Introduction to Treatment and Wrap up

Valerie M. O’Hara, DO, FAAP, ABOM
Allen F. Browne, MD, FACS, FAAP, ABOM

Objectives

- Relate the latest developments in the application of advanced tools for pediatric weight management
  - Algorithms
  - Pharmacotherapy
  - Devices
  - Metabolic-bariatric surgery
Algorithms and Pharmacotherapy
Valerie O’Hara, D.O.

Staged Treatment

• Stage 1: Prevention Plus
• Stage 2: Structured Weight Management
• Stage 3: Comprehensive Multidisciplinary Intervention
• Stage 4: Tertiary Care Intervention

Move to next stage if no change in 3 months of treatment
Pediatric Obesity Treatment Algorithm

- Metabolic & Bariatric surgery
- Increased pediatric access
- Improvement of obesity related comorbidities

- Pharmacotherapy
- Emerging pediatric data mirroring adult results
- Research ongoing

- Professionally-directed Lifestyle Change by multidisciplinary team
- Adjustment of any weight promoting medications
- Coordination of specialists to ensure non-weight promoting treatments that may benefit more than one comorbidity

- Research shows poor weight loss effects especially in patients with severe obesity
- Self-directed Lifestyle Change
- Most patients told to “eat less and move more”

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Corresponding AAP Stage
- Stage 1-2
- Stage 3 Pediatric obesity expert
- Stage 4 Bariatric surgeon

Weight goals: Weight Stability AND improvements in health targets over 12 weeks

Microenvironment Targeted Therapy
- Nutrient Signaling, Muscle Activity, Stress, Sleep, Circadian Rhythm, Weight-Promoting Medications

Pharmacological Directed Therapy
- Weight goals: >5% BMI reduction from baseline (or index value of BMI trajectory change/stability over 12 weeks)

Metabolic and Bariatric Surgery
- Surgical Criteria: BMI ≥120% of 95th% with comorbidity or ≥140% of 95th%
<table>
<thead>
<tr>
<th>FDA Approved</th>
<th>Off-Label, w/ Pediatric Evidence in Obesity Treatment</th>
<th>Off-label, no pediatric data for Obesity Treatment</th>
<th>FDA approval pending</th>
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</thead>
<tbody>
<tr>
<td>Phentermine age &gt;16 years [4.1% BMI reduction at 6 months]</td>
<td>Metformin [BMI reduction -0.86]</td>
<td>Phenteramine/Topiramate</td>
<td>Setmelanotide (-20-50kg weight loss in select patients)</td>
</tr>
<tr>
<td>Orlistat &gt;12 years [-2.61 kg at 1 year]</td>
<td>Topiramate [BMI reduction -4.9% on 75mg dose x 3 months]</td>
<td>Naltrexone/bupropion SR</td>
<td></td>
</tr>
<tr>
<td>Exenatide (BMI - 3.42% at 3 months)</td>
<td>Liraglutide (BMI - 5.0% at 6 months)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lisdexamfetamine (2.5 pounds over 4 weeks on 70mg)</td>
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Srivastava et al. Obesity 2019
Kelley, et al, NEJM 2020

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**Pediatric Obesity Algorithm 2018-2020**

Core Author:
Suzanne E. Cuda, MD, FAAP, FOMA, Dipl. ABOM

Contributing Authors:
Marisa Censani, MD, Dipl. ABOM
Madeline Joseph, MD, FAAP, FACEP, Dipl. ABOM
Valerie O’Hara, DO, FAAP, Dipl. ABOM
Nancy T. Browne, MS, PPCNP-BC, CBN, FAANP

BMI Pediatric Obesity Algorithm III - Effective September 2019
Set Point and BMI

How set is the set point?

