Nutritional Growth Solutions

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Clinical Trials Demonstrate Efficacy and Safety of Dietary Supplement to Achieve Height and Weight Increases in Short and Lean Children

SUMMARY OF FINDINGS

Dietary Supplement Demonstrates Efficacy in Short and Lean Children

Overview

A two-phase prospective, randomized, double-blinded, placebo-controlled trial of nutritional supplementation involving 200 healthy, lean, short, prepubertal children aged 3 to 9 years over a period of 6 months found that the formula was an effective and safe option for promoting height and weight without an increase in body mass index. Of the 85.5% of participants (171) who completed the 6-month, Phase I trial, 150 continued in an open labeled, Phase II extension to 12 months. Out of 150 children in Phase II, 86% (129) completed the trial. Those who had been in the Phase I nutritional supplement formula treatment group continued to show improvements in height and weight during the extension period, and those who had been in the Phase I placebo treatment group saw similar statistically significant increases in height and weight without increases in body mass index during the 6-month extension.[1,2]

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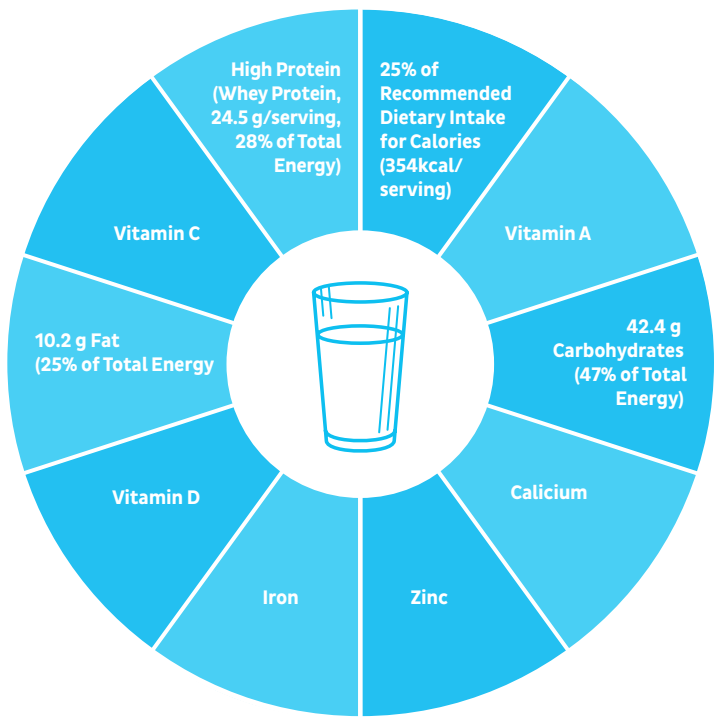
Adequate and balanced nutrition is essential for optimal growth and development. Short and lean children are frequently characterized as picky eaters and often are unwilling or unable to consume an adequate diet. Researchers at the Institute for Endocrinology of the Schneider Children's Medical Center of Israel explored whether the growth rate of short and lean healthy children might be improved with a nutritional supplement.[1]

200 children were recruited into a 2-phase, placebo-controlled study to determine if a protein, vitamin and mineral rich nutritional formula would facilitate increases in height and weight. Inclusion criteria were healthy, short, and lean prepubertal children aged 3 to 9 years with height and weight at or less than 10th percentile and weight percentile less than height percentile for age and sex using the 2000 U.S. Centers for Disease Control growth charts. The children came from middle-class families and had been referred for growth assessment. Children with chronic or gastrointestinal diseases (malabsorption, genetic syndromes, malignancy and any chronic medical treatment) were excluded from the trials.[1]

Nutritional Supplement Formula

Using a formula containing about 25% of recommended dietary intake for calories (354kcal/serving), high protein (whey protein, 24.5 g/serving, 28% of total energy), 42.4 g carbohydrates (47% of total energy), 10.2 g fat (25% of total energy), vitamins A, C, and D and calcium, iron and zinc, the researchers randomized 100 children to the formula treatment group and 100 children to a placebo treatment group with a low-caloric (60kcal/serving), low-protein (3.3 g/serving) mixture unfortified with vitamins and minerals. Each participant received 1 sachet of formula to mix with 200mL of water to be consumed after dinner each day in addition to their regular meal. Good consumption was defined as $\geq$50% of the liquid mixture and poor consumption was $\leq$50% of the mixture.[1] Researchers found efficacy was related to dose. Those who were good consumers



of the product demonstrated height and weight increases while those who consumed less than the effective dose did not achieve statistically significant height and weight increases. No serious adverse events were reported in either Phase I or the extension Phase II.[1,2]

