

ORIGINAL ARTICLE

MICRONUTRIENT STATUS AND ENERGY INTAKE IN MODERATE ACUTE MALNOURISHED CHILDREN AFTER INTAKE OF HIGH ENERGY NUTRITIONAL SUPPLEMENTS FOR FOUR WEEKS: A RANDOMIZED CONTROLLED STUDY

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Background: Undernutrition including micronutrient deficiency results in adverse health-related outcomes in children of low-medium income countries. This study aims to explore the effect of four weeks of Lipid-based nutritional supplement (LNS) on energy intake, anthropometry and micronutrient status in moderate acute malnourished children. **Methods** Thirty-four children with mean age 7.08 ± 1.47 years and a BMI Z score between -2 and -3 SDS were randomized into LNS and Placebo groups in a single blind randomized control trial. Energy intake, fasting blood samples, and anthropometric measurements were obtained prior to and after four weeks of LNS (535 kcal) or Placebo (92kcal) supplementation in addition to their habitual dietary intake. **Results:** During four weeks of supplementation, energy intake (kcal) [(611±155) to (987±224), $p < 0.001$], weight (kg) [(17.5±2.83) to (18.1±3.24), $p < 0.001$], mid-upper arm circumference (cm) [(14.8±0.91) to (15.1±0.84), $p = 0.005$] and BMI (kg/m^2) [(12.9±0.33) to (13.3±0.45), $p = 0.002$] was significantly improved in the LNS group compared to Placebo. A significant increase in hemoglobin (g/ml) [(12.2±1.14) to (13.7±1.69), $p < 0.01$] and iron levels ($\mu\text{g}/\text{dl}$) [(0.36±0.09) to (0.67±0.20), $p < 0.001$] were observed in the LNS group. No significant differences were detected in the copper and zinc levels. **Conclusion:** Lipid-based nutritional supplement is effective in improving energy intake, nutritional outcomes and iron but not copper and zinc. The trial was registered at www.isrctn.com under reference: ISRCTN147181521.

Keywords: Micronutrients; Energy intake; LNS; Moderate acute malnutrition

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INTRODUCTION

Moderate acute malnutrition (MAM) is extremely pervasive and devastating condition that affects all age groups, including pregnant women and children. MAM is more prevalent with three times greater risk of mortality and morbidity compared to severe acute malnutrition (SAM).¹ Approximately 50% of children are malnourished and 83% of child deaths are ascribed to MAM.² Pakistan has the second most astounding rate of undernourished children where poverty, illiteracy, poor hygiene and lack of nutritionally rich foods are considered the major determinants of malnutrition. In Pakistan one out of every four children below five years of age is undernourished.³

Micronutrient (vitamins and trace minerals) deficiency is one of the significant public health issues affecting millions of people worldwide. In children, micronutrient status is of explicit interest as they can have significant adverse effects on growth, cognitive and physical development. Iron (Fe), Zinc (Zn) and Copper (Cu) are amongst the important trace elements

that are essential for structural and functional activities of all cells in the body, especially for health nutritional recovery of MAM.⁴ According to the National Nutritional Survey (NNS) of Pakistan, Fe and Zn deficiency in under five children is estimated up to 28.6% and 18.6% respectively.⁵ In addition, approximately 25% of the malnourished children are affected from copper deficiency worldwide.⁶

Despite various advances in child health along with the overall decreasing percentage of undernourished children in the current years, MAM still remains undetected; however, management of MAM remains debated specifically in low- and middle-income countries. The most commonly used approach to treat MAM is the Targeted Supplementary Feeding Program (TSFP) including "Ready-to-use supplementary food" (RUSF) as nutritional supplements. These products are rich in vitamins, proteins, carbohydrates, fats and minerals, which are used to enhance nutritional rehabilitation.⁷ Several studies have demonstrated the effectiveness of nutritional supplements to improve nutritional outcomes, recovery rate, quality of life,

weight-for-height Z-score (WHZ) in undernourished children and also had a positive impact on blood nutrient levels.⁸ However, one recent study found no benefit of nutrient supplements in malnourished children⁹, or the overall effect of supplements was lower than expected¹⁰.

Lipid based nutritional supplements (LNS) are high energy dense pastes (with a high lipid content) that have been designed for the prevention of stunting and wasting. Due to its high energy content, long-shelf life and microbiologically safe packaging they are much effective in promoting rapid weight gain in undernourished children, both SAM and MAM.¹¹ However, use of LNS supplement and their effect on the levels of micronutrients among MAM school going children is not investigated widely. Therefore, the current study aims to investigate the effect of four weeks of LNS on plasma levels of micronutrients (Fe, Zn and Cu), energy intake and recovery from malnutrition in free-living children with MAM attending school.

