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Impact of Protein Supplementation and Care and Support on Body Composition and CD4 Count among HIV-Infected Women Living in Rural India: Results from a Randomized Pilot Clinical Trial

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Abstract

Body composition in HIV-infected individuals is subject to many influences. We conducted a pilot six-month randomized trial of 68 WLA (women living with AIDS) from rural India. High protein intervention combined with education and supportive care delivered by HIV-trained village women (Asha [Activated Social Health Activist] Life [AL]) was compared to standard protein with usual care delivered by village community assistants (Usual Care [UC]). Measurements included CD4 counts, ART adherence, socio-demographics, disease characteristics (questionnaires); and anthropometry (bioimpedance analyzer). Repeated measures analysis of variance modeled associations. AL significantly gained in BMI, muscle mass, fat mass, ART adherence, and CD4 counts compared to UC, with higher weight and muscle mass gains among ART adherent (≥ 66%) participants who had healthier immunity (CD4 ≥ 450). BMI of WLA improved through high protein supplementation combined with education and supportive care. Future research is needed to determine which intervention aspect was most responsible.

Keywords

Nutrition; AIDS in rural women; ART; protein; body composition

INTRODUCTION

Nutritional status is known to influence susceptibility to as well as recovery from infectious disease. Immune defense mechanisms are much more effective in well-nourished individuals than in poorly fed ones (1). Scarce amounts of nutritious food, appetite loss, and decreased nutrient absorption are important predictors of weight loss and body composition changes in HIV-infected individuals (2).

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Most trials of macronutrient consumption among HIV patients have been conducted in high-income countries. However, many of the trials conducted in developed countries have not included measures of mortality, morbidity or disease progression (2). Therefore, it is unclear whether nutrition trials influence HIV-progression and, in particular, it is not known how effective nutrition trials might impact health outcomes in developing countries where hunger and malnutrition are more common.

Body composition is an important determinant of HIV prognosis. Weight loss and wasting are associated with lower CD4 counts and independently predict mortality (3). In addition, patients receiving highly active antiretroviral therapy (HAART) have an increased risk of death if weight loss exceeds 10% of weight at baseline (4).

Food Insecurity in India

In India, food insecurity lends itself to both underweight and overweight trends. In Andhra Pradesh (AP), 31% of women between 15 to 49 years of age are considered overweight or obese, with a BMI of > 25.0 kg/m2, a cutpoint used in their study to indicate obesity (5). In AP, 19% of rural residents have high levels of cholesterol and triglycerides, and 31% have abnormally low high density lipoproteins (HDL) (6). When compared to those uninfected, persons living with HIV/AIDS had total cholesterol and triglycerides levels 65% to 75% higher (7).

The rural women living in India have a major role in attaining, preparing and distributing food among the family. The first portion of the food is generally allocated to the breadwinner (it may be the man or in case of widow, it may be the woman of the house). Then the remaining food is allocated among the other members of the family including children and others. As a result, women in India are given less importance to healthy eating due to their patriarchal system. It is not surprising therefore, that most rural women in India are anemic.

Relationship between Food Insecurity and HIV

While little information exists about food insecurity and HIV, there is some evidence that food insecurity increases a women’s risk of exposure to HIV. Food insecurity is defined as limited or uncertain access to enough nutritionally adequate and safe food for an active, healthy life (8). Recent studies conducted in sub-Saharan Africa suggest that severe food insecurity is associated with reduced condom use and with increased occurrence of symptoms that may indicate sexually transmitted disease among sexually active women (9). These findings suggest that interventions that target sexual risk reduction behaviors are unlikely to be optimally effective if food insecurity is not taken into account.

In our Asha study, while it was a challenge for us to ensure the extra nutritional supplements provided to the women was actually consumed by the women themselves, our Asha played a major role by interacting and building rapport with family members as well as the target women living with AIDS (WLA). The Asha trained the family about the importance of the WLA to consume the supplemental food. The Asha also counseled the family to continue purchasing the usual amount of food weekly as the supplemental food was targeted for the WLA solely. As each WLA was very motivated to improving her overall physical and mental health so as to continue supporting her children and other family members, the women and their families complied.

