

Sibutramine Helped Obese Teens Cut Risk Factors

The drug allowed 12- to 16-year-olds to lower BMI and improve triglycerides, HDL, and insulin levels.

BY JANE SALODOF MACNEIL
Contributing Writer

LAS VEGAS — Sibutramine (Meridia) enabled obese adolescents to shed weight and improve obesity-related risk factors in a 12-month, randomized, double-blind, placebo-controlled trial.

The proportion of teenagers who lost at least 5% of body mass index (BMI) was more than three times greater in the sibutramine group compared with the control group—62% vs. 18%, Robert I. Berkowitz, M.D., reported at the annual meeting of North American Association for the Study of Obesity. When BMI loss of 10% or more was tallied, the sibutramine advantage was 39% vs. 6% of the patients.

Along with declines in glucose, insulin, and triglyceride levels, sibutramine helped the teenagers improve their psychological and emotional well-being and their school and social functioning, said Dr. Berkowitz, psychiatrist-in-chief at Children's Hospital of Philadelphia's behavioral health center.

"The improvements were significantly greater in the sibutramine group than in the placebo group," he said.

Few long-term studies have addressed adolescent obesity. Mainly they have looked at behavioral changes in diet and exercise. "Most report a loss of only 1-4 kg, with participants still overweight at the end of the study," Dr. Berkowitz said.

Sibutramine is not approved for patients under age 16.

The trial enrolled 498 patients aged 12 to 16 years (mean age 13.6 years), who had a BMI two units above the 95th percentile for their ages. Two-thirds of the patients were female.

"These were very overweight teenagers," Dr. Berkowitz noted, reporting that the population had a mean BMI of 36 kg/m². The investigators drew conclu-

sions from changes in BMI rather than absolute weight because teenagers are still growing in height.

All the patients started the trial on 10 mg of sibutramine or placebo in the morning. If they had lost less than 10% of body weight at 6 months, the dose was increased to 15 mg. The regimen also included behavioral programs for all of the participants.

The patients on sibutramine reduced their BMI by 8.2% on average, with a mean absolute reduction of 2.9 kg/m². A control group on placebo achieved only a 0.8% reduction, with a mean absolute reduction of 0.3 kg/m².

Changes in risk factors were more significant, Dr. Berkowitz reported at the meeting, which was cosponsored by the American Diabetes Association. The sibutramine arm had a 5.9% reduction in triglyceride, vs. a 9% elevation in the teenagers on placebo. HDL cholesterol increased 7% with sibutramine

but stayed the same with placebo. Insulin levels went down 10.8% in the sibutramine arm, but rose 30.2% in the control group.

Systolic blood pressure and pulse rates were similar in the two groups, as were the rates of most adverse events (headaches and flu being the most frequent). Tachycardia was significantly greater with sibutramine: 13% vs. 6%.

Three-fourths of 368 teenagers on sibutramine completed the study, but less than two-thirds of 130 in the placebo group continued to the end, perhaps because of dissatisfaction with the amount of weight loss. Only 5% of the sibutramine arm and 6% of the control group withdrew because of adverse events.

Pending Food and Drug Administration review of data from the study, Dr. Berkowitz said physicians might consider using sibutramine off label in obese teenagers with serious medical problems. He cautioned, however, that physicians should be very careful to use it as indicated in the labeling for adults.

Dr. Berkowitz received grant support from and is a consultant to and advisory board member of Abbott Laboratories, which markets sibutramine. ■

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Obese Men Have Markers for Infertility, Lower Sperm Motility

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

NEW ORLEANS — Here's one more reason to advise overweight men to shed pounds: Obese men have serum markers of compromised fertility, and men who have fathered children tend to have lower body mass indexes than do those without children.

It's long been established that excess weight can impair female fertility. But a study presented in a poster session at the annual meeting of the Endocrine Society indicates that increasing body mass index (BMI) in males is associated with decreased testosterone and inhibin B levels.

