Dietary Intake and Micronutrient Deficiency in Children with Cancer

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Disclosures

• None
Background
RESEARCH ARTICLE

A randomized trial of the effectiveness of the neutropenic diet versus food safety guidelines on infection rate in pediatric oncology patients

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Effectiveness of the Neutropenic Diet (ND) vs Food Safety Guidelines (FSG)

- **BACKGROUND:** This prospective randomized controlled trial evaluated the difference in neutropenic infection rates in pediatric oncology patients randomized to the Food and Drug Administration's FSGs versus the ND+FSGs during one cycle of chemotherapy.
  - The ND is prescribed to avoid introduction of bacteria into a host's GI tract and reduce infection.
  - The FSG are *evidence-based* food handling recommendations for immunocompromised populations.

- **PROCEDURE:** Pediatric patients receiving cancer treatment with myelosuppressive chemotherapy were eligible. Neutropenic infection was the primary outcome.

- **RESULTS:** 150 patients were randomly assigned to FSGs (n = 73) or ND+FSGs (n = 77). There was no significant difference between the groups in the percentage of patients who developed neutropenic infection: FSGs 33% versus ND+FSGs 35% ($p = 0.78$). However, patients randomized to ND+FSGs reported that following the diet required more effort than those on FSGs alone and dissatisfaction with restrictive food choices.

- **CONCLUSION:** The ND offers no benefit over FSGs in the prevention of infection in pediatric oncology patients undergoing myelosuppressive chemotherapy and adherence requires more effort for patients and families. Institutions caring for children with cancer should consider replacing ND guidelines with FSGs.
Neutropenic Diet

• Avoid raw vegetables
• Avoid fruits that can’t be peeled
• Avoid takeout/fast foods
• Avoid aged cheese
• Avoid raw nuts and fresh nut butters
• Avoid yogurt
• Avoid unpasteurized juice, milk, cheese
• Cook all products to well done
• Avoid deli meats

Food Safety Guidelines

• Shopping
  • Safe packaging, expiration dates, pasteurized, separate raw meats to decrease contamination
• Food storage
  • Refrigerator and freezer temp, cook/freeze by recs
• Food preparation
  • Wash hands, foods, sanitize, don’t cross-contaminate
• Safe Cooking
  • Cook until well-done
• Safe serving of food
  • Hot foods hot, cold foods cold, leftover recs
Methods
Objectives of Secondary Analysis of Data

1. To compare differences in %RDI of *macronutrients* between diet arms
2. To compare differences in % RDI of food group servings between diet arms and US healthy children
3. To compare differences in %RDI of *micronutrients* between diet arms
4. To compare serum micronutrient levels between diet arms.
5. To compare serum micronutrient levels to dietary micronutrient intake.
6. To compare quality of life in patients with sufficient vs deficient micronutrient levels.
Data Analysis

• Weekly 24-hour diet recalls using the multiple pass method.
  • A dietician converted the intakes into % RDI for food group servings

• FoodWorks was used to evaluate overall nutrition content of diets.
  • Software calculated macro- and micronutrients by % RDI corrected for age and gender

• The nutritive content of the diets was compared between the two groups with dietary recommendations and population norms
Health Related Quality of Life Inventories

- Peds QL™ Pediatric Quality of Life Inventory and Cancer Module
  - Child self report (ages 5 – 21)
  - Parent proxy report (ages 2 – 21)
- European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30
  - Self report (ages 22 – 30)

- HRQL inventories were available in English and Spanish and are validated and reliable for group comparisons in this population.

- Examples of QOL variables:
  - Pain and hurt, Nausea, Procedural and treatment anxiety, Worry, Cognitive problems, Health and activities
Results
## Study participant demographics

### BASELINE DEMOGRAPHIC CHARACTERISTICS BY TREATMENT GROUP

<table>
<thead>
<tr>
<th></th>
<th>Food safety diet (N = 73)</th>
<th>Neutropenic diet (N = 77)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, Mean</strong></td>
<td>11</td>
<td>12</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Sex, N (%)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>male</td>
<td>46 (63)</td>
<td>44 (57)</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Race N (%)</strong></td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>White</td>
<td>28 (38)</td>
<td>18 (23)</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>9 (12)</td>
<td>18 (23)</td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>29 (40)</td>
<td>36 (47)</td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>5 (7)</td>
<td>3 (4)</td>
<td></td>
</tr>
<tr>
<td>other</td>
<td>2 (3)</td>
<td>2 (3)</td>
<td></td>
</tr>
</tbody>
</table>

