Micronutrients and Immune Function

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Brief bio:

1) Treating HIV(+) individuals since 1984

2) Currently consults with over 250 HIV(+) individuals worldwide

3) Frequent prescriber of antiviral meds (HAART)

4) Goal --> Achieve a useful integration of natural and pharmaceutical interventions
Micronutrients and Immune Function

Why is gut health so important to the treatment of HIV infection?

1) Absorbs all nutrients
2) Maintains a complement of CD4 cells that comprises > 60% their total number
3) Regulates glucose metabolism and the body’s insulin response; produces vitamin micronutrients
4) Processes fecal contents promptly so fermented waste products do not get reabsorbed into the blood

The GI system performs the following fx’s:
Living a Normal Lifespan with HIV

“Leaky Gut Syndrome”

Micronutrients and Immune Function


- Chronic immune activation is a better predictor of HIV disease outcome than plasma viral load
- Circulating microbial products, derived from the GI tract, are a cause of HIV-related immune activation
- This process is significantly contributed to by a compromised GI mucosal surface

Micronutrients and Immune Function


“Injury to the immune component of the GI mucosal surface, along with damage to the intestinal epithelial microenvironment with its antimicrobial functions, may effect systemic immune activation during the chronic phase of HIV infection through the increased translocation of luminal microbial products”

Micronutrients and Immune Function

How can we maintain the integrity of the intestinal mucosa in chronic HIV infection?
Micronutrients and Immune Function

1) A Healthy Diet
2) Pre and Probiotic Supplementation
3) L-Glutamine Supplementation
4) Elimination of Intestinal Parasites
Living a Normal Lifespan with HIV

- Metronidazole 500 mg 2X/day
- Paromomycin 500 mg 2X/day
- Albendazole 200 mg 2X/day

Take for 15 days

Retest 1 month after completion of treatment
<table>
<thead>
<tr>
<th>Parasitology Microscopic Exam Results</th>
<th>Parasitology EIA Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Echinococcus granulosus (Dogs), Echinococcus multilocularis</strong></td>
<td><strong>Brusia</strong></td>
</tr>
<tr>
<td><strong>Endocytosis</strong></td>
<td><strong>Cryptosporidium</strong></td>
</tr>
<tr>
<td><strong>Entamoeba coli</strong></td>
<td><strong>Eliotrypanum</strong></td>
</tr>
<tr>
<td><strong>Eosinophilic vacuoles</strong></td>
<td><strong>Giardia</strong></td>
</tr>
<tr>
<td><strong>Giardia trophozoites</strong></td>
<td><strong>Helicobacter pylori</strong></td>
</tr>
<tr>
<td><strong>Helicobacter pylori</strong></td>
<td><strong>Iodophor</strong></td>
</tr>
<tr>
<td><strong>Iodophor</strong></td>
<td><strong>Isospora</strong></td>
</tr>
<tr>
<td><strong>Isospora</strong>*</td>
<td><strong>Leishmania</strong>*</td>
</tr>
<tr>
<td><em><em>Leishmania</em> trophozoites</em>*</td>
<td><em>Note: Results not available</em></td>
</tr>
</tbody>
</table>

*Reference Ranges for EIA tests is negative.*
Micronutrients and Immune Function

Clinical Trials

- Numerous studies have reported a high prevalence of nutrient deficiencies in patients with HIV infection
- Micronutrient deficiencies are associated with a higher incidence of infection, faster disease progression and increased HIV mortality
Micronutrients and Immune Function

Clinical Trials

- Broad-spectrum micronutrient intervention is associated with fewer symptoms, delayed disease progression and reduced HIV-related mortality
- Broad-spectrum micronutrient intervention is also associated with increased in CD4 count in patients on and off HAART

Micronutrients and Immune Function

Broad-Spectrum Micronutrient Therapy

3 Randomized Clinical Trials
- The Thai Study
- The African Study
- The U.S. Study
Micronutrients and Immune Function


- A Double-Blinded, Placebo-Controlled, Randomized Clinical Trial (n=481)
- At the end of one year there were 50% fewer deaths in the micronutrient group compared to placebo
- Major difference in mortality rate was seen in patients with less than 200 CD4 cells (HR=0.37)

Fawzi, et al. *NEJM* 2004

- A daily micronutrient supplement was provided to 269 pregnant HIV(+) women in Tanzania (n=1078)
- Six years later, the micronutrient group had a significantly higher mean CD4 count and lower mean viral load
- There were significantly fewer symptoms, less disease progression, and lower mortality in the micronutrient supplemented patients
Dr. Fawzi's Conclusion:

- Multivitamin supplements delay the progression of HIV disease and provide an effective, low-cost means of delaying the initiation of antiretroviral therapy in HIV-infected (patients)


Mitochondria

- Energy power-houses
- Have their own DNA
- Mitochondrial DNA is replicated by a separate enzyme to nuclear DNA
The HIV Micronutrient Study

Funded by:
Bristol-Myers Squibb Virology
The HIV Micronutrient Study

Methods

- A prospective, double-blinded, placebo-controlled randomized clinical trial
- Study duration -> 12 weeks
- Forty patients were randomized and enrolled at four independent research sites in the US (New York, Los Angeles, Philadelphia, SF)