"Lower inhibin B levels are indicative of dysfunction in the seminiferous tubules," said Eric Pauli, M.D., of the Pennsylvania State University, Hershey. "Our findings indicate that these lower serum inhibin B levels point to decreased tubule function, and that inhibin B might even be a more sensitive way of detecting compromised fertility in men than a semen analysis," he said.

Dr. Pauli analyzed semen and serum fertility markers in 87 men aged 19-48 years whose BMIs ranged from 16 to 47 kg/m². The men were drawn from two settings: parents of babies born in an obstetrics practice, and couples who were seeking fertility assistance. In the latter group, only men without a history suggestive of infertility were included.

In addition to providing blood and semen samples, the men had their skinfold thickness measured and underwent testicular examinations to document testicular volume and rule out undi-

agnosed disease. They also answered questions about paternity status, history of infertility in self or partner, and alcohol and tobacco use.

Blood was tested for inhibin B, FSH, luteinizing hormone, testosterone, and free testosterone. Semen was examined for motility, volume, and concentration.

Almost 70% of the men had a history of paternity; they had lower BMIs (26 kg/m² vs. 31.6 kg/m²) and skinfold thicknesses (24.7 mm vs. 34.1 mm) than did the men who were not fathers.

Patients whose BMIs were around 42.5 kg/m² had serum testosterone levels ranging between 150 ng/dL and 400 ng/dL, compared with a range of about 400-700 ng/dL in men with BMIs of around 24 kg/m².

Men with BMIs of about 42.5 kg/m² had inhibin B levels of up to 225 pg/mL, compared with up to 325 pg/mL in men with BMIs of around 24 kg/m², and had FSH levels of up to 5 U/L, compared to levels of up to 10 U/L in those with BMIs of around 24 kg/m².

There was no association of body fat with luteinizing hormone or with any semen analysis factor. However, lower inhibin B levels were associated with lower sperm motility. Free testosterone was not associated with body fat.

"These guys seem to make normal amounts of sperm, because their sperm count and sperm motility are not different from normal-weight men," Dr. Pauli said. "However, their inhibin B, which is a marker for normal sperm cell production, is lower, suggesting that their testes make sperm that is in some way dysfunctional. We don't know the nature of this dysfunction, yet." ■

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Obese Men Spend Nearly \$700 More per Year on Medicine

NEW ORLEANS — Obese men spend nearly four times more on prescription drugs than do those who are of normal weight, Thomas G. Allison, Ph.D., said at the annual scientific sessions of the American Heart Association.

Overweight men fall midway between the two poles in terms of prescription medicine costs, added Dr. Allison, a cardiovascular rehabilitation specialist at the Mayo Clinic, Rochester, Minn.

The higher prescription drug costs associated with overweight and obesity are a reflection of the significantly increased prevalence of a wide range of chronic rheumatologic, gastrointestinal, neurologic, and psychiatric health problems in this population, he added.

Dr. Allison reported on 328 middle-aged businessmen who presented for comprehensive executive physical exams at the Mayo Clinic.

Only 52 of the executives were of normal weight; their monthly prescription drug costs for medications they were already on or began taking as a result of findings from their physical exam averaged \$22.84.

In contrast to that, monthly

prescription drug costs averaged \$39.27 in the 172 men who were overweight and \$80.31 in the 104 obese businessmen.

None of the men in the study had coronary disease.

However, the prevalence of all of the standard cardiovascular risk factors, with the exception of smoking, increased with rising body mass index class, Dr. Allison said.

So did the prevalence of degenerative joint disease, low back pain, gout, depression, sleep apnea, gastroesophageal reflux, and erectile dysfunction.

Previous studies have estimated the cost of illnesses attributable to overweight and obesity at more than \$130 billion per year.

But that might actually be an underestimate, according to Dr. Allison.

He noted that although his study found more weight-related health problems than have been reported by some other investigators, the executive physical exam offered at the Mayo Clinic is more thorough and comprehensive than the physical examinations typically provided through health plans.

—Bruce Jancin