Community Health Workers and Possible Influences on Food Insecurity

While there is no data available on how community health workers (CHW) assist persons living with HIV/AIDS (PLWHA) in terms of food supplementation, CHWs are valuable members of the clinical team who provides services to PLWHA. These services include support for ART adherence, accompaniment to the hospital and clinics and nutritional assessment and referral (10). CHWs aid PLWHA in complying with the strict ART drug regiment by providing them with adequate counseling on issues such as the nature of the treatment, possible side effects and the disadvantages of poor adherence (11). CHWs can make a valuable contribution to community development by improving access to and coverage of communities with basic health services. For example, there is robust evidence that CHWs can undertake actions that lead to improved health outcomes (12), including expanding immunization coverage and TB treatment (13). These actions not only improve health but also result in increased life expectancy (13). The CHWs also provide support for mental health/emotional problems related to HIV disease and active support for disclosure of HIV status, which further helps the PLWHA comply with their treatment (11).

In India specifically, as there is a shortage of physicians and nurses in many resource-limited settings (14), trained CHWs have successfully reduced health disparities and improved a wide range of physical and mental health outcomes. CHWs have participated in diverse activities including cancer education and screening (15), mammography (16), and diabetes (17), heart disease and stroke prevention (18), in multiple settings with different populations (19-21). The use of lay CHW was also associated with a reduced risk of neonatal death and stillbirth and improved antenatal and neonatal practice indicators in five trials conducted in South Asia (22).

Development of Asha in India

To advance health promotion efforts with the vulnerable rural population, the Government of India launched the National Rural Health Mission (NRHM) in 2005 (23). Part of this mission is to assist the most underserved populations, especially women and children, by engaging Asha (Accredited Social Health Activists) who are trained to act as a bridge between the community and the health care system. The focus of Ashas are to promote good health practices, create an awareness of health, mobilize the community towards local planning, and increase utilization and accountability of existing health services. The current areas of focus include creating awareness of healthy nutrition, basic hygiene, sanitation, clean water, neonatal health, providing information on existing health services and promoting healthy living and working conditions.

In a study originating from rural Lucknow conducted by Singh et al. (23), the greatest use of Asha occurred among young, educated women with low parity. In Uttar Pradesh, Srivastava et al. (24) examined the role of Asha as liaisons between the community and health service providers and found that when properly trained and supervised, the Asha functioned very effectively. Ashas were able to gain the trust of community members and achieved a high degree of job satisfaction. Currently, the impact of village community assistants on nutrition of the PLWHA has not been studied.

In the current study, we investigated the combination of nutritional supplementation, with supportive care, and education delivered by Ashas in a six-month randomized trial. Caloric supplementation consisted of a high protein dal mixture. The combined intervention was compared to a control condition of education and group meetings provided by Community Health Workers in combination with supplementation of a usual protein dal mixture.

METHODS

Design

A total of 68 rural women living with AIDS (WLA) participated in a prospective, clinical trial designed to determine the impact of having HIV-trained village women, Asha

(Activated Social Health Activist), provide supportive care in collaboration with other health care providers. These grant-trained village women were not part of the government-trained Asha who primarily assist women with maternal-child health issues post pregnancy.

In this study, two of 16 high prevalence HIV/AIDS villages in rural Andhra Pradesh (AP) that were demographically similar and served by a distinct Public Health Center (PHC), were randomized into intervention vs. control villages so that cross-contamination would not be a biasing factor.

The intervention Asha-Life (AL) was compared to a Usual Care (UC) control group receiving standard care. The nutritional intervention consisted of a high protein supplement (1 kg of Urad dal [black gram]/month, and 1 kg of Toor dal [split pigeon peas]/month, that was included as part of the AL intervention. A standard protein supplement (1 kg of Chana dal [Split chick peas]/month) was provided to the UC group. Human Subjects Protection Committees and an Ethics Committee provided approval to conduct the study both in the US and in India, respectively.

Sample and Setting

Inclusion criteria for the study were: a) WLA between the ages of 18-45; b) screened as receiving antiretroviral therapy (ART) for a minimum of three months; and c) not a participant of an earlier qualitative study. An exclusionary factor was CD4 cell count less than 100. One village was randomly selected to engage the intervention group, while the second engaged the UC group.

Procedure

As presented in greater detail elsewhere (25), qualitative research provided the foundation for refining the intervention study based on the perspective of WLA, rural HIV physicians, nurses and reproductive health-focused Ashas (26,27). Lay village women who were trained as Ashas for the intervention group were selected by the project director (PD) if they were high school educated, interested in caring for WLA, and lived in a similar village as the WLA in the intervention group. The Asha were of similar caste as the WLA, and while not matched in religion, were either Hindu or Christian in religion – as were the WLA.

