Macronutrients

As Part of HIV Treatment

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Macronutrients as part of HIV treatment

- Background
- State of research
- Our study
- Research vs. Implementation
Background

Nutrition and Sub-Saharan Africa

- 24.7 million people in sub-Saharan Africa (SSA) with HIV/AIDS and 4.3 million new infections
- 2 million on treatment in Dec 2006, increase of 700 million in one year (WHO)
- SSA > 30% insufficient food intake
- WFP 2006: “2 million tons - valued at US$600 million” plus 2 million tons donated in kind
Coincident HIV and Malnutrition

Adults and children estimated to be living with HIV in 2006

North America
1.4 million
(1.4 million)
(880 000–2.2 million)

Caribbean
250 000
(190 000–320 000)

Latin America
1.7 million
(1.3–2.5 million)

Western and Central Europe
740 000
(580 000–970 000)

North Africa and Middle East
460 000
(270 000–760 000)

Sub-Saharan Africa
24.7 million
(21.8–27.7 million)

Eastern Europe and Central Asia
1.7 million
(1.2–2.6 million)

East Asia
750 000
(460 000–1.2 million)

South and South-East Asia
7.8 million
(5.2–12.0 million)

Oceania
81 000
(50 000–170 000)

Total: 39.5 (34.1–47.1) million
Coincident HIV and Malnutrition

Hunger map

- Undernourished population
- Undernourished population
- Población subnutrida

FAOSTAT 2002-2004
Malnutrition-infection complex

- Macro-micronutrient deficiencies
- Organ-specific manifestations
- Acute phase response
- Infections

- HIV
- Pathogenicity
- Behaviour

- Decreased intake
- Decreased absorption
- Increased requirements
- Increased excretion

Adapted Friis 2005
HIV Adversely Affects Nutrition

- Nutrition modified in HIV
  - Decreased intake (most important)
  - Decreased absorption
  - Increased protein turnover
  - Increased resting energy expenditure

- Coinfections with TB, malaria, parasitic disease increase metabolic demand

- Weight loss can define stage, ART initiation
Decreased Food Intake

CNS disease

Medication

Depression

Systemic Infection

Poverty

GI pathology

Decreased Food Intake
Nutrition Has Marked Effect On Pediatric Survival

- Poor growth strongly and independently associated with poor survival in US HIV-infected hemophilia populations. (Hilgartner 2001)
- Ugandan infants with low weight in the first year of life had a 5-fold increase in risk of death by age 25 mos. (Berhane 1997)
- In well nourished children on antiretrovirals, poor growth is an independent risk factor for death (McKinney 1994, Benjamin 2003, Carey 1998)
Growth Failure Associated with Increased Risk of Mortality, Uganda

Average Weight-for-Age Z Scores in Year 1 of Life

Odds Ratio for Mortality by 2 Years

2.74
3.39
4.87

Berhane R et al, Pediatrics 1997;100 (1)

Courtesy S. Arpadi
Nutritional status predicts progression of HIV among children on ART

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<td>1.8,67.7</td>
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Benjamin 2004
Nutritional status predicts survival of HIV among adults on ART

- BMI less than 18.5 at initiation of HAART is significantly associated with overall mortality (Jerene 2006)
- Weight loss during first four weeks of treatment is associated with death (Van der Sande 2004)
- Initiation of ART is a high risk time period
What happens if you act on the poor nutritional status of HIV-infected patients on ART?

- Weak evidence base
- Indirect support: biologic rationale, programmatic experience, data in HIV-uninfected individuals
- UN General Counsel/WHO Technical Advisory Group: advocate integration of nutrition into HIV/AIDS care & treatment programs
- Others
Macronutrient Research

- Data lacking
  - Pubmed “Macronutrient + HIV” = 13 citations
  - Pubmed “Macronutrient + AIDS” = 13 citations
  - Pubmed “Food HIV Africa” Limit: RCT
    - Oct 2007: 48 citations – 28 Vitamin, 15 Breastfeeding, 3 Food supplementation, 2 other
  - Pubmed “malnutrition or wasting, AIDS or HIV” = 302063 citations
  - Cochrane review 2007
Unanswered Questions
Macronutrients and HIV

- **Patient**
  - Response of BMI
  - Clinical outcomes of macronutrient interventions
  - Clinical criteria to give supplementation

- **Intervention**
  - Best type of macronutrient combo
  - Timing in disease course
  - Duration of intervention required

