Effectiveness of ready-to-use therapeutic food compared to a corn/soy-blend-based pre-mix for the treatment of childhood moderate acute malnutrition in Niger

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Summary

Standard nutritional treatment of moderate acute malnutrition (MAM) relies on fortified blended flours though their importance to treat this condition is a matter of discussion. With the newly introduced World Health Organization growth standards, more children at an early stage of malnutrition will be treated following the dietary protocols as for severe acute malnutrition, including ready-to-use therapeutic food (RUTF). We compared the effectiveness of RUTF and a corn/soy-blend (CSB)-based pre-mix for the treatment of MAM in the supplementary feeding programmes (SFPs) supported by Médecins Sans Frontières, located in the Zinder region (south of Niger). Children measuring 65 to <110 cm, newly admitted with MAM [weight-for-height (WHM%) between 70% and <80% of the NCHS median] were randomly allocated to receive either RUTF (Plumpy'Nut®, 1000 kcal day^{-1}) or a CSB pre-mix (1231 kcal day^{-1}). Other interventions were similar in both groups (e.g. weekly family ration and ration at discharge). Children were followed weekly up to recovery (WHM% $\geq$ 85% for 2 consecutive weeks). In total, 215 children were recruited in the RUTF group and 236 children in the CSB pre-mix group with an overall recovery rate of 79.1 and 64.4%, respectively ($p < 0.001$). There was no evidence for a difference between death, defaulter and non-responder rates. More transfers to the inpatient Therapeutic Feeding Centre (I-TFC) were observed in the CSB pre-mix group (19.1%) compared to the RUTF group (9.3%) ($p = 0.003$). The average weight gain up to discharge was 1.08 g kg^{-1} day^{-1} higher in the RUTF group [95% confidence interval: 0.46–1.70] and the length of stay was 2 weeks shorter in the RUTF group ($p < 0.001$). For the treatment of childhood MAM in Niger, RUTF resulted in a higher weight gain, a higher recovery rate, a shorter length of stay and a lower transfer rate to the I-TFC compared to a CSB pre-mix. This might have important implications on the efficacy and the quality of SFPs.

Key words: child nutrition disorder, wasting, fortified blended flour, ready-to-use therapeutic food, Niger, randomized controlled trial.

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Introduction

Standard nutritional treatment of moderate acute malnutrition (MAM) relies on fortified blended flours though their importance to treat this condition is a matter of discussion [1]. With the newly introduced World Health Organization (WHO) growth standards [2], nutritional programmes formerly using the weight-for-height percentage of the

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median (WHM%) [National Center for Health Statistics (NCHS) reference] may expect to admit up to eight times more severely malnourished children (Z-score WHO reference) switching from the NCHS moderately malnourished category [3]. Consequently, those children, previously classified as moderately malnourished, will be treated following the dietary protocols as for severe acute malnutrition, including ready-to-use therapeutic food (RUTF).

Made from peanuts, powder milk, sugar, vegetable oil, vitamins and minerals, RUTFs have important advantages compared to fortified blended flours. They are energy-dense pastes that do not require any preparation before consumption. Also, they are manufactured in individual packages, easy to store and to preserve from bacterial contamination. In Malawi, three studies have evaluated the superiority of RUTF on standard therapy for the treatment of moderately wasted children [4, 5] or for children at risk of manutrition [6]. All showed a better recovery rate and a higher weight gain for RUTF. In 2006, Médecins Sans Frontières (MSF) started to use RUTFs in its home-based Supplementary Feeding Programme (SFP) in Niger with encouraging results [7].

There is a crucial need to develop and evaluate specific treatment for children at an early stage of acute malnutrition and, in the meantime, it is important to evaluate the effectiveness of available RUTFs in the rehabilitation of those children. We compared the clinical effectiveness of RUTF and a corn/soy-blend (CSB)-based pre-mix for the treatment of moderately malnourished children in Niger.

Material and Methods

Study setting

The study was conducted in two Supplementary Feeding Centres (SFCs) supported since 2006 by MSF in the remote and difficult-to-access villages of Mallawa and Bangaza (Magaria department, Zinder region, South of Niger). These two SFCs were part of a larger programme with a total of 14 Ambulatory Therapeutic Feeding Centres and 2 inpatient Therapeutic Feeding Centres (I-TFC). The area is affected by chronic food insecurity marked each year with a 'hunger gap', period when the previous year's stocks have run out but the new crop is not yet ready for harvest. This period usually lasts from 3 to 6 months between May and October. In the Zinder region, in 2006, stunting among children <5 years of age was estimated at 59% and wasting at 11% [8].

