High Protein Nutritional Supplementation increases Serum IGF-I Concentrations in Short Children with Low IGF-I

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Introduction

Milk supplementation increases serum insulin-like growth factor I (IGF-I) concentrations in healthy children and the effect may be attributed to elevation of insulin and/or direct effects of milk proteins. Low serum IGF-I concentrations are common among children with short stature and may be associated with a continuum of various degrees of GH deficiency and GH insensitivity, the latter commonly associated with poor nutrition/malabsorption. Effects of nutritional supplementation in short children with low serum IGF-I levels has not previously been studied.

Objectives

- To investigate whether 7 days high protein nutritional supplementation increases serum IGF-I levels in short prepubertal children with low serum IGF-I.
- To evaluate the IGF-I response as a potential diagnostic marker of the cause of low baseline IGF-I in short children (malnutrition or GH deficiency)

Methods

- This is a prospective, single group, seven day intervention trial as outlined in figure 1.
- Short, prepubertal 3-13 year-old children with low serum IGF-I concentrations were given a milk based protein supplementation of 18 g/10 kg body weight and day during 7 days.
- 17 children were included in the study.
- Diet was assessed using a three days food record prior to the baseline visit and the three last days of the intervention.
- Baseline and end of intervention serum IGF-I and markers of GH/nutritional status were obtained
- Hormonal analysis were performed using commercially available assays.

