

Genes influence effectiveness of weight-loss drug

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Obese patients with a specific genetic make-up lose more weight when taking the weight loss drug sibutramine and undergoing behavioral therapy compared to those without this genetic make-up, reports a new study in *Gastroenterology*, the official journal of the American Gastroenterological Association (AGA) Institute.

The obesity epidemic continues to be an increasingly global problem: an estimated 1.6 billion adults worldwide are overweight (body mass index [BMI]>25) and 400 million are obese (BMI>30). In addition, the incidences of diabetes and other debilitating diseases attributable to obesity continue to rise.

While there are numerous options for the treatment of obesity, this study examined sibutramine, a medication approved for the long-term treatment of obesity. The drug creates a feeling of fullness, prevents decline in metabolic rate associated with low calorie diets and causes weight loss, especially when combined with behavioral therapy. However, weight loss with the drug is highly variable. Therefore, a research team at the Mayo Clinic assessed the influence of specific markers of candidate genes controlling serotonergic and adrenergic mechanisms ($\alpha 2A$ -receptor, 5-HTTLPR and GN β 3) on weight loss/body composition in response to sibutramine or placebo.

"We found significantly lower values for weight, BMI and proportion of body fat in patients taking sibutramine. The candidate gene variations provided useful markers of enhanced response to the drug," said Michael

Camilleri, MD, AGAF, of the Mayo Clinic and lead author of the study. "Gene variations may help select obese patients who are more likely to experience improved outcome with this treatment. Since the different markers were present in almost 50 percent of patients, inclusion of screening for these genetic markers before prescribing the medication may even be cost-effective from a public health perspective."

In this randomized, double-blind, pharmacogenetic study, Dr. Camilleri and colleagues evaluated behavioral therapy and sibutramine (10 or 15 mg daily) or placebo for 12 weeks in 181 overweight or obese participants. They measured body weight, BMI, body composition, gastric emptying and genetic variation.

Study results showed that sibutramine at both doses, given in combination with behavioral therapy, caused significant weight loss ($p = 0.009$). The drug resulted in lower values for weight, BMI and proportion of body fat compared to placebo (p

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