ORIGINAL ARTICLE

The short-term impact of high energy nutritional supplements on energy balance in underweight primi-gravidae: A randomized controlled trial

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Abstract

Objective: To determine the impact of high-energy nutritional supplements on appetite, appetite regulators, energy intake and macronutrients level among underweight primigravidae.

Method: The single-blind randomised controlled trial was conducted from April 26, 2018, to August 10, 2019, in tertiary care hospitals of Khyber Pakhtunkhwa province of Pakistan, after approval from the ethics review committee of Khyber Medical University, Peshawar, and comprised underweight primigravidae who were randomly allocated to high energy nutritional supplement group A and placebo group B. Appetite questionnaires were filled and blood samples were obtained in fasting state, at 30, 60, 120, 210 and 270 minutes to measure blood glucose, insulin, peptide YY and cholecystokinin. Breakfast and lunch were served at 30 minutes and 210 minutes after supplementation, respectively. Data was analysed using SPSS 20.

Results: Of the 36 subjects, 19(52.8%) were in group A and 17(47.2%) were in group B. The overall mean age was 18.66 ± 2.5 years. Energy intake in group A was significantly higher than group B ($p<0.001$), and so were mean protein and fats ($p<0.001$). The subjective appetite perceptions for 'hunger' and 'desire to eat' were significantly lower ($p<0.001$) before lunch in group A. Plasma concentrations of appetite hormones corresponded to the appetite perceptions and were significantly higher in group A after breakfast and lunch for peptide YY, cholecystokinin and insulin compared to group B ($p<0.001$).

Conclusion: High-energy nutritional supplement was found to have short-term suppressive effect on energy intake and appetite.

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Introduction

In developing and low-income countries, the major public health issue and concern is malnutrition.[1] It is also a leading cause of pregnancy-related complications and determines the lives of the mothers and their families.[2] Globally, Pakistan is among the three countries that have the highest burden of foetal, child and maternal mortality.[3] The major underlying cause of malnutrition is poverty.[4,5] Many studies have suggested that high-energy nutritional supplements (HENS) improve nutritional and energy intake, enhance body weight and further produce a positive impact on clinical health in patients by decreasing the risk of having to get hospitalised.[6] During pregnancy the fulfillment of nutritional requirements are important in order to secure the mother and the child from pregnancy-related complications, as pregnancy is considered a risk factor of nutritional deficiency.[7]

The supplements, including ingredients like energy, fats, proteins, vitamins, minerals and iron, are normally used during pregnancy to overcome nutritional deficiency.[8] Majority of oral supplements are mixture of multinutrients containing micro- and macro-level nutrients. These oral supplements are prescribed during pregnancy to improve the clinical health outcomes.[9] The developing countries are highly concerned towards maternal and child health issues arising from low body mass index (BMI), which is indicative of maternal undernutrition.[10] In the low-income population, poor diet deficient in nutrients causing repeated infections contributes to malnutrition.[11,12] Malnutrition at the time of pregnancy and during pregnancy influences maternal and foetal health, and can be preventable if identified in time and followed up by effective and efficient treatment.[13]

Nutritional supplements affect the appetite and desire to eat directly or indirectly[14] and a positive improvement in appetite among women has been observed.[15] The effect of nutritional supplements on appetite parameters, like

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hunger, fullness, satiety, desire etc., and hormonal control, like insulin, glucose, peptide YY (PYY) and cholecystokinin (CCK). and energy intake using different subjects have been determined in healthy adults[16,17] but its short- and long-term effects in underweight primigravidae have not been adequately documented.

The current study was planned to explore the effect of HENs on energy intake, appetite and appetite modulators in healthy underweight primigravidae.

Subjects and Methods

The single-blind randomised controlled trial (RCT) was conducted from April 26, 2018, to August 10, 2019, in tertiary care hospitals of Khyber Pakhtunkhwa (KP) province of Pakistan. After approval from the ethics review committee (ERC) of Khyber Medical University (KMU), Peshawar, the sample size was calculated using OpenEpi calculator[18] in the light of literature[19,20] while keeping power 85% and confidence interval (CI) 95%.

The study protocol was based on the recommendations of the Consolidated Standards of Reporting Trials (CONSORT) statement.[21] The trial with registered with ISRCTN clinicalTrial.gov Identifier: https://www.isrctn.com/ISRCTN10088578.

