TREATMENT GUIDE FOR PHYSICIANS

Lifestyle & Diet

OVERVIEW

Obesity, type II diabetes, and prediabetes are associated with many comorbidities and increased cardiovascular disease risk. Current treatment for these conditions includes lifestyle interventions, dietary counseling, exercise, and pharmacologic therapies. Research suggests that an altered intestinal microbiome may also play a role in the development and progression these conditions, and as such, may present a new target area for treatment [1].

INDICATIONS FOR SMARTGUT TESTING

- BMI >30 or BMI >25 and any comorbidities
- Failure to achieve weight loss goals with diet and exercise counseling
- Potential need for more invasive treatment such as medications or surgery
- Abdominal obesity with waist circumference ≥102 cm (40 in) in men, or ≥88 cm (35 in) in women, PLUS any two of the following:
  - Elevated triglycerides ≥150 mg/dL or on cholesterol medication
  - HDL <40 mg/dL in men and <50 mg/dL in women, or on cholesterol medication
  - Hypertension or on antihypertensive medication
  - Prediabetes or diabetes
- Any obesity-related comorbidities (e.g. fatty liver, polycystic ovary syndrome, sleep apnea, etc.)

RELEVANT SMARTGUT RESULTS

- Low microbiome diversity [2-6]
- High or low levels of Lactobacillus (the abundance of different members of Lactobacillus is variable with BMI) [7]
- Low levels of at least one of the following: *Akkermansia muciniphila* [4,8], *Alistipes* [9], *Anaerotruncus colihominis* [10], *Bifidobacterium* [8,11], *Butyrivibrio crossotus* [4], *Methanobrevibacter smithii* [12,13] *and Roseburia* [14].

CLINICAL TREATMENT SUGGESTIONS BASED ON SMARTGUT RESULTS

MONITOR THE FOLLOWING CLINICAL MARKERS:

- Microbiome diversity score: Studies suggest that microbiome diversity will increase with weight loss and reduction in BMI [3].
- Levels of *Akkermansia muciniphila*: Studies suggest higher levels of this anti-inflammatory bacteria may be associated with improved metabolic markers and weight loss [4].
- Levels of *Bifidobacterium:* Some studies show that low BMI is associated with increased levels of this genus [8].
- Levels of other microorganisms, such as *Alistipes, Anaerotruncus colihominis, Butyrivibrio crossotus, Methanobrevibacter smithii* and *Roseburia.*

INTERVENTIONS TO CONSIDER:

- Suggest a Mediterranean diet: Dietary changes can change the microbiome within 24 hours of initiation. The optimal diet for patients can be variable, but in general a Mediterranean diet has been shown to improve microbiome profile [15,16].
- Prescribe an exercise routine: Studies show that exercise improves microbiome diversity. If patient can tolerate, recommend 30 minutes of moderate intensity 5-7 days/week [17].
- Prescribe probiotics, prebiotics or synbiotics: While there have been limited clinical studies on dosing and type of probiotic for these conditions, studies have shown the following to have a beneficial effect on weight reduction and/or improved metabolic profile:
    - Lactobacillus gasseri SBT 2055 (in fermented yogurt): 2 doses of 100g/day of 5 x 1010 cfu [18,19].
    - Combination probiotic with *Lactobacillus, Bifidobacterium,* and *Streptococcus thermophilus* (VSL#3) [20].
    - The use of prebiotics and/or dietary fiber (from different plant sources) can help to restore the gut microbiome and decrease body fat [21]. The optimal dose of prebiotics is still unknown, although studies in humans suggest that the use of 10 g inulin/day or 21 g oligofructose/day may be beneficial. Sources of prebiotic fiber include soybeans, inulins, unrefined grains, and non-digestible oligosaccharides, among others [22-25].
    - A multispecies synbiotic supplement (containing both prebiotics and probiotics) may help metabolic profiles in diabetic patients: *L. acidophilus* (2 × 109 CFU), *L. casei* (7 × 109 CFU), *L. rhamnosus* (1.5 × 109 CFU), *L. bulgaricus* (2 × 108 CFU), *Bifidobacterium breve* (2 × 1010 CFU), *B. longum* (7 × 109 CFU), *Streptococcus thermophilus* (1.5 × 109 CFU), and 100 mg fructo-oligosaccharide [26].
- Recommend eliminating artificial sweeteners: Animal studies suggest that artificial sweeteners alter the gut microbiome and increase risk of obesity and metabolic disease [27].
- Avoid antibiotic use when possible: This may be most important in the perinatal period and young childhood. Studies in animals suggest antibiotics during this time lead to an obese phenotype even well after antibiotics are discontinued [28,29]. An epidemiological study showed a connection between the repeated use of certain antibiotics in adults and the risk of diabetes [30].

- Consider prescribing metformin: Animal studies have shown that metformin improves metabolic markers as well as increasing levels of Akkermansia muciniphila [31,32].
- Avoid proton pump inhibitors: Studies show these medications may alter the gut microbiome towards less healthy profiles [33,34].
- Consider fecal microbiota transplant (FMT) in the future: Fecal microbiota transplant for metabolic syndrome is currently considered an investigational new drug by the FDA and requires a special permit for clinical or research use, but may become a clinical option in the future [35-37].

POTENTIAL OUTCOMES

- Improvement in weight, BMI, and abdominal obesity
- Improvement in metabolic markers including lipid panel, blood pressure, fasting glucose
- Improvement in microbiome profile towards more diversity and more beneficial microbes
- Reduction in risk of diabetes, cardiovascular disease, and obesity-related comorbidities
- Ability to decrease and/or avoid medication for diabetes, blood pressure, and elevated cholesterol

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