Growth in Children with Steroid Sensitive Nephrotic Syndrome

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Abstract

Background: Nephrotic syndrome in children usually has an onset between 2-8 years of age and steroids form the mainstay of management. Therapy may affect growth in children with relapsing nephrotic syndrome. This study was carried out to correlate growth with the cumulative dose of steroids in children with steroid sensitive nephrotic syndrome (SSNS).

Methods: Data of 35 children with SSNS was analysed retrospectively. They were divided into two groups. Group I received prednisolone only and Group II received levamisole and or cyclophosphamide in addition to steroids. Their heights were recorded at the time of inclusion and again one year later. The SD scores for age were determined. Growth rate as a change in the SD score over one year (Δ SD score) was correlated to the cumulative dose of steroids over the same period using the Pearson's correlation.

Result: There were 24 (68.6 %) boys and 11 (31.4 %) girls (M:F ratio 2.18:1) in the age group of 17 months to 11 years at inclusion. Group I constituted 19 (54.2 %) and Group II, 16 (45.8 %). Pearson's correlation coefficients for all children, Groups I and II were -0.341, -0.441 and -0.255 respectively indicating "Fair correlation". This indicates that as the cumulative dose of steroid increases the growth retardation becomes more apparent.

Conclusion: Growth retardation is proportional to the cumulative dose of steroids in children with SSNS.

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Key Words : Steroids; Cumulative dose; Nephrotic syndrome; Growth

Introduction

Growth is an essential feature of childhood. It depends on genetic, nutritional, social and emotional factors. It is affected by chronic systemic disease. Growth follows a sigma shaped curve with a high velocity in the early postnatal period and during puberty, but a steady rate during mid-childhood. Nephrotic syndrome occurs most commonly in the age group of 2-8 years when the growth rate is at a steady state. Patients having frequent relapses and requiring repeated courses of steroids often develop steroid toxicity, including growth retardation [1]. It is known that daily, supraphysiologic doses of glucocorticoids inhibit growth by multiple mechanisms including impaired release of growth hormone and decreased activity of insulin-like growth factor-1 (IGF-1) in growing bones. However their effect in Indian children with steroid sensitive nephrotic syndrome (SSNS) has not been described. This study correlates the growth rate with the cumulative dose of steroids in children with steroid sensitive nephrotic syndrome.

Material and Methods

The data of 35 children with SSNS on regular follow-up for a minimum period of one year at the nephrology clinic of a tertiary level hospital was analyzed retrospectively. These

children were divided into two groups. Groups 1 received prednisolone in the standard dose for the initial episode at 2 mg/kg/day for six weeks followed by 1.5mg/kg on alternate days for six weeks and relapses were treated with 2 mg/kg/day till remission followed by 1.5 mg/kg/day for four weeks as per the guidelines of the Indian Academy of Pediatrics [2]. Group II consisted of children who in addition to the steroids had received steroid sparing agents like levamisole and or cyclophosphamide during the year of study.

The height was measured using a stadiometer on at least two occasions, first at the time of inclusion in the study and second time a year later. The height was converted into an SD (standard deviation) score (Z score) using the software "CDC EPI Info 2002" which requires age and height for calculation. The change in SD scores over one year was noted as Δ SD score. The cumulative dose of steroids received during the year was calculated for each patient and recorded as mg/kg/year. Correlation of the growth rate as a change in the SD score over one year was done with the cumulative dose of steroids using the Pearson's correlation and its significance noted. Children with steroid resistance or those with a poor follow-up during the study period were excluded from the study.

Results

Records of 35 children with SSNS were analysed. There were 24 (68.6 %) boys and 11 (31.4 %) girls with the M: F ratio

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of 2.18:1. Their age ranged from 17 months to 11 years at inclusion in the study. Group I constituted of 19 (54.2 %) children and Group II had 16 (45.8 %), the details of which are given in Table 1.