MATERIAL AND METHODS

This was a single blind randomized controlled study conducted in various government schools (both boys and girls) of Hayatabad. Research procedures took place in the clinical trial room of Institute of Basic Medical Sciences, Khyber Medical University, Peshawar, Pakistan over a period of 8 months (from September, 2017 to April, 2018). The study population was moderate acute malnourished school going children between 5–10 years of age. Ethical approval was obtained from the Research Ethics Committee of Khyber Medical University (approval no: DIR/KMU-EB/EN/000455). After obtaining consent from school principals and parents of the participants, anthropometric measurements were obtained following WHO standard procedures and were used to calculate BMI Z-scores using the WHO standards. A total of 37 children having BMI Z-score between -2 and -3 were recruited for the study and were randomly allocated into two groups, LNS (n=19) and Placebo (n=18) using Computer Randomizer software version 30. Children suffering from eating disorders, allergies, using supplements or having any gastrointestinal tract disorders were excluded. The nutritional composition of both the supplements is shown in table-1.

Two main trial days were conducted with a 4-week difference in between and all the participants came to the clinical trial room in the fasted state. On the morning of both of the trial days, fasting blood samples and anthropometric measurements including weight, height, mid upper arm circumference (MUAC), skinfold thickness measures and waist to hip ratio were taken from all the participants and were subsequently served with either LNS (535 Kcal/day; Acha Mum by WFP) or Placebo (92 Kcal/day) on the basis of group

allocation. Placebo was prepared with 58 g low fat milk (Nesvita) providing (24 kcal) and 42g roasted chickpeas (68 kcal). After taking the LNS or Placebo, participants were served *ad libitum* buffet breakfast and lunch at 90 and 240 minutes respectively. Sociodemographic data regarding parent's characteristics, i.e., (status, occupation, education and monthly income), number of siblings, number of family members and family accommodation expenditure were also collected from the participants. The supplements (LNS/Placebo) were provided to the participants for four weeks on a daily basis at the school and were requested to take these supplements in small portions between meals in addition to their regular diet. Furthermore, empty packets of the supplements were collected to check compliance.

Ad libitum meals comprised of a variety of foodstuffs served three times in a greater quantity than expected to be consumed by the participant. Kitchen weighting scale was used to measure the weight of each food offered in the buffet meals. *Ad libitum* breakfast contained a variety of foods including paratha, fried and boiled eggs, bread, jam, cream, black milk tea, milk and sometimes juice according to participants choice. While in *ad libitum* lunch biryani, chicken korma, kaabli pulao, red kidney bean curry, raita and naan roti was usually served. About half an hour time was given to the participant and was requested to eat according to their desire. Same type and same amount of food was delivered using same utensils, served in the same setting on both the trial days to avoid any changes in eating behaviour. Likewise, the researchers were not present in the room at the time of meal consumption by the participants to avoid any impact of their food intake.

Multiple pass dietary recalls were used to collect the dietary data of the participants for three consecutive days that is three days (3d) before the initial trial visit (day 1st), 3d after the start of the trial initiation and 3d at the end of intervention. However, after ending of the trial interventions (30 days) no dietary data was collected. This was done to measure and to compare the difference between the regular intake of participants before and after the supplement from their regular diet and to check the effect of supplementing on routine dietary intake and energy compensation. Energy intake was calculated with the diet analysis software Windiet 2005. For enhancing results accuracy and minimize estimation bias, three researchers had individually carried out the dietary intake analysis and mean values of each were considered as final.

Blood was obtained from antecubital vein using aseptic techniques. Serum was separated through centrifugation and stored at -80 °C. Blood samples were taken for the analysis of plasma iron, zinc and copper levels using flame atomic absorption spectrometry (FAAS); Perkin Elmer Atomic Absorption Spectrometer (model AAS-700) in Centralized Research

Laboratory (CRL), Peshawar and Hb levels were assessed using haematology analyzer. A proper wet acid digestion method was used to digest plasma before the analysis.

Statistical analysis of data was done using Minitab version 17. Student's t test (paired t-test) was used as a test of significance. Chi-square test was used for categorical data. A p-value less than 0.05 were considered significant.

RESULTS

Total nine hundred fifty-seven (n=957) children were screened out from different government schools. One hundred thirty-one (13.7%) participants were found to be in the moderately acute undernourished category. Out of which 26 participants were excluded based on the exclusion criteria and 68 participants refused to participate. A total of thirty-seven (37) MAM children with BMI-Z score of -2.35 ± 0.29 and mean age 7.07 ± 1.42 years were recruited in this study. Three participants dropped out therefore a total thirty-four participants completed the study trial (figure-1).

