

Adolescents Benefit from Roux-en-Y Gastric Bypass

BY JANE SALODOF MACNEIL
Southwest Bureau

PHOENIX — Benefits and complications resulting from Roux-en-Y gastric bypass procedures are similar for both adolescents and adults, according to data presented by Mike K. Chen, M.D., at the annual meeting of the American Pediatric Surgical Association.

A multicenter review of 37 adolescents who underwent the procedure showed

that average body mass index decreased by 20.7 kg/m² at 1 year, said Dr. Chen, a surgeon at the University of Florida, Gainesville. He also reported significant improvements in key metabolic syndrome markers.

"While there are considerable risks with bariatric surgery, early experience suggests that these risks are offset by health benefits in these patients," Dr. Chen said.

Five surgeons performed the operations on adolescents aged 13-21 years at three pediatric centers: Dr. Chen's institution, Children's Hospital of Alabama (University of Alabama, Birmingham), and Cincinnati Children's Hospital Medical Center (University of Cincinnati).

In 36 cases, the surgeons attempted laparoscopic procedures. Two were converted to open procedures, however, bringing to three the number of open procedures in the sample. Roux limb lengths were reported as 75-150 cm, and gastric pouch size as 30-45 cc.

Average body mass index at baseline was 56.5 kg/m² for the first 31 patients. Twelve months later, it was 35.8 kg/m² for 30 survivors. A control group of 12-13 adolescents who received nonsurgical care went from 47.2 kg/m² at baseline to 46.0 kg/m²—a decrease of only 1.2 kg/m².

Dr. Chen itemized the metabolic data as follows: fasting insulin decreased by 21.3 μU/mL in 14 patients, fasting glucose by 12 g/dL in 10 patients, homeostasis model assessment—insulin resistance (HOMA-

IR) by 4.6 in 9 patients, triglycerides by 65.1 mg/dL in 17 patients, and total cholesterol by 29.7 mg/dL in 18 patients.

Because of the small sample size, Dr. Chen and his coauthors did not calculate rates for individual complications but reported adverse events in categories.

They classified a complication as minor if the patient was readmitted to the hospital for less than 7 days of treatment, which could be endoscopy or diagnostic

A severe complication could be a life-threatening event, a major organ system failure, or sequelae lasting more than 30 days. Only two patients had a severe complication: a teenager who died 9 months after surgery from colitis that developed during rehabilitation for osteoarthritis, and one who experienced beriberi with sequelae for 2 months. The rest of the complications were mild to moderate, and 22 patients (61%) had none at all.

Dr. Chen said the surgeons undertook the analysis in response to a call for outcome studies in recently published guidelines for bariatric surgery in patients between the ages of 13 and 21 (Pediatrics 2004;114:217-23).

He cited one previous report of efficacy and complication rates, noting it was limited to 33 adolescents treated over 20 years at a single adult institution (J. Gastrointest. Surg. 2003;7:102-7).

"The vast majority of patients who undergo bariatric surgery are adults in their fifth decade of life," Dr. Chen said, adding that outcome data clearly support the procedure's efficacy in the older population.

About 15.5% of adolescents are overweight, he said, adding that "50%-75% of these obese kids become obese adults." Without a successful intervention, he warned, the consequences can include physical and psychosocial conditions and lost years of life. ■

VYTORIN® (ezetimibe/simvastatin)

VYTORIN: There are insufficient data for the safe and effective use of VYTORIN in pediatric patients. (See *Ezetimibe and Simvastatin* below.)

Ezetimibe: The pharmacokinetics of ezetimibe in adolescents (10 to 18 years) have been shown to be similar to that in adults. Treatment experience with ezetimibe in the pediatric population is limited to 4 patients (9 to 17 years) with homozygous sitosterolemia and 5 patients (11 to 17 years) with HoFH. Treatment with ezetimibe in children (<10 years) is not recommended.

