

Effect of oral nutritional supplementation on growth and recurrent upper respiratory tract infections in picky eating children at nutritional risk: a randomized, controlled trial

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Abstract

Objectives: To evaluate the effect of oral nutritional supplementation (ONS) plus dietary counselling (DC) (intervention) versus DC alone (control) on growth and upper respiratory tract infection (URTI) in nutritionally at-risk, picky eating children in India.

Methods: We performed a 90-day, prospective, randomized, controlled trial. A total of 255 children aged 24–72 months with a weight-for-age z-score ≥ -2 and < -1 , picky eating behaviour, and acute URTI were randomized to the control ($n = 128$) or intervention group ($n = 127$). The outcomes included the change in weight-for-age z-score from days 1 to 90 and the URTI incidence.

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Results: The mean age was 44.0 ± 14.3 months. The intervention group showed a significantly greater increase in mean weight-for-age and body mass index-for-age z-scores compared with the control group from day 10 onwards. Higher energy intake in the intervention group was observed at all follow-up visits, except for day 10. The incidence of URTI in the control group was 2.01 times higher than that in the intervention group, controlling for confounding factors.

Conclusions: ONS plus DC is effective for improving weight and reducing the incidence of URTI in nutritionally at-risk, picky eating children with an acute URTI episode.

Keywords

Oral nutritional supplementation, picky eating, growth, upper respiratory tract infection, dietary counselling, energy intake

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Background

Picky eating is typically characterized in children who eat a limited number of foods, are unwilling to try new foods, have restricted intake of vegetables and other food groups, and have strong food preferences.¹ This condition is common during childhood^{2–6}, and frequently causes parental concern because of the potential risk for nutritional deficits and inadequate weight gain.^{7,8} Compared with non-picky eating children, picky eaters are typically reported to have lower consumption of fruits, vegetables and meat, as well as lower intake of energy, protein, vitamin C, vitamin E, calcium, iron, zinc, fibre, and folate.^{6,9} All of these are important for healthy growth and development.^{6,7,9}

Poor nutrition during childhood is closely associated with repeated infections, worsening through repeated cycles.¹⁰ Inadequate nutrition in picky eating children may have a negative effect on defence against infection. Infectious illness can exacerbate poor nutrition and micronutrient deficiencies due to a reduced nutrient intake, and increased demand for nutrient and energy expenditure.¹⁰ Severe and moderate undernutrition,

defined as a z-score < -2 , is a major risk factor for respiratory tract infection resulting in increased childhood mortality.¹¹ However, even mild undernutrition, defined as a z-score ≥ -2 and < -1 , is associated with increased child mortality from respiratory tract infections.^{12,13} Therefore, early diagnosis of mild growth deficits followed by appropriate nutritional intervention may help break the persistent cycle of undernutrition and infection in children with nutritional risk.

In previous studies, oral nutritional supplementation (ONS), which is a nutritionally complete supplement that contains a blend of macro- and micronutrients, was shown to be an effective method of improving nutritional status^{14,15}. Additionally, ONS reduced the incidence of upper respiratory tract infection (URTI) during the course of the intervention in picky eating children with nutritional risk.¹⁴

This study aimed to compare the effect of an intervention using ONS together with dietary counselling (DC) against DC alone on growth and the incidence of URTI in nutritionally at-risk children with picky eating behaviour in India.

Methods

Study design and participants

We conducted a prospective, randomized, controlled, open-label, parallel group, multicentre study between August 2013 and April 2014. This study was performed in six clinics and hospitals across different cities in India. There was no difference in the rate of undernutrition between the clinics and hospitals. All clinics were in urban areas and had a similar socioeconomic status.

Children aged 24–72 months (2–6 years) who had picky eating behaviour, a weight-for-age between the 3rd and 15th percentiles based on the WHO Child Growth Standards, and were diagnosed with URTI at the various paediatric outpatient centres by paediatricians were eligible for inclusion. We selected children in the age group of 2–6 years for this study because the incidence of picky eating declines from 20% to 2% between 2 and 11 years, and stabilizes at approximately 3% after 6 years.¹⁶ Furthermore, the incidence of acute infections is greater in children identified as picky eaters.¹⁷ Eligible subjects were recruited on the same day if they satisfied the inclusion criteria. The diagnosis of URTI included rhinitis, tonsillitis, pharyngitis, otitis media, or bronchitis that did not require hospitalization. Picky eating was defined as having at least two of the following: 1) eating only a limited number of foods; 2) being unwilling to try new foods; 3) refusing to eat vegetables and/or foods from other food groups; 4) showing strong food likes and dislikes; and 5) displaying behaviour that disrupted mealtimes.^{2,18} Children who had the following conditions were excluded: current medical conditions requiring hospitalization; gastrointestinal tract infections or inflammatory bowel disease; active tuberculosis; acute hepatitis B or C; human immunodeficiency virus or

malignancy; cystic fibrosis; immunodeficiency syndromes, congenital abnormalities of the respiratory tract, such as lung and respiratory cilia; an unsuspected foreign body in the respiratory tract; asthma; and known metabolic disorders, renal impairment, or rheumatic diseases and diabetes. Children who had dysphagia, aspiration risk, a known allergy, or intolerance to any ingredients in ONS were also excluded from the study. Other exclusion criteria included children who had received antibiotic treatment within the last 2 weeks of enrolment, or were taking medications and agents that could potentially modulate body weight. These included diuretics, appetite stimulants, steroids, and growth hormones.