The socioeconomic condition of both the groups included in the study shows that all the participants were from low socioeconomic background (5000 to 35000 PKR). The professional status of the participant's parents shows that 17 (100%) of the fathers in LNS and 16 (94.1%) in Placebo were on job and mostly are drivers, laborers and guards. Similarly, 15 (88.24%) of the participant mothers in LNS were housewives. Moreover, Literacy rate among the parents were low too. The educational status reveals that 23.5% of the fathers in both the groups [LNS and Placebo] were illiterate while 17.6% were educated up to primary, middle or high school levels. On the other hand, 58.8% mothers in LNS and 82.4% in Placebo were uneducated. Furthermore, data taken about the household status shows that majority of the children from both the groups were living in separate houses, having residence in urban areas and majority had consumed community tap water [14 (82.35) in LNS, 15 (88.24%) in Placebo].

The anthropometric characteristics of both the groups are shown in table-2. There was significant weight gain in the LNS group [(17.5±2.83) to (18.1±3.24), $p < 0.01$] compared to Placebo ($p = 0.29$). In addition, a significant increase was observed in the mean value of mid upper arm circumference [(14.7±0.91) to (15.1±0.84), $p = 0.005$] and BMI [(12.9±0.33) to (13.3±0.45), $p = 0.002$] in LNS compared to Placebo.

Comparison for energy intake (EI) and macronutrient intake between the LNS and Placebo groups on both the main clinical trial days, day 1 (1st main day) and day 31 (2nd main day) are presented in

figure-2. The supplements (LNS/ Placebo) were served to the participants in the morning before the breakfast.

During the breakfast and lunch (without considering energy from the supplement), the EI was significantly declined in the LNS group (492.7 ± 185.7) in contrast with Placebo (776.4 ± 300.8) on the 1st main day. Similarly, a significant decline was also found in intake of proteins ($p < 0.05$), fats ($p < 0.05$) and CHO ($p < 0.01$) in LNS group as compared with Placebo, when the macronutrient intake of breakfast and lunch (without including the supplement) was summed up. However, no significant difference was observed between both the groups when the total EI of breakfast, lunch and the energy from the supplement was combined. Whereas, a significant decrease was found only in CHO ($P < 0.01$) in LNS group as compared with Placebo, as summarized in figure-2.

Moreover, on the 2nd main trial day (day 31), no significant differences were found in the EI between both groups (LNS vs Placebo, 627.9 ± 300.1 vs 740.9 ± 311.9 , $p = 0.290$) during the breakfast and lunch (without including supplement). However, the overall EI in the LNS group was higher (879.3 ± 327.1) as compared to Placebo (772.4 ± 316.8) when the EI during the breakfast, lunch and the supplement was analyzed combined. Whereas, in case of macronutrient intake, only a significant increase ($p < 0.005$) in fats intake was found in LNS group in comparison to Placebo when the sum of the intake during breakfast, lunch and the supplement was calculated.

Dietary recalls were recorded three days (3d) before the initial trial visit (day 1st), 3d after the start of the trial initiation and 3d at the end. However, after ending of the trial, no dietary data was collected. There was no significant difference ($p = 0.981$) found in energy and macronutrient intake before the start of the trial, however, significantly high energy and macronutrients intake were observed 3d after starting the trial ($p < 0.001$) and at the end ($p < 0.001$) in the LNS group compared to Placebo as shown in table-3.

Haemoglobin levels were significantly higher in LNS group ($p < 0.01$) compared to Placebo ($p = 0.065$). Iron levels were significantly increased in both groups with more obvious increase in LNS group. In contrast, a non-significant increase in the levels of copper and a decrease in zinc levels were noticed in both groups (Table-4).

Hedonic scale was used to know about the taste and acceptability of the supplement. Majority of the study population liked the taste of LNS and Placebo with no statistical differences between the two groups. While 1 child from LNS and 2 children from Placebo group slightly dislike the taste of the supplement

Table-1: Nutritional Composition of LNS (Achaa Mum) and Placebo as supplementary foods

	LNS 100 g/day	Placebo 100 g/day
Energy (kcal)	535	92
Macronutrients		
Proteins (g)	14	5.54
Carbohydrates (g)	22	14.2
Fats (g)	30	0.58
Minerals		
Zinc (mg)	11	-
Iron (mg)	10	0.22
Copper (mg)	1.4	-
Calcium (mg)	535	0.16
Vitamin D (mcg)	15	-
Vitamin C (mg)		0.02

Table-2: Changes in Body Composition after four weeks of supplementation in LNS and Placebo groups