Simvastatin: Safety and effectiveness of simvastatin in patients 10-17 years of age with heterozygous familial hypercholesterolemia have been evaluated in a controlled clinical trial in adolescent boys and in girls who were at least 1 year post-menarche. Patients treated with simvastatin had an adverse experience profile generally similar to that of patients treated with placebo. **Doses >40 mg have not been studied in this population.** In this limited controlled study, there was no detectable effect on growth or sexual maturation in the adolescent boys or girls, or any effect on menstrual cycle length in girls. Adolescent females should be counseled on appropriate contraceptive methods while on therapy with simvastatin (see *CONTRAINDICATIONS and PRECAUTIONS, Pregnancy*). Simvastatin has not been studied in patients younger than 10 years of age, nor in pre-menarchal girls.

Geriatric Use

Of the patients who received VYTORIN in clinical studies, 792 were 65 and older (this included 176 who were 75 and older). The safety of VYTORIN was similar between these patients and younger patients. Greater sensitivity of some older individuals cannot be ruled out. (See *CLINICAL PHARMACOLOGY, Special Populations and ADVERSE REACTIONS*.)

ADVERSE REACTIONS

VYTORIN has been evaluated for safety in more than 3800 patients in clinical trials. VYTORIN was generally well tolerated.

Table 1 summarizes the frequency of clinical adverse experiences reported in ≥2% of patients treated with VYTORIN (n=1236) and at an incidence greater than placebo regardless of causality assessment from 3 similarly designed, placebo-controlled trials.

Table 1*
Clinical Adverse Events Occurring in ≥2% of Patients Treated with VYTORIN and at an Incidence Greater than Placebo, Regardless of Causality

Body System/ Organ Class Adverse Event	Placebo (%)	Ezetimibe 10 mg (%)	Simvastatin** (%)	VYTORIN** (%)
<i>Body as a whole – general disorders</i>	n=311	n=302	n=1234	n=1236
Headache	6.4	6.0	5.9	6.8
<i>Infection and infestations</i>				
Influenza	1.0	1.0	1.9	2.6
Upper respiratory tract infection	2.6	5.0	5.0	3.9
<i>Musculoskeletal and connective tissue disorders</i>				
Myalgia	2.9	2.5	2.6	3.5
Pain in extremity	1.3	3.0	2.0	2.5

* Includes 2 placebo-controlled combination studies in which the active ingredients equivalent to VYTORIN were coadministered and 1 placebo-controlled study in which VYTORIN was administered.

** All doses.

Post-marketing Experience: The adverse reactions reported for VYTORIN are consistent with those previously reported with ezetimibe and/or simvastatin.

Ezetimibe: Other adverse experiences reported with ezetimibe in placebo-controlled studies, regardless of causality assessment: *Body as a whole – general disorders*: fatigue; *Gastrointestinal system disorders*: abdominal pain, diarrhea; *Infection and infestations*: infection viral, pharyngitis, sinusitis; *Musculoskeletal system disorders*: arthralgia, back pain; *Respiratory system disorders*: coughing.

Post-marketing Experience: The following adverse reactions have been reported in post-marketing experience, regardless of causality assessment: Hypersensitivity reactions, including angioedema and rash; elevated creatine phosphokinase; elevations in liver transaminases; hepatitis; thrombocytopenia; pancreatitis; nausea; cholelithiasis; cholecystitis; and, very rarely, myopathy/rhabdomyolysis (see *WARNINGS, Myopathy/Rhabdomyolysis*).

Simvastatin: Other adverse experiences reported with simvastatin in placebo-controlled clinical studies, regardless of causality assessment: *Body as a whole – general disorders*: asthenia; *Eye disorders*: cataract; *Gastrointestinal system disorders*: abdominal pain, constipation, diarrhea, dyspepsia, flatulence, nausea; *Skin and subcutaneous tissue disorders*: eczema, pruritus, rash.

The following effects have been reported with other HMG-CoA reductase inhibitors. Not all the effects listed below have necessarily been associated with simvastatin therapy. *Musculoskeletal system disorders*: muscle cramps, myalgia, myopathy, rhabdomyolysis, arthralgias.

Nervous system disorders: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, dizziness, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy, psychic disturbances.

Ear and labyrinth disorders: vertigo.

Psychiatric disorders: anxiety, insomnia, depression, loss of libido.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included 1 or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, dermatomyositis, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, eosinophilia, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

Gastrointestinal system disorders: pancreatitis, vomiting.

Hepatobiliary disorders: hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma.

Metabolism and nutrition disorders: anorexia.