The study was approved by the Institutional Review Board or Independent Ethics Committee. Written informed consent was obtained from each child's parents or legal guardian. The study was performed in accordance with the ethical principles that had their origin in the Declaration of Helsinki. The study was registered at Clinical Trial Registry India (ctri.nic.in) and Clinicaltrials.gov with the registration numbers CTRI/2014/07/004717 and NCT02056275, respectively.

Randomization

Recruited children were randomly allocated to one of the two study groups (DC, $n=128$ [control group]; ONS plus DC [intervention group], $n=127$) at day 1 (baseline visit) in a 1:1 ratio. Sealed envelopes containing the subject study group assignment were prepared by Abbott Nutrition for each site using SAS programming to generate block randomization tables. The forms were folded so that the treatment group assignment was internal and research staff would not be able to see through the envelope. As eligible children were enrolled, they were assigned a

subject number sequentially starting with the first envelope.

Intervention and control

The age-specific recommendations for energy and nutrient requirements for Indian children were used as the target intakes for the intervention and control groups. The intervention group received DC at baseline and each post-baseline visit plus instructions for ONS to be consumed daily over the 90-day period. The control group received DC at baseline and each post-baseline visit. The post-baseline visits were scheduled at days 3, 10, 30, 60, and 90.

DC in both groups was conducted by dietitians who were trained on the protocol. A total of six dietitians participated in the study. Parents in the intervention group were provided advice about appropriate food groups to include in food preparation and information about the importance of meal frequency, including three main meals and two to four snacks, to meet the child's nutritional requirements. Parents were instructed to reconstitute the ONS in powder form with water and provide it to the child during snack time between main meals. Children aged 24 to <48 months were asked to consume at least one serving (224 mL) and those aged 48 to 72 months to consume two servings (448 mL) of ONS. The ONS was a commercially available powder product (PediaSure; Abbott Healthcare Private Limited, Mumbai, India). The nutritional characteristics of ONS are shown in Table 1. When ONS is consumed at the recommended amount, it provides at least 20%–30% of the energy and 35%–60% of the daily protein recommendations for children aged 24–72 months. Parents in the control group received advice on the importance of meal frequency including three main meals and 2–4 snacks between main meals. Parents also received information to help them

Table 1. Nutrient composition of the nutritional supplement

Nutrients	Oral nutritional supplement per serving (45.5 g)
Energy (kcal)	213
Protein (g)	6.4
Fat (g)	10.6
Carbohydrate (g)	22.8
Vitamin A (µg)	138.8
Vitamin C (mg)	20.0
Vitamin B1 (mg)	0.41
Vitamin B2 (mg)	0.46
Niacin (mg)	3.19
Vitamin B6 (mg)	0.46
Vitamin B12 (µg)	0.68
Pantothenic acid (mg)	1.41
Biotin (µg)	7.28
Choline (mg)	53.7
Vitamin D2 (µg)	1.43
Vitamin E (mg)	5.01
Vitamin K (µg)	7.96
Folic acid (µg)	45.5
Calcium (mg)	175.6
Iron (mg)	2.5
Iodine (µg)	17.3
Magnesium (mg)	89.1
Phosphorus (mg)	109.2
Zinc (mg)	1.59
Selenium (µg)	5.60
Manganese (mg)	0.45

select foods rich in energy and protein for food preparations that would meet the child's nutritional requirements.

Outcomes

The primary outcome was the change in weight-for-age z-score from baseline to day 90. Secondary outcomes included the change in height-for-age and body mass index (BMI)-for-age z-scores, the number of sick days from URTI, the number of acute URTI episodes over the study period, and the energy consumption at each post-baseline time point. Other outcomes included parental

assessment of the child's appetite and palatability, and the child's compliance with ONS consumption in the intervention group.

Anthropometric assessment

Anthropometric measurements were performed by dietitians who were trained in standardized methods for taking such measurements. Body weight was measured with light clothes without shoes and jackets using an electronic weighing scale after calibrating the scale to zero (Wensar Aliston, Sanjay Scientific Co., Mumbai, India) and recording the weight to the nearest 0.1 kg. Height was measured without shoes or hat using a stadiometer (Prestige Stadiometer, Sanjay Scientific Co., Mumbai, India) and recording it to the nearest 0.1 cm. BMI (kg/m^2) was calculated using measured weight and height.

Nutritional status

Weight-for-age, BMI-for-age, and height-for-age are expressed as sex-age-specific z-scores using the WHO Child Growth Standards.

Dietary assessment

Dietary intake was collected using a 24-hour food recall method implemented by trained dietitians at each study site during baseline and at each subsequent study visits. At the baseline visit, parents were interviewed about the child's intake for the last 3 days. For post-baseline visits, one 24-hour food recall was completed. Using a compiled list of the most commonly consumed foods and drinks based on the Indian food composition tables published by the National Institute of Nutrition,¹⁹ the average energy intake was calculated by a dietitian based on the 24-hour dietary recall at baseline, and on days 3, 10, 30, 60, and 90.

Compliance of ONS and incidence of acute URTI

Parents in the intervention group were provided a diary to record the volume of ONS consumed by the child daily. A child was considered compliant if the actual consumption of ONS was at least 75% of the recommended volume for the entire study period of 90 days.