Once selected, these intervention Ashas (n = 4) were trained by the research staff over a three-day period. The Asha training included education about the study, understanding of needs of WLA, the basics of HIV/AIDS and progression, importance of adherence to ART, strategies to assist these women in coping with their illness, and understanding their role in implementing the intervention arm of the study. Quality assurance assessments were done quarterly. The Asha, paid a small stipend monthly that consisted of Rs.1750/per month, were employed full time. The grant-trained Asha model appears to be as sustainable as the government model where ASHA were paid stipends for providing services to women and children in need.

Each intervention Asha visited 4-5 WLA weekly, monitored barriers to ART adherence, assisted in recording ART adherence, assisted in assessing the nature and outcome of hospital and clinic visits of the WLA, accompanied WLA to all appointments, and provided other assistance that removed barriers the WLA faced in accessing health care or the prescribed treatment.

A similar process of selection was undertaken for two control village community assistants. The separate training, over a two-day period, included a review of the study, basics of HIV/AIDS and progression, importance of adherence to ART, and understanding their role in implementing the standard arm of the study. Each UC village community assistant visited

8-9 WLA monthly, to assist in monitoring ART adherence on a monthly basis, and assisted in assessing the nature and outcome of hospital and clinic visits of the WLA.

Enrolling Participants

The study was announced in each PHC by means of flyers posted in the large waiting area where patients collected. Participants interested in the study contacted the PD for further information about the study. After a description was provided, and all questions were answered, interested WLA signed the first informed consent, which enabled the PD to administer a brief two-minute structured questionnaire that inquired about age, education and other socio-demographic characteristics, including HIV and ART status; these questions determined eligibility for the study and provided basic socio-demographic information on refusals.

If eligibility was met, the PD discussed the need for CD4 testing; after a second informed consent was signed, a venipuncture was conducted in the PHC. Within four days, the WLA met with the PD to discuss the test results, and if the CD4 cell count were not less than 100, the final informed consent was signed and the baseline survey was administered. WLA were then enrolled in the study. All respondents were paid $5 (Rs 225) for completing the screening procedures, $10 (Rs 450) for returning for test results and completing the baseline questionnaire (same day), $5 for each of the group sessions received and $20 (Rs 900) upon completion of the six-month questionnaires.

AL Intervention

In addition to the Asha intervention, AL participants received six (6) program-specific sessions following a needs assessment that was conducted by the PD. Sessions included the following topics: a) HIV/AIDS and dealing with the illness; b) learning about ART and ways to overcome barriers to adherence; c) maintaining a healthy home environment; d) how to improve coping, overcome stigma and care for their family members; e) basics of good nutrition and easy cooking tips; and f) engagement in Life skills, such as computer skills, marketing and embroidery. Each session provided real life examples about how the learned skills could be followed. The women were very interactive in clarifying the information provided. The sessions that both AL and control participants received were didactic and provided by a healthcare expert, such as a community physician, nurse or the Project Director. Participants were encouraged to ask questions or have content further explained in ways that may have been more relevant for the women.

WLA received nutrition packages including 1kg bags each of black gram and Toor dal monthly. Per 100 grams, the black gram consisted of 347 calories, 24 grams of protein, 1.4 grams of fat and 59.6 grams of total carbohydrate. The Toor dal per 100 grams consisted of 335 calories, 22.3 grams of protein, 1.7 grams of fat and 57.6 grams of carbohydrate.

All nutritional intervention materials were purchased from a local area provider in Kovur. Each package of nutritional supplement was consistently mixed in prescribed amounts, weighed, and allotted to each participant depending on their intervention group membership.

The intervention women were told that the dal provided was an extra nutritional supplement to what they usually cook for them and their families. The Toor dal is basically used in the sambar or with cooked vegetables or cooked with green chillies salt and lime. The Urad dal is used for the breakfast, such as idli, dosai, and vaada or for evening snacks. The women generally consumed 50 grams of Toor dal per day and 75 grams of Urad dal per day.

Usual Care Program

The UC participant sessions were matched in terms of number and length of group sessions to the AL program. The UC sessions generally included the following topics: a) HIV/AIDS and dealing with the illness; b) learning about ART and ways to overcome barriers, and Positive Parenting. Additional question and answer sessions brought the total to six sessions. These WLA received 1kg bags of Chana dal; of which per 100 grams consisted of 360 calories, 17.1 grams of protein, 5.3 grams of fat and 60.9 grams of total carbohydrate. The UC women were provided 1 kg of Chana each month for the 6 month period and they were freely able to divide into portions as they saw fit. The dal is often soaked in water and boiled or cooked in a pressure cooker and served over rice.