Variables	Before LNS	After LNS	p-value	Before Placebo	After Placebo	p-value
Height (cm)	115.7±8.99	116.2±9.39	0.12	122.3±9.54	122.5±9.44	0.39
Weight (kg)	17.5±2.83	18.1±3.24	0.0005***	19.4±2.92	19.7±3.41	0.29
BMI (kg/m ²)	12.9±0.33	13.3±0.45	0.002**	12.9±0.31	13.0±0.70	0.56
SDS Height	-0.98±1.41	-0.98±1.47	0.96	-0.09±1.26	-0.15±1.24	0.10
SDS Weight	-2.19±1.05	-1.99±1.18	0.007**	-1.57±0.85	-1.58±0.74	0.90
SDS BMI	-2.35±0.28	-1.96±0.34	0.001**	-2.37±0.31	-2.36±0.79	0.95
MUAC (cm)	14.7±0.91	15.1±0.84	0.005**	15.2±0.79	15.5±0.93	0.10
Biceps (mm)	3.91±1.02	3.92±1.15	0.96	3.67±1.00	3.73±1.17	0.57
Triceps(mm)	6.35±1.42	6.64±1.75	0.18	6.44±1.55	6.45±1.94	0.95
Mid abdomen(mm)	4.49±1.45	4.77±1.56	0.13	4.98±1.59	5.08±1.7	0.39
Sub scapular (mm)	4.59±0.64	4.63±0.75	0.62	4.72±0.80	4.75±0.83	0.71
Waist/Hip	0.86±0.05	0.85±0.04	0.07	0.85±0.07	0.82±0.05	0.07

Abbreviations: MUAC, Mid upper arm circumference, BMI, basal metabolic index, SDS, standard deviation score (*p<0.05, **p<0.01, ***p<0.001)

(Before LNS and Placebo means before supplementation on 1st trail day, After LNS and Placebo means after 4 weeks of supplementation on 2nd trial day)

Table-3: Comparison between the total energy intake and Macronutrient intake of both the groups on three days before and after 1st day trial and three days at the end

	LNS (n=17)	Placebo (n=17)	p-value
Three days before 1st day trial			
Energy (kcal)	611.4±155.5	610.2±139.90	0.981
Proteins (g)	18.6±4.20	19.2±5.61	0.752
Fats (g)	24.5±8.30	23.6±8.34	0.736
CHO (g)	83.9±19.81	85.7±15.4	0.765
Three days after 1st day trial			
Energy (kcal)	1008.7±170.4	660.9±168.7	<0.001***
Proteins (g)	30.7±6.18	22.7±5.88	0.001**
Fats (g)	47.1±10.1	23.1±9.04	<0.001***
CHO (g)	93.7±16.7	93.3±21.4	0.96
Three Days at the end (at 26, 27 and 28th day of the trial)			
Energy (kcal)	987.8±224.1	708.5±159.8	<0.001***
Proteins (g)	29.2±7.81	23.3±4.88	0.01*
Fats (g)	43.6±10.4	43.6±8.01	<0.001***
CHO (g)	102.1±30.2	100.1±22.7	0.824

Abbreviations: CHO, carbohydrates (*P<0.05, **P<0.01, ***P<0.001)

Table-4: Comparison between the Haemoglobin and plasma levels of Iron, Zinc and Copper before and after Supplementation and as N (%) values

Parameters	LNS (n=16)			Placebo (n=16)		
	Before LNS	After LNS	p-value	Before Placebo	After Placebo	p-value
Hb (g/mL)*	12.2±1.14	13.7±1.69	0.007**	12.7±0.95	13.57±1.52	0.065
N (%)	2 (13.3)	0 (0)		0 (0)	0 (0)	
Iron (µg/dl)**	35.8±9.04	67.1±14.0	<0.001***	45.6±15.19	66.95±6.35	<0.001***
N (%)	15 (93.7)	0 (0)		9 (56.2)	0 (0)	
Copper (µg/dl)***	8.45±2.11	9.21±2.33	0.095	8.79±2.88	9.99±2.12	0.145
N (%)	16 (100)	16 (100)		16 (100)	16 (100)	
Zinc (µg/dl)****	14.8±13.6	13.3±1.6	0.709	23.1±17.7	16.17±16.6	0.309
N (%)	16 (100)	16 (100)		15 (93.7)	16 (100)	

Abbreviations: Hb, hemoglobin, (Deficient (<11 g/ml*), Deficient (<55 µg/dl**), Deficient (<85 µg/dl***), Deficient (<60 µg/dl****)

