Nutritional Challenges in Children with Autism

Cade Nylund, MD, MS
Major, United States Air Force, Medical Corps
Assistant Professor of Pediatrics
Uniformed Services University of the Health Sciences

Disclosure

• I have no financial relationships to disclose or conflicts of interest to resolve.
• The views expressed here are my own and do not reflect the official policy of the United States Air Force, the Department of Defense, or the U.S. Government.

Objectives

• Identify the specific nutritional risks of children with autism
• Understand unique features of autism which place children at risk of malnutrition
• Review recent developments on specific nutritional supplements or diets in children with autism
What is Autism?

Autism Spectrum Disorder (ASD)
- Lifelong Disorder
- Spectrum of Neurodevelopmental Conditions
- Deficits in Communication and Social Interactions
- Repetitive Behaviors
- Restricted interests and activities
- CDC Reports 1/68 Children affected

Baio J. MMWR March 2014

Case 1

- 5 year old boy diagnosed with ASD at age 3
- Non-verbal and significant cognitive delay
- Has severe selective feeding disorder
  - Brand specific macaroni and cheese
  - Brand, flavor, and color specific fish crackers
  - Will eat no other foods
  - Mother has tried “everything” to try to broaden his nutritional intake

Case 1

- Height 109 cm Weight 15.2 kg
- BMI 12.8 kg/m² Z Score -3.17
- 25-OH Vitamin D 16.2 ng/ml
- CBC and Iron panel normal
- Treatment Plan
  - Treated Vitamin D deficiency
  - Made referral to intensive inpatient feeding program
  - Feeding team sent the patient back to have an EGD prior to enrollment in their feeding program
Case 1

• Esophagogastroduodenoscopy Performed

• Identified Eosinophilic Esophagitis (EoE)

Case 1

• Topical steroid treatment for EoE
• Repeat EGD proved adequate treatment
• Enrolled in inpatient intensive behavioral feeding program
• Broadened diversity of this diet
• 6 month follow up BMI Z-score -1.8

Case 2

• 17 year old male with ASD
• Developmental delay, but verbal
• On atypical antipsychotic for behavioral outbursts
• BMI 36 kg/m²
• Dietary/Activity History: 2-3 gallons of sweet tea per day, and No activity
• Increased aminotransferases suggestive of NAFLD or NASH
Case 2

- Artificial Sweetened Beverages replaced his sweet tea
- Encouraged to walk his Yorkshire Terrier twice a day
- 3 months later he had lost 12 kg
- Aminotransferases levels improved

Why Nutritional Challenges?

- Undernutrition
  - Frequent feeding disorders
  - Self-initiated selective eating
  - Parent-initiated selective diets
- Overnutrition/hyperalimentation
  - Decreased physical activity
  - Rewarded with preferred foods
  - Selective eating of high calorie/low nutrient dense (aka junk) foods
  - Medications which may stimulate appetite

Military Health Care Data on Children with ASD

- Have large population of children
  - Around 1 million at any time
- Demographically, geographically, and socioeconomically diverse background
- Largest single cohort of children with ASD
Military Health Database

Study Population
4 million

Children 2-18
Oct 2002-Sept 2013

1:5 Match

Matched Controls
243,810

ASD
48,762

Percent of Children in each BMI Percentile

% of Total Population

48,762 Children
ASD

243,810 Children
No-ASD


Percent of Children in each BMI Percentile

% of Total Population

ASD

No-ASD

Association of a Diagnosis of ASD with Obesity and Metabolic Comorbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>1.85 (1.78, 1.92)</td>
</tr>
<tr>
<td>T2DM</td>
<td>2.60 (2.41, 2.96)</td>
</tr>
<tr>
<td>HTN</td>
<td>2.04 (1.84, 2.27)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>2.01 (1.90, 2.13)</td>
</tr>
<tr>
<td>NAFLD/NASH</td>
<td>2.74 (2.06, 3.65)</td>
</tr>
</tbody>
</table>