- **Programmatic**
  - How is food used and shared in the household
  - Ability of programs to engage in valid research
  - Distraction from other HIV activities
  - Cost
Macronutrients as Part of HIV Treatment

A Pilot Study of a Six Month Macronutrient Supplementation Program for Patients Initiating Antiretroviral Therapy in Central Kenya

Stephen Arpadi, Wafaa El-Sadr (PI), Juma Rashid, Murugi Ndirangu, Mark Hawken, Richard Deckelbaum
Study Questions

- For ambulatory patients with BMI between 14.5 and 18.5, does macronutrient supplementation during the first six months of ART therapy:
  - Change BMI vs. ART/MMS/counseling alone?
  - Affect clinical outcomes, QOL, food security, food frequency?
  - Affect laboratory indicators?
  - Safety, Logistics and Costing
Study Design

- Answering questions is not easy
- Medicalizing food in areas of seasonal food insecurity
- Other designs problematic: individual randomization, index patient vs. family, RUTF vs. food, programmatic limitations
- Step toward global goal to integrate macronutrient supplementation into HIV treatment
- We must determine what is effective given scarcity of data and limited resources
Pilot Study Design

Control Site

n=100

Ambulatory, starting ART
BMI 14.5-18.5

Treat with ART and MMS
Nutrition Counseling

6 and 12 month Follow Up
Home Visit at 3, 9 months

Intervention Site

n=100

Ambulatory, starting ART
BMI 14.5-18.5

Treat with ART and MMS
Nutrition Counseling

PLUSS
Treat with 6 months Macronutrient Supplement
(Maize, beans, oil, porridge)

6 and 12 month Follow Up
Home Visit at 3, 9 months
Study Outcomes

Anthropometrics
BMI at 6 months – Primary Outcome
BMI at 12 months
MUAC at 0, 6, 12 months
Skinfold Thickness at 0, 6, 12 months

Questionnaires
Food Frequency at 0, 6, 12 months
Food Security at 0, 6, 12 months
Quality of Life at 0, 6, 12 months
Clinical Events at 0, 6, 12 months
Household food inventory at 3, 9 months

Laboratory
CD4 Counts
Complete Blood Count
Pre-Albumin
Ferritin
Retinol Binding Protein

Cost
Macronutrients as Part of HIV Treatment

- Can we advocate for specific macronutrient supplementation as part of HIV treatment based on the evidence?
Macronutrients as Part of HIV Treatment

- Can we advocate for specific macronutrient supplementation as part of HIV treatment based on the evidence?
- No

- Programmatic dilemma because of lack of data, limited resources
Macronutrients as part of HIV treatment

- WHO 2005 - “There is an urgent need to develop and test a series of nutritional supplements for the maintenance and improvement of nutritional status in HIV/AIDS.”
Current Needs

- Well-designed studies, that are:
  - Implementable
  - Scalable – along with ART
  - Use minimal operational, human, and fiscal resources from fragile infrastructures
- Face the design challenges
- Collaboration
Macronutrients as Part of HIV Treatment

- Food is not monotherapy for HIV
- Interesting nutrition-related growth questions in children
Nutritional therapies for HIV wasting

- Treatment of underlying disease
- Food-based therapies
- Formula and protein supplements
- Appetite stimulants
- Non-volitional feeding - enteral, TPN
- Anabolic agents
- Cytokine inhibitors
- Resistance training exercise
Summary of experience in a AIDS wasting

- Many modalities increase caloric intake
- Increased food intake does not lead to Body Cell Mass repletion (↑↑wt and fat, ± FFM and ht)
- Anabolic agents promote BCM repletion
- Resistance exercise and cytokine inhibitors also promote BCM repletion
- Anti retrovirals are essential
Are growth and body composition disturbances reversed with increased dietary intake?

- “Pre-HAART” studies found enteral supplements via oral and tube feedings improve wt and fat stores but not ht or lean body mass (Miller 1995, Henderson 1994).

- Similar results with appetite stimulant e.g. megestrol (Clarick 1997).
# Z score changes with tube feedings (Henderson 1994)

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<tr>
<td>Ht for age</td>
<td>-1.93 (.80)</td>
<td>-1.74 (1.64)</td>
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<td>Wt for age</td>
<td>-2.13 (.71)</td>
<td>-1.46 (1.38)*</td>
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<td>Wt for Ht</td>
<td>-1.07 (.96)</td>
<td>-0.13 (1.04)*</td>
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<td>AMC</td>
<td>-1.24 (.86)</td>
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<td>Arm fat area</td>
<td>-1.75 (1.31)</td>
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* p<0.05