Study participants

All children measuring 65 to <110 cm (used as a proxy for the age of 6–59 months), newly admitted to the Mallawa and Bangaza SFCs with MAM and good appetite were eligible for inclusion. MAM was defined as a WHM% from 70 to <80% (NCHS reference), without oedema and with a mid-upper arm circumference (MUAC) ≥110 mm. Children requiring hospitalization as well as those who had been hospitalized or admitted in a nutritional programme in the previous 2 months were excluded. Due to high workload during the hunger gap, children with a MUAC ≥135 mm and apparently healthy were not admitted to the SFP.

Study design and intervention

We conducted a field-randomized trial. The allocation sequence (blocks of 10) was computer generated and concealed in sealed envelopes. After informed consent of the caretaker, children were individually randomized to receive either RUTF [Plumpy'Nut® (Nutriset, Malaunay, France) two packs daily, i.e. 1000 kcal day^{-1}] or, as suggested in the nutritional national protocol, a CSB pre-mix (1750 g of CSB, 175 ml of vegetable oil and 105 g of sugar, i.e. 1231 kcal day^{-1}). Haemoglobin concentration was screened at admission for all children and daily iron and folic acid supplementation was given to all children presenting with a haemoglobin <9 g dl^{-1}. In addition, in the CSB pre-mix group only, children with a haemoglobin ≥9 and <11 g dl^{-1} were given a weekly iron supplementation (100–200 mg according to weight), as recommended by the nutritional national protocol. No iron supplementation was given to children with a haemoglobin ≥11 g dl^{-1} to prevent increased risk of malaria infection [9, 10]. Other interventions were similar in both groups and included at admission: measles vaccination, single vitamin A and folic acid supplementation, deworming and malaria testing (rapid diagnosis test: Paracheck®) and treatment when positive. Nutritional advices, medical examination and appropriate treatment were provided on a weekly basis. A family ration of CSB (2450 g), oil (140 ml) and sugar (140 g) in separate containers was given every week and a ration at discharge (50 kg of cereals, 7.5 kg of legume and 7.5 l of oil).

Children were re-assessed on weekly basis until their recovery (programme discharge criteria: WHM% ≥85% for 2 consecutive weeks), death or transfer to the I-TFC. Transfer criteria were medical (e.g. severe infectious diseases, severe anaemia and severe dehydration) and/or nutritional (development of oedema, weight loss with anorexia or deterioration of general condition). In practice, transfer decision remained at clinician discretion. Children who did not reach the discharge criteria after 16 weeks of treatment were classified as 'non-responders'. Those who missed three consecutive visits were classified as 'defaulters' and were traced by field

workers. Children who recovered were followed up to 6 months after their discharge.

Study objectives

Our primary objective was to compare the weight gain ($g\,kg^{-1}\,day^{-1}$) and the recovery rate in the two groups. Secondary objectives focused on transfer to the I-TFC, mortality, non-responder and defaulter rates, length of stay, MUAC gain and haemoglobin gain during treatment, relapse and height gain 6 months after discharge.

Study outcomes and data collection

Weight was measured weekly by trained staff with 100 g precision using a 25 kg Salter scale. Height (children $\geq$85 cm) or length (children $<$85 cm) was measured once every second week with 1 mm precision. MUAC (left arm) was measured at admission and at exit. Presence of oedema and Paracheck® results were collected from medical records filled by trained nurses. Haemoglobin was measured on capillary blood at admission and discharge using HemoCue® 201 or 301 according to the site. A questionnaire was administered to the caretaker of the child at admission and discharge to collect socio-demographic characteristics, medical history and information on adherence to the nutritional treatment.

Sample size

To detect a $1\,g\,kg^{-1}\,day^{-1}$ weight gain increase in the group receiving RUTF compared to the CSB pre-mix group (expected average weight gain $\pm$ SD: $2.0 \pm 2.5\,g\,kg^{-1}\,day^{-1}$), 99 children were required per group (80% power; $\alpha = 0.05$; two sided). To have the same chance to detect a 10% absolute increase in the cure rate in the RUTF group, we needed 313 children per group. To compensate for possible contamination, we aimed to recruit 400 children per group.

Statistical analysis

Data were double entered in Epidata 3.1 (Odense, Danemark) and analysed using STATA 9 (College Station, Texas, USA). Nutritional indicators (NCHS reference) were calculated using EpiNut (Epi Info 6.0). Proportions were compared by using Chi-square tests or Fisher's exact test when appropriate. Means and medians were compared using *t*-tests and Mann–Whitney tests, respectively. Weight gain differences were estimated with their 95% confidence intervals (CIs). Adjusted analyses were conducted using multiple linear regression.