T2DM=Type 2 Diabetes Mellitus, HTN = Hypertension

Percentage of Pediatric Patients with ASD and Controls Requiring Medication for Metabolic Complications of Obesity

![Graph showing percentage of pediatric patients requiring medication for metabolic complications of obesity]

T2DM=Type 2 Diabetes Mellitus, HTN = Hypertension

ASD and Obesity in Adulthood

- 92 Adult subjects with ASD
- 45 % were obese or overweight
- 15 % Hyperlipidemia
- 11 % Hypertension
- 10% Diabetes

Jones KB. Autism 2015 July. Epub ahead of print
Association of Psychotropic Medications with Obesity for Children with ASD


ASD, Obesity, and Age

- Younger children with ASD take in significantly less calories than controls
- The risk of obesity is highest in the teenagers (12-20 years old)

Hyman SL. Pediatrics 2012 Nov 130:S145-153

ASD, Obesity and Micronutrient Deficiency

- Despite excess in calorie intake, children with ASD and obesity consume insufficient
  – Iron
  – Calcium
- More likely to be vitamin D deficient

Shmaya Y. Research in Developmental Disabilities. 2015 Mar 38, pg 1-6
Summary Obesity and ASD

• Nearly twice as likely to be obese
• Metabolic Complications of Obesity
  – Hypertension
  – Type 2 Diabetes Mellitus
  – Hyperlipidemia
  – NAFLD/NASH
  – More likely to be prescribed medication, suggests less likely to respond to nutritional intervention and exercise alone
• Psychotropic Medication are associated with obesity in children with ASD
• Children with ASD often have micronutrient deficiency despite excess in calories

Malnutrition

• Micronutrient deficiencies common
• 16 % diagnosed with malnutrition
• 10 % with diagnosis of failure to thrive

Feeding Disorders in ASD, and Malnutrition

- 6.5% of children with ASD are diagnosed with a feeding disorder
- 0.8% of controls
- Odds Ratio 8.0 (7.5-8.5)
- Feeding disorder is a red flag for malnutrition

Among those with ASD
Risk of Malnutrition if Patient Diagnosed with Feeding Disorder
Eosinophilic Esophagitis (EoE)

- Feeding disorders are the most highly associated comorbid diagnosis in pediatric onset EoE
- Feeding disorders are often assumed to be behavioral in children with ASD
- Children with ASD are at an increased risk of EoE
  - Odds Ratio 2.94 (2.45-3.53)
- ASD w/ Feeding disorder Odd Ratio of EoE
  - 24.2 (8.1-72)
- No ASD w/ Feeding disorder Odds Ratio of EoE
  - 21.8 (5.3-87.9)

Heifert et al. NASPGHAN 2015

Feeding Disorders and ASD

- Feeding disorders should not be assumed to be behavioral
- EGD should be performed

- EoE is a treatable disease which potentially lead to improved caloric intake

Picky Eaters

- Pathologic feeding disorder
  - Evidence of malnutrition
  - <10-20 foods
- Picky Eater
  - No evidence of malnutrition
  - Eats a variety of foods maybe doesn’t like specific textures, colors, etc.
• Pathologic feeding disorder
  – Rule out EoE or other organic cause, aspiration, swallowing problem etc.
  – Refer to a specialty feeding therapy program

• Picky
  – Recommend “Just Take a Bite” as first step for parents
  – Referral to pediatric speech therapist

Special Diets and ASD

• Inconclusive evidence that Gluten-Free, Casein-Free (GFCF) diet or any other diet improves the primary symptoms of autism
• Children may require special diets for other comorbid conditions

ASD and Special Diets

- Specific diets may be required to treat specific disorders in those with ASD
  - Eosinophilic Esophagitis
  - Celiac disease
  - Food Allergies