The study was designed as an ‘open label’ intervention because whole villages were randomized to each condition. In addition, because both groups received food, neither believed they were being deprived of anything.

Instruments

Several instruments were previously tested with WLA in the U.S. (28-30) and India (31).

Socio-Demographic information—A structured questionnaire was used to collect: age, education, employment status, relationship status and number of children.

CD4 Cell Counts—Blood samples were sent to the designated lab for CD4 determination by flow cytometry. The absolute numbers of CD4 are obtained by multiplying % from flow cytometry by total white blood cell count (determined by Act Diff Coulter).

Adherence—Pill count was observed by the interviewer who visited the home of each client during the three-day baseline procedure period. Adherence was calculated based on the number of pills consumed during the baseline month divided by the number of pills prescribed during the same month with adherence measured monthly thereafter.

Depressive Symptomatology—The CES-D is a 20-item scale that measures frequency of depressive symptoms on a 4-point continuum. The CES-D has well-established reliability and validity. Scores on the CES-D range from 0-60, with higher scores representing greater depression. Internal consistency for this scale in our Indian population was 0.94 (32).

Body Composition Measurement

Trained research staff conducted all anthropometric measurements at baseline, at three months and at six months. WLA were weighed barefoot. Heights were measured by a standard clinic height ruler. Body weight was measured by a calibrated scale. A 310e Bioimpedance analyzer (Biodynamics, Inc, Seattle, WA) was used to measure percent body fat, fat mass and lean mass. Body mass index (BMI) was computed as weight in kilograms divided by height in meters squared. We constructed BMI categories using the World Health Organization (WHO) International Criteria for all populations (<18.5 kg/m^2; 18.5 – 24.9 kg/m^2; 25 – 29.9 kg/m^2; > 30 kg/m^2) (5).

Statistical Analysis

Variable construction, calculation and statistical analyses were performed using SAS version 9.2 (Statistical Analysis System, Cary NC). We evaluated the effectiveness of village random allocation by comparing participant characteristics and baseline measurements of the two study groups using one-way analysis of variance (ANOVA) (for continuous variables) and Chi-square tests (for categorical variables). We adjusted all statistical models for variables that significantly differed at baseline.

Univariate and multivariate Repeated Measures Analysis of Variance (rANOVA) using a modified mixed approach described subject effects of changes over three time points (baseline, 3 months and 6 months) for the total study sample, between treatment group effects, and changes over time by treatment group interactions. We evaluated whether the equality of variance assumption was met for ANOVA and rANOVA models by testing for homogeneity of variance for the outcome variables at each time point according to group membership. We conducted stratified analyses according to median ART adherence and median CD4 count taken from computed means of both variables over all time points. All data are presented as means ± standard deviation of the mean (SD).

RESULTS

Sociodemographic Characteristics

A total of 68 WLA were enrolled and remained in the study until completion; 34 in the AL intervention and 34 in the UC group. Baseline socio-demographic characteristics of the study population are described in Table 1, with further detail provided elsewhere (26). Mean age of participants was 31.2 years old (SD 5.2). Participants were primarily Hindu (66%) and married (52%). About one in five (22%) received at least four years of education. About half of the women were diagnosed with HIV for four or more years. Almost half had been taking ART just over 18 months in duration and over half (54%) of the women were depressed (CES-D ≥ 16). Mean compliance with ART at baseline was 48.3 (SD 16.1).

In bivariate analysis modeled by ANOVA and chi-square, baseline age, marital status and being on medication more than 18 months were not significantly associated with program, while education, being Hindu, duration of HIV, depression and compliance with ART differed significantly between programs. In particular, the AL intervention group was more likely to have at least four years of education, to have lived more than four years with HIV, and to be depressed compared to the UC group. In addition, AL participants were less likely to be Hindu and their ART compliance at baseline was lower than that of the UC group. As randomization of villages at baseline produced somewhat different socio-demographic distributions, adjustment of all statistical models for these variables was undertaken.

Body Composition and Immune Parameter Assessments

Body composition measurements at baseline indicated that participants were underweight (Table 2). Average body-mass index (BMI) was 19.7 kg/m^2 (SD 3.0), with average weight at 45.0 kg (SD 5.6) (99 pounds), and average height at 151 cm (SD 5.4) (59.4 inches). No group differences modeled by ANOVA were found in body composition and immune parameter measurements at baseline. We tested for homogeneity of variance for all mean outcome variables at each time point according to group membership. Assumptions of equal variance were met for all variables.

