Effects of ColoPlus® in Treatment of Patients with HIV-associated Diarrhoea in Northern Uganda.

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Background: HIV/AIDS remains a major public health problem the world over, with high morbidity and mortality. Northern Uganda, a region that is just emerging from over 20 years of conflict, has HIV prevalence of about 8.2%, much higher than the national average of 6.4%. Chronic diarrhea is a common manifestation in patients with acquired immunodeficiency syndrome (AIDS) in developing countries. With inadequate food availability in poor households, HIV-associated diarrhoea often leads to malnutrition and worsening of HIV disease especially for those with no access to anti-retroviral therapy. Nutritional intervention is a key component of comprehensive management of HIV/AIDS patients. ColoPlus, a nutritional product made from bovine colostrum, is rich in nutrients, immunoglobulin, growth factors and peptides that have anti-bacterial effects. The aim of the study was to determine the effects of ColoPlus on stool frequency, nutritional and immunological status of patients with HIV-associated diarrhoea.

Method: The study was carried out between October 2007 to June 2008 at Gulu Referral Hospital and 4 other outreach clinics in internally displaced persons' camps in Gulu and Amuru districts. Eighty seven patients participated in the open-labeled randomized clinical trial. Forty five patients received 50 grams of ColoPlus twice a day for 4 weeks, besides "regular care". The control group of 42 patients received only the "regular care" for diarrhoea which included fluid and electrolyte replacement, antibiotic and anti-diarrhoeic drug use. Participants were followed up for 9 weeks. Effects of ColoPlus on daily stool frequency, fatigue level, body weight, and body mass index, haemoglobin, serum albumin and CD4+ cell counts were measured for all patients.

Results: There was a significant decrease in mean daily stool frequency from 7.5 ± 2.9 to 1.3 ± 0.7 (±SD) in patients on ColoPlus, representing 83% reduction. Patients on regular treatment had a 60% reduction in mean daily stool frequency (6.9±3.2 to 2.7±1.8). On average, diarrhoea ceased by day 7 for patients on ColoPlus and day 21 for the controls. Self-estimated fatigue remarkably reduced by 85% for patients on ColoPlus compared to 43% for the controls. Mean weight and body mass index (BMI) increased by 11% in patients on ColoPlus with no significant change in the controls. Patients on ColoPlus had a 14% increase in mean CD4+ cell count compared to a 12% reduction in the controls. No significant effect of ColoPlus was demonstrated on serum albumin and haemoglobin by week 9.

Conclusion: ColoPlus is an effective treatment of HIV-associated diarrhoea.

Effects of ColoPlus in treatment of HIV-associated diarrhea

Uganda Medical Association Scientific Conference, Gulu

27th February 2009

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Background

HIV/AIDS remains a global public health problem

HIV prevalence in conflict affected N. Uganda, stands at 8.2%, compared to national average of 6.4%.

Chronic diarrhea is a common manifestation in patients with acquired immunodeficiency syndrome (AIDS) in developing countries.

Background

With inadequate food availability in poor households, HIV-associated diarrhoea often leads to malnutrition and worsening of HIV disease especially for those with no access to anti-retroviral therapy.

Background

Nutritional intervention is a key component of comprehensive management of HIV/AIDS patients.

Innovations in scaling up nutritional interventions in care of PLWHA is needed

Several studies have demonstrated that use of bovine immunoglobulins and colostrum preparations decreases diarrhea in HIV/AIDS patients

Background

ColoPlus, a nutritional product made from bovine colostrum, is rich in nutrients, immunoglobulin, growth factors and peptides that have anti-bacterial effects.

Background

An open-label observational study in Nigeria showed clinical, nutritional and immunological benefits in patients with HIV-associated diarrhea.

Background

We conducted the first RCT aimed at evaluating the effect of ColoPlus on diarrheal frequency, nutritional and immunological status of patients with HIV-associated diarrhoea in Gulu and Amuru districs of northern Uganda.

Study objectives

1. To determine the effect of ColoPlus on the frequency of stool evacuations in patients with HIV-associated diarrhoea.

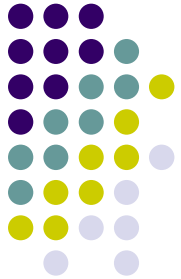
2. To determine the effect of ColoPlus on self-estimated fatigue levels in the study patients.

Study objectives

3. To determine the effect of ColoPlus on the nutritional status of the study patients.

4. To determine the effect of ColoPlus on the immune response (change in CD4+ cell count) in the study patients.

Methods: study setting and population



- Study was carried at between October 2007 and June 2008 at Gulu Referral Hospital and 4 outreach clinics
- HIV-infected adults attending care at study sites were enrolled. Inclusion criteria:
  - 18 years +
  - Prolonged diarrhea, 4+ motions/day for 7+ days
  - Not on ARVs
  - No known allergy / intolerance to milk and milk-products
  - Informed consent

Methods: sample size

- Formula by Corlien et al
  - Proportion of patients with HIV assoc diarrhea resolving on regular treatment = 35% and on bovine colostrum immunoglobulin = 72.4%;
  - 95% CI, Power 90%;
  - 20% loss to follow-up

- Minimum sample size of 40 patients for each study arm was used.