Those included were healthy, underweight primigravidae having BMI <18.5kg/m^2. The exclusion criteria included underweight primigravidae having any major illness, such as gestational diabetes mellitus (GDM), pregnancy-induced hypertension (PIH), thyroid diseases, liver diseases etc., or having been previously on any long-term medication and having allergy to supplements. Also, those having any previous history of gastrointestinal (GIT) anomalies, surgeries and eating disorders, like bulimia nervosa, anorexia nervosa and purging disorders, were excluded.

The recruitment of the first participant was done one week after ERC approval. After taking written informed consent from the participants, they were randomised using Computer Randomiser version 3.0 to HENS group A receiving MAAMTA[22] and placebo group B.

Data was collected using a predesigned questionnaire containing detailed medical history.

Same type of ad libitum breakfast and lunch were served to the participants of both the groups. The ad libitum breakfast consisted of parathas, fried eggs, boiled eggs, white bread slices, jam, cream, mixed tea. This menu was prepared on the participants' choice. The ad libitum lunch consisted of brown rice, chicken curry, yogurt, naan, salad containing cucumber, and fruits consisted of bananas and apples because these are available throughout the year. All of these were measured before and after serving and were presented in small portions.

To determine the short-term effect of supplement/placebo, the participants were asked to visit the trial room of the hospital concerned. They were provided 10 minutes to rest and acclimatise with the environment, and then anthropometric measurements were taken. Afterwards, the baseline blood sample was collected for the determination of glucose and appetite hormones insulin, PYY and CKK, and to fill a validated appetite questionnaire.[19] Appetite profile was measured using anchored 100mm visual analogue scales (VAS). On the trial day, the questionnaires were completed in the fasting state, at 30 minutes after supplementation, at 60, 120 minutes after breakfast, 210 and 270 minutes after lunch. The questions asked were, 'How hungry are you?'and 'How satiated are you?'. Possible answers ranged from 'not at all' to 'very'. Blood samples were collected in the fasting state, at 30 minutes after supplementation, at 60, 120 minutes after breakfast, and at 210, 270 minutes after lunch. The participants were provided with ad libitum buffet breakfast and ad libitum lunch according to the wish of each participant, which was asked from them a day before the trial.

A total of 20ml of blood was taken over the course of the day. In the fasting state, 5ml was taken of which 1ml was put in an Eppendorf tube containing 200µl of aprotonin, a protease inhibitor, and 2ml each was put into a gel tube and an ethylenediaminetetraacetic acid (EDTA) tube. At the rest of the time points, 3ml blood was taken. Insulin was determined by chemo-luminescent immunoassay (CLIA), while enzyme-linked immunosorbent assay (ELISA) was used for PYY and CCK. Glucose was determined by colorimetric method using Cobas 111. Energy and macronutrient intake were calculated using Windiet software.

Data was analysed using SPSS 20. Student t test was used to compare the parameters between the two groups, while analysis of variance (ANOVA) was used to compare the appetite regulators at different time points on the main trial day. Area under the curve (AUC) was used for calculating the pre-breakfast (0-60min) and pre-lunch (0-120min) responses. It is calculated by' trapezoidal rule' or 'trapezium rule'.

[(a+ b)/ 2 x Time] was used to compute the AUC.

(a=trapezium 1) and (b=trapezium 2).

All the measurements taken at different time and different duration for both the groups were taken as a mean value with standard deviation. P<0.05 was considered statistically significant.

Results

Of the 36 subjects, 19(52.8%) were in group A and 17(47.2%) were in group B. The overall mean age was 18.66±2.5 years. All the 36 participants (100%) were housewives. By profession, the husbands of 9(24.3%) of them were jobless, 4(10.8%) were abroad, 5(13.5%) were government servants, and most of them were labourers 6(21.6%). The monthly income of the participants' households was PKR5000-15,000 in 5(24%) cases in group A compared to 9(53%) in group B, PKR16,000-25,000 in 5(24%)cases in group A compared to 3(18%) in group B, and PKR26,000-35,000 in 9(53%) cases in group A compared to5(29%) in group B.