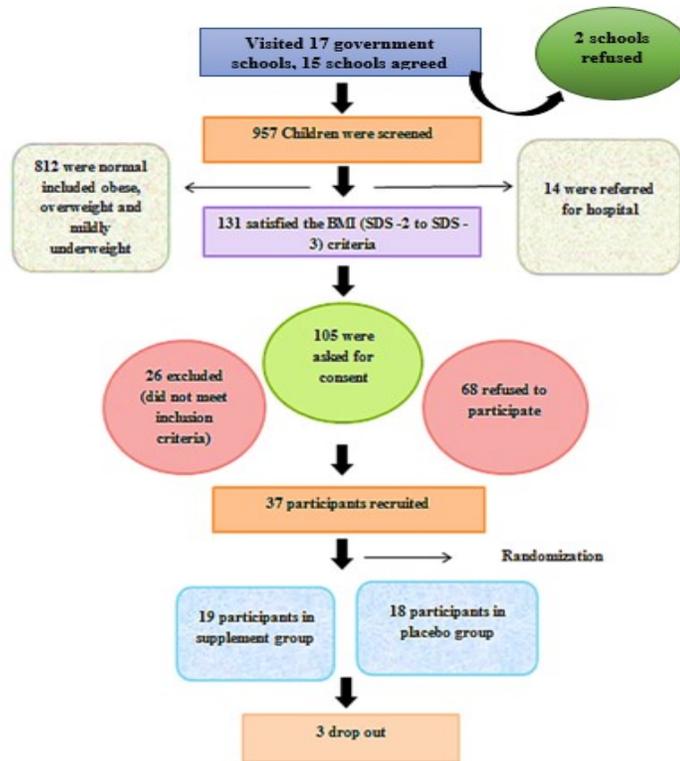


Figure-1: Diagrammatic representation of participant’s recruitment and treatment allocation

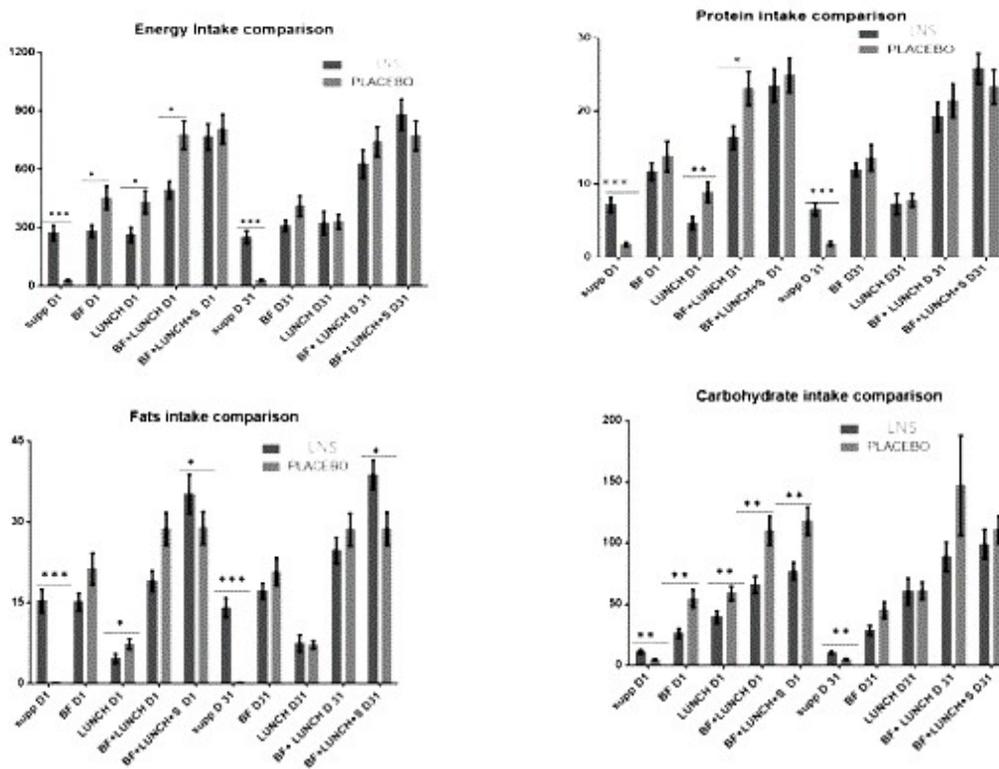


Figure-2: Bar charts representation for the comparison of the energy intake and macronutrients intake (CHO, Proteins and Fats) between LNS and Placebo during breakfast and lunch at both the main trial days. BF, breakfast; S, supplement.

DISCUSSION

Malnutrition, micronutrient deficiency and low socioeconomic status can result in adverse health and preventing millions of children from attaining their full growth. This study was designed to observe the efficacy of high caloric dense supplement (LNS) versus low energy dense (Placebo) for a period of one month (four weeks); in improving the micronutrient status and nutritional intake of children with MAM. We observed energy intake calculated through multiple pass 24 hours' dietary recalls significantly improved in the LNS group ($p < 0.001$) in contrast to Placebo after supplementation although no difference was observed at baseline (Before the three days of trial). Previous studies also documented an increase in the energy intake after supplementation.¹² At baseline, energy intake of our study population was extremely low (611Kcal) compared to the normal estimated average requirement (EAR) of children between 5–10 years age (1500–2000 Kcal) per day¹³. However, after LNS supplementation a significant improvement was observed in their energy intake and close to their normal estimated values but still it is quite lower.