In this study, parents were asked to record the incidence and duration of recurrent acute URTIs in the diary over the study period. At each visit to a physician, the physician verified any acute infections that had been recorded in the diary based on medical records or proof of diagnosis of URTI. Parental reporting of child health outcomes, including infections, has shown to be a reasonable approach.²⁰⁻²²

Appetite score

At each study visit, parents rated the appetite of the child in the past 24-hour period using a visual analogue scale ranging from 0 to 10. In this scale, a score of 0 indicates a very poor appetite and 10 is a very good appetite.

Palatability score

Palatability of the ONS was assessed by the parent using a hedonic scale in which 1 represented "does not like it at all" and 5 represented "likes it a lot".

Statistical analyses

The sample size was calculated using NQuery Advisor[®] Version 5.0 (Statistical Solutions, Los Angeles, CA, USA). A sample size of 128 children (64 per group) had 80% power to detect a difference of 0.5 SD in a mean change in weight-for-age WHO z-score from days 1 to 90, using the two-sample t-test with a 0.05 two-sided significance level. Enrolment of 256 children

was needed for an estimated attrition rate of 50%.

All of the statistical analyses were performed on an intent-to-treat (ITT) basis using SAS version 9.3 (SAS Institute, Cary, NC, USA). Descriptive results, including anthropometric measurements, energy, and macronutrient intake, and the incidence of URTI over the study period are shown by the mean, median and SD. Categorical variables are shown by the number of subjects (n) and as a percentage (%). All continuous variables were checked for normality using the Shapiro–Wilk test, histograms, and normality probability plots, and determined as non-normal if found significant ($p < 0.001$). Nonparametric tests, including the Wilcoxon rank sum and signed rank tests, were used to examine differences between the two groups and within groups respectively, for continuous variables with non-normal distribution.

The incidence of acute URTI over the study period was analysed using Poisson regression analysis, controlling for age (months), sex, and change in growth parameters, such as weight-for-age, height-for-age, and BMI-for-age z-score changes over 90 days. Categorical variables were analysed using the Cochran–Mantel–Haenzel test, with adjustment for the study site (chi-square or Fisher’s exact test). Repeated measures analysis of variance or the two-sample two-sided Wilcoxon rank sum test was used to examine the improvement in growth outcomes over time using weight-for-age, BMI-for-age, and height-for-age z-scores as measured at days 30, 60, and 90. The effects of the intervention on growth parameters and the incidence of URTI were also examined using the evaluable data set. Subjects who consumed at least 75% of the recommended dose of ONS and attended at least two sessions of DC were included in the evaluable analysis.

Results

Study subjects

Two hundred eighty-one children were screened, of whom 255 were enrolled and randomized to the intervention (127 children) and the control (128 children) groups. Of the 255 randomized children, 13 children (8 in the intervention group and 5 children in the control group) did not complete the study (Figure 1).

Table 2 shows the children’s characteristics at baseline. The mean age was 44.0 ± 14.3 months. Two thirds of children were boys. The mean age and sex distribution were not different between the two groups. Mean weight was not different between the two groups. However, children in the control group were significantly taller than those in the intervention group ($p = 0.0024$). This resulted in a significantly lower mean height-for-age z-score ($p < 0.0001$) and a correspondingly higher mean BMI and BMI-for-age z-score ($p < 0.0001$ and $p = 0.0002$, respectively) in the intervention group compared with the control group at baseline.

Acceptance and compliance of ONS

Based on parental reporting, the children’s liking for ONS increased over the study period ($p < 0.05$). Therefore, there was a high compliance with consumption of ONS in the intervention group, and 98.4% of children consumed at least 75% of the recommended volume of ONS. Additionally, nearly all children in both groups attended at least two sessions of DC over the study period.

Change in growth outcomes

Figure 2a and 2b shows the mean weight and height gain in both study groups, respectively. The intervention group demonstrated a significant weight gain at day