On the main experimental day, the participants were given supplement/placebo before breakfast, the energy intake in the form of supplement to test groups before breakfast was significantly high in group A than group B ($p< 0.001$). No significant difference was observed in energy intake after breakfast between group A 487.55±212.61 and group B515.53±279.78 ($p>0.05$). After lunch, a significant decline was observed in the energy intake of group A 746.59±420.44 compared to group B 474.45±161.25 ($p<0.05$). When the total energy intake, taken as a sum of both breakfast and lunch, was calculated, a significant difference ($p<0.05$) was found with lower energy intake in group A than group B. However, when the overall energy intake of breakfast, lunch and supplement/placebo was calculated, no significant difference was seen between the groups (Figure 1).

The supplement provided to group A had a significantly high level of mean protein and fats level ($p<0.001$) compared to the placebo in group B. However, during breakfast, there was no significant difference in the macronutrient intake ($p>0.05$). The pattern of macronutrients intake was also high for group B, such as the mean carbohydrate intake after lunch was significantly higher ($p<0.05$) than group A. A significant increase ($p<0.05$) in the total carbohydrate intake was also seen in group B compared to group A (Table 1).

Appetite regulators at different points in time showed a highly significant increase in PYY in group A

Table-1: Comparison of macronutrients and energy intake in HENS and Placebo groups on trial day.

Intake Pattern	Bio-chemical Parameters	HENS Mean±SD	Placebo Mean±SD	*p*-value
Placebo or supplement	Carbohydrates(gm)	34.06±37.24	17.03±8.70	0.082
	Proteins(gm)	7.23±2.89	1.79±0.88	<0.001***
	Fats(gm)	17.92±4.79	0.36±0.16	<0.001***
	Energy intake(kc)	283.25±102.65	97.65±62.29	<0.001***
Breakfast	Carbohydrates(gm)	47.31±28.81	54.61±24.36	0.425
	Proteins(gm)	20.66±10.05	20.81±13.35	0.969
	Fats(gm)	25.28±10.97	27.21±16.26	0.673
	Energy intake(kc)	487.55±212.60	515.53±279.78	0.732
Lunch	Carbohydrates(gm)	82.95±36.71	138.48±81.78	0.010
	Proteins(gm)	24.50±12.59	32.41±19.60	0.151
	Fats(gm)	10.97±7.10	13.52±12.63	0.448
	Energy intake(kc)	474.45±161.25	746.59±420.44	<0.05*
Breakfast ±Lunch	Carbohydrates(gm)	65.13±37.24	96.54±73.07	<0.05*
	Proteins(gm)	22.58±11.41	26.61±17.52	0.243
	Fats(gm)	18.12±11.65	20.37±15.92	0.492
	Energy intake(kc)	962±276.65	1262.12±555.21	<0.05*
Total	Carbohydrates(gm)	43.42±43.30	70.04±70.57	<0.05*
	Proteins(gm)	17.46±11.92	18.34±18.50	0.767
	Fats(gm)	18.05±9.92	13.70±16.06	0.088
	Energy intake(kc)	1245.25±311.94	1359.76±560.32	0.439

HENS: High-energy nutritional supplements SD: Standard deviation. Significant difference (*$p<0.05$, **$p<0.01$, ***$p<0.001$).

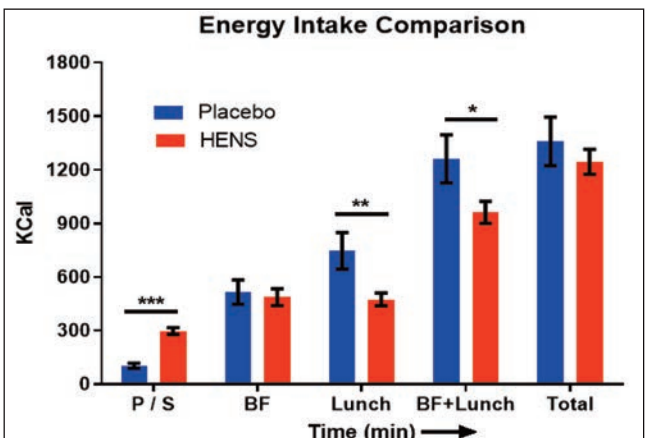

Figure-1: Energy intake of the participants on trial day.
HENS: High-energy nutritional supplements, P: Placebo, S: Supplementation.