Results of Phase I[1]

At the outset of Phase 1, the children's anthropometric measurements were taken and a 3-day food diary was recorded by the child's parents before each clinical visit. Dietary intake was assessed at baseline and after 6 months. Good consumers of the nutritional supplement formula gained height-SDS (P<.001) and weight-SDS (P=.005) with no change in body mass index when compared with the poor consumers of the nutritional supplement and those in the placebo treatment group. Lebenthal et al reported positive dose response correlations between the amount of formula consumed and the incremental increase in height and weight but no correlations in the placebo group. During Phase I, 19 participants (7 from the formula group and 12 from the placebo group) reported sporadic mild gastrointestinal adverse events (stomach ache, vomiting, nausea) with no significant different in the rates of those adverse events between the groups (P=0.301).

The authors concluded that those in the nutritional supplement group had a significant improvement in height and weight without a commensurate increase in BMI, suggesting growth without obesogenic effect as shown in Table 1. Dietary intake of both groups, exclusive of the supplements, were similar suggesting that the growth was dependent on the formula and not due to an increase in dietary intake.

Results of Phase II[2]

Following the positive results of Phase I, researchers continued the study for an additional 6 months during which all participants were offered the opportunity to join an open-labeled extension. Of the 179 children who completed Phase I, 150 continued in the trial. Anthropometric measurements and a 3-day food diary were assessed at Phase II 6-month baseline and after 12 months of intervention.

129 of the 150 children completed the open-labeled extension. Good consumers (≥50% of the formula) through Phases I and II continued to gain weight and height, with a total gain in height-SDS (height Z-score) of 0.19±0.14 SD. Good consumers randomized to the Phase I placebo group significantly improved their growth rate (gain in height-SDS during Phase I with the placebo was 0.04±0.13, while gain in height-SDS during Phase II with the formula was 0.12±0.11; P=.001) echoing the results of the good consumers during the blinded phase (0.12±0.12). No increase in BMI was reported with formula consumption. Poor consumers (≤50% of recommended dose) did not see statistically significant improvements in their height-SDS. As in Phase I, significant dose response correlations were observed between the amount of the nutritional supplement formula consumed and the incremental increase in height-SDS and weight-SDS achieved. During Phase II, mild gastrointestinal adverse events after consumption of the formula were reported by 11 participants (sporadic stomach ache n=7; vomiting n=2; nausea n=1) No laboratory adverse events were reported, and no serious adverse events were reported during the study period.

Discussion

The children given the formula in Phase I had statistically significant increases in both height and weight when compared to the placebo treatment group. When given formula in Phase II of the study, the placebo group in Phase II confirmed the findings of Phase I. With these results, it was determined that the nutritional formula is safe and effective at promoting growth in both height and weight without a commensurate increase in body mass index in the population of short and lean prepubertal children. Due to these encouraging findings, new research will continue to explore the optimal formulation for other pediatric populations.

TABLE 11

Anthropometric changes after 6-month intervention with formula and placebo by poor and good consumption volume based on 171 completers (Formula n=80; Placebo n=91).

Consumption Categories	Formula (POOR)	Formula (GOOD)	Placebo (POOR)	Placebo (GOOD)	*P*
N (after 6 months at baseline)	37/57	43/43	18/27	73/73	<.001
Δ Height-SDS	0.00±0.14*	0.12±0.12†	-0.02±0.12*	0.05±0.16*,†	<.001
ΔWeight-SDS	0.02±0.30*	0.28±0.35†	0.06±0.30*	0.12±0.35*,†	.005
ΔBMI-SDS	0.08±0.65	0.23±0.47	0.09±0.47	0.09±0.59	.559

NOTE: Good consumption – intake of ≥50%; Poor consumption – intake of ≤50% of recommended dose.

P represents the difference among groups and consumption categories using 1-way ANOVA.

Rates with superscripts (*,†) differ significantly from each other in that row at P <.05; rates with no superscripts do not differ significantly from others in that row.