Significant decline in energy intake was observed during the breakfast in LNS group as compared to Placebo on 1st day, which could be due to energy dense supplement (535 Kcal, LNS) before breakfast that might suppress energy intake during breakfast. Similar reductions were observed in energy intake results during breakfast¹², along with immediate and short-term suppression in the energy intake of meal after supplement intake¹⁴. However, in our study we observed a prolonged suppression of energy intake in moderately malnourished children which extends up to lunch time. Moreover, on the 1st trial day, the total energy intake showed no significant difference between the two groups. This is in contrast to underweight females where overall energy intake was increased in the supplement group.¹² Likewise, at the end of the trial the overall energy intake was higher in LNS group compared to Placebo. Thus, it shows that if the LNS are given on daily basis, children adapt and there is less suppression of the energy intake from the regular habitual diet. Although, with LNS there is an overall increase in energy intake, however, this increase is less than expected as observed previously. Further mechanistic studies are required in children to assess the extended impact of lipid-based supplements on energy intake.

In our study children like the taste of supplements which is also a well reported factor for the confirmation of its regular intake. Only 1% of the children dislike the taste of the supplement in our

study, which is in contradiction with other studies where 29% dislike the supplement taste.¹⁰ Thus, it could not have an effect on the data of regular energy intake from participants in the present study. Moreover, throughout the trial it was noticed that parents of the children from both the groups were more cautious about their child eating behaviours. Both the LNS and Placebo supplements were similar in taste, colour and had the same consistency. Also, we had run a pilot study regarding identification of Placebo. Forty participants were asked to taste and only 20% have identified Placebo correctly. However, instead of this, the overall average energy intake was much greater in LNS due to its high energy rich constituents. Furthermore, during the trial we had asked the questions from the participants regarding whether they were eating the LNS or Placebo. Only 20% of the participants were able to identify the supplement correctly. Nutritional counselling was also given to the participants in both the groups and we have found that after nutritional counselling there is an increase in the energy intake and the interest of the participants or parents regarding supplement use were improved.

Another important finding in the LNS group showed a significant improvement in some anthropometric measures particularly weight, MUAC and BMI, although, the weight gain was much lower (0.62 kg) than the expected (2 kg) [Provision of daily extra 500kcal energy for one month increased a weight gain of 2 kg (expected result)]. Our results are in line with previous findings where weight gain was substantively less compared to predicted with supplements.¹⁵ This might be due to acute suppression of appetite after supplementation, where children eat less and more energy spending because of physical activities. Moreover, sharing of the supplements with siblings/colleagues might be the factors influencing the expected weight gain. Likewise, BMI and MUAC in LNS group was significantly improved compared to Placebo. This is in accordance with study by Fabiansen, *et al.* in underweight children.¹⁶ Moreover, the low socio-demographic status may have an impact on nutritional and anthropometric status as it is considered among one of the important factors that have deleterious effects on the health and growth of children.¹⁷

Furthermore, haemoglobin and iron levels were significantly increased in the LNS group compared to Placebo. Although at baseline, majority of the participants had low iron levels (LNS; 0.36 ± 0.09 mg/L), which is in line with the results of a study by Kiran Bains, *et al.* where 84.6% children had low serum iron levels (0.35 ± 0.01 mg/L).¹⁸ This significant change in iron levels could be possible

due to the high caloric lipid-based supplements with high iron concentration. Furthermore, a highly significant increase was observed in the iron status in Placebo group compared to baseline values. This might be due to nutritional counselling at the start, and previous study has revealed that nutritional counselling could be as effective as specialized (food-based interventions) for the management of MAM.¹⁹ Low Cu levels were observed, which is in accordance with previous findings in malnourished population. The serum concentration of copper could be affected by various factors including intake of copper amount in routine diet, absorption by the intestine, accumulated iron, Cu: Zn ratio and others. It is possible that our participants might have a deficiency due to consumption of food deficient in copper. However, after four weeks of supplementation slight improvement in copper levels was observed but this effect did not reach significance. Other studies had also observed improvement²⁰, however, only few studies have observed the impact of LNS supplement on Cu levels. Furthermore, Zn levels of both the groups' participants were very low at the baseline. Previous studies also observed considerably low levels of zinc in malnourished children at the baseline.²¹ In Pakistan it is already documented in 2018 survey that 18.6% of the children are zinc deficient.⁵ Insufficiency of zinc micronutrients' status has an impact on diverse health disorders such as growth retardation, less immunity and, impairment of absorption. Moreover, in the current research after the supplementation of four weeks, no improvement was found in zinc levels, in contrast, a slight decrease was observed in both groups. Many studies found no improvement in zinc levels after intake of multiple micronutrient supplements or ready to use supplements including a cluster randomized trial by Ackatia-Armah, *et al.*²² However, a study in which zinc supplements were given alone an improvement in zinc levels were found.²³

