Prebiotics as a method to decrease bodyweight in overweight and obese children

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Abstract
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Methods: An exhaustive search of available medical literature was performed using MEDLINE-Ovid, CINAHL-EBSCO Host, and Web of Science. Keywords included: inulin-type fructan, prebiotic, obesity, overweight, body weight, and children. Studies were assessed for quality using GRADE.

Results: Eighty-two articles were assessed for relevancy to the clinical question. Two studies were found both of which were randomized controlled trials. In 1 of the studies, body weight z-scores significantly decreased in the prebiotic group. However, the low quality of the studies necessitates further studies with larger sample sizes.

Conclusion: Prebiotics should not be the sole therapy to decrease body weight in overweight and obese children but could augment other healthy lifestyle changes.

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Prebiotics as a Method to Decrease Bodyweight in Overweight and Obese Children

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A Clinical Graduate Project Submitted to the Faculty of the
School of Physician Assistant Studies
Pacific University
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Biography

[redacted]
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Acknowledgements

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Table 1: Quality Assessment of Reviewed Studies

List of Abbreviations

DXA Dual-energy X-ray absorptiometry
Prebiotics as a Method to Decrease Bodyweight in Overweight and Obese Children

BACKGROUND

The obesity epidemic in the United States has reached staggering levels. Currently more than 2 out of 3 U.S. adults and approximately 1 of 3 children are overweight or obese.\(^1\) One of the risk factors of excess weight as an adult is carrying extra weight as a child. Simmons et al\(^2\) found that the likelihood of a child or adolescent with obesity to be obese as an adult was 5 times greater than non-obese individuals.

Overweight and obesity put a strain on the healthcare system with increases in preventable disease such as type 2 diabetes, stroke, osteoarthritis, certain types of cancer, and coronary heart disease.\(^1\) As a consequence of obesity, medical costs were estimated to be $147 billion in 2008 dollars. Obesity is also related to increased rates of depression and anxiety.\(^3\) By decreasing the prevalence of overweight and obesity, U.S. health dollars could be saved and quality of life could be improved.

One strategy to address the number of adults living with overweight or obesity is to intervene early in life with childhood weight. Past studies have shown a relationship between the gut microflora and
obesity. For example, Ley et al\textsuperscript{4} demonstrated that ratios of gut bacteria were different in lean and obese individuals and could be manipulated with weight loss. As a result, making changes to the gut microbiome could be a potential therapeutic avenue to pursue. Prebiotics are components of food that are not digested and are used by bacteria in the gut. Insulin concentrations, glucose levels after meals, and satiety improved with prebiotic supplementation in previous adult studies.\textsuperscript{5} The aforementioned changes could be the effects that influence weight reduction with prebiotics. Thus, clinicians need to know if prebiotics can decrease bodyweight in overweight and obese children.

**METHODS**

The subject of this literature review began with finding an article on ScienceDaily.\textsuperscript{6} A comprehensive literature search was conducted using MEDLINE-Ovid, CINAHL-EBSCO Host, and Web of Science. Keywords included were inulin-type fructan, prebiotic, obesity, overweight, body weight, and children. Eligibility criteria included studies relevant to the clinical question in English and on human subjects. For other resources, bibliographies of relevant studies were reviewed. The quality of the articles was determined using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE).\textsuperscript{7}
RESULTS

Eighty-two articles were reviewed to determine applicability to the clinical question. Two articles fit inclusion criteria, both of which were randomized controlled trials.\textsuperscript{5,8} See Table 1. Searching through the bibliographies of the two studies did not yield additional articles.