Mulloy A et al. Research in Autism and Developmental Disorders 2010

Existing Evidence for GFCF diet

- Randomized Study of 20 children in Norway
- All children had abnormal urinary peptides
- 1 year GFCF diet
- Follow up blinded assessments
- Significant improvement in multiple developmental domains for those on the diet


GFCF Diet Study Issues

- Small study of 10 kids with ASD
- All had abnormal peptides excreted in the urine
- Children with ASD on GFCF diet had 19% reduced cortical bone thickness

Nutritional Supplements & ASD

- Omega-3 FA -- evidence inconclusive
- Methylcobalamin and L-Methylfolate evidence still inconclusive and further studies needed
  - May be related to an association in the MTHFR gene in only some children


Clinical Study
Effectiveness of Methylcobalamin and Folic Acid Treatment on Adaptive Behavior in Children with Autistic Disorder Is Related to Glutathione Redox Status

Richard L. Frye, Virginia Malveaux, George Fuchs, John R. Jobe, Sarah J. Lang, Alexander J. Hubscher, David W. Gobes

Department of Pediatrics, John Hopkins Hospital (Baltimore, MD, USA), and Department of Pediatrics, University of Maryland School of Medicine (Baltimore, MD, USA)

Aims: To determine the effectiveness of Methylcobalamin and Folic Acid Treatment on adaptive behaviors in children with autistic disorder and to explore any potential association between plasma glutathione redox status and treatment response.

Methods: A randomized, double-blind, placebo-controlled study was conducted. Subjects were children aged 2 to 10 years with a diagnosis of autistic disorder. The study was divided into two treatment groups: Methylcobalamin and Folic Acid, and Placebo. Each group received the respective treatment for 12 weeks. Blood samples were collected at baseline and after 12 weeks of treatment. Glutathione redox status was determined by measuring glutathione/GSSG ratios.

Results: The Methylcobalamin and Folic Acid treatment group showed a significant increase in plasma glutathione redox status compared to the Placebo group (p < 0.05). There was a positive correlation between improved adaptive behaviors and increased plasma glutathione redox status in the treatment group.

Conclusions: These findings suggest that Methylcobalamin and Folic Acid treatment may improve adaptive behaviors in children with autistic disorder and that plasma glutathione redox status may be a potential biomarker for treatment response.
Methylenetetrahydrofolate Reductase (MTHFR)
- 1672 with ASD vs. 6760 without ASD
- Several specific C677T polymorphisms associated with ASD
  - Odds ratios range for various polymorphisms was 1.42-1.86


Folic Acid Review
- Folate required for DNA/RNA synthesis and cell repair
- Critical during times of cell growth
  - One of the signs of deficiency is anemia
- Involved in neurotransmitter synthesis
  - Dopamine
  - Serotonin
  - Norepinephrine
Dihydrofolate

Folic Acid

Dihydrofolate reductase

Tetrahydrofolate

MTHFR

5-methyl-tetrahydrofolate

L-methylfolate

Happy neurotransmitters
DNA synthesis

Methionine

Methionine Synthase + Vitamin B12

Homocysteine

Methionine

Cyanocobalamin

Methylcobalamin

Why the methylcobalamin?
L-Methylfolate and Methylcobalamin Approach

- There is evidence that MTHFR enzyme deficiency is linked to autism in some children
- Supplementation may be helpful only in children who have a MTHFR mutation
- Genetic testing is available
- “Poor man’s test” = homocysteine level
- All children with ASD on a multivitamin

Children with ASD Nutritional Call to Action

- Early health nutritional maintenance/supervision as routine care for all children with ASD
- Early parent education on nutritional risks
- Identify pathological cause of symptoms (EoE)
- Parent training and referral to speech/feeding therapy for selective feeding or feeding disorders
- Multidisciplinary approach
  - RD, Speech Therapy, Occupational Therapy, Psychiatry, GI, Developmental Peds, PCM

Questions?