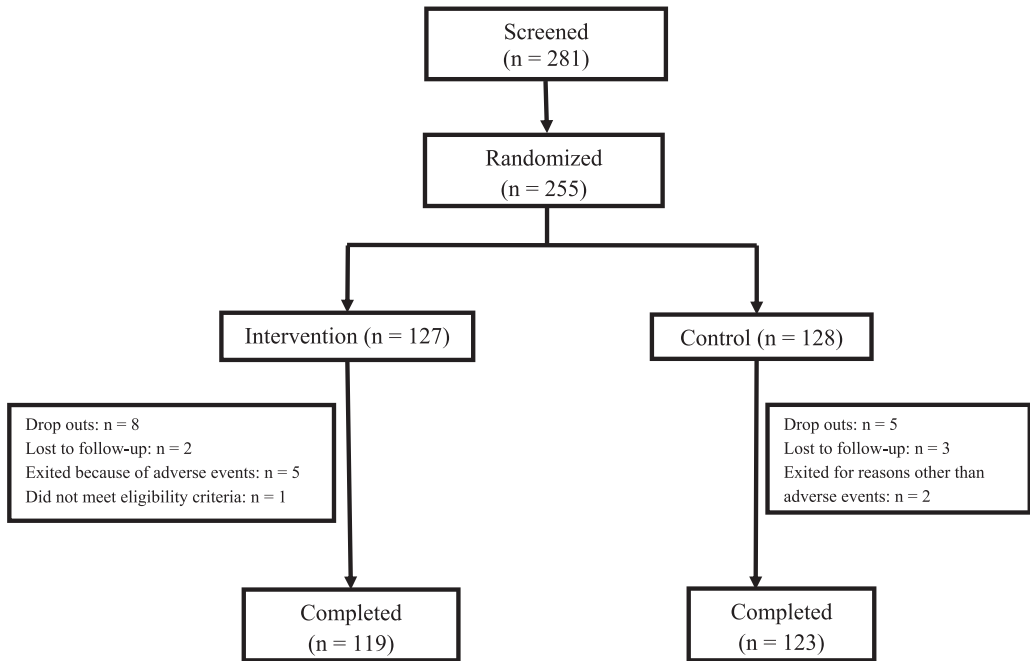


Figure 1. Study flow chart

Table 2 Baseline characteristics of the children

Characteristics	Total	Intervention (n = 127)	Control (n = 128)	p value
Age (months), mean (SD)	44.0 (14.3)	42.8 (14.0)	45.2 (14.4)	0.1876 ^a
Sex				
Male, n (%)	160 (62.7)	80 (63.0)	80 (62.5)	0.9352 ^b
Female, n (%)	95 (37.3)	47 (37.0)	48 (37.5)	
Weight (kg), mean (SD)	12.8 (2.0)	12.6 (1.94)	13.0 (2.03)	0.1186 ^a
Height (cm), mean (SD)	94.4 (10.2)	92.5 (10.13)	96.3 (9.82)	0.0024 ^a
BMI (kg/m ²), mean (SD)	14.4 (1.6)	14.8 (1.75)	14.0 (1.41)	0.0002 ^a
Weight-for-age z-score, mean (SD)	-1.5 (0.3)	-1.55 (0.26)	-1.51 (0.26)	0.2774 ^c
BMI-for-age z-score, mean (SD)	-0.9 (1.3)	-0.63 (1.37)	-1.24 (1.17)	0.0002 ^c
Height-for-age z-score, mean (SD)	-1.4 (1.3)	-1.76 (1.35)	-1.11 (1.10)	<0.0001 ^c

^aThe p value was obtained by the Wilcoxon rank sum test.

^bChi-square test.

^cThe p value was obtained from an analysis of variance model adjusted for study group, study site, sex, and the interaction term of treatment group and sex.

BMI, body mass index; SD, standard deviation.

10 compared with the control group ($p = 0.0002$). By day 90, the intervention group showed a mean weight gain that was almost twice that of the control group

($p < 0.0001$) (Figure 2a). In contrast, the change in height was not significantly different between the two groups across all assessment time points. However, there