Inclusion criteria

- Prepubertal
- Age 3-13 years
- Height SDS < -2
- Serum IGF-I SDS <-1

Exclusion criteria

- Chronic illness
- Syndromes

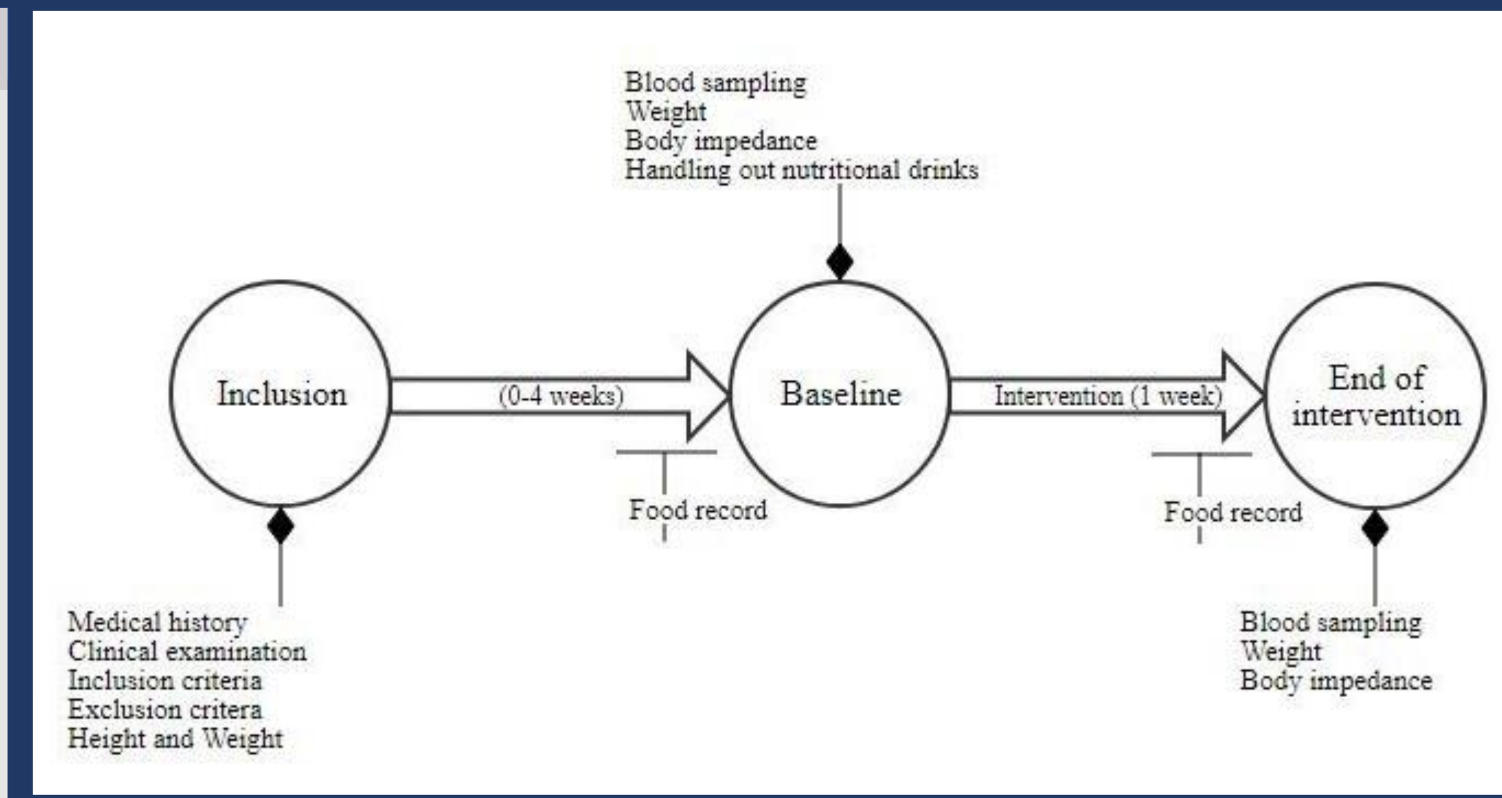

Figure 1. Flowchart showing the study design.

