Study compares effectiveness of weight-loss drugs

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In an analysis that included nearly 30,000 overweight or obese adults, compared with placebo, orlistat, lorcaserin, naltrexone-bupropion, phentermine-topiramate, and liraglutide were each associated with achieving at least 5 percent weight loss at 52 weeks, and phentermine-topiramate and liraglutide were associated with the highest odds of achieving at least 5 percent weight loss, according to a study appearing in the June 14 issue of *JAMA*.

Approximately 1.9 billion adults are overweight and 600 million are obese worldwide. Identifying effective long-term treatment strategies for overweight and obesity is of paramount importance. The U.S. Food and Drug Administration (FDA) has approved 5 weight loss drugs (orlistat, lorcaserin, naltrexone-bupropion, phentermine-topiramate, and liraglutide) for long-term use in obese (body mass index [BMI] > 30) or overweight (BMI > 27) individuals with at least 1 weight-associated condition (type 2 diabetes, hypertension, hyperlipidemia). Data on the comparative effectiveness of these drugs are limited.

Siddharth Singh, M.D., M.S., of the University of California, San Diego, La Jolla, and colleagues conducted a systematic review and meta-analysis of randomized clinical trials that included overweight and obese adults treated with FDA-approved long-term weight loss agents for at least 1 year compared with another active agent or placebo. Twenty-eight randomized clinical trials with 29,018 patients (median age, 46 years; 74 percent women; median baseline body weight, 222 lbs.; median baseline BMI, 36.1) were included.

The researchers found that a median 23 percent of placebo participants had at least 5 percent weight loss vs 75 percent of participants taking phentermine-topiramate, 63 percent of participants taking liraglutide, 55 percent taking naltrexone-bupropion, 49 percent taking lorcaserin, and 44 percent taking orlistat. All active agents were associated with significant excess weight loss compared with placebo at 1 year: phentermine-topiramate, 19.4 lbs.; liraglutide, 11.7 lbs.; naltrexone-bupropion, 11 lbs.; lorcaserin, 7.1 lbs.; and orlistat, 5.7 lbs. Compared with placebo, liraglutide and naltrexone-bupropion were associated with the highest odds of adverse event-related treatment discontinuation.

"Ultimately, given the differences in safety, efficacy, and response to therapy, the ideal approach to weight loss should be highly individualized, identifying appropriate candidates for pharmacotherapy, behavioral interventions, and surgical interventions. Historically, concerns regarding the long-term safety profile of pharmacotherapy for weight loss have limited their clinical use, particularly among medications with significant adrenergic actions or central appetite-suppressing actions. Short-term clinical trials may not provide comprehensive information on the long-term safety of these agents, and prospective postmarketing surveillance studies are warranted," the authors write.

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