Adjusted Model of Mean Body Composition and Immune Parameters

Table 3 contains means and standard deviations from the modified mixed repeated measures analysis of variance models (rANOVA) that evaluated within subject changes according to group membership over time. Models were adjusted for age and baseline ART adherence, because these variables were shown to be significantly and marginally significantly different in relation to group membership at baseline. Other variables such as depression, years of education, years since diagnosis, and religion, were also shown to be significantly different at baseline according to group membership. However adding these variables sequentially to the repeated measures models did not change the estimates and the variables were therefore excluded from the final analysis models.

All body composition variables, weight, BMI, lean weight, fat weight, as well as CD4 count and ART adherence were significantly different according to group membership over time. The AL intervention greatly improved in all parameters, with significant weight gain, change in lean and fat weight, increase in CD4 count, and improvement in ART adherence when compared to UC. P-values presented, all of which were below 0.01, indicate interaction between within subject change over time and group membership.

ART adherence and immune status may play important mediating roles in relationship to nutrition and body composition. We adopted a judicious approach in evaluation of interactive effects due to our small sample size and the high likelihood that power would be compromised. We constructed rANOVA models of body composition change stratified according to median ART adherence and median CD4 count (see Table 4). Differences between UC and AL were significant ($p < 0.01$) for total body weight and lean muscle mass among participants who were ART adherent (ART adherence ≥ 66%), but were not significant among participants who had reduced adherence to their ART medication (ART adherence < 66%). We also stratified by median CD4 count to determine if the associations were differential according to immune status. The total body weight and lean muscle mass differences according to intervention group were strongest for participants with CD4 counts that exceeded the median of 450.

Subtle differences at baseline may have influenced differences between groups. While lean muscle mass and total body weight at baseline were not significantly different according to group membership, because the AL group appeared to have larger means at baseline than the UC group, we further adjusted our repeated measures analysis of variance models for lean muscle mass and total body weight at baseline. Lean weight change according to group membership, when additionally adjusted for baseline lean weight, was slightly less significant (p=0.005). Estimates of total body weight change, according to group membership, did not change when additionally adjusted for baseline weight (p=0.0001). Finally, CD4 count dramatically increased from baseline in the AL group, from 439 to 714, a 39% increase.

DISCUSSION

The nutritional supplementation provided to the AL participants over a six month time period, in combination with education delivered in group sessions and supportive care by Asha, significantly improved body composition, muscle mass, fat mass, ART adherence, and CD4 count compared to the UC group. These results have great importance for women living with AIDS in rural India.

Nutrition for women living in rural India is marked by low caloric intake and micronutrient deficiency (33). The nutrient deficiencies coupled with a semi-starvation state is made far worse when combined with infection from HIV. Both the disease and treatment for disease alter body composition. In a longitudinal study of HIV-infected adults, parameters associated with disease severity such as baseline viral load, CD4 cell count, and change in CD4 cell count predicted alterations in trunk fat, extremity fat, and lean mass (34). The pathogenesis of HIV, particularly in developing countries already suffering from malnutrition, results in slow and progressive weight loss from anorexia and gastrointestinal disturbances and rapid episodic weight loss from secondary infection (34,35).

We observed differences in weight and lean muscle mass according to group membership when we stratified by ART adherence, with weight and lean muscle mass gains observed in the AL group limited to participants who were ART adherent. Our results suggest that participants with a greater adherence to ART coupled with receiving higher protein and additional care may have gained more total weight and muscle mass compared to participants who received normal protein and usual care. Because of power constraints, we could not evaluate whether interactions were significant. These observations are consistent with changes in body composition that occur with ART, and perhaps ART adherence coupled with higher protein led to the increased muscle and overall weight gain (36). The world-wide dissemination of ART has dramatically decreased mortality among HIV-infected individuals. In Asia, 37% of those infected with HIV are receiving ART, while the percentage in India is higher due to the fact that India accounts for roughly half of Asia's HIV prevalence (37). With the increasing number of HIV-infected persons receiving ART, nutrition becomes an important component to health improvement. Previous studies have shown being underweight at initiation of ART independently predicts mortality (38-40). Weight gain therefore becomes an increasingly important health parameter to accompany successful treatment of HIV. Malnutrition leads to a sub-optimal ART response, but also food insecurity can promote poor self-efficacy and poor ART adherence.

