Nutritional Growth Solutions

SAN DIEGO, CA

Healthy Heights Academic Summary Grow Daily Boys 10+

Effect of a nutritional supplementation on growth and body composition in short and lean preadolescent boys: A randomized, double-blind, placebo-controlled study.

Healthy Heights Academic Summary: Grow Daily Boys 10+

Overview

The first part of a two-phase, double-blind, placebo-controlled trial of the effects of nutritional supplementation on short and lean prepubertal 10-14.5-year-old boys found that the formula resulted in significant increases in fat-free mass and muscle mass over the course of the clinical trial, suggesting that the supplement not only promotes growth but also more optimized body composition.

Additionally, the participants over the age of 11.4 years who were in the formula group had the added benefit of maintaining their height percentile (statistically defined and studied as Height SDS), which typically decreases in boys who have relatively delayed puberty as compared to their peers.

Effect of a nutritional supplementation on growth and body composition in short and lean preadolescent boys: *A randomized, double-blind, placebo-controlled study*

INTRODUCTION

Children go through two stages of rapid growth that have wide-ranging and long-lasting biological consequences, in large part determining their adult characteristics such as height, weight and body composition.

The first stage is within the first year of infancy, in which the intake of key macro and micronutrients is easier to achieve as it is provided by breast milk or formula.

The second stage takes place within the pubertal period, commonly taking place from the ages of 10-14.5 years old. Both of these phases are resource-intensive and highly taxing on the body's metabolic systems, but it is often this second stage that goes understudied. Although there have been a multitude studies on the effect nutrition plays on pubertal development within developing nations, there has been a notable lack of research into this phase of growth within already developed nations, due largely to the misperception that optimal nutritional intake has become an insignificant issue within developed nations.

However, many children even in developed nations are unable to consistently receive the nutrients necessary for ideal growth rates due to a lack of availability and affordability of nutritionally dense foods. Naturally, these children can often suffer from poor nutrition that likely has significant negative impacts on their rate of physical development.

As males and females undergo rapid growth associated with the pubertal period, they require differing levels of energy. As they require more energy, boys often face significant hurdles due to their below-average physical development, often subject to both physical limitations and social ostracization that can have long-lasting, negative ramifications on their future.

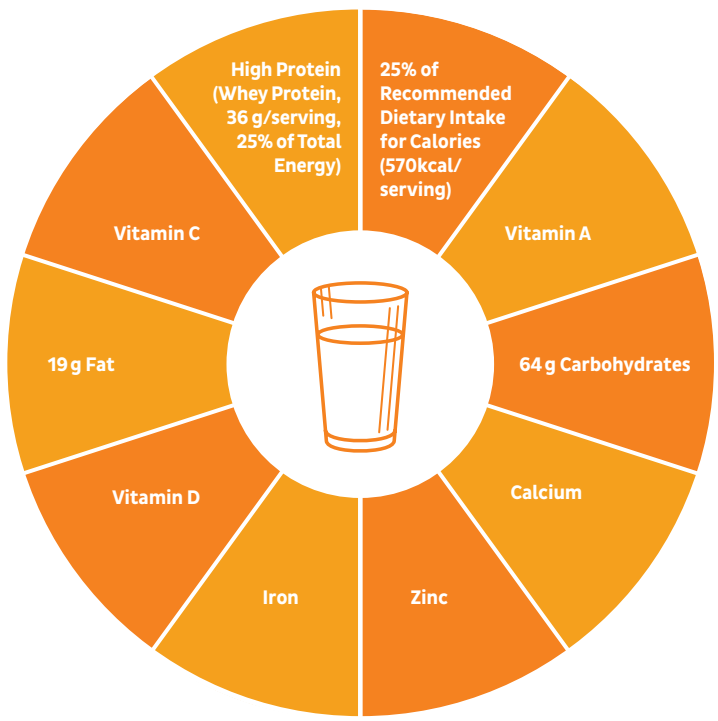
METHODOLOGY

160 male children between the ages of 10 and 14.5 years old were enrolled in the first phase of a 12-month, double blind, placebo-controlled study to test the effectiveness of a new nutritional supplement designed to deliver optimum levels of the key nutrients crucial for healthy pubertal growth. In addition to their age, the children were selected based on a number of other inclusion factors, such as being at Tanner Stage 1 (pre-pubertal stage) of physical development and measuring at or under the 10th percentile of height and weight for boys their age according to the CDC Growth Charts.

Several criteria for exclusion were also established, focusing on pre-existing conditions that could skew the results of the trial. Such exclusion criteria included chronic diseases, gastrointestinal diseases, genetic syndrome and growth hormone deficiencies.

Of the 160 participants, 86 of the enrolled participants were randomly assigned to the formula group and 74 into the placebo group - at baseline, no significant differences were recorded in the health of enrolled participants.

