“Plant-Based, No-Added-Fat or American Heart Association Diets: Impact on Cardiovascular Risk in Obese Hypercholesterolemic Children and Their Parents”

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Michael Macknin, M.D.
Professor of Pediatrics, General Pediatrics
Cleveland Clinic Lerner College of Medicine of CWRU
Introduction

• General pediatrician
  – Spent majority of time in direct patient care
    – Previous research has been on common problems observed in a general pediatrician’s office
      – Otitis Media
      – Teething
      – Upper respiratory infections
      – Immunizations
      – Bicycle and motor vehicle injury prevention
  – Most common chronic problem now
    – Overweight and obese children
      – Significant cardiovascular risk factors
Generation of Study Concept

• Jane Esselstyn
  – Her children were my patients
  – She talked of the benefits of a Plant-Based (PB) diet for years
  – I finally did some reading on the PB diet
  – Met with her father, Dr. Esselstyn
    – Discussed his experience with the PB diet
    – Realized what I could contribute
      – A prospective randomized trial of PB diet in obese hypercholesterolemic children and adults
Study Aims and Design

• Importance
  – Plant-based diets may promote weight loss, improve lipoprotein profiles and insulin sensitivity and possibly prevent cardiovascular disease (CVD) in adults. This is the first randomized trial of CVD risk reduction from a plant-based no added fat diet (PB) and the American Heart Association Diet (AHA) in children.
Study Aims and Design

• Hypothesis
  – Both diets would be associated with improvements from baseline in measures of CVD risk and the PB diet may have more improvements than the AHA diet.

• Design
  – Four-week prospective study, randomized to PB or AHA diet with weekly 2-hour nutrition education classes.

• Setting
  – Large Midwestern hospital system’s predominantly middle class outpatient pediatric practices.
Study Aims and Design

• **Population:**
  – Thirty children (9-18 years old)
  – One participating parent per child
  – Last recorded BMI >95th percentile
  – Cholesterol >169 mg/dL

• No significant differences between AHA and plant based groups at baseline
  – Demographics
  – Nutrient intake
  – Clinical outcomes
Enrollment families

Letters mailed meeting eligibility requirements (n=1278)

Excluded (n=65)
- Not meeting inclusion criteria (n=14)
- Declined to participate (n=13)
- Interested but enrollment closed (n=37)
- Consented but withdrew before randomization (n=1)

Enrollment participants

No response (n=1183)
- Letters returned undeliverable (n=43)
- No phone call response to letter (n=1140)

Randomized (n=30)

Allocated to plant-based diet (n=16)
- Received allocated intervention (n=16)
- Did not receive allocated intervention (n=0)

Allocated to AHA diet (n=14)
- Received allocated intervention (n=14)
- Did not receive allocated intervention (n=0)

Allocation

Lost to follow-up (n=2)
Discontinued intervention (weeks 1 and 4 for unknown reasons) (n=2)

Lost to follow-up (n=0)
Discontinued intervention (n=0)

Follow-Up

Analyzed (n=14)
- Excluded from analysis (did not attend last session, therefore no end of study data) (n=2)

Analyzed (n=14)
- Excluded from analysis (n=0)

Analysis
Study Aims and Design

• **Intervention:**
  – Weekly education sessions with cooking demos and recipes held in the kitchen/classrooms of Cleveland Clinic’s Wellness Institute
  – Both child and parent to follow assigned diet for four weeks
  – Saturday sessions to accommodate family participation and retention
  – $50 per family per week to compensate for time spent on study
What are the diets?

• The **plant-based diet**:  
  – Whole grains  
  – Fruits  
  – Vegetables  
  – No added oil  
  – Limited nuts and seeds  
  – No limitations on the amount of food intake  
  – Animal products are not allowed
What are the diets?

- The **American Heart Association diet**:  
  - Emphasizes fruits and vegetables  
  - Allows healthy fats  
  - Low-fat meats  
  - Fish  
  - Low-fat dairy in moderation  
  - Daily requirements  
    - <30% calories from fat  
    - <7% calories from saturated fat  
    - <300mg cholesterol  
    - <1500 mg of sodium
Education Classes

• 4 weekly 2-hour education classes
  – Nutrition education (1 hour)
    – 2 hours the first week
    – Weeks 1 & 2
      – Reading labels, where to buy food, food preparation, how to stay on diets when eating out
    – Weeks 3 & 4
      – Review of healthy food choices, the effects of diet on health, discussion of what worked and what didn’t work
  – Hands on cooking classes (1 hour)
    – Weeks 2-4
    – Optional 5th week, after all final labs and measurements completed
      – Introductory class to the diet they were not assigned
Pre- and Post-Measures

• Food diary
  – 2 weekdays and 1 weekend day both before and during the study

• Physical activity questionnaires for children

• Measurements of:
  – Height
  – Weight
  – Waist circumference
  – Mid-arm circumference
  – Blood pressure

• Post Study Food Acceptability Questionnaire
Pre- and Post-Measures

• Fasting Blood Test:
  – Lipid panel
  – High-sensitive C-reactive protein
  – Myeloperoxidase
  – IL6
  – Insulin
  – Glucose
  – Hgb A1C
  – ALT
  – AST
Funding