**Liber and Szajewska**

This randomized, double-blind, placebo-controlled trial\textsuperscript{8} examined the effect of oligofructose supplementation, a type of prebiotic, on body weight in overweight and obese children. Eligibility criteria included age of 7-18 years and BMI-for-age >85th percentile. Subjects were categorized as overweight if BMI-for-age was between 85th and 97th percentile. Subjects were categorized as obese if BMI-for-age was above the 97th percentile. Overweight or obesity as a result of genetic syndromes, endocrine disease, or using drugs that can affect weight or appetite were the exclusion criteria. Ninety-seven subjects were randomized into an oligofructose group (n=48) and a placebo group (n=49). The baseline characteristics of the 2 groups were similar in regards to prognostic balance. The treatment was 2 oral doses of oligofructose per day for 12 weeks. Subjects were instructed to take the supplement dissolved in water before breakfast and dinner. The dose was 8 g per day for 7-11 year olds and 15 g daily for 12-18 year
olds. The placebo was maltodextrin which was made by the pharmacy in the same packaging and given in equal caloric doses. Both groups and their parents received the same advice from the dietician on diet, instructed to eat the same amount of calories during the study, and be physically active 1 hour per day.8

A computer system was responsible for randomization. During the course of the study, all subjects and investigators were blinded to the group. The placebo (maltodextrin) and the treatment (oligofructo-se) are both white powders that resemble each other with texture and odor and were packaged in the same type of container.6

BMI-for-age z-score was the primary outcome. Secondary outcomes included percentage of body weight reduction, mean BMI-for age z-score, self-reported energy intake, number of children with a BMI-for-age <85th percentile, number of children with dyslipi-daemiaes, number of children with hypertension, and physical activity. A physical examination including blood pressure, weight, height, and BMI, as well as laboratory tests such as fasting glucose, cholesterol levels, and total body fat with dual-energy X-ray absorptiometry was completed before the intervention. A dietician reviewed a 3 day food record from each subject. The International Physical Activity Questionnaire was used to determine physical activity levels. Subjects were
asked to keep a symptom diary throughout the study. At the end of 12 weeks, weight, height, BMI, and body fat with DXA were measured again and the food record, physical activity questionnaire, and symptom diary were collected. If there were abnormalities in laboratories at the beginning of the study then the tests were repeated at 12 weeks. Only weight, height and BMI were measured for the follow-up period of 24 weeks.\(^8\)

There was not a difference in BMI-for-age z-scores between the oligofructose group and the placebo group. No significant differences were found among the secondary outcomes.\(^8\)

One of the limitations of this study was the high overall dropout rate of approximately 19%. However, the dropout rate was similar in both groups. The authors’ method of measuring compliance may have been inadequate. The authors had subjects only return the unused packets. In addition, according to the subjects, the oligofructose formed lumps when stored at room temperature which may have influenced blinding.\(^8\)

**Nicolucci et al**

This randomized, double-blinded, placebo-controlled trial\(^5\) examined the effect of prebiotic oligofructose-enriched inulin on body weight in overweight and obese 7-12 year old children. Eligibility criteria in-
cluded children above the 85th percentile for BMI, Tanner developmental stage 3 or less, and otherwise healthy. Diabetes, liver disease, cardiovascular issues, use of drugs that can affect appetite, weight, or metabolism, on a weight loss diet, more than 3 kg of weight loss 12 weeks before the first day of the study, major changes in exercise in the preceding 4 weeks, or antibiotic use in the last 3 months were all reasons to be excluded. Forty-two subjects were randomized into the prebiotic group (n=22) and the placebo group (n=20). The 2 groups were prognostically balanced. The treatment group consumed 8 g of prebiotic daily while the placebo group consumed 3.3 g of maltodextrin daily, which is equal in calories to the treatment. The 2 powders were packaged similarly and subjects were instructed to dissolve the powder in 250 ml of water and consume 15-20 minutes before dinner. Subjects were advised to take half of the dose for the initial 2 weeks and then the full dose for the rest of the study. Both groups were advised to eat for fullness and continue their current physical activity level.5

A computer system was responsible for randomization. Both research staff and subjects were blinded to the treatment. Compliance was measured with empty and unused packets.5