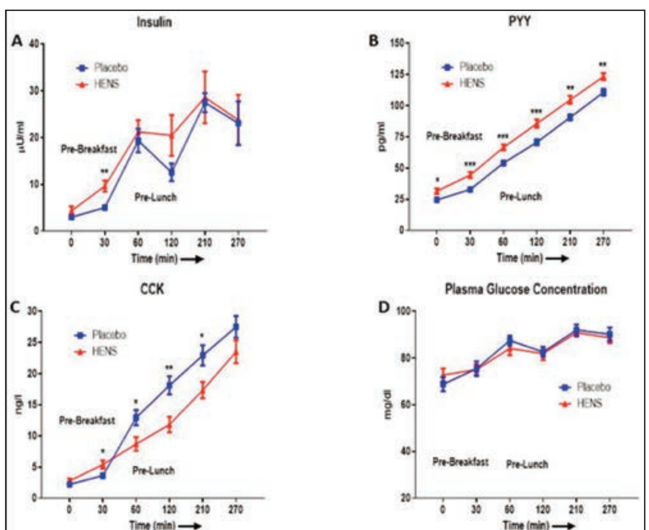

Figure-2: Plasma concentrations of appetite regulators at different time points during the trial.
PYY: Peptide YY, CKK: Cholecystokinin, HENS: High-energy nutritional supplements.
Values presented as mean ± standard error (SE).

31.57±9.27compared to group B 24.55±5.45 in fasting state (*p*<0.01), 44.68±10.16 in group A and 32.83±5.95 in group B post-supplementation (*p*<0.001), 67±9.53 versus 54.05±7.9 at breakfast (*p*<0.001) and 104.84±13.05 versus 90.66±9.72 at lunch (*p*<0.01). A significant increase in CCK concentration was seen in group B 12.92±5.20 compared to group A 8.69±4.79 at breakfast (p<0.05) and 22.94±6.92 and 17.36±5.79, respectively, one hour after lunch (*p*<0.05). Insulin was significantly increased in group A 9.64±5.18 compared to 5.04±1.93 post-supplementation (*p*<0.01).

No significant difference was seen in the plasma glucose pattern, taken as glycaemic index, between the groups (Figure 2).

AUC suggested that in the pre-breakfast period, appetite responses for fullness (*p*<0.01) and prospective food consumption (*p*<0.01) were significantly increased in group A compared to group B. There was a significant decrease in hunger response before lunch in group A than group B (*p*<0.001. In the pre-lunch period, appetite responses, like hunger (*p*<0.001) and desire to eat (*p*<0.001), were significantly increased in group B. It was observed that graphically the pattern of decrease in hunger, desire to eat, prospective food consumption and increase in fullness and satiety were similar with increasing time in both the groups (Figure 3).

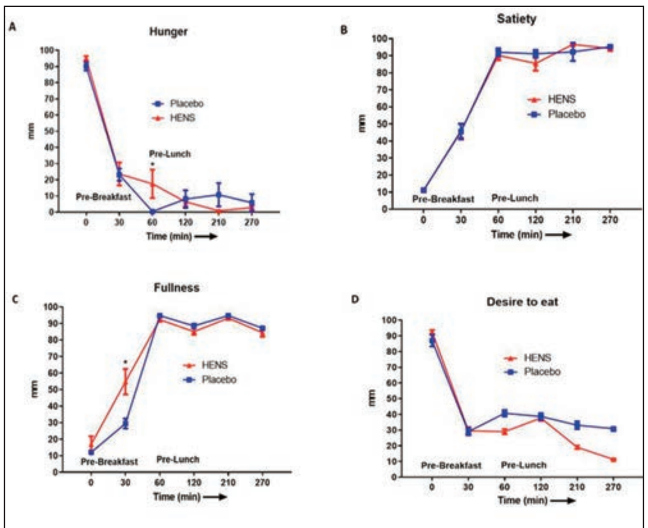

Figure-3: Comparison of appetite responses between high-energy nutritional supplements (HENS) and Placebo groups on trial day.
Values presented as mean ± standard error (SE).

Table-2: Total micronutrients intake.

Bio-chemical Parameters	HENS Mean±SD	Placebo Mean± D	*p*-value
Calcium(mg)	223.5±120	185.02±216.	0.243
Iron(mg)	4.20 ±3.79	3.02±2.78	0.073
Vit.A(µg)	214.8±168	140.2±199	0.038*
Vit.D(µg)	3.26±3.72	0.99±1.92	<0.001***

HENS: High-energy nutritional supplements, SD: Standard deviation, Vit: Vitamin. Significant difference (**p*<0.05, ***p*<0.01, ****p*<0.001)

In terms of micronutrients, vitamins A and D levels were significantly higher in group A compared to group B (Table 2).