Ethics

The study was approved by the Comité Consultatif National d'Ethique of the Ministry of Health in Niger and by the Comité de Protection des Personnes, Ile de France XI, Saint-Germain en Laye, France.

Results

Recruitment took place from August to October 2007 with the 6-month follow-up ending in July 2008. During the course of the study, due to communication problems with those remote SFCs, children weighing $\geq$8 kg at any time during their treatment were provided with three daily packs of RUTF instead of two as planned in the study protocol. Consequently, we excluded these children from the analysis. In total, 215 children in the RUTF group and 236 children in the CSB pre-mix group are included in the analysis (Fig. 1). Group characteristics were balanced at baseline (Table 1).

Overall recovery rate was 79.1% in the RUTF group and 64.4% the CSB pre-mix group ($p < 0.001$) (Table 2). There was no statistical evidence for a difference between death, defaulter and non-responder rates. More transfers to the I-TFC were observed in the CSB pre-mix group (19.1%) compared to the RUTF group (9.3%) ($p = 0.003$). At the time of transfer, average weight gain, age, WHM%, length of stay in the SFP were similar in both groups (data not shown). Reasons for transfer did not differ between groups; 29% having been transferred because of deterioration of their nutritional status, 15% because of medical complications and others because of a combination of both. A total of 15 children were transferred because they had reached a WHM% $<$70% or because they had developed nutritional oedema (5 in the RUTF group; 10 in the CSB pre-mix group).

The average weight gain up to discharge was $1.08\,g\,kg^{-1}\,day^{-1}$ higher in the RUTF group compared to the CSB pre-mix group (95% CI: 0.46–1.70). Among all children, the difference in average weight gain during the first 2 weeks of treatment was $1.86\,g\,kg^{-1}\,day^{-1}$ (95% CI: 1.04–2.67) in favour of the RUTF (Table 3). Analysis adjusted on age, sex, WHM% at entry showed similar results as well as analysis conducted after excluding 40 children (21 in the RUTF group; 19 in the CSB pre-mix group) who were discharged before or after having reached the discharge criteria (data not shown).

Regarding the secondary outcomes, the length of stay up to discharge was shorter in the children receiving RUTF (median: 4 weeks vs. 6 weeks; $p < 0.001$). There was no evidence for a difference in either haemoglobin or MUAC gain during treatment. No adverse events attributed to the nutritional product were reported.

At discharge, mothers reported that 82.9% of the children receiving RUTF were able to finish the daily ration but only 53.0% of those receiving CSB pre-mix ($p < 0.001$). According to the caretaker's information, contamination was very limited with

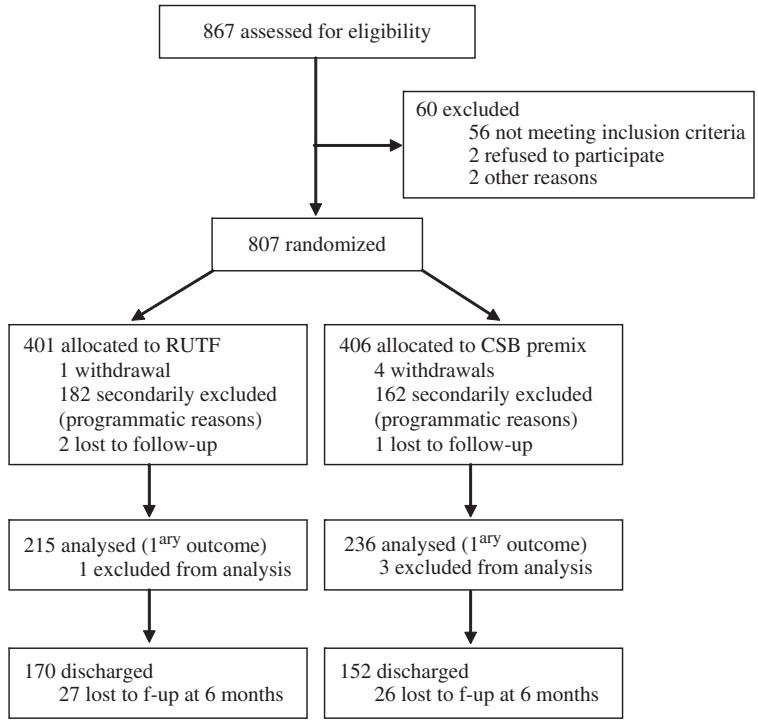

FIG. 1. Flowchart of the participants.