Inclusion Criteria

- HIV-positive, CD4 count ≥100 cells/mm3
- At least 3 months on a stable HAART regimen that included D4T and/or DDI
- Clinical signs or symptoms of peripheral neuropathy
The HIV Micronutrient Study

Study Intervention

- All patients were given a foil packet containing 8 pills (micronutrients or placebo) to be taken twice daily with food
- The micronutrient treatment was permitted to be taken at the same time as antiviral medications

The HIV Micronutrient Study

Micronutrient Supplement - total daily dosage

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beta-Carotene</td>
<td>20,000IU</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>2,000mg</td>
</tr>
<tr>
<td>Bioflavonoids</td>
<td>300mg</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>800IU</td>
</tr>
<tr>
<td>Vitamin B-6</td>
<td>260mg</td>
</tr>
<tr>
<td>Vitamin B-1</td>
<td>60mg</td>
</tr>
<tr>
<td>Vitamin B-2</td>
<td>60mg</td>
</tr>
<tr>
<td>Niacinamide</td>
<td>60mg</td>
</tr>
<tr>
<td>Pantothenic acid</td>
<td>60mg</td>
</tr>
<tr>
<td>Choline</td>
<td>60mg</td>
</tr>
<tr>
<td>Inositol</td>
<td>60mg</td>
</tr>
<tr>
<td>Folic Acid</td>
<td>800mcg</td>
</tr>
<tr>
<td>Biotin</td>
<td>50mcg</td>
</tr>
<tr>
<td>Vitamin D3</td>
<td>400IU</td>
</tr>
<tr>
<td>Betaine HCL</td>
<td>150mg</td>
</tr>
<tr>
<td>L-Glutamine</td>
<td>200mg</td>
</tr>
<tr>
<td>Vitamin B12 (methylcobalamin)</td>
<td>2.5mg</td>
</tr>
</tbody>
</table>
### The HIV Micronutrient Study

#### Micronutrient Supplement - total daily dosage

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>Dosage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium (Citrate)</td>
<td>800 mg</td>
</tr>
<tr>
<td>Magnesium (Citrate)</td>
<td>400 mg</td>
</tr>
<tr>
<td>Iron (Picolinate)</td>
<td>18 mg</td>
</tr>
<tr>
<td>Iodine (Iodide)</td>
<td>150 mcg</td>
</tr>
<tr>
<td>Copper (Picolinate)</td>
<td>2 mg</td>
</tr>
<tr>
<td>Manganese (Picolinate)</td>
<td>10 mg</td>
</tr>
<tr>
<td>Zinc (Picolinate)</td>
<td>30 mg</td>
</tr>
<tr>
<td>Selenium (Picolinate)</td>
<td>200 mcg</td>
</tr>
<tr>
<td>Chromium (Picolinate)</td>
<td>100 mcg</td>
</tr>
<tr>
<td>Molybdenum (Picolinate)</td>
<td>300 mcg</td>
</tr>
<tr>
<td>Potassium (Citrate)</td>
<td>99 mg</td>
</tr>
<tr>
<td>Boron (Picolinate)</td>
<td>2 mg</td>
</tr>
</tbody>
</table>

#### Potent Antioxidants

- Alpha Lipoic Acid 400 mg
- Acetyl-L-carnitine 1000 mg
- N-acetyl-cysteine (NAC) 1200 mg
The HIV Micronutrient Study

Endpoints

- **Immunologic**
  - CD4/CD8 cells, HIV-1 RNA

- **Metabolic**
  - ALT, AST, electrolytes, serum creatinine
  - Fasting insulin levels, glucose, and lipids
  - Plasma lactate levels

- **Clinical**
  - Effect on peripheral neuropathy symptoms
  - Effect on quality of life measures (MOS-HIV)
The HIV Micronutrient Study

Conclusions

- Micronutrient supplementation can significantly improve CD4 cell counts in HIV-infected patients taking HAART.
- The micronutrient supplement tested was well-tolerated over 12 weeks.
- Micronutrient supplementation may hold promise as adjuvant therapy in HIV. Further investigation is warranted.


The United Kingdom

- 60,000 HIV-infected patients
- 15,000 antiviral naïve patients

- $28,000 per patient x 11,000 patients equals
The HIV Micronutrient Study

The United Kingdom

- 60,000 HIV-infected patients
- 15,000 antiviral naïve
- A two year delay of HAART saves the NHS -- £10,000 per pt
- £10,000 per patient x 15,000 patients equals

£150,000,000
Savings
Over 2 years
### Micronutrients and Immune Function

**Future Studies planned:**

- **Canadian Micronutrient Study**
  - Safe delay of HAART trial
  - Endpoint: $\Delta$ CD4 count and cost savings

- **Case Western Reserve Study**
  - Immune Modulator Trial
  - Endpoint: $\Delta$ CD4 count / $\downarrow$ morbidity

- **Kaiser-Permanente of Northern CA**
  - Safe delay of HAART trial
  - Endpoint: $\Delta$ CD4 count and cost savings

*Immune Support Formula*

www.KPAX.us

(www.KPAXvitamins.co.uk)
Micronutrients and Immune Function

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