During the study, the participants arrived every three



months to a clinical study visit. All participants were given a three-month supply of either the formula or the placebo, along with specific instructions on consumption and tracking. Each participant was instructed to consume one sachet of formula or placebo mixed in 200ml of water, after dinner. To best replicate how such nutritional supplementation would be delivered outside the controlled parameters of the study, the researchers identified two issues that could significantly impact the results of the experiment and took necessary steps to ensure such impact would be kept to a minimum.

The first was the possibility for user error - the powder formula was distributed in single-serving sachets that parents and children would likely be familiar with from other nutritional supplements available on the mass market and could be quickly and easily prepared as part of a daily schedule.

The second was concerns about compliance to the treatment plan. Thus, participants were also asked to monitor and track how diligent they were in taking the formula itself, with the researchers defining both a “good” and a “poor” level of consumption of their assigned beverage. Good consumption was defined as an average intake over 50% of the total dose, while poor consumption was defined as an average intake less than 50% of the total dose.

The participants’ height, weight, body fat mass, body fat percent, fat-free mass and muscle mass were assessed by the researchers three times: at baseline, then at 3 months, and then again at 6 months, concluding phase 1 of the trial.

Finally, the parents were also asked to record all food and beverage intake over 3 days the week before each of the scheduled check-ins, allowing the researchers to see to what degree the formula was supplementing nutritional deficiencies and thus how effective it was as a tool of dietary intervention.

TRIAL RESULTS

The results showed statistically significant differences between “good” consumers, “poor” consumers, and participants within the placebo-group. Differences were most significant between the formula group and the placebo group, demonstrating that those who were given the formula showed significant changes in weight-SDS, BMI-SDS, fat-free muscle mass, and muscle mass.

Within the formula group, the results were dose-dependent - dependent on good consumption vs poor consumption. Participants who were “good” consumers of the formula showed significant increases in weight-SDS, BMI-SDS, and muscle mass in comparison to those who were classified as poor consumers of the nutritional formula.

This adds an important distinction to the results: the supplement was not only shown to be effective, but that how effective it would ultimately be dependent on the rate of consumption and the level of compliance with the treatment instructions. As the clinical trial was conducted on prepubertal boys already

deemed to be below-average within the growth parameters established by the CDC, increases in BMI-SDS should be considered a positive result, especially when said result is paired with the increases in fat-free muscle mass.

Although the experiment did not show significant improvements to height-SDS within the formula group, we can attribute this to the analysis not being able to control for the confounding variable of puberty progression. Once the results were stratified by participant age, the researchers were able to identify significant effects in the children ages 11.4+.

In participants over the age of 11.4 years, good consumption of the formula was shown to maintain their existing height-SDS, resulting in an improved growth rate not seen within the poor consumers and placebo-group participants of the same age, who showed a decrease in height-SDS. The decrease in height-SDS in these 11.4+ participants was due to a slower than average growth velocity rate as compared to their peers, which is typical in children with relatively late pubertal development.

Significantly, all participants, regardless of treatment, showed consistent age ranges for the progression into puberty during the course of the experiment. When such consistency is coupled with the findings of the study, the researchers concluded that the supplement did not affect the onset of puberty.

Discussion

Given the positive dose-response correlations found within the formula group (and absent from the placebo group), the researchers concluded that consistent supplementation with the formula was safe and effective for increasing weight, fat free mass, and muscle mass. In prepubertal boys ages 11.4+, for whom growth velocity is usually decreased as compared to their peers, the formula was safe and effective for maintaining growth velocity.

The results were dose-dependent, with the outcomes differing not just between the formula group and the placebo group but also the "good" consumers of the formula and the "poor" consumers of the formula. "Good" consumers of the formula had positive results above that of the "poor" consumers and the placebo group, indicating that the level of supplementation within the formula group has a direct effect on the developmental outcome.

As natural growth tempos can vary at this stage of development, it cannot be conclusively stated that the formula resulted in height gains for all participants. However, the "good" consumers aged over 11.4 years old maintained their height-SDS, and thus their growth velocity, when "poor" consumers and those in the placebo group did not see the same result, indicating that the formula helped these participants avoid declines in their growth trajectory.

The changes in weight seen in the formula group were not modulated by age of the participants. "Good" consumers of the formula

on average showed significant increases when compared to “poor” consumers and the placebo group. Notably, these increases did not come at the expense of healthy body composition: the formula increased weight-SDS and BMI-SDS, being predominantly increases in muscle mass and fat-free mass. From this, the researchers concluded that the weight gain was non-obesogenic.

These results, coupled with the lack of adverse effects observed within the participants, demonstrate that the formula is not only likely to be highly effective but also a safe option for parents concerned with their young boy’s growth. Further research is needed to determine optimal nutrition and the timing of interventions in adolescence.