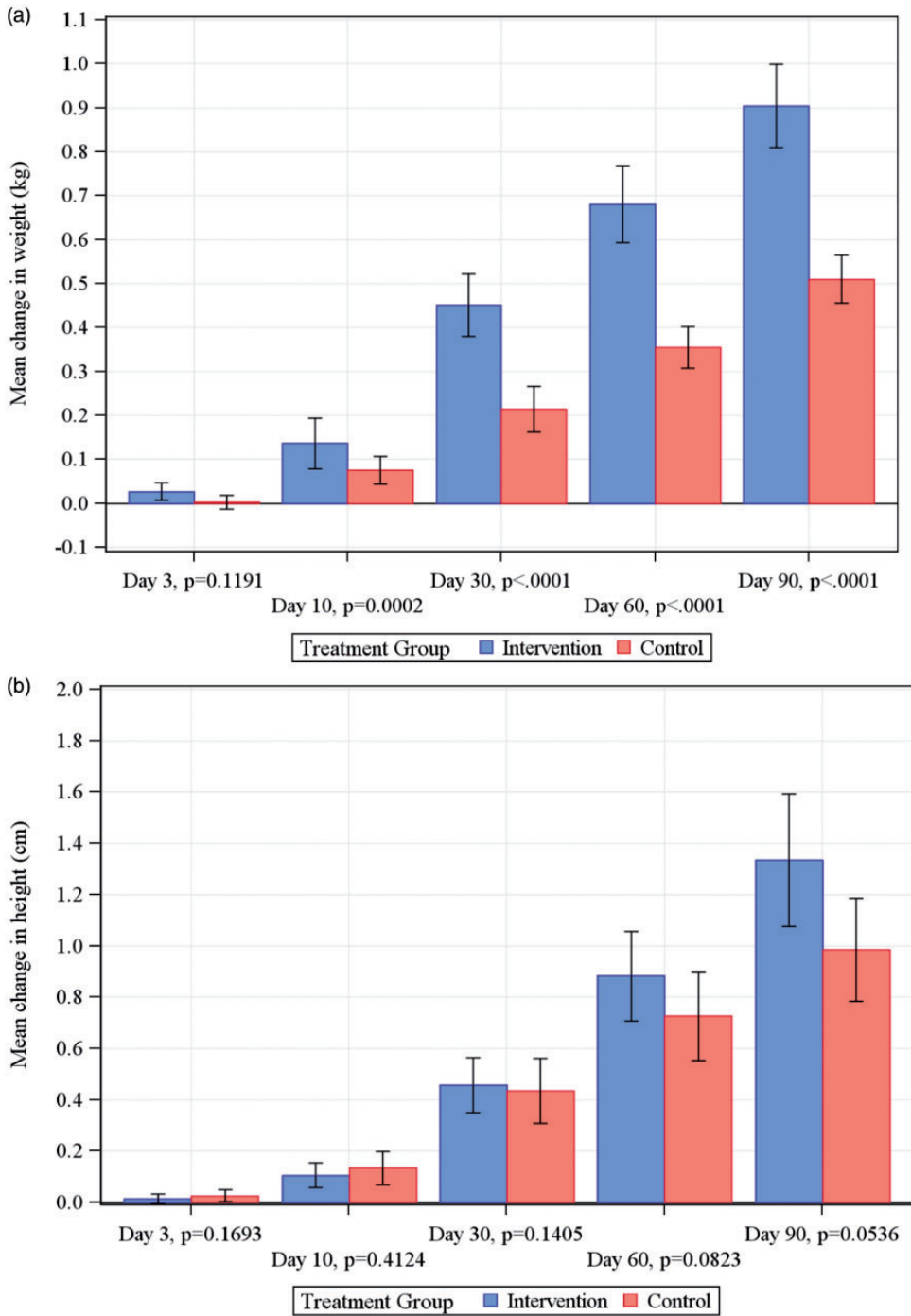


Figure 2. Mean change in (a) weight (kg) and (b) height (cm) from baseline to each post-baseline time point in each treatment group. Bars represent the standard deviation. The p values in panels a and b were obtained by the Wilcoxon rank sum test.

was a tendency for height gain in the intervention group observed from day 60 onwards ($p=0.0823$ and $p=0.0536$ at days 60 and 90, respectively) (Figure 2b).

When we expressed growth using WHO Child Growth Standards, the intervention group maintained their baseline weight-for-age z-score at day 3 ($p=0.5063$), while the control group experienced a drop in weight-for-age z-score ($p=0.0293$) (data not shown). A significantly larger increase was observed in the weight-for-age z-score in the intervention group from day 10 onwards compared with the control group ($p<0.0001$) (Figure 3a). Similarly, the gain in BMI-for-age z-score in the intervention group was significantly higher than that in the control group for all post-baseline time points after day 3 (Figure 3b). However, both groups showed a decrease in height-for-age z-scores over the 90-day period ($p<0.05$, data not shown), although there was a lower reduction over the total 90-day period in height-for-age z-score for the intervention group (Figure 3c).

Evaluable analyses produced similar results to the ITT analysis regarding significant increases in weight-for-age and BMI-for-age z-scores (data not shown).

Energy intake and appetite

In accordance with improvement in weight status, total energy consumption was significantly higher in the intervention group compared with the control group at all post-baseline time points, except for day 10 ($p<0.05$) (Figure 4). Additionally, parents reported a significant improvement in appetite in the intervention group at day 30 compared with the control group (mean score: 4.98 in the intervention group versus 4.50 in the control group, $p=0.0055$) (data not shown).

Incidence of URTI

There was a total of 21 and 34 events of URTI reported for the intervention and control groups, respectively. The incidence rate of URTI was 13.0% and 17.0% for the intervention and the control groups, respectively. Similar findings on the effect of reducing the incidence of URTI were also found in the evaluable analysis (data not shown). Table 3 shows a model of factors associated with the incidence of URTI over the 90-day period using the ITT and evaluable populations. Changes in various growth parameters over the study period were fitted in the model and the change in height-for-age Z score appeared to best predict the incidence of URTI. After controlling for baseline age (months), sex, and change in height-for-age Z score, the incidence of URTI was 2.01 times more frequent in the control group than in the intervention group over the study period ($p=0.0361$), using the ITT population.

Adverse events were reported in 24 (18.9%) and 28 children (21.9%) in the intervention and control groups, respectively. These events were related to respiratory and gastrointestinal symptoms, such as intolerance to ONS. ONS-related adverse events were reported in four (3.1%) children. There were no serious adverse events reported.

Discussion

To the best of our knowledge, this is the first study to evaluate the efficacy of ONS on children's nutritional status in an Indian population of picky eating children who experience recurrent URTI and are at nutritional risk. Our study showed that a nutritional intervention comprising ONS and dietary counselling was effective. Our intervention led to improved energy intake and prevented weight loss during the first 3 days of an acute infection in nutritionally at-risk