• Pilot Funding Obtained
  – $25,000 total from Cleveland Clinic Research Program Committee and Pediatric Research Fund Grants

• Review committees saw great significance

• Study logistics impossible
Research Team

• Collaborators Established
  – Two masters level dietary students
    – Tammy Kong, MS, RD
    – Adam Weier, MS, RD
  – Two Biostatisticians
    – Sara Worley, MS
    – Anne Tang, MS
  – Pediatric Gastroenterologist
    – Naim Alkhouri, MD
    – Exhaled breath analysis of volatile organic compounds
Research Team

— Director of Lifestyle 180, our Wellness Program
  — Mladen Golubic, MD, PhD

— Diet Instructors
  — Jane Esselstyn, RN
    — Author
    — Taught the plant based diet
  — Alicia Thomas, MS, RD, LD
    — Research Bionutrition Manager for the Case Western Reserve University Clinical and Translational Science Collaborative and CRU's
    — Taught the AHA diet and contributed to study design
Clinical Research Unit

• The Clinical Research Unit
  – Supported by the National Center for Advancing Translational Sciences of the National Institutes of Health (UL1TR000439)

  – Stacy Payne, BS
  – Megan Villarreal, BA
  – Kay Stelmach, RN
Study Logistics

• Informed consent process handled:
  – Calls to identified participants
  – Consent appointments made for convenience of participant at many different Cleveland Clinic entities (Family Health Centers, Wellness Center)
  – Education re: sample collection (e.g., stool) for first and last visit

• Study Site Preparation:
  – Evaluated Wellness facility for study flow, space, layout
  – Created study data collection stations
  – Created visit flowsheet/checklist
  – Study kits
  – Site preparation night before visits occurred
Clinical Research Team

• Personnel
  – CRU Research Nurses, Study Coordinators, and Lab personnel sufficient to accomplish
    – 60 visits in one 2 hour time limit prior to diet instruction
    – Collect all data measures on first and last day of study
  – Pediatric Department volunteers

• Sample Integrity
  – Breath samples transported every two hours to meet two-hour processing time limit
  – Blood samples transported twice per study session to assure timely analysis

• Assisted with regulatory and compliance procedures
Sample Size calculation

• Based on data from Rip Esselstyn’s Engine 2 Diet Book

• 6-7 patients per group
  - Power of 90% at a significance level of .05
    - Detect the within-group changes from baseline in total CHO (mean +/- SD decrease of 60 +/- 26mg/dL)
      VS
    - Null hypothesis mean decrease of 25 +/- 26mg/dL
  - Did not power the study to demonstrate statistically significant differences between 2 effective dietary interventions

• 60 participants total
  - Each group: 15 adults and 15 children
  - Calculated with 20% dropout rate
  - Still nearly twice the sample size needed
Results Plant-based Children and Adults

- Nutrition
  - Total energy and intake of almost all measured nutrients were decreased in both groups in children and adults.
  - Intent-to-treat analysis: Results no longer significant in children*; adults**

<table>
<thead>
<tr>
<th>Significantly lower than AHA</th>
<th>Significantly Higher than AHA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Cholesterol</td>
<td>Total Carbohydrates</td>
</tr>
<tr>
<td>Total Saturated Fat</td>
<td>Total Dietary Fiber</td>
</tr>
<tr>
<td>% Calories from Fat **</td>
<td></td>
</tr>
<tr>
<td>% Calories from Saturated Fat</td>
<td></td>
</tr>
<tr>
<td>Total Protein **</td>
<td></td>
</tr>
<tr>
<td>Animal Protein</td>
<td></td>
</tr>
<tr>
<td>Vitamin D *</td>
<td></td>
</tr>
<tr>
<td>Vitamin B12</td>
<td></td>
</tr>
</tbody>
</table>
Nutrients within Group

Children

Parents

AHA group

PB group

Percent change from baseline

P>=0.05: Mean change

P<0.05: Mean change

P<0.01: Mean change

95% confidence interval

95% confidence interval
## Nutrient Intake Changes in Children

<table>
<thead>
<tr>
<th>Outcomes (RDA)</th>
<th>Plant-Based</th>
<th>AHA</th>
<th>Change</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>During Study</td>
<td>Baseline</td>
<td>During Study</td>
<td>Change</td>
</tr>
<tr>
<td>Calcium, mg (1300)</td>
<td>807</td>
<td>396</td>
<td>-411</td>
<td>612</td>
</tr>
<tr>
<td>Iron, mg* PB</td>
<td>16</td>
<td>15</td>
<td>-1</td>
<td></td>
</tr>
<tr>
<td>Iron, mg** AHA</td>
<td></td>
<td></td>
<td></td>
<td>12</td>
</tr>
<tr>
<td>Omega-3 FA, g</td>
<td>1.3</td>
<td>0.6</td>
<td>-0.7</td>
<td>1.6</td>
</tr>
</tbody>
</table>