Results from phase 2 of the clinical study have not yet been reported.

References

1. Fisch Shvalb N, Lazar L, Demol S, Mouler M, Rachmiel M, Hershkovitz E, Shamir R, Phillip M, Yackobovitch-Gavan M. Effect of a nutritional supplementation on growth and body composition in short and lean preadolescent boys: A randomised, double-blind, placebo-controlled study. *Acta Paediatr.* 2021 Aug 4. doi: 10.1111/apa.16054. Epub ahead of print. PMID: 34346091.

TABLE 3

Tanner stage and changes in anthropometrics, body composition and nutrition intake (regular intake and study supplementation) after 6 months of intervention with formula vs. placebo, according to adherence to consumption.

	Formula (POOR) **n = 35**	**Formula** (GOOD) **n = 30**	**Placebo** (POOR) **n = 14**	**Placebo** (GOOD) **n = 47**	P_1
Tanner stage* *n (%)*					
1	18 (52.9%)	22 (78.6%)	8 (66.7%)	28 (62.2%)	0.462
2	15 (44.1%)	6 (21.4%)	4 (33.3%)	15 (33.3%)	
3	1 (2.9%)	0	0	2 (4.4%)	
Δ Height-SDS	−0.06 ± 0.12	0.00 ± 0.10	-0.05 ± 0.12	-0.03 ± 0.11	0.180
All participants	P_2 = 0.005	P_2 = 0.810	P_2 = 0.139	P_2 = 0.118	
≤11.4 yrs	*n* = 15	*n* = 15	*n* = 9	*n* = 22	
	0.00 ± 0.09	0.00 ± 0.08	0.01 ± 0.09	0.02 ± 0.09	0.881
	P_2 = 0.956	P_2 = 0.824	P_2 = 0.956	P_2 = 0.956	
>11.4 yrs	***n* = 20**	***n* = 15**	***n* = 5**	***n* = 25**	
	-0.11 ± 0.12[b]	**-0.01 ± 0.12[a]**	**-0.17 ± 0.09[b]**	**-0.07 ± 0.11[ab]**	
	P_2 = 0.001	P_2 = 0.664	P_2 = 0.016	P_2 = 0.006	**0.033**
Δ Weight-SDS	-0.02 ± 0.31[a]	0.33 ± 0.32[b]	0.01 ± 0.20[a]	0.10 ± 0.26[a]	<0.001
	P_2 = 0.668	P_2 = 0.001	P_2 = 0.907	P_2 = 0.008	
Δ BMI-SDS	0.04 ± 0.46[a]	0.50 ± 0.48[b]	0.04 ± 0.41[a]	0.20 ± 0.38[ab]	<0.001
	P_2 = 0.652	P_2 = 0.001	P_2 = 0.713	P_2 = 0.001	
Body composition	***n* = 26**	***n* = 21**	***n* = 11**	***n* = 36**	p_1
Δ Fat mass (kg)	0.21 ± 0.58	0.74 ± 0.99	0.60 ± 0.68	0.24 ± 0.67	0.037
	P_2 = 0.075	P_2 = 0.003	P_2 = 0.016	P_2 = 0.043	
Δ Fat mass percentage	0.04 ± 1.70	1.1 ± 2.3	1.2 ± 2.3	0.08 ± 1.9	0.127
	P_2 = 0.909	P_2 = 0.045	P_2 = 0.108	P_2 = 0.818	
Δ FFM (kg)	1.4 ± 0.97[a]	2.3 ± 1.4[b]	1.4 ± 0.61[a]	1.6 ± 0.83[a]	0.009
	P_2 = 0.001	P_2 = 0.001	P_2 = 0.001	P_2 = 0.001	
Δ Muscle mass (Kg)	1.3 ± 0.98[a]	2.2 ± 1.33[b]	1.3 ± 0.59[a]	1.5 ± 0.78[a]	0.021
	P_2 = 0.001	P_2 = 0.001	P_2 = 0.001	P_2 = 0.001	

Note: 'Good' consumption—intake ≥50%; 'Poor' consumption—intake <50% of the recommended dose. P_1 represents the difference between groups and consumption categories (using 1-way ANOVA and post-hoc Tukey). Rates with different superscripts (a, b) differ significantly from each other at $p \leq 0.05$; rates with no superscripts do not differ significantly from each other. P_2 represents a one-sample *t* test analysis evaluating the null hypothesis that change in height-SDS = 0. A significant test represents a significant change in height-SDS. *At baseline, all participants were in Tanner stage 1. Seven participants refused to have a Tanner stage evaluation by a paediatric endocrinologist.

Values in bold represents the analysis for the change in Height-SDS, stratified according to age group for participants with a baseline age >11.4 years.