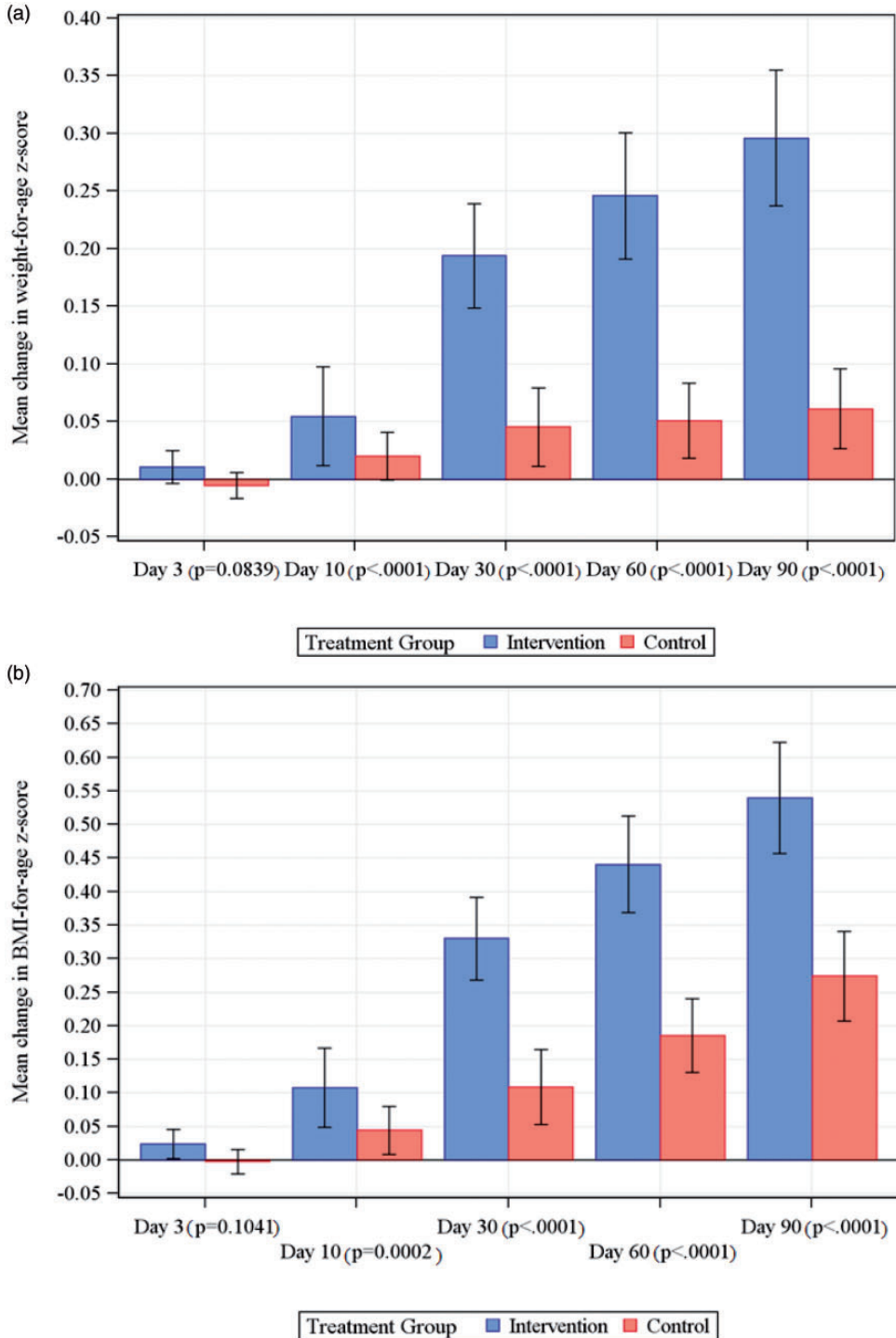


Figure 3. Mean change in (a) weight-for-age, (b) body mass index-for-age, and (c) height-for-age z-scores from baseline to each post-baseline time point in each treatment group. Bars represent the standard deviation. The p values in all of the panels were obtained by the Wilcoxon rank sum test. BMI, body mass index.