*RDA Iron PB (9-13yrs: 14.4 mg) (14-18yrs: male 14.8 mg, female 27 mg)
**RDA Iron AHA (9-13yrs: 8 mg) (14-18yrs: male 11 mg, female 15 mg)
### PB vs. AHA Significant Children Nutrient Intake Changes

<table>
<thead>
<tr>
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<th></th>
<th>AHA</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>During</td>
<td>Change</td>
<td>Baseline</td>
</tr>
<tr>
<td>Total Protein, g*</td>
<td>64</td>
<td>40</td>
<td>-24</td>
<td>60</td>
</tr>
<tr>
<td>Vitamin D, IU (600)*</td>
<td>163</td>
<td>59</td>
<td>-104</td>
<td>151</td>
</tr>
<tr>
<td>Vitamin B12, ug (6)*</td>
<td>5</td>
<td>2</td>
<td>-3</td>
<td>3</td>
</tr>
</tbody>
</table>
Results in Children

• Statistically Significant Anthropometric and Laboratory Outcomes Within-Group
  – Plant-based children had lower: (Also Significantly > AHA*)
    – BMI-Z scores* (-0.14)
    – Systolic Blood Pressure (-6.43 mmHg)
    – Total Cholesterol (-22.5 mg/dL)
    – LDL Cholesterol (-13.14 mg/dL)
    – hsCRP* (-2.09 mg/L)
    – Insulin (-5.42 uU/mL)
Results in Children

• **Plant-based and AHA children had lower:**
  - Weight(-3.05/-1.14 kg)
  - Mid-arm circumference (-2.02/-1.55 cm)
  - Myeloperoxidase (-75.34/-69.23 pmol/L)

• **AHA children had lower:**
  - Waist circumference (-2.96 cm)
Results in Adults

• Statistically Significant Anthropometric and Laboratory Outcomes Within-Group
  – Plant-based adults had lower: (Also significantly >AHA*)
    – Mid-arm circumference (-1.32 cm)
    – Systolic Blood Pressure (-7.96 mmHg)
    – Total Cholesterol* (-33.79 mg/dL)
    – LDL* (-27.0 mg/dL)
    – HgbA1c* (-0.16 %)

  – Plant-based and AHA adults had lower:
    – Weight (-3.64/-2.01 kg)
    – BMI (-1.29/-0.73 kg/m2)
Labs within Group

Children

Parents

Percent change from baseline

AHA group

PB group

Cleveland Clinic Children’s
Food Acceptability Questionnaire

• Difference between the AHA and PB:
  – Both children and parents in the PB group reported more difficulty purchasing the necessary food for their diet

• No differences in:
  – How well they liked the food
  – Liked the taste
  – Appearance appeal
  – How boring
  – Ease of preparation
  – Ease of maintaining diet at restaurants
  – Effort to stay on diet
  – Effect on cost of food purchases
  – Satisfaction felt after meals
  – Overall satisfaction
Discussion

• HgbA1c increased in both PB and AHA children:
  – PB children had significantly lowered insulin levels
  – The only homeostasis model assessment of insulin resistance
    that changed significantly was an improvement in the Children’s
    PB group
  – In the adult PB group, HgbA1c decreased significantly
  – Therefore I doubt there was significance in increase in
    children's HgbA1c
Discussion

• HDL-Cholesterol Significantly Lower in AHA Children and Adults and PB Adults
  – Reported previously to decrease in vegan diets in adults
  – However AHA and PB are both associated with decreased risk of heart disease
  – Heterogeneity in composition and function of the HDL-C
    – Further characterization of HDL-C after exposure to diets might help establish significance of HDL-C changes
Nutrient Intake

• A nutritionally well-educated compliant patient can probably attain a balanced diet on both the PB and AHA diet with B12 supplementation for the PB diet

• However, particularly in children on the PB, vitamin D supplementation is probably warranted

• Monitoring consumption of protein, n-3 fatty acids, iron, zinc, iodine, and calcium in long term vegans is also recommended
Difficulties with Long-term Compliance on PB diets

• Difficulties in purchasing
• Effort required for PB was described as a potential barrier in a previous study
• Cost may be a barrier in lower socioeconomic populations
• Children feel good even when obese and hypercholesterolemic
  — May not see the benefits or feel better switching to a PB diet
• Barriers to easy, affordable access to PB foods need to be reduced
• Studies have described good acceptability and compliance with a PB diet
Limitations to our Study

• Small study
• Short period of time
• Select group of middle-class patients
• Less than completely reliable measures of compliance
• No direct health outcomes measured
• No placebo group
  - AHA is considered standard of care
• Concerns about long-term compliance
Conclusions

• “PB diets generally are recognized as safe for children and adolescents as long as the intake of key nutrients is monitored and appropriate supplements are provided. The results of our study suggests that the documented benefits of PB in adults, including, but not limited to, decreasing overweight and obesity and decreased cardiovascular risk, most likely would be seen in children. These benefits, especially given the known onset of CVD in childhood, could improve the lifetime health of those populations who choose to eat a PB beginning in childhood.”