**Body Mass Index (N = 70)**
- Underweight 9%
- Normal weight 59%
- Overweight 13%
- Obese 20%
### Medical Characteristics

<table>
<thead>
<tr>
<th>Diagnosis N (%)</th>
<th>Food safety diet (N = 73)</th>
<th>Neutropenic diet (N = 77)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brain Tumors</td>
<td>6 (8)</td>
<td>7 (9)</td>
<td>NS</td>
</tr>
<tr>
<td>ALL</td>
<td>25 (34)</td>
<td>23 (30)</td>
<td></td>
</tr>
<tr>
<td>AML</td>
<td>3 (4)</td>
<td>2 (3)</td>
<td></td>
</tr>
<tr>
<td>Soft Tissue Sarcoma</td>
<td>2 (3)</td>
<td>7 (9)</td>
<td></td>
</tr>
<tr>
<td>Bone Sarcoma</td>
<td>21 (29)</td>
<td>16 (21)</td>
<td></td>
</tr>
<tr>
<td>Hodgkins Disease</td>
<td>5 (7)</td>
<td>9 (12)</td>
<td></td>
</tr>
<tr>
<td>NHL</td>
<td>5 (7)</td>
<td>5 (6)</td>
<td></td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>4 (5)</td>
<td>2 (3)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>2 (3)</td>
<td>2 (3)</td>
<td></td>
</tr>
</tbody>
</table>
Macronutrient Intake

Dietary Intake (N = 150)

- Fat: 30%
- Carbohydrates: 53%
- Protein: 17%

Recommended Macronutrient Intake

- Fat: 20 – 35%
- Carbohydrate: 45 – 65%
- Protein: 10 – 35%

<table>
<thead>
<tr>
<th>Macronutrient</th>
<th>ND (% RDI)</th>
<th>FSG (% RDI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kcals</td>
<td>83</td>
<td>75</td>
<td>0.08</td>
</tr>
<tr>
<td>Protein</td>
<td>190</td>
<td>166</td>
<td>0.08</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>165</td>
<td>141</td>
<td>0.03</td>
</tr>
<tr>
<td>Fiber</td>
<td>30</td>
<td>29</td>
<td>---</td>
</tr>
</tbody>
</table>

NIH, Food and Nutrition Board of the Institute of Medicine, National Academy of Sciences
Percentage of USDA Recommended Food Group Servings

Average Intake by Diet Compared to US 11 - 18 y.o.
## Micronutrient Intake

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>Neutropenic diet (% RDI)</th>
<th>Food safety diet (% RDI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium</td>
<td>74</td>
<td>61</td>
<td>NS</td>
</tr>
<tr>
<td>Magnesium</td>
<td>78</td>
<td>88</td>
<td></td>
</tr>
<tr>
<td>Manganese</td>
<td>34</td>
<td>26</td>
<td></td>
</tr>
<tr>
<td>Vitamin E</td>
<td>52</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>123</td>
<td>106</td>
<td></td>
</tr>
<tr>
<td>Vitamin D</td>
<td>17</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Vitamin A</td>
<td>42</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Vitamin C</td>
<td>230</td>
<td>165</td>
<td></td>
</tr>
<tr>
<td>Pantothenic Acid</td>
<td>31</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Copper</td>
<td>147</td>
<td>129</td>
<td></td>
</tr>
<tr>
<td>Iron</td>
<td>152</td>
<td>121</td>
<td></td>
</tr>
<tr>
<td>Folic Acid</td>
<td>127</td>
<td>94</td>
<td></td>
</tr>
</tbody>
</table>
Micronutrient Deficiency – Preliminary Analysis of 23 random patients at endpoint

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>(%) deficient N=23</th>
<th>(%) RDI ± SD N=150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin E</td>
<td>4.3%</td>
<td>455 ± 54.5%</td>
</tr>
<tr>
<td>Zinc</td>
<td>50%</td>
<td>124% +/- 112%</td>
</tr>
<tr>
<td>25-OH Vitamin D</td>
<td>84%</td>
<td>11.2% +/- 21%</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>4.3%</td>
<td>43% ± 70.6%</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>42%</td>
<td>161% ± 107%</td>
</tr>
<tr>
<td>Selenium</td>
<td>4.3%</td>
<td>136% ± 125%</td>
</tr>
<tr>
<td>Pre-albumin</td>
<td>35%</td>
<td>102% ± 75%</td>
</tr>
</tbody>
</table>

*There were no significant associations between intake and serum levels.
Pediatric oncology patients are more deficient in micronutrients

<table>
<thead>
<tr>
<th>Micronutrient</th>
<th>Pedi Onc % Deficient</th>
<th>US % Deficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc</td>
<td>50%</td>
<td>&lt;10%</td>
</tr>
<tr>
<td>25-OH Vitamin D</td>
<td>84%</td>
<td>42%</td>
</tr>
<tr>
<td>Vitamin C</td>
<td>42%</td>
<td>5-17%</td>
</tr>
</tbody>
</table>

*NHANES 2009*
Micronutrient Deficiency and Quality of Life

- The only relationship between QOL domains and micronutrients (Vitamin C, D, and zinc) analysis was an inverse correlation between Vitamin C and nausea ($p = 0.03$).