Methods: study design

- Open-label RCT
  - 45 patients received regular care for diarrhea plus 50gm of ColoPlus twice a day for 4 weeks, 95% compliance.
  - 42 patients received regular care for diarrhea only

- All patients were followed up at weekly intervals for 9 weeks.

Methods: measurements

- Baseline data:
  - socio-demographics information
  - clinical data by clinicians
  - 24 hr stool freq – on dairy card
  - self-estimated fatigue levels – Visual analogue scale(0 – 10)
  - weight, BMI
  - stool microscopy, Hb, Alb, CD4+

- **Measures were repeated at weeks 4 and 9, except for CD4+ at 9 weeks.**

Methods: Data analysis

- Data was entered in EPI Info and analyzed SPSS
- Chi-square tests for categorical variables; Independent and paired sample t-tests for continuous variables.
- Baseline values were compared with week 4 and 9 values to answer study objectives

Methods: Ethical approvals

- IRC of Gulu University Faculty of Medicine
- UNCST,
- NDA Clearance
- Ethics Committee of Kund University, Sweden

Results

Table 1: Baseline characteristics of study participants, N = 87.

	ColoPlus n=45	No ColoPlus n=42	Total N=87
Sex, F	28 (62.2)	32(76.2)	60(69.0)
Mean age, yrs	34.5(8.1)	39.1(9.7)	36.7(9.1)
Diarrhea Mean freq Mean duration	 7.5(2.9) 16.4(11.0)	 6.9(3.2) 16.8(10.9)	 7.2(3.1) 16.6(10.9)
Mean Temp °C	36.1(3.3)	36.6(0.6)	36.3(2.4)

Table 2: Baseline characteristics of study participants, N = 87.

	ColoPlus n=45	No ColoPlus n=42	Total N=87
Education None	9(20.0)	8(19.0)	17(19.5)
Primary	28(62.2)	33(78.6)	61(70.1)
Secondary	8(17.8)	1(2.4)	9 (10.3)
Occupation			
Not employed	30(66.7)	27(64.3)	45(65.5)
Employed	15(33.3)	15(35.7)	42(34.5)
Septrin prophylaxis			
Yes	40(88.9)	41(97.6)	81(93.0)
No	5(11.1)	1(2.4)	6 (7)
Other Abs, Yes	8(17.8)	9(21.4)	17(20)
No	37(82.2)	33(78.6)	70(80)

Table 3: Effect of ColoPlus on frequency of diarrhea

	N	Mean motions per day	P-value
Baseline			
ColoPlus	45	7.5(2.9)	
No ColoPlus	42	6.9(3.2)	0.376
Week 1			
ColoPlus	43	3.5(1.5)	
No ColoPlus	41	4.7(3.8)	0.059
Week 4			
ColoPlus	42	1.6(0.7)	
No ColoPlus	41	2.9(1.8)	<0.001
Week 9			
ColoPlus	33	1.3(1.6)	
No ColoPlus	40	2.7(3.5)	0.041