Discussion

The study was planned to determine the effect of HENS on appetite and energy intake of underweight primigravidae. On the main experimental trial day, the study results showed a significant decrease in the energy intake of HENS group during the breakfast period compared to the Placebo group. This suppression in energy intake continued till lunch. Our results are in accordance with the previous studies done on healthy underweight females.[19] In the study conducted on underweight females, the suppression in energy intake was observed after the intake of HENS drink. Similarly, in a study done on underweight children, who were given ready-to-use therapeutic food (RUTF) for a month, showed that about 2/3rd of the energy consumed was compensated by other meal times in terms of eating less than usual.[23] The reason for this suppression in that energy intake may be the energy-rich supplement 'MAAMTA' which contains about 533kcal of energy/100gms provided to the group A in the current study compared to 184.13kcal/100gms to the other group.

However, this suppression in appetite and energy intake was sustained in the current study till lunch, which was in contradiction to a study.[19] Similar findings were shown by a study done on underweight school-going children in which the energy suppression was prolonged till lunch.[24] Moreover, in the study the overall energy intake (sum of breakfast, lunch and supplement/placebo) showed no significant difference between the groups, In an earlier study, there was an increase in the overall energy intake after the intake of -energy supplement drinks by underweight healthy females.[25] A study done on bolus feeding in healthy men reported an increase in overall energy intake although there was a partial reduction in food intake20. The reason for the current findings may be explained by the role of pregnancy and sex hormones' interference with taste and food intake in pregnant women.[26]

The current study observed that during the breakfast period, the energy intake and macronutrients intake was decreased in the HENS group. A study on healthy athletes showed that the supplements usually have a long-term effect on nutritional requirement and consumption of energy as they reduce the intake of macronutrients from other energy sources.[27] The high-protein oral nutritional supplements provide long-lasting calories and diminish the need of carbohydrate as energy source6. This was because of the lipid-based nutrient rich supplement provided to the participants. Although after supplementation, the intake of macronutrients was higher in the HENS group with a significant increase in the fats and proteins intake, this increase in the macronutrients intake was not seen during the pre-lunch and post-lunch period because the supplement had a suppressive effect on appetite and food intake. Similar findings have been reported earlier.[25]

In the pre-breakfast period, an increase was seen in the plasma concentrations of anorexigenic hormones CCK, PYY and insulin after supplement intake in the HENS group compared to the placebo group. This can be explained by the lipid- and protein-rich supplement given to the HENS group. This increase in the PYY was sustained throughout the pre-lunch period as well, while the impact of CCK and insulin was short-lived, as also shown by previous studies.[17,28] The appetite responses 'fullness' and "perspective food consumption' showed a significant increase in the HENS group in the pre-breakfast period, while appetite responses like' hunger' and 'desire to eat' were significantly increased in the placebo group in the pre-lunch period. This 'fullness' and 'reduced hunger' in HENS group during post-supplementation period coincided with lower energy intake during ad libitum breakfast, but energy provided by combined intake of the supplement and breakfast was still significantly higher in the HENS group than the placebo group.[6,13] The result of the current study showed that the given supplement had a direct effect on 'hunger' and 'desire to eat'. The supplementation covered the energy needs and provided a good source for short-time energy requirement. Therefore, the 'desire to eat' and 'hunger' level decreased before lunch. The finding is in accordance with previous studies.[29,30]

The current study showed correspondence between the responses of appetite scores and responses of hormones with regard to PYY, CCK and insulin in the pre-breakfast and pre-lunch period, such that the increased concentration of PYY, CCK and insulin in the pre-breakfast period led to increased fullness in the HENS group. This sustained increase in the PYY led to decreased 'desire to eat' and 'hunger' in the HENS group compared to the placebo group.

The strengths of the current study include random allocation of the participants to the two groups, low dropout rates, compliance of the participants, and a high level of standardisation and quality assurance during data-collection because data was collected by the same investigator from all the participants.

The limitations of the current study include a small sample size and short duration. Larger community-based trials with longer duration are recommended.

Conclusion

Women in the HENS group had a short-term suppressive effect on the total energy intake and appetite on the experimental day trial. Continuation of the antenatal supplementation nevertheless had beneficial effects on nutritional and pregnancy outcomes.

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Conflict of Interest: None.

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