We observed sizeable increases in muscle mass and overall body weight among women in the AL intervention group. The present study design did not enable us to determine the individual contribution from the nutrition portion of the intervention, nor could we determine whether changes in weight and body composition were related to more protein and not just more food. Evidence from other studies point to an important role that protein supplementation could play. One study supplemented AIDS patients with a triglyceride formula that lacked protein, and found, compared to controls without supplementation, no significant differences in weight or in fat-free mass (41). A small clinically-focused randomized trial among AIDS patients compared patients receiving multiple nutrients including protein to patients receiving no supplementation. During the 12-week intervention period, usage of antiretroviral therapy remained unchanged. Leucine, a marker of protein catabolism, was significantly decreased in the supplementation group compared to controls, and lean muscle mass was significantly increased in the supplementation group compared to controls. There was no change in weight for participants in either group (42).

In another study of amino acid supplementation compared to an isocaloric carbohydrate (maltodextrin) supplement condition, the amino acid group significantly gained in total weight and lean body mass compared to the carbohydrate group (6). Evidence from these three studies suggests that increased calories without protein resulted in no weight or lean mass changes, while only protein compared to isocaloric carbohydrate resulted in gains of both weight and lean body mass. The present nutritional intervention consisted of a protein, fiber, fat, and carbohydrate mixture, whereas the intervention group received more protein and calories than the control group. We can infer that the increased protein in combination with increased calories contributed to the muscle mass and total body weight gains that we observed in our study, although we cannot separate out the individual contributions from each, nor can we determine what portion of body composition improvement can be assigned to nutrition.

The observed increases in muscle mass and body composition could have resulted from improved ART adherence and not protein and caloric supplementation. In a longitudinal study of 190 HIV-positive anti-retroviral naïve patients with no nutritional supplementation, body composition measures and CD4 counts were taken before HAART treatment initiation, and at six month follow-up (43). The study population showed an overall significant increase in all body composition measures including weight, lean mass and fat mass, which suggests that the study population enrolled in the current study could have also gained weight and muscle mass because of improved adherence and not necessarily increased supplementation. The present study design was not set up, however, to determine which aspect of the intervention was most responsible for the observed changes.

Immune status may also influence response to ART as well as weight gain from the protein intervention. We stratified our repeated measures analysis of variance models according to median CD4 count, and found that participants in the higher protein group had significantly higher total weight and muscle mass gains if they also had CD4 counts that were above the median. Body composition gains may reflect improved immune status. Increased protein consumption may be related to both. These results suggest an inter-dependence between immunity, ART, nutrition and body composition in relationship to HIV.

Independent of HIV infection, protein and calorie malnutrition can suppress both innate and acquired immunity (38). Acquired immune parameters such as diminished effector T and B cell response and suppressed production of lymphocytes in general occurs in conditions of protein-calorie malnutrition (44-46). Protein-energy malnourishment also promotes impairment of innate immune factors such as complement and diminished phagocytic activity (47). Improvement in nutrition can therefore have direct beneficial effects on immune parameters known to protectively influence recovery from infectious diseases such as HIV and other related infections.

Several randomized controlled trials of macronutrient supplementation for adults with HIV in the developed world reviewed in Koethe et al. (38), as well as one interventional study of nutritional supplementation of HIV-infected individuals in South India have mixed results in relationship to impact of supplementation on body weight (6,7,41,42, 48-53). Supplementation in all trials included increased protein in the experimental condition, either through amino acid supplementation, protein powder, protein shakes, or fortified mixtures. While several trials observed weight gain or gain in lean weight in the experimental condition (6,7,42) only one observed a decrease in CD4 count (50), but did not observe weight gain in the experimental condition. Except for the interventional trial in India, all trials occurred among well-nourished individuals in the developed world (6,7,41,42,48-52). The interventional trial in India did not result in significant weight gain in the supplement group compared to usual care and did not result in an improved CD4 count (53). Baseline BMI in the Indian interventional trial was similar (20.6 kg/m^2) in comparison to the present study (19.7 kg/m^2), however a large percentage of subjects did not complete the Indian interventional trial (43%) suggesting that the two study populations may not be comparable. In addition, the Indian interventional trial was not randomized and appeared to have a larger number of baseline differences that required statistical adjustment than the present study which could have compromised their power to detect differences.

Findings of our study also revealed the importance of Asha support of WLA in relationship to ART adherence and education about healthy behaviors. Asha were impactful in helping WLA and their family members to understand the importance of healthy eating, healthy living, and healthy thinking in relationship to their multiple roles of healthy mother, wife, and sister. We observed significant body composition changes in the intervention group compared to usual care controls that most likely resulted from combined supportive care, education, and nutritional supplementation.