TABLE 1
Baseline characteristics of the participants

	RUTF $n=215$	CSB pre-mix $n=236$
Girls	124 (57.7)	128 (54.2)
Age (months)		
6–11	23 (10.8)	28 (11.9)
12–23	151 (70.9)	150 (63.8)
24–35	39 (18.3)	53 (22.6)
≥36	0 (0.0)	4 (1.7)
Weight (kg)	6.6 ± 0.7	6.6 ± 0.7
Height (cm)	70.6 ± 3.7	70.7 ± 3.8
MUAC (mm)	120.9 ± 4.9	120.0 ± 5.6
Weight for height (% median, NCHS)	76.7 ± 2.6	76.4 ± 2.4
Height for age (*Z*-score, NCHS)	–2.71 ± 0.98	–2.77 ± 0.99
Accompanied by their mother	201 (93.9)	218 (92.4)
Breastfed	170 (80.2)	173 (73.6)
Positive Paracheck®	103 (49.5)	132 (58.4)
Haemoglobin ($g\,dl^{-1}$)		
[4 ; 6[	15 (9.2)	21 (11.7)
[6 ; 9[	66 (40.5)	74 (41.3)
[9 ; 11[	54 (33.1)	61 (34.1)
[11 ; 15[	28 (17.2)	23 (12.9)

Data are *n* (%) or mean ± SD.

<1% of the children in the CSB pre-mix group having received some RUTF or the opposite. Six months after discharge, about one-fifth of the cured children relapsed. During follow-up, height and height-for-age gains were similar in children who had received RUTF or CSB pre-mix (Table 3).

Discussion

Among children who recovered in our study, weight gain was on average $1.08\,g\,kg^{-1}\,day^{-1}$ higher in the RUTF group compared to the CSB pre-mix group. Although the recovery and eligibility criteria, and the food protocols were different, our results fit with previous observations in Malawian children at risk of malnutrition, moderately malnourished or severely malnourished in the second treatment phase [4–6]. In those studies, weight gain was 0.4–$1.7\,g\,kg^{-1}\,day^{-1}$ significantly higher in the group receiving RUTF [4–6].

Although we do not know the proportion of the food supplement actually eaten by the children, >80% of the children in the RUTF group finished their daily ration compared to only half of the children receiving the CSB pre-mix according to the caretakers. This had an obvious direct impact on the weight gain. The high energy density of the RUTF reduces significantly the food volume compared to

TABLE 2
Cure, transfer, death, defaulter and non-responder rates

	RUTF *n* (%)	CSB pre-mix *n* (%)	Difference (%) (95% CI)	*p*-value
Recovered	170 (79.1)	152 (64.4)	14.7 (6.5 to 22.8)	<0.001
Transfer to I-TFC	20 (9.3)	45 (19.1)	−9.8 (–16.1 to –3.4)	0.003
Death	7 (3.3)	7 (3.0)	0.3 (–2.9 to 3.5)	0.86
Defaulter	5 (2.3)	11 (4.6)	−2.3 (–5.7 to 1.0)	0.18
Non-responder	13 (6.0)	21 (8.9)	−2.9 (–7.7 to 2.0)	0.25

TABLE 3
Weight gain, length of stay and secondary outcomes

	RUTF		CSB pre-mix		*p*-value
	n	Mean ± SD/ median (min–max) %	*n*	Mean ± SD/ median (min–max) %	
Weight gain ($g\,kg^{-1}\,day^{-1}$)					
During the first 2 weeks (all children)[a]	204	5.34 ± 4.15	217	3.48 ± 4.32	<0.001
Up to discharge (cured children)[b]	170	5.67 ± 3.02	152	4.59 ± 2.59	<0.001
Length of stay up to discharge (weeks)	170	4 (2–16)	152	6 (2–16)	<0.001
MUAC gain up to discharge ($mm\,day^{-1}$)	162	0.37 ± 0.29	150	0.32 ± 0.24	0.11
Haemoglobin gain up to discharge ($g\,dl^{-1}\,week^{-1}$)	101	0.30 ± 0.63	102	0.29 ± 0.51	0.77
Status 6 months after discharge					0.48
Dead	3	1.8	0	0.0	
Relapse	33	19.4	33	21.7	
Weight for height ≥80% (NCHS median)	107	62.9	93	61.2	
Lost to follow-up	27	15.9	26	17.1	
Height gain ($mm\,day^{-1}$) 6 months after discharge[c]	107	0.30 ± 0.09	93	0.31 ± 0.10	0.67
Height for age gain (*Z*-score) 6 months after discharge[c]	106	0.17 ± 0.51	93	0.16 ± 0.50	0.86