Trend: mean daily freq of diarrhea

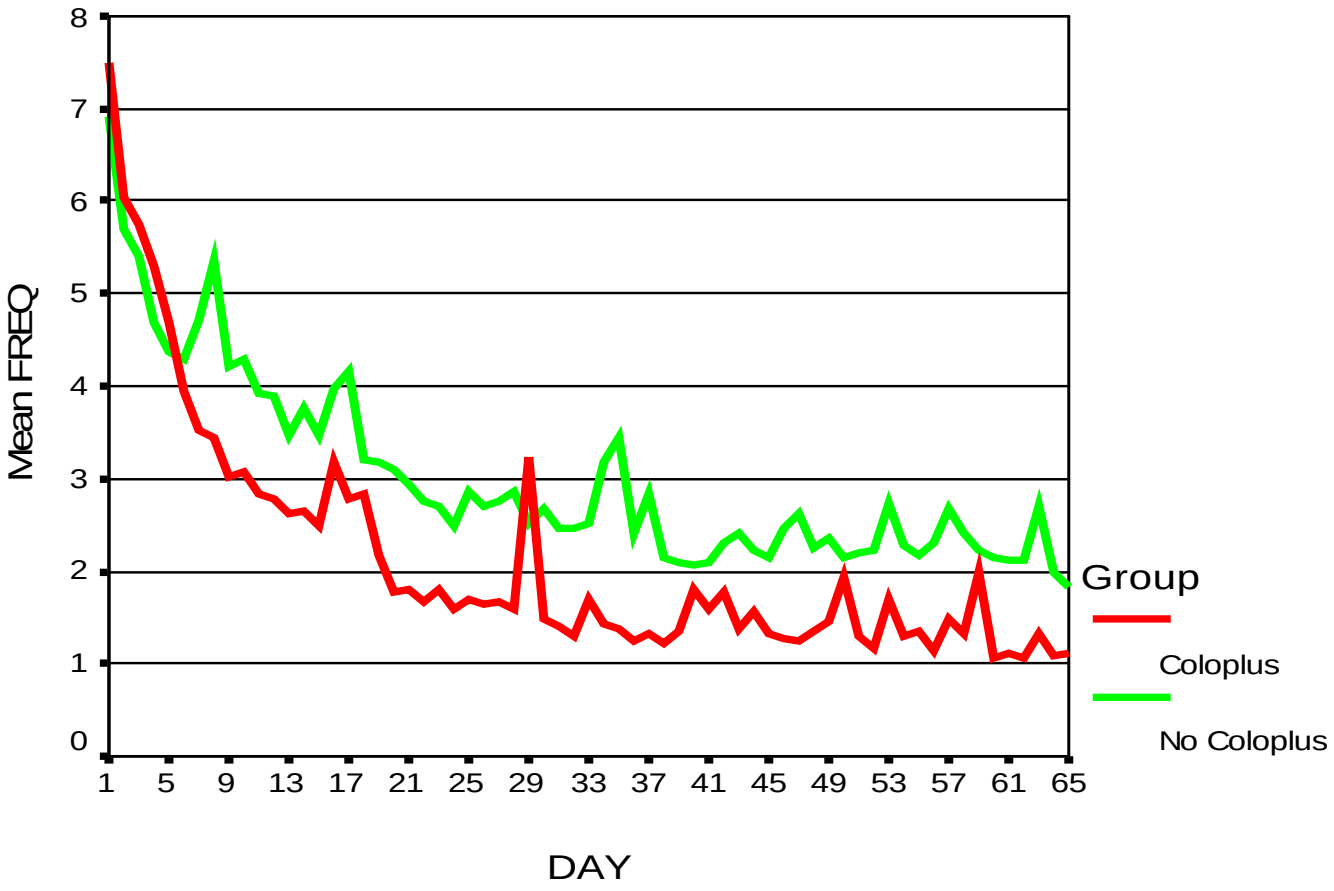


Table 4: Effect of ColoPlus on fatigue

	Mean VAS Score			Mean decrease (week 9)	P-value
	Baseline	Wk4	Wk9		
ColoPlus	52.8	25.1	7.9	44.8	
No ColoPlus	46.4	35.5	26.6	20.0	<0.001

Table 5: Effect of ColoPlus on nutritional status

	Mean values			Mean decrease	P-value
	Baseline	Wk4	Wk9	Week 9	
Weight, kg					
ColoPlus	51.7	54.1	57.6	5.8	<0.001
No ColoPlus	54.0	54.0	53.5	-0.1	0.251
BMI					
ColoPlus	19.5	20.4	21.7	2.2	<0.001
No ColoPlus	20.4	20.5	20.4	-0.1	0.591
Serum albumin				1.0	0.244
ColoPlus	3.6	3.7	4.7	-0.2	0.146
No ColoPlus	3.9	3.9	3.8		
Haemoglobin					
ColoPlus	11.7	11.9	12.0	0.2	0.337
No ColoPlus	12.2	12.3	11.9	-0.4	0.334

Table 6: Effect of ColoPlus on CD4+ cell count

	Mean CD4+		Mean increase	P-value
	Baseline	Wk9		
ColoPlus	379	433	53	<0.001
No ColoPlus	492	432	-60	<0.001

Study limitations

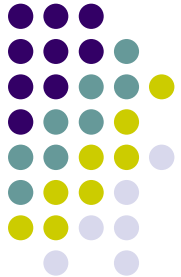
The open-label RCT study design might have introduced some observational / reporting bias during follow-up e.g. patient self-estimated fatigue levels or observed clinical measures. However, laboratory tests that are less prone to such bias still showed favourable outcomes for patients on ColoPlus compared to their controls.

We did not monitor HIV viral load in this study to assess whether immunological response (increase in CD4+ count) was associated with reduction in viral replication.

Conclusions

- ColoPlus is an effective treatment of HIV-associated diarrhea
- ColoPlus also remarkably reduces fatigue levels thereby improving patient wellbeing and functionality.
- Patients treated with ColoPlus achieved greater weight gain, increase in body mass index and good immunological response demonstrated by a rise in CD4+ count.

Recommendations

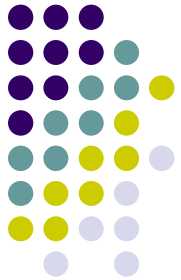


- We recommend a wider use of ColoPlus as an innovative therapeutic nutritional product in the management of HIV /AIDS patients, especially those with persistent diarrhoea and HIV wasting syndrome.

- A large scale phase IV trial is recommended in scaling up ColoPlus use a component of comprehensive HIV/AIDS care programmes.

Acknowledgements

- Swedish Embassy, Kampala, Uganda
- Gulu Women Economic Development and Globalization (GWED-G), Gulu Uganda
- ColoPlus AB, Malmö Sweden, Sweden
- Lund University
- Gulu University and GRRH
- JCRC, Gulu
- Communities and Participants



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