The correlation of cumulative dose of steroids (mg/kg/yr) and Δ SD scores for height are depicted in Table 2 and Fig. 1 along with the Pearson's correlation. Pearson's correlation coefficients for the entire study population, and in Groups I and II were -0.341, -0.441 and -0.255 respectively and indicate "Fair correlation". This indicates that as the cumulative dose of steroids (as mg/kg/year) increases the Δ SD score decreases, thereby confirming that growth retardation worsens. However, this was statistically significant ($p=0.045$) for patients in both the groups.

Discussion

A major cause of growth retardation in patients with nephrotic syndrome in the pre-corticosteroid era was protein calorie malnutrition secondary to poor appetite, protein loss in the urine and malabsorption due to edema of the gut. Today, the major cause is corticosteroid therapy, though probably emotional deprivation and chronic anxiety may also play a role. The dosage and duration of glucocorticoid treatment in nephrotic syndrome and the evolution of renal function are predominant factors affecting growth. Prolonged high-dose corticosteroid administration suppresses growth rates [3].

The loss of insulin-like growth factor-I (IGF-1) and IGFBP-3 found in nephrotic children may directly prompt growth defect and retardation. In addition, glucocorticoids are believed to be associated with overt elevation of serum IGF-I levels suggesting potential development of IGF resistance, one of the main factors responsible for persistent growth retardation [4].

Our study shows that there is a fair correlation between reduced growth rate and the cumulative dose of steroids in Indian children with SSNS. In a similar study the growth in both boys and girls, assessed by

changes in height standard deviation score (Δ SD scores), worsened significantly with chronological age. There was a significant negative correlation between Δ SD score and duration of treatment in boys but not in girls [5].

In a long term study of adults who had steroid sensitive nephrotic syndrome in childhood, final adult height (median SD score 0.4, range 3.3 to +1.3) and body mass index (BMI) were normal. Growth and renal function were normal, and overall morbidity was low [6]. Another study shows that overweight and obesity appears to be protective against glucocorticoid-related growth retardation in SSNS [7]

Children with minimal change nephrotic syndrome are usually responsive to glucocorticoids. The initial daily administration of glucocorticoids can usually be reduced to alternate-day therapy in a relatively short time. Growth failure was observed only in children with prolonged daily steroid therapy, while alternate day steroids were not associated with significant growth impairment [8], and there was no indication for growth hormone therapy (rhGH). However, rhGH has been used in steroid dependent nephrotic syndrome with a significant positive effect on height, bone mineralization, and body composition, but a relative acceleration of bone age [9]. The significant increase in growth associated with diminished use of steroids makes the use of steroid sparing agents (like alkylating agents) reasonable for children with nephrotic syndrome who show signs of decreased growth velocity [10,11]. This is noted in our study as well, where children who had received steroid sparing agents also had significant growth retardation but this did not correlate well (Pearson's correlation: -0.255, p 0.34) with the cumulative dose of steroids which

Fig 1 : Correlation of cumulative steroids with Δ SD scores for height over one year

Table 1

Age and gender distribution (n=23)

Category	Number	Boys	Girls	M:F ratio	Median age (months)
All patients	35	24	11	2.18:1	54
Gp I	19	14	5	2.8:1	42
Gp II	16	10	6	1.66:1	60

Table 2

Correlation of cumulative dose of corticosteroids and growth over one year

Category	Number	Mean cumulative steroids (mg/kg/yr)	Average Δ SD scores	Pearson's correlation	Significance
All patients	35	160.9	- 0.422	-0.341	0.045
Patients on steroids only (Group I)	19	125.7	- 0.363	-0.441	0.059
Patients on steroids and other drugs (Group II)	16	198.2	- 0.484	- 0.255	0.341

was the highest in this group (198.2 mg/kg/year). This may in part be explained by some catch up growth once steroid sparing agents were administered and the steroids tapered.

At present, the best way to prevent growth impairment is to avoid an unnecessary prolonged course of treatment with large doses of corticosteroid, to provide adequate intake of calories and proteins, regularly monitor growth and to try to decrease psychological stress.

Conflicts of Interest

None identified

Intellectual Contribution of Authors

Study Concept : Col M Kanitkar

Drafting & Manuscript Revision : Lt Col K R Mohan

Statistical Analysis : Lt Col K R Mohan, Col M Kanitkar

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