Data are mean ± SD; median (minimum–maximum); or percentages.
[a]30 children absent, transferred or dead before the second week of treatment.
[b]4 children absent at the Week 2 visit.
[c]Relapses, dead and lost to follow-up excluded.

the CSB pre-mix prepared as porridge. Also, due to its individual packaging, RUTF might be interpreted as a therapeutic product and less prone to intra-household sharing than a CSB pre-mix easily assimilated to local food. In addition, by allowing the caretaker to follow the nutritional advices without interrupting daily activities, the 'ready to use' feature of RUTF might have facilitated the treatment compared to the CSB pre-mix that should be cooked several times a day.

Because of the higher weight gain in the RUTF group, we observed a 2-week shorter length of stay in the programme. This may have an important impact on the organization of SFC (e.g. higher treatment capacity with the same number of staff) and, more importantly, it might enhance the adherence to the nutritional treatment (e.g. caretakers are involved for a shorter time period in the programme and might recognize more easily the effectiveness of the treatment).

In this study, we cannot differentiate whether the observed accelerated weight gain is on account of lean or fat tissue deposition. Lean tissue growth requires appropriate nutrient intake while adipose tissues needs mainly energy. There is some evidence that, in Malawi [4] milk and non-milk-based RUTF have a similar impact on weight gain despite their different components. Therefore, indicators other than weight gain might better assess the quality of the nutritional recovery. We tried to approach this issue by comparing the gain in haemoglobin level between the two groups. Overall, there was no evidence for a difference although this result should be interpreted with caution since iron supplementations differed between study groups and according to baseline level of haemoglobin. Also, the duration of

the iron supplementation might have been too short to show a measurable improvement in haemoglobin level.

Recovery rates were better in the RUTF group when compared to the CSB pre-mix group but this might have been biased by the higher transfer rate to I-TFC in the CSB group. In our study, none of the nurses was blinded to the food product given to the participants but, since the characteristics of children at the time of the transfer were similar in both groups, it is likely that similar transfer criteria were applied for all children. This deserves further investigation since reducing the transfer rate to the I-TFC would definitely improve the acceptability of the nutritional programme by the caretakers and reduce its cost.

We found no difference in death, non-responders, defaulters, post-recovery relapse rates or in height growth up to 6 months after recovery. Supplementation with fortified spreads has been reported to influence on growth [11] among moderately malnourished children but when given for a longer time period than in our study.

The main limitation of our study is the secondary exclusion of children who did reach a weight of $\geq$8 kg during their treatment. This resulted in selection of younger children, more often breastfed, with a lower height and weight at admission. However, this secondary exclusion was evenly distributed in both treatment groups. Child characteristics remained balanced at baseline and our study population remained relevant to address the issue of MAM in Niger where wasting and mortality rates affect especially children <2 years of age [8].

The distribution of a weekly family and discharge rations probably influenced not only the weight gain, which was quite high in our study, but also the length of stay, the recovery and defaulter rates. I am not sure this is perfect. The message is that the rations (both family and discharge) did influence the weight gain, the length of stay, the recovery rate, and the defaulter rates.

In conclusion, our study identified a series of advantages of RUTF over a CSB pre-mix for the treatment of MAM in children <5 years of age in South of Niger. These advantages have direct implications on patients' outcomes and management (higher weight gain, shorter length of stay and faster recovery, less transfer to the I-TFC) and might lead to a better adherence to the treatment. Also, by increasing organizational capacity of the SFPs, these advantages would enhance the effectiveness of the nutritional programmes to tackle MAM in the community.

Currently, ready-to-use products remain more expensive than fortified blended flours but several aspects of RUTF might significantly reduce the overall treatment cost. The shorter treatment duration observed with RUTF, the limited transfer rate to the I-TFC, its easier transport, storage, distribution (no need to be mixed), consumption (no need to be cooked) and, its longer shelf-life allow, on the one hand, the SFP to save human, logistical resources and food products. For caretakers, on the other hand, this might limit transport and cooking fuel expenditure, as well as opportunity costs of attending the SFP. Economic implications of the use of RUTF to treat MAM deserve an in-depth evaluation.

Our results provide additional evidence on the role of RUTF in the treatment of MAM. Further research on ready-to-use food is needed to identify the most appropriate and cost-effective product to treat MAM.

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