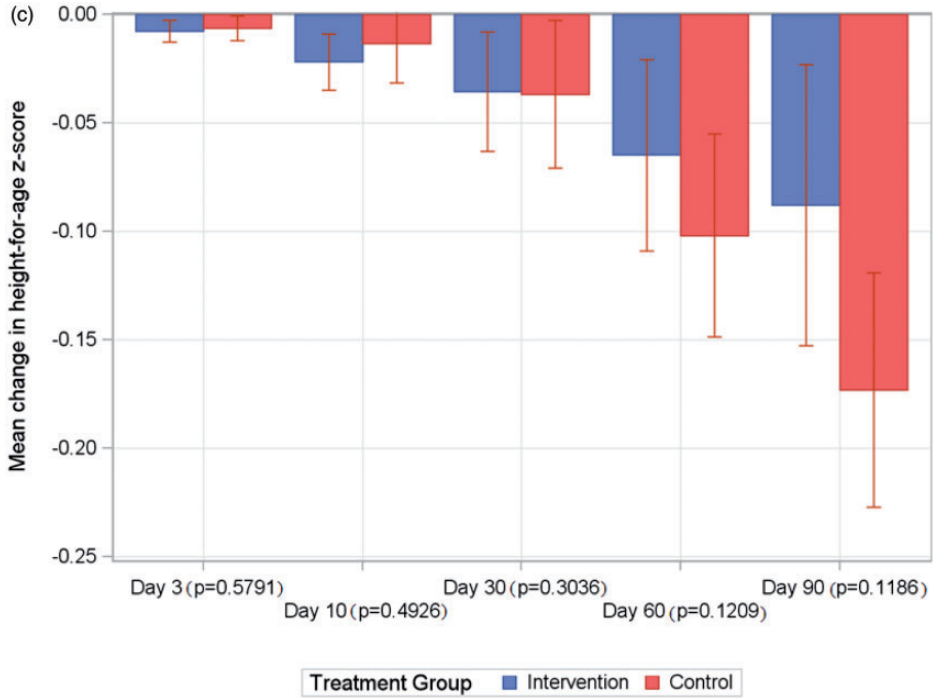


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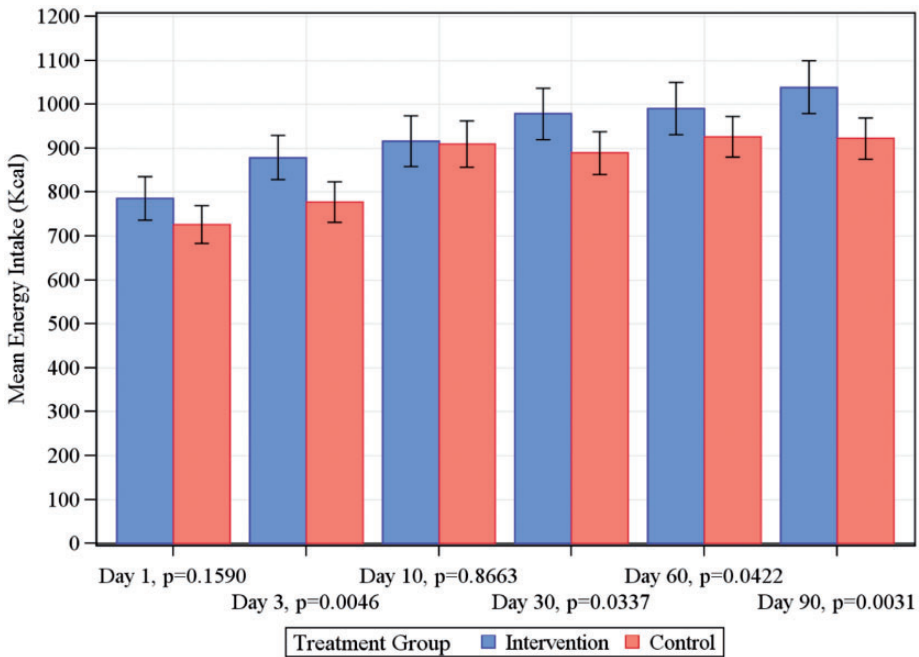


Figure 4. Mean energy intake at baseline and each post-baseline time point in each treatment group. Bars represent the standard deviation.

Table 3. Poisson regression model of recurrent upper respiratory tract infection during the 90-day period

Factors	ITT		Evaluable	
	Incidence rate ratio (95% CI)	p value ^a	Incidence rate ratio (95% CI)	p value ^a
Age (months)	1.03 (1.01, 1.06)	0.0114	1.03 (1.01, 1.06)	0.0132
Sex				
Male	1.00	0.3876	1.00	0.4486
Female	1.35 (0.69, 2.65)		1.31 (0.66, 2.61)	
Change in height-for-age z-score	0.3 (0.15, 0.6)	0.0017	0.3 (0.14, 0.61)	0.0020
Treatment				
Intervention	1.00	0.0361	1.00	0.0317
Control	2.01 (1.03, 3.91)		2.07 (1.05, 4.1)	

^aThe p value was obtained by Poisson regression analysis. ITT, intent-to-treat; CI, confidence interval.

children who were diagnosed with acute URTI. Additionally, the nutrition intervention strategy of ONS and DC over the study period increased the weight-for-age z-score, and there was a lower recurrence rate of URTI in this group compared with those who received DC alone. These significant findings were consistent in ITT and evaluable analyses.

The synergistic and cyclical relationship between poor nutrition and infections is well recognized and the strength of this association increases with the severity of undernutrition.^{10,13} During an acute infection, reduced food intake and increased nutrient requirements for metabolic responses lead to a further deterioration in the nutritional status of children who are nutritionally compromised.¹⁰ This consequently predisposes the child to the cycle of undernutrition and recurring infection.¹⁰ Picky eating behaviour may pose an additional influence on the child's nutritional status during an acute infection because of existing nutrient deficiency and its effect on immunity.^{6,9} Reducing child undernutrition along with timely and appropriate treatment for respiratory tract infections will help improve the child's overall health. We implemented this nutritional

intervention in picky eating children with mild undernutrition who were concurrently being treated for URTI in this study. Children receiving ONS plus DC had a significantly higher energy intake compared with those who received DC alone when experiencing an acute infection. The intervention maintained weight of these children, but those in the control group experienced weight loss during the period of acute illness. Therefore, use of ONS helped minimize the negative effect of acute infection on the child's nutritional status, which may play a role in breaking a persistent cycle of infection and undernutrition.

In our study, the two groups showed significantly improved weight-for-age from baseline to day 90. However, the intervention group showed a significant improvement in this growth parameter from baseline as early as day 10. An improvement in weight from baseline in the control group was not observed until much later, at day 60. The weight-for-age z-score gain was significantly better in the intervention group from day 10 onwards compared with the control group. Our findings are consistent with previous studies that compared the effects of ONS plus DC versus DC alone

in picky eating children at nutritional risk.^{14,23} Consuming an adequate range of different food groups to meet daily nutrient recommendations can be challenging,²⁴ especially with children who have poor appetites or feeding difficulties (e.g., picky eating behaviour). Therefore, paediatric ONS can help overcome the challenge of a nutritional intervention that relies solely on foods to meet the child's nutritional requirements for improving growth and health in at-risk children.