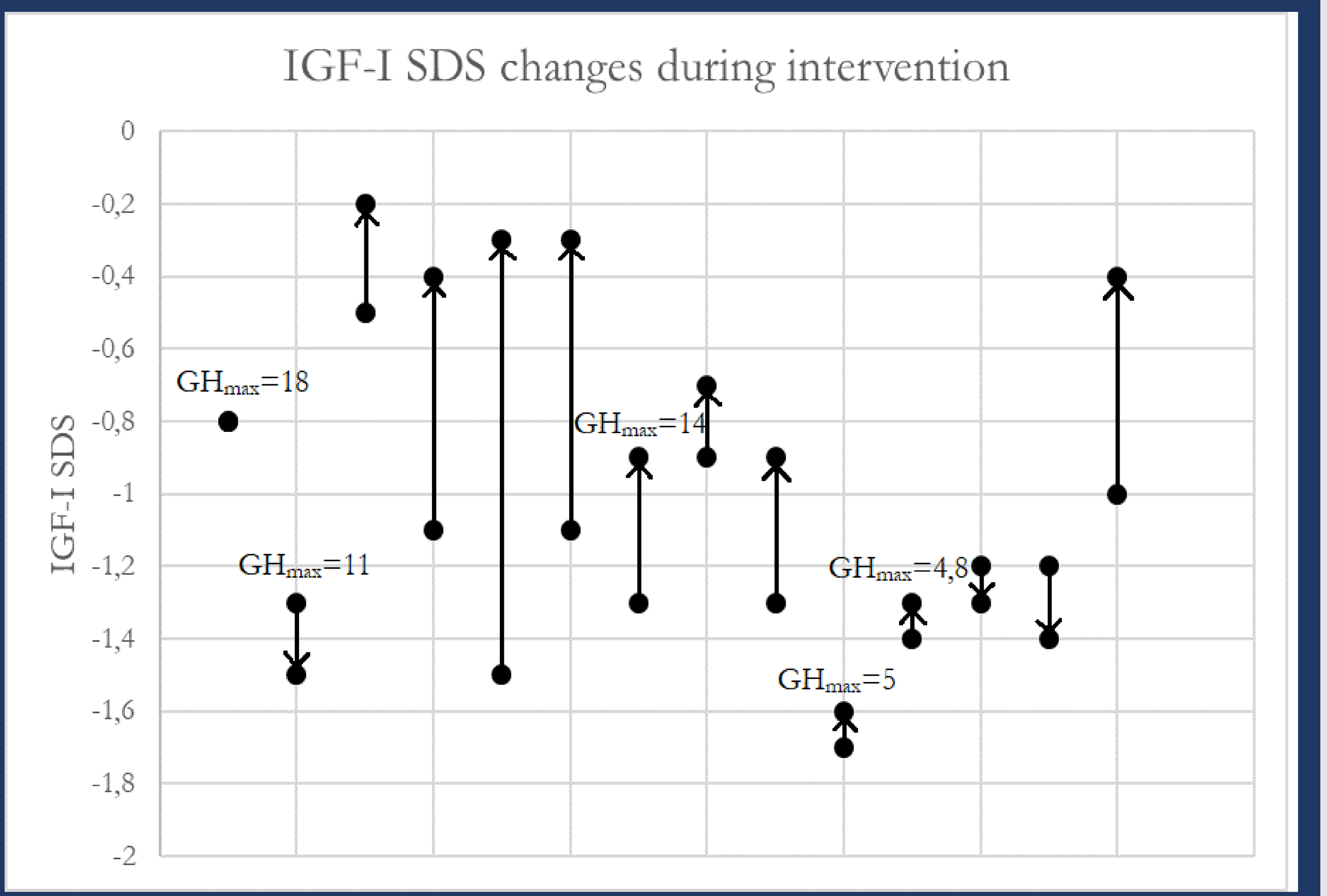

Figure 2. Individual IGF-I SDS at baseline and after intervention and GHmax from overnight profiles in those patients that based on clinical suspicion of GHD was further evaluated.

	Baseline	End of intervention	Number	P values
IGF-I$_{RIA}$ (µg/L)	82.9 ± 24.9	92.4 ± 31.4	14	0.017*
IGF-I$_{RIA}$ (SDS)	-1.16 ± 0.3	-0.86 ± 0.49	14	0.015*
IGFBP-3 (µg/L)	3130 ± 629	3042 ± 606	14	0.28
IGFBP-3 (SDS)	0.39 ± 0,94	0.26 ± 0.76	14	0.37
Insulin (mIE/L)	3.6 (2.9:5.0)	5.5 (3.05:7.0)	13	0.35
SHBG (nmol/L)	160 ± 23.2	136 ± 35.4	14	0.0083*

Table 1. IGF-I, IGFBP-3, insulin and SHBG at baseline and end of intervention. Values are expressed as mean ± SD or median and inter quartile range (IQR). Statistics performed by paired t-test or Wilcoxon's signed Rank Test.

Results

- 14 of 17 patients finished the 7 days intervention.
- Protein intake increased significantly (P< 0.001) while fat energy percentage decreased (p=0.005). Intake of total or weight based energy and carbohydrate energy percentage were unchanged.
- Children increased their mean body weight by 0.39 ± 0.29 kg (P<0.001).
- IGF-I SDS increased corresponding to an increase of 11.1 ± 14.7 % (P=0.017).
- Fasting morning Insulin was unchanged although suppression of insulin regulated SHBP suggests increased nightly insulin release.
- IGFBP-3 SDS was not low at baseline and did not change.
- There were no correlation among clinical markers of nutritional state at baseline or their changes during the intervention (weight SDS, BMI SDS, 3-day energy or protein intake and IGF-I/IGFBP-3 ratio) and there was no correlation to the IGF-I increase. IGF-I changes and weight SDS at baseline tended to correlate (r=-0.51, p=0.063).
- GH release was evaluated based on clinical suspicion of GHD and GHmax < 10 was found in 2 children with a minimal IGF-I response. In the remaining three, GHmax > 10 ug/L was associated with increased, slightly decreased or unchanged IGF-I, respectively.

Conclusions

- High protein supplementation has the potential to increase IGF-I from a low baseline level in short children. The possibility that this may have long term effect on height should be investigated.
- The lack of correlation among common clinical markers of nutritional deficiency underlines the need for a specific and sensitive diagnostic marker. Larger studies that include GH testing are warranted.
- Low IGF-I and normal IGFBP-3 SDS at baseline (claimed to indicate malnutrition) does not exclude GHmax < 10 ug/L.

Acknowlegements and disclosures

The authors have nothing to disclose.

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