Limitations

Our capacity to generalize to other populations under similar conditions is limited due to our small sample size. Despite the small sample size, however, we observed sizeable differences in body composition and immune parameters that have direct impact on recovery from HIV. Several demographic and prognostic variables were found to differ at baseline between intervention and control groups. Randomization was conducted according to village and not individual. Therefore baseline differences could not be avoided. In spite of the baseline differences however, model estimates adjusted for the baseline differences were similar to unadjusted model estimates.

We also did not measure compliance to the nutritional supplement intervention. That is, we could not determine if compliance might have been greater among the intervention group, or if compliance was less among the control group. The two nutritional supplements were created to be equally palatable. The nutritional supplements were not isocaloric, but rather the protein intervention contained more protein and more calories. In addition, we did not undertake baseline dietary assessment. Therefore we could not measure the background diet and whether diet had changed as a result of the intervention. Potential dietary compensation effects would need to be sizeable, however, to explain the differences that we observed.

Our intervention consisted of protein supplementation combined with education, focused nutrition training, and supportive care designed to increase treatment adherence. The increase in ART adherence, for instance, could have contributed to a diminished viral load and/or increased CD4 count. Body composition improvements could have resulted from better compliance to ART treatment rather than the nutritional intervention. In another longitudinal study of HIV-infected individuals, HAART was associated with an increase in lean mass among women with HIV compared to HAART naïve users, although total weight increases were not observed. In the same study, viral load changes were not associated with body composition alterations, however positive increases in CD4 cells were associated with gains in extremity lean mass (34). Evidence demonstrating the increases in weight and muscle mass from HAART (34, 43), and evidence showing increases in muscle mass and body weight resulting from protein suggest that both were important in promoting an improved body composition among the intervention group compared to usual care controls.

Finally, the current design did not permit us to separate out the influence of food from education and supportive care. Most likely all elements contributed to improvements in body composition and immune status. Future research using a factorial design will enable us to parcel out which element(s) of the intervention were responsible.

Conclusion

Our randomized pilot intervention trial conducted among 68 rural Indian women with AIDS, found that high protein caloric supplementation combined with additional care, focused nutrition education, and targeted efforts to improve ART adherence provided by trained Ashas resulted in significant increases in body composition and improvements in immune functioning, compared to standard protein in combination with usual care. The increases in muscle mass and overall body weight were greater among rural Indian women who were ART adherent and had healthier immune responses, suggesting that adherence and immune functioning were important mediating influences. These results are preliminary and derived from a small sample that did not have a control condition without nutritional supplementation. Further research is needed to determine which aspect of the intervention was primarily responsible for the observed body composition improvements.

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Table I

Sociodemographic Characteristics by Program and Overall

	AL[a]		UC[b]			
Baseline Variable	**M**	**SD**	**M**	**SD**	**Total M/SD**	**p value[c]**
Age (20-45)	32.2	5.3	30.1	5.2	31.2/5.2	.102
Compliance with ART (29-100)	41.7	9.5	54.9	16.9	48.3/16.1	.001
	N	%	N	%	Total %	p value[c]
Hindu	15	45.5	29	85.3	65.7	.001
Married	15	44.1	20	58.8	51.5	.225
At least 4 years of school	11	32.4	4	11.8	22.1	.041
More than 47 Months since HIV Diagnosis	22	66.7	11	32.4	49.3	.005
More than 18 Months on Medication	18	52.9	15	45.5	49.3	.540
Depressed[b]	24	70.6	13	38.2	54.4	.007

[a]Asha-Life

[b]Usual Care

[c]p-value derived from Chi-square or one-way ANOVA

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Table II

Biologic Characteristics Based on Group Membership at Baseline

	AL[a]		UC[b]		Total Sample		
Variable	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**p-value[c]**
Weight (kg)	46.2	7.9	43.8	7.1	45.0	5.6	0.20
Height (cm)	151.8	5.1	150.2	5.7	151.0	5.4	0.22
Body Mass Index	20.0	3.4	19.4	2.5	19.7	3.0	0.35
Lean Weight	33.4	5.2	31.8	5.4	32.6	5.3	0.23
Fat Weight	12.8	4.0	12.0	3.0	12.4	3.5	0.35
Percent Fat (%)	27.2	5.4	27.2	4.7	27.2	5.0	0.97
CD4 count	439.1	217.6	447.5	260.0	443.3	238.0	0.89