$\downarrow$ Vitamin C : $\uparrow$ Nausea
Conclusions and Future Directions
Why are levels low in Vitamin C and Zinc despite sufficient intake?

- Possibilities include
  - Malabsorption
    - In mucositis? -- Vitamin C and Zinc are absorbed in intestinal cells
    - Absence of dietary promoters (human milk and animal proteins) or presence of inhibitors (phytic acid found in grains, legumes, nuts/seeds)
  - Consumption or Inhibition of production
    - Oxidative catabolism of ascorbic acid is accelerated in patients with severe iron overload.
    - Inhibition of production of endogenous zinc (damage to pancreas, enterocytes, intestinal mucosa)
  - Increased excretion
    - Due to renal damage? -- Vitamin C is freely filtered by kidneys due to its molecular weight and reabsorbed in renal proximal tubule
Micronutrient Deficiencies may be related to morbidity in Children with Cancer

• Children with cancer have low levels of vitamins D, C, and zinc
  • Vitamin D deficiency
    • leads to poor calcium absorption and secondary osteopenia with fractures and bone malformations
    • in HSCT patients has led to increased mortality.
    • associated with decreased QOL with effects on mood in cognition, cardiovascular and autoimmune diseases.
  • Vitamin C deficiency
    • associated with hematologic toxicity, diminished immune function, and poor wound healing
  • Zinc deficiency
    • also associated with diminished immune function and poor wound healing.
    • associated with rash, stomatitis, diarrhea, fatigue
    • disrupts host protective mechanisms against cancer
      • lower levels associated with inferior prognosis in cervical cancer patients (PR/NR vs CR)
      • may be a primary risk factor in development of certain GI malignancies
Conclusions

• Children with cancer have poor diets, similar to or worse than general population.

• Effects of poor diets are unclear but worrisome.

• Children with cancer suffer from micronutrient deficiencies despite high or adequate intake.
  • Deficiencies in Vitamins C, D, and Zinc are clinically relevant in children with cancer because deficiency is associated with morbidity.
  • Understanding nutrient deficiencies and the incongruence between intake and nutrition status will increase awareness of malnourishment as a contributor to adverse events and treatment related toxicities.
Future Directions

• Prospective study measuring serum levels and dietary intake in specific tumor types and treatments over time.

• Studies of the etiology of micronutrient deficiencies including microbiome, metabolism, and excretion.

• Studies comparing outcomes in patients with vitamin deficient to vitamin sufficient patients and possibly those exposed to vitamin replacement.
Implications

• Future research could lead to the development of new guidelines for children with cancer that include screening for diet quality and micronutrient status.
  
  • New dietary guidelines would be expected to lead to improved nutritional status of cancer patients which correlates with a better prognosis.
  
  • Improved health status could result in improved tolerance to and delivery of chemotherapy, decreased infections, better wound healing, and possibly decreased late effects and improved overall survival and quality of life.
Thank you

PI: Karen Moody, MD
Rebecca Baker, MPH, CCRP
Abby Johnson, MS, RD, LD
Joya Chandra, PhD

Statistics: Diane Liu, MS
Acknowledgements

• CHAM Research support
  • Ruth Santizo
  • Jon Gill MD

• AECC support
  • Richard Gorlick, MD
  • CJ Segal-Isaacson Ed.D.
  • Judy Wylie-Rosett Ed. D., RD
  • Mimi Kim, PhD

• IU/Riley
  • Aaron Carrol MD
  • Becca Baker MPH

• Affiliate Institutions
  • Jeannie Spies PNP, Rady Children's Hospital, CA
  • Inan Olmez, MD, Maimonides Medical Center, NY
  • Linda Granowetter MD, Robin Dulman MD, & Amanda Buthmann RD NYU Hospital and Medical Center, NY
  • Birte Wistinghausen MD, Mount Sinai Hospital and Medical center, NY
  • Kanya Ayyanar Kosair Childrens Hospital
Questions