It has been observed that iron and copper in diet interfere with the plasma level of zinc as both compete for absorption in the small intestine or transportation in liver or blood. This fact is quite obvious in our study where significant increase was observed in average plasma iron levels but the average levels of plasma zinc were further decreased. In addition, the influence of the presence of parasites on the availability and absorption of Zn is well studied.²⁴ It also might be a possible reason that intestinal infections, secondary to the presence of parasites in the gut, affect the metabolism of Zn which might result in lowering the levels of Plasma Zn. However, in our study we dewormed all the participants before coming to the trial.

Researchers believed that increased Cu levels are strongly associated with increased haemoglobin and inverse with Zn levels, the special condition can be seen in the children with hyperactivity.²⁵ Extreme elemental components of zinc, iron and copper in the supplements were necessary to measure as it may result in reduction of another component. Hence a specific model with the optimum ratio of these micronutrients should be recommended and considered necessary before LNS supplements.²⁶

Like other studies, our study also acknowledges some strength and limitations. The main strength of our study was the good compliance in both LNS and Placebo group. The major reason was that supplement was provided daily and the empty sachets were collected on the same day along with nutritional counselling of parents and children. Furthermore, multiple pass 24 hours dietary recall were used that reduces the misreporting bias and it estimates the exact portion of the food size consumed which helps in the exact intake by the children. In our study children like the taste of supplements which is also a well reported factor for the confirmation of its regular intake.

Main limitation of our study is that we could not check the level of other biomarkers such as CRP and Albumin that have a huge impact on zinc and copper levels in blood. These would have provided a broader and complete picture of the nutritional status of these children. Furthermore, four weeks' supplementation was a short duration to study the impact on anthropometric parameters especially the height of these children. Moreover, the study was conducted in a small district of Peshawar with a small cohort and therefore our findings cannot be generalized to a larger population. In addition, a comparison with a healthy control would have provided a more robust comparison and the results could be applicable to healthy children.

CONCLUSION

The conclusion of this study is that LNS improves nutritional outcomes and micronutrient levels especially iron levels of moderate acute malnourished children in a community setting. Moreover, LNS increased the overall energy intake of the malnourished children but the increase was lower than expected.

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AUTHORS' CONTRIBUTION

SF conceived, designed and did statistical analysis, data interpretation and editing of manuscript. FN did data collection, statistical analysis and manuscript writing. SHH and KG did critical review, data interpretation and editing, final approval of manuscript. SN and RN did review and final approval of manuscript

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Competing Interest: None to declare