We did not observe any significant improvement in height within each treatment group or between the two groups, similar to a previous study.¹⁴ There was a trend towards improved height gain in the intervention group. However, this gain was inadequate to maintain or improve the z-score compared with the WHO growth standards. Children in our study might have started the intervention during a period of acute infection for which the nutrients were used to replenish nutrients lost because of the illness. Furthermore, the amount of ONS provided to children in our study (224 mL for 24 to <48 months and 448 mL for those aged 48–72 months) was smaller than the dosage used in a previous study where the amount of ONS recommended was based on the child's body weight (e.g., for children aged 36–72 months, this would have been 40 mL/kg/day).¹⁴ In a previous study, preschool children aged 3–4 years at risk of undernutrition who did not have acute URTI or picky eating behaviour received 450 mL of ONS.²⁵ This previous study showed a significant improvement in height from baseline, but this was only found from week 24 onwards. This suggests that a longer treatment period may be necessary for a significant improvement in height.

In our study, along with markedly improved nutritional status, the intervention group showed a reduction in the incidence of URTI over the intervention period.

A positive effect of ONS on reducing acute infections in children at nutritional risk has been reported in various studies. A previous 3-month nutritional intervention study investigated picky eating children who showed a reduction in growth, but the children were clinically healthy at the start of the intervention.¹⁴ This previous study showed that the recurrence rate of developing URTI was significantly lower in the group of children who received ONS and DC compared with those who received DC only (28% versus 51%).¹⁴ Other studies showed a significant reduction in the number of sick days due to gastrointestinal and respiratory tract infections over the study period.^{23,25} Compared with children living in safe and secure environments, children living in a developing country (e.g., India) may have a greater need for additional nutrient support to cope with additional oxidative and environmental stresses due to overcrowding or air pollution. These are risk factors for respiratory tract infections.^{26,27} In this regard, ONS and DC may be more effective than only providing DC alone for improving the nutrient intake of at-risk children. This intake supports children's needs for earlier and improved growth, while boosting their immune system for protection against infections. All of the essential nutrients are required to be in the diet in adequate amounts to support growth and maintain immune function. Therefore, our findings and those from other clinical studies show that paediatric ONS formulated with a specific blend of macro- and micronutrients can be an effective tool to reduce acute respiratory infection in picky eating children who are nutritionally compromised or at nutritional risk.

This study has some limitations. This study was a non-blinded, open-label study. Therefore, there may have been bias in administering the assigned treatment to each study group and assessing the study outcomes, especially regarding subjective

parental self-assessment of the child's appetite level. The use of three 24-hour recalls at baseline versus a single 24-hour recall at post-baseline may result in less comparable dietary intake data across study visits. However, the improvement in energy intake is in accordance with the improvement in weight. This finding suggested that a single 24-hour recall at post-baseline provided a relative measure of dietary intake compared with the three 24-hour recalls completed at baseline. One other limitation is the presence of confounding factors known to be associated with a child's health, especially in developing countries. Details of parental education, overcrowding, living conditions, sanitation, and immunization status were not available for controlling in the analysis of factors associated with the incidence of URTI. Nonetheless, a randomized, controlled study design may help to reduce the effect of these study characteristics. The use of weight-for-age for screening nutritionally at-risk children is another caveat because height was not considered in the assessment of nutritional status at enrolment. Nonetheless, these children presented with acute infections during which weight rapidly responded to a reduced food intake and increased metabolism. Therefore, weight-for-age is a sensitive indicator for evaluating the effect of an intervention. Additionally, because the standard growth curve of the weight-for-age z-score is not available for children older than 5 years, we used BMI-for-age z-scores for a consistent comparison across the different age groups. Finally, parental reporting of child health outcomes might have been a limitation of this study. However, the following evidence suggests that this was a reasonable approach. Validation of 100 hospital admissions showed that parental recall for respiratory illness and infection was 99% valid by checking parental reports against hospital case notes and morbidity coding.²⁰

Parental reports of respiratory infections in infants was found to be strongly associated with hospitalization with respiratory infection, suggesting its validity.²¹ Additionally, a validation study that evaluated the validity of parental reporting of the child's acute otitis media on a monthly basis for 3 months showed an excellent agreement between parental reports of acute otitis media with a history of over the previous month and medical records, with a weighted kappa of 0.88 (95% confidence interval: 0.76–0.94).²² The positive predictive value of a parental report of an acute otitis media episode within the previous month was 85.0% and the negative predictive value was 99.1%.²²

Conclusions

The study shows that a nutritional intervention of ONS and DC in nutritionally at-risk picky eating children with URTI helps to maintain their weight during acute infections. Use of ONS is effective for improving the nutritional status as measured by weight-for-age and BMI-for-age, and it enhances protection against relapse of URTI over the intervention period. India has a considerable health economic and clinical burden of child undernutrition and respiratory tract infection. Our findings suggest that a long-term nutritional intervention that measures the health economic impact of ONS on child growth and infections is required.

Authors' contributions

AG, BK, IS, and VS conceived and designed the study. AG, BK, AK, DC, PP, and SS were responsible for recruitment of the subjects and data collection. AG, BK, IS, VS, AK, TS, PP, SS, YB, YLL, VMHT, and DH participated in data analysis and interpretation. DH drafted the manuscript. All authors read and approved the final manuscript.

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Declaration of conflicting interest

The author(s) declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: IS, VS, YLL, VT, and DH are employees of Abbott Nutrition. Y.B. is an employee of Cognizant Technologies Solution Pvt. Ltd, which is a Contract Research Organization providing statistical services to Abbott Nutrition.

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