Skin and subcutaneous tissue disorders: alopecia, pruritus. A variety of skin changes (eg, nodules, discoloration, dryness of skin/mucous membranes, changes to hair/nails) have been reported.

Reproductive system and breast disorders: gynecomastia, erectile dysfunction.

Eye disorders: progression of cataracts (lens opacities), ophthalmoplegia.

Laboratory Abnormalities: elevated transaminases, alkaline phosphatase, γ-glutamyl transpeptidase, and bilirubin; thyroid function abnormalities.

Laboratory Tests

Marked persistent increases of serum transaminases have been noted (see *WARNINGS, Liver Enzymes*). About 5% of patients taking simvastatin had elevations of CK levels of 3 or more times the normal value on 1 or more occasions. This was attributable to the noncardiac fraction of CK. Muscle pain or dysfunction usually was not reported (see *WARNINGS, Myopathy/Rhabdomyolysis*).

Concomitant Lipid-Lowering Therapy

In controlled clinical studies in which simvastatin was administered concomitantly with cholestyramine, no adverse reactions peculiar to this concomitant treatment were observed. The adverse reactions that occurred were limited to those reported previously with simvastatin or cholestyramine.

Adolescent Patients (ages 10-17 years)

In a 48-week controlled study in adolescent boys and girls who were at least 1 year post-menarche, 10-17 years of age with heterozygous familial hypercholesterolemia (n=175), the safety and tolerability profile of the group treated with simvastatin (10-40 mg daily) was generally similar to that of the group treated with placebo, with the most common adverse experiences observed in both groups being upper respiratory infection, headache, abdominal pain, and nausea (see *CLINICAL PHARMACOLOGY, Special Populations and PRECAUTIONS, Pediatric Use*).

Gastric Bypass Less Effective for Black Women Than Whites, With Possible Biologic Basis

BY DAMIAN MCNAMARA
Miami Bureau

ORLANDO — African American women in general lose less weight after gastric bypass surgery than do white women, but the reasons are unknown. A recent study found that diet, eating behavior, and psychosocial status do not explain the disparity, but changes in fat mass seem to be the key.

"We know that African American women are generally more obese overall," Cynthia K. Buffington, Ph.D., said in an interview at a poster presentation during the annual meeting of the American Society for Bariatric Surgery.

Dr. Buffington and her associates compared morbidly obese African American and white women with no significant differences in preoperative body mass index, ideal body weight, or fat mass.

The study included 39 African American women with a mean BMI of 51 kg/m² and 114 white women with a mean BMI of 48.5.

Investigators also compared 39 of the African Americans to a subgroup of 39 whites matched for preoperative weight (a mean 143 kg). One year later, the African American women lost 62% of their excess weight to a mean of 94 kg,

whereas the white women lost 80% of excess weight to a mean of 78 kg.

In the full cohort, the investigators determined psychosocial status using the Minnesota Multiphasic Personality Inventory-2 and the Millon Behavioral Medicine Diagnostic instruments. African American women had fewer psychosocial issues

than did white women in the study, perhaps because obesity is more culturally accepted in the African American community, Dr. Buffington said.

"African American women are more self-confident and have fewer psychosocial issues related to their obesity," said Dr. Buffington, director of research at U.S. Bariatric in Fort Lauderdale, Fla.

Specifically, African American women demonstrated significantly less depression, emotional instability, introversion, inhibition, and feelings of isolation or rejection; fewer adjustment problems; and better social adjustment than did white women in the study.

Dr. Buffington and her associates assessed patient diet histories and scores on

eating-behavior questionnaires.

The researchers found no significant differences in macronutrient intake or eating behaviors such as binge eating, food cravings, or eating control to explain the reduced effectiveness of surgery in African Americans.

"Both groups were consuming large

amounts of calories, but there were no differences in carbohydrates or proteins," Dr. Buffington said. "Both were consuming high amounts of fat, but there were no differences between

groups."

African Americans had a 47% change in fat mass 1 year after surgery that was far less than the 63% change for whites, Dr. Buffington said. "This was strongly correlated to total weight loss."

"We think it means there is a biological basis for surgery not to induce as much fat loss in a morbidly obese population of African Americans versus [whites]," Dr. Buffington said. She said other investigators are finding reduced oxidation of fat in the muscle of African American females. ■



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