The primary outcome of this study was reduction in percent body fat. DXA was used to measure fat mass and lean mass. At baseline
and every 4 weeks, height, weight, and waist circumference were measured. Hologic QDR software was used to estimate android and gynoid fat. Godin’s Leisure-Time Exercise Questionnaire was used at the beginning of the study, the half-way point, and the last test day.\textsuperscript{5}

Absolute body weight increased in the treatment and the placebo groups; however, the increase was 2.4 times greater in the placebo group. In the treatment group, body weight z-score significantly decreased by -0.07 +/- 0.02. BMI did not change in the treatment group however the placebo group had a significant change in BMI with an increase of 0.4 +/- 0.2.\textsuperscript{5}

This study’s limitations included a small sample size of 38 subjects. Another limitation of this study is the mostly Caucasian sample.\textsuperscript{5}

**DISCUSSION**

The cause of childhood obesity is multifactorial. New research is revealing the importance of the gut microbiome on weight and health. To mitigate the resource stress of overweight and obesity on the U.S. healthcare system, it is imperative to keep looking for ways to address this growing issue. Prebiotics may be a therapeutic way to decrease body weight in overweight and obese children.

This systematic review resulted in 2 studies\textsuperscript{5,8} that examine how prebiotics influence bodyweight in overweight and obese children. A
significant effect of prebiotics on bodyweight in overweight and obese children was only demonstrated in 1 study. The GRADE method was used to evaluate the studies (Table 1).

The 2 studies’ combined limitations are high dropout rate, compliance measurement concerns, risk of unblinding, small sample size, and non-diverse demographic of subjects. Both studies reported a double-blind study. However, Liber and Szajewska noted that blinding may have been hindered because some of the subjects noticed that their powder became clumpy. After the study concluded, the results were unblinded and it was only the prebiotic powder that became clumpy. This is unlikely to decrease the validity of this study unless the subjects knew that the prebiotic would become clumpy versus the maltodextrin placebo.

Only the Nicolucci et al study showed a significant difference in bodyweight. Body weight technically increased in both treatment and placebo groups however the placebo increased by 2.4 times the treatment group. It is important to remember that children are supposed to be growing so the clinical use of the prebiotic might be to help keep children on a healthy growth curve. Because of the small sample size, lack of diversity of the subjects, and subjects were otherwise healthy,
we cannot make wide-sweeping conclusions to all overweight and obese children.

To be able to have more concrete support of the efficacy of probiotics to decrease bodyweight in overweight and obese children, the subject needs to be studied further. Due to the low quality attributed to both studies, the reliability of the data is in question. Data from a larger randomized controlled trial with a more diverse population may result in more trustworthy conclusions.

**CONCLUSION**

At this point, the effect of prebiotics on bodyweight in overweight and obese children remains unsettled because of the conflicting results and the low quality of the 2 available studies. Because of the positive effect of prebiotics in the most recent study, this supplement remains a promising avenue for future research as it is not expensive nor invasive. In the 2 studies, subjects noted few side effects which could lead a clinician to suggest prebiotics to a pediatric patient who is overweight or obese along with other healthy lifestyle suggestions.
References


Table 1. Quality Assessment of Reviewed Articles

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Downgrade Criteria</th>
<th>Upgrade Criteria</th>
<th>Quality</th>
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</thead>
<tbody>
<tr>
<td>Liber and Szajewska³</td>
<td>RCT</td>
<td>Limitations: Serious¹ Indirectness: Not Serious Inconsistency: Serious² Imprecision: Not Serious Publication bias: Unlikely</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Nicolucci et al⁵</td>
<td>RCT</td>
<td>Limitations: Not Serious Indirectness: Not Serious Inconsistency: Serious² Imprecision: Serious³ Publication bias: Unlikely</td>
<td>None</td>
<td>Low</td>
</tr>
</tbody>
</table>

³ Large number lost to follow-up
⁴ The two studies have conflicting findings
⁵ The Nicolucci et al study had a small sample size of 38 subjects