REFERENCES

- Girma A, Woldie H, Mekonnen FA, Gonete KA, Sisay M. Undernutrition and associated factors among urban children aged 24–59 months in Northwest Ethiopia: a community based cross sectional study. *BMC Pediatr* 2019;19(1):214.
- James P, Sadler K, Wondafraash M, Argaw A, Luo H, Geleta B, *et al.* Children with moderate acute malnutrition with no access to supplementary feeding programmes experience high rates of deterioration and no improvement: results from a prospective cohort study in rural Ethiopia. *PLoS One* 2016;11:e0153530.
- Hirani SAA. Malnutrition in young Pakistani children. *J Ayub Med Coll* 2012;24(2):150–3.
- Marasinghe E, Chackrewarthy S, Abeysena C, Rajindrajith S. Micronutrient status and its relationship with nutritional status in preschool children in urban Sri Lanka. *Asia Pac J Clin Nutr* 2014;24(1):144–51.
- Imanzadeh F, Olang B, Khatami K, Hosseini A, Dara N, Rohani P, *et al.* Assessing the Prevalence and Treatment of Malnutrition in Hospitalized Children in Mofid Children's Hospital During 2015–2016. *Arch Iran Med* 2018;21(7):302–9.
- Golden MH. Proposed recommended nutrient densities for moderately malnourished children. *Food Nutr Bull* 2009;30(3 Suppl):S267–342.
- Cawood AL, Elia M, Sharp SK, Stratton RJ. Malnutrition self-screening by using MUST in hospital outpatients: validity, reliability, and ease of use. *Am J Clin Nutr* 2012;96(5):1000–7.
- Kang M, Kim DW, Jung HJ, Shim JE, Song Y, Kim K, *et al.* Dietary supplement use and nutrient intake among children in south Korea. *J Acad Nutr Diet* 2016;116(8):1316–22.
- Poustie VJ, Russell JE, Watling RM, Ashby D, Smyth RL. Oral protein energy supplements for children with cystic fibrosis: CALICO multicentre randomised controlled trial. *BMJ* 2006;332:632–6.
- Fatima S, Malkova D, Wright C, Gerasimidis K. Impact of therapeutic food compared to oral nutritional supplements on nutritional outcomes in mildly underweight healthy children in a low-medium income society. *Clin Nutr* 2018;37:858–63.
- Thakwalakwa C, Ashorn P, Phuka J, Cheung YB, Briend A, Puimalainen T, *et al.* A lipid-based nutrient supplement but not corn-soy blend modestly increases weight gain among 6- to 18-month-old moderately underweight children in rural Malawi. *J Nutr* 2010;140:2008–13.
- Fatima S, Gerasimidis K, Wright C, Tsiountsioura M, Arvanitidou EI, Malkova D. Response of appetite and potential appetite regulators following intake of high energy nutritional supplements. *Appetite* 2015;95:36–43.
- European Food Safety Authority (EFSA). Outcome of public consultations on the Scientific Opinions of the EFSA Panel on Nutrition, Novel Foods and Food Allergens (NDA) on Dietary Reference Values for sodium and chloride. EFSA Supporting Publications [Internet]. 2019 Sep [cited 2021 Jan];16(9). Available from: <https://data.europa.eu/doi/10.2903/sp.efsa.2019.EN-1679>
- Fatima S, Gerasimidis K, Wright C, Malkova D. Impact of High Energy Nutritional Supplement Drink consumed for five consecutive days on cardio metabolic risk factors in underweight females. *Proceedings of the Nutrition Society* 2015;74:OCE1.
- Thapa BR, Goyal P, Menon J, Sharma A. Acceptability and efficacy of locally produced ready-to-use therapeutic food nutrient in the management of severe acute malnutrition in comparison with defined food: a randomized control trial. *Food Nutr Bull* 2017;38:18–26.
- Fabiansen C, Phelan KP, Cichon B, Ritz C, Briend A, Michaelsen KF, *et al.* Short children with a low midupper arm circumference respond to food supplementation: an observational study from Burkina Faso. *Am J Clin Nutr* 2016;103(2):415–21.
- Letourneau NL, Duffett-Leger L, Levac L, Watson B, Young-Morris C. Socioeconomic status and child development: A meta-analysis. *J Emot Behav Disord* 2013;21:211–24.
- Bains K, Kaur H, Bajwa N, Kaur G, Kapoor S, Singh A. Iron and zinc status of 6-month to 5-year-old children from low-income rural families of Punjab, India. *Food Nutr Bull* 2015;36(3):254–63.
- Nikiema L, Huybregts L, Kolsteren P, Lanou H, Tiendrebeogo S, Bouckaert K, *et al.* Treating moderate acute malnutrition in first-line health services: an effectiveness cluster-randomized trial in Burkina Faso. *Am J Clin Nutr* 2014;100(1):241–9.
- Weisstaub G, Medina M, Pizarro F, Araya M. Copper, iron, and zinc status in children with moderate and severe acute malnutrition recovered following WHO protocols. *Biol Trace Elem Res* 2008;124(1):1–11.
- Prado EL, Abbedou S, Yakes Jimenez E, Somé JW, Ouédraogo ZP, Vosti SA, *et al.* Lipid-based nutrient supplements plus malaria and diarrhea treatment increase infant development scores in a cluster-randomized trial in Burkina Faso. *J Nutr* 2015;146(4):814–22.
- Ackatia-Armah RS, McDonald CM, Doumbia S, Erhardt JG, Hamer DH, Brown KH. Malian children with moderate acute malnutrition who are treated with lipid-based dietary supplements have greater weight gains and recovery rates than those treated with locally produced cereal-legume products: a community-based, cluster-randomized trial. *Am J Clin Nutr* 2015;101(3):632–45.
- Mozaffari-Khosravi H, Shakiba M, Eftekhari M-H, Fatehi F. Effects of zinc supplementation on physical growth in 2–5-year-old children. *Biol Trace Elem Res* 2009;128(2):118–27.
- Yones DA, Galal LA, Abdallah AM, Zaghlool KS. Effect of enteric parasitic infection on serum trace elements and nutritional status in upper Egyptian children. *Trop Parasitol* 2015;5(1):29–35.
- Ugwuja E, Ejikeme B, Ugwu N, Obidoa O. A comparative study of plasma trace elements (copper, iron and zinc) status in anaemic and non-anaemic pregnant women in Abakaliki, Nigeria. *Online J Health Allied Sci* 2011;10(2):1–3.
- Gregory PJ, Wahbi A, Adu-Gyamfi J, Heiling M, Gruber R, Joy EJ, *et al.* Approaches to reduce zinc and iron deficits in food systems. *Glob Food Secur* 2017;15:1–10.

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