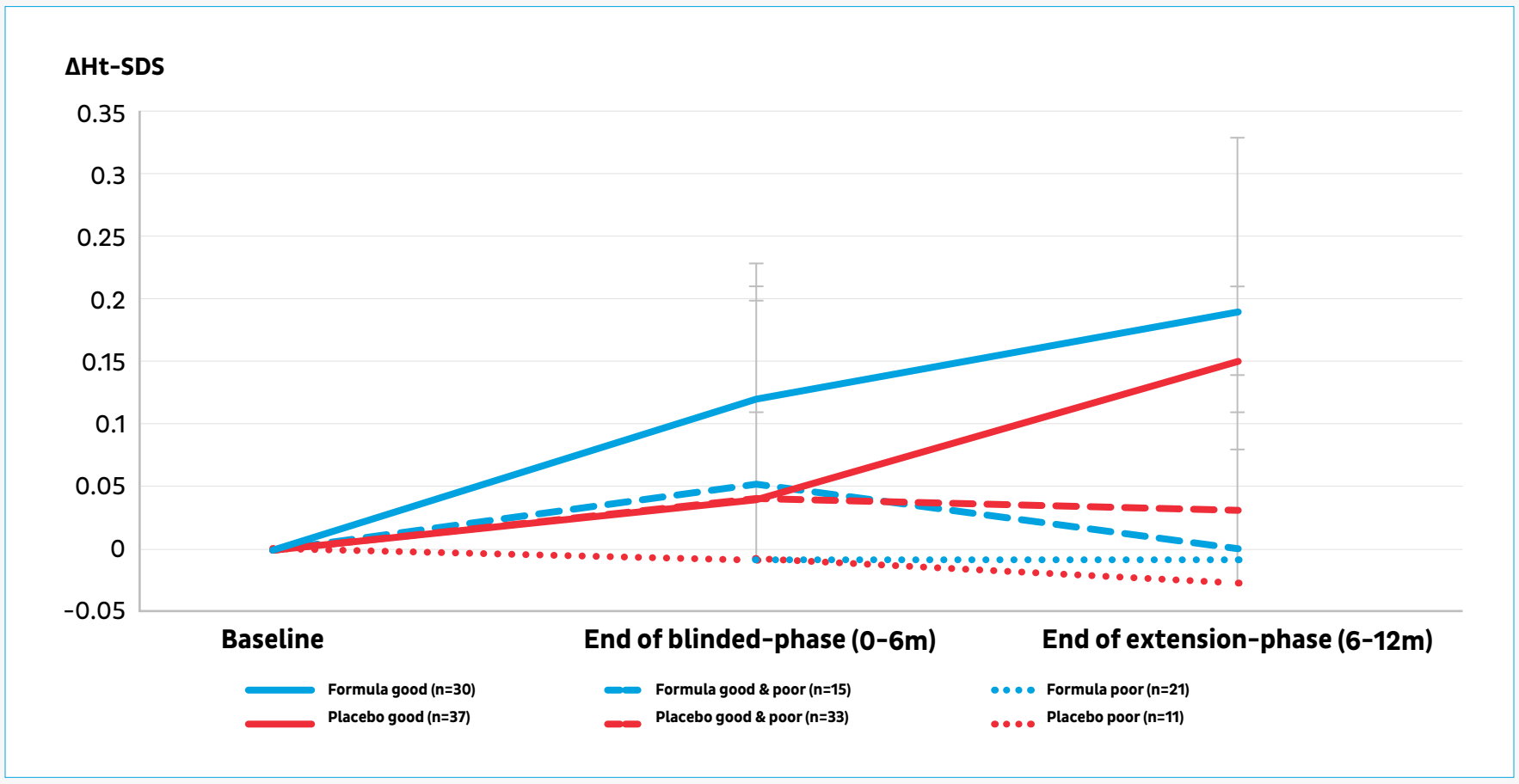
References

1. Lebenthal Y, Yackobovitch-Gavan M, Lazsar L, Shalitin S. Tenenbaum A, Shamir R, et al. Effect of a nutritional supplement on growth in short and lean prepubertal children: a prospective, randomized, double-blind, placebo-controlled study. J Pediatr. 2014:165:1190-3.

2. Yackobovitch-Gava M, Lebenthal Y, Lazar L, Shalitin S, Demol, S, Tenenbaum A, et al. Effect of nutritional supplementation on growth in short and lean prepubertal children after 1 year of intervention. J Pediatr. 2016.

FIGURE 12

Linear growth over 12 months of good and poor consumers of nutritional supplement formula versus placebo.[2]



NOTE: Linear growth after 12 months of nutritional intervention. This figure shows changes in height-SDS over time during the double-blind placebo-controlled phase and the open-label extension phase using only the nutritional supplement formula. Good consumption – intake of ≥50%; Poor consumption – intake of ≤50% of recommended dose.