BMI

20 22 24 26 28 30 32 34 36 38 40 42 44 46 48 50 52 54 56 58 60

Courtesy of Lee Kaplan, MD, MPH, Harvard Medical School

Weight Loss Varies Widely Among Patients

Diet (Low-carbohydrate)

Drug (Liraglutide)

Device (Duodenal liner)

Surgery (Gastric Bypass)
Thinness is also a heritable and polygenic trait

RESEARCH ARTICLE
Genetic architecture of human thinness compared to severe obesity
Fernando Riveros-McKay1, Vanisha Mistri2, Rebecca Boundse1, Audrey Hendricks1, Julia M. Keogh3, Hannah Thomas5, Elana Henning8, Laura J. Corbin6,7, Understanding Society Scientific Group5, Stephen O’Rahilly3, Eleftheria Zeggini1, Eleanor Wheeler1, Inês Barroso6,7, 1, Sadaf Farooqi1,2

Healthy, thin individuals have a lower burden of genes that increase susceptibility to obesity

Conclusion: Understanding genetic variation can help guide clinical care

Treatment
- Precision obesity medicine
  - Identifying obesity subtypes
  - Choosing the best treatment for each patient
- Ability to predict treatment outcomes will decrease treatment risk and cost
- Knowledge of genetics driving common obesity could reduce stigma/bias

Prevention
- Early diagnosis could facilitate prevention strategies
- Implications for childhood obesity
Patients need realistic weight loss goals.

**Weight Loss Devices (WLDs)**

Allen Browne, M.D.
Weight Loss Devices (WLD)

- Have to adjust physiology/set point
- Safe
- Adjustable
- Reversible/Temporary
- Use with multidisciplinary team
- All “off-label” for children and adolescents

Weight Loss Devices (WLD)

- Can be prelude to MBS
- Can be used:
  - Sequentially
  - PRN
  - Scheduled
- Can be combined with pharmacotherapy
- ? Take advantage of “plasticity” of obesity in children
WLD Procedures

- Laparoscopy
- 2 endoscopies
- Endoscopy
- Swallowed and excreted spontaneously

Mechanisms of WLD

- Affect vagus nerve
- Affect pressures in stomach
- Affect gastric emptying
- Bypass duodenum
- Change duodenal surface
- ???
Electrical modulation

Vagus nerve

Stomach

Space Occupying Balloon
Space Occupying Hydrogel Beads

Restriction

Trans-pyloric shuttle

Adjustable gastric band
Gastric drainage

Duodenal effectors

A. Mucosal resurfacing
B. Balloons
C. Bypass sleeve
Metabolic and Bariatric Surgery
Allen Browne, M.D.

Metabolic and Bariatric Surgery (MBS)

- Moves the set point - it’s physiologic
- Long term safety and efficacy data
- Not adjustable, permanent
- Use with multidisciplinary team
- AAP recommendation - 2019
### MBS is Physiologic

<table>
<thead>
<tr>
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<th>RYGB</th>
<th>Restrictive dieting</th>
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<tbody>
<tr>
<td>Energy Expenditure</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Appetite</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Hunger</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Reward-Based Eating</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Satiety</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Stress Response</td>
<td>-</td>
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</tr>
<tr>
<td>Gut Peptides</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Ghrelin</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>GLP-1, PYY, CCK, Amylin</td>
<td>+</td>
<td>-</td>
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### MBS

**RYGB - Gastric Bypass**

**Gastric Sleeve Resection**
Risk/Benefit of Pediatric MBS

• Safer than cholecystectomy (MBSAQIP data in adults)
• Growth - normalized (Alqahtani, 2014)
• Sexual maturation - normalized
• Long term effects - largely unknown
• Vitamin and mineral deficiencies

Results – Resolution of Obesity Complications after MBS in adolescents

Teen LABS Study

Inge 2016

• Resolution of type 2 DM - 19/20
• Resolution of prediabetes - 13/17
• Resolution of dyslipidemia - 84/128
**Results – Resolution of Obesity Complications after MBS in adolescents**

AMOS Study
Olbers, 2017

- 5 year follow-up
- T2DM - 3/81 to 0/79
- Elevated fasting insulin 56/79 to 3/76
- Dyslipidemia 56/81 to 11/76
- Elevated LFT’s 25/81 to 4/76

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**Results – Resolution of Obesity Complications after MBS in children**

Saudi Arabia
Alqahtani, 2014

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**Cumulative Remission and Improvement**

- Prediabetes
- Diabetes Mellitus
- OSA
- Prehypertension
- Hypertension
- Cholesterol
- HDL
- LDL

3 months 6 months 1 year 2 years 3 years
Keeping patients engaged and managing expectations is an important part of the therapeutic obesity alliance.

Thinking Out of The Box
Q & A

Thank you!