with rhGH. A significant increase in serum creatinine and creatinine excretion with a constant weekly creatinine clearance and the increase in mid-arm muscle circumference were indications of an improvement in lean body mass. In addition, there was an improvement in the pattern of plasma amino acids and an increase in serum albumin, possibly as a result of the improvement of protein metabolism [24]. In another study, weight gain and an increase of IGF-1 and transferrin levels was found in malnourished dialysis patients treated with rhGH. A decrease of BUN level was also documented, despite the constant oral intake, suggesting that short-term rhGH administration was associated with an anabolic reaction in these patients [25]. In addition a significant increase of lean body mass was found in thirty-three prepubertal patients with CRF treated for two years with rhGH [26].

In summary, available evidence suggests that growth retardation might be the result of late referral and/or suboptimal clinical care. [27]. Management of malnutrition, renal osteodystrophy, metabolic acidosis, salt wasting and anemia should be optimal before rhGH initiation. Finally there is some recent evidence that the beneficial effect of rhGH on height might result in an eventual increase in adult height [18, 28].

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