[a] Asha-Life

[b] Usual Care

[c] p-value derived from one-way ANOVA

Table III

Adjusted* mean body composition, immune parameters, and ART adherence according to group over time

Variable	Mean AL[a] Measures ± S.D.			Mean UC[b] Measures ± S.D.			p-value[c]
	Baseline	3 Month	6 Month	Baseline	3 Month	6 Month	
Weight (kg)	46.2 ± 7.9	49.1 ± 7.9	51.4 ± 6.9	43.8 ± 7.1	41.9 ± 9.0	42.6 ± 8.3	0.0001
Body Mass Index (kg/m^2)	20.0 ± 3.4	21.3 ± 3.0	22.3 ± 3.0	19.4 ± 2.5	18.6 ± 3.6	18.8 ± 3.0	0.0001
Lean Weight (kg)	33.4 ± 5.2	33.7 ± 6.2	36.1 ± 4.9	31.8 ± 5.4	31.4 ± 6.0	30.8 ± 6.1	0.0045
Fat Weight (kg)	12.8 ± 4.0	14.7 ± 4.0	15.3 ± 3.3	12.0 ± 3.0	12.3 ± 2.8	11.1 ± 3.6	0.0001
Percent Fat (%)	27.2 ± 5.4	29.6 ± 4.2	29.6 ± 4.2	27.2 ± 4.7	28.7 ± 5.1	26.0 ± 5.7	0.0009
CD4 count[d]	439.1 ± 217.6		714.4 ± 293.3	447.5 ± 260.0		416.6 ± 234.9	0.0001
ART adherence (%)[e]	40.0 ± 11.0		99.0 ± 0.02	53.0 ± 0.2		67.0 ± 0.2	0.0001

[a] Asha-Life (AL)

[b] Usual Care (UC)

[c] p-value for interaction between change over time and group membership

[d] CD4 count measured at baseline and end of intervention

[e] ART adherence modeled as a main term

* Models adjusted for age and ART adherence at baseline

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Table IV

Mean total and lean weight by group over time stratified by ART adherence and CD4 Count adjusted for age at baseline

ART Adherence < 66%

Variable	**AL[a]**			**UC[b]**			**p-value[c]**
	Baseline	**3 Month**	**6 Month**	**Baseline**	**3 Month**	**6 Month**	
Weight (kg)	42.9 ± 7.5	44.1 ± 8.3	46.4 ± 9.7	39.9 ± 10.4	39.9 ± 10.4	42.0 ± 7.4	0.36
Lean Weight (kg)	31.1 ± 5.0	34.1 ± 5.0	31.1 ± 8.8	31.0 ± 4.3	31.1 ± 5.1	30.6 ± 5.1	0.16

ART Adherence ≥ 66%

Variable	AL[a]			UC[b]			p-value[c]
	Baseline	3 Month	6 Month	Baseline	3 Month	6 Month	
Weight (kg)	47.5 ± 7.8	51.5 ± 6.6	53.9 ± 5.7	43.8 ± 8.5	42.7 ± 9.2	43.2 ± 9.2	0.0001
Lean Weight (kg)	34.4 ± 5.0	36.9 ± 4.7	34.8 ± 4.6	32.9 ± 6.5	31.9 ± 7.2	31.1 ± 7.5	0.0002

CD4 Counts < 450

Variable	AL[a]			UC[b]			p-value[c]
	Baseline	3 Month	6 Month	Baseline	3 Month	6 Month	
Weight (kg)	45.1 ± 6.1	47.4 ± 6.0	50.4 ± 6.9	43.2 ± 6.7	39.2 ± 9.7	41.4 ± 6.9	0.19
Lean Weight (kg)	32.8 ± 4.8	35.1 ± 4.7	31.7 ± 8.3	30.8 ± 4.5	30.5 ± 5.5	29.9 ± 5.6	0.05

CD4 Counts ≥ 450

Variable	AL[a]			UC[b]			p-value[c]
	Baseline	3 Month	6 Month	Baseline	3 Month	6 Month	
Weight (kg)	46.7 ± 8.8	51.2 ± 8.1	53.2 ± 7.4	45.1 ± 8.1	44.1 ± 9.2	44.1 ± 9.8	0.0001
Lean Weight (kg)	33.7 ± 5.4	36.7 ± 4.9	34.8 ± 4.6	33.8 ± 6.4	33.3 ± 6.8	32.4 ± 7.0	0.006

[a]ASHA Life (AL)

[b]Usual Care (UC)

[c] p-value for interaction between change over time by group membership