

Obesity Drugs' Benefits May Not Outweigh Risks

The impact on morbidity and mortality is unknown as trial attrition rates were high.

BY ROBERT FINN
San Francisco Bureau

Clinical testing on current weight-loss drugs has been inadequate to determine whether their benefits outweigh the risks of long-term use, according to a literature review by Canadian researchers.

The review, by Dr. Raj S. Padwal and Dr. Sumit R. Majumdar of the University of Alberta, Edmonton, took a close look at the two drugs currently approved by the Food and Drug Administration for the treatment of obesity—*orlistat* (Xenical) and *sibutramine* (Meridia)—and at another drug, *rimonabant* (Acomplia), that has not yet received FDA approval (Lancet 2007;369:71-7).

Although the three drugs all work by different mechanisms,

clinical trials show that they tend to result in about the same modest degree of weight loss: an average of 5 kg (11 lbs), or roughly 5% of body weight. They all have side effects, but in general the side effects have been judged to be tolerable.

None of the drugs has been subjected to long-term testing. It's unknown, for example, whether the weight loss induced by these drugs translates to decreases in obesity-related morbidity and mortality. Dr. Padwal and Dr. Majumdar describe this as "a major gap in knowledge."

It's also unknown whether use of the drugs results in improvements in some of the other consequences of obesity, such as osteoarthritis, gastroesophageal reflux disease, sleep apnea, and reduced quality of life.

Furthermore, the existing clin-

ical trials for *orlistat*, *sibutramine*, and *rimonabant* were all marred by high levels of attrition. In general, 40%-50% of all the patients enrolled in those trials dropped out before the trials were concluded. This makes it difficult to assess the drugs' true levels of efficacy and safety in the general population.

"We think that antiobesity drug trials powered to show clinically important reductions in major obesity-related morbidity and mortality should be required either before these drugs are approved for widespread use or as a condition of ongoing approval," the authors wrote.

They advanced three justifications for this conclusion. First,

drugs that improve secondary end points, such as weight loss, may not in the long run improve more clinically relevant end points, such as cardiovascular morbidity and mortality.

Second, a drug's toxicity may not be apparent on initial release. *Rimonabant*, for example, appears to decrease hunger by blocking endocannabinoid receptors in the brain. Preliminary data suggest that endocannabinoids may work to prevent stroke, limit the size of myocardial infarctions, and inhibit cancer-cell proliferation. Blocking endocannabinoid receptors on a long-term basis may therefore have unintended negative consequences.

Third, new drugs are expen-

sive, and the enormous potential market for obesity drugs amplifies their cost to society. The lack of proof that these drugs improve overall outcomes makes it difficult to justify those costs.

Bariatric surgery is the only treatment proven to produce consistent and effective long-term weight loss, but Dr. Padwal and Dr. Majumdar described bariatric surgery as "neither a feasible nor desirable population-based treatment for obesity."

They wrote that although it's important to address all aspects of the environment that encourage obesity, the search for novel drug treatments is both legitimate and necessary.

"However," they wrote, "in our efforts to fill the therapeutic void" that characterizes contemporary obesity management, "the benefits of obesity pharmacotherapy must outweigh the risks and costs." ■

New drugs are expensive, and the potential market for them amplifies their cost to society. The lack of data makes it difficult to justify those costs.

Providers' Time, Commitment Can Improve Diet Adherence

BY MARY ELLEN SCHNEIDER
New York Bureau

RENO, NEV. — Improving patient adherence to a diet program requires an investment of time that must include providing specific weight loss goals and asking patients about their progress at every visit, Lora E. Burke, Ph.D., said at the annual meeting of the American College of Nutrition.

Checking in with patients regularly by phone is also important in maintaining compliance, though the calls do not have to be made by the physician, said Dr. Burke, who offered evidence-based tips for getting patients to stick to dietary changes.

"There is no segment of the population that is immune to nonadherence," she said. When assessing adherence to a diet regimen, give patients permission not to be 100% compliant and acknowledge the challenges they face. It's often better to ask tactfully what a patient is doing to comply, and how, than to ask yes-or-no questions, she added.

It is critical to define weight loss goals for the patient. Patients going to a nutritionist will often say that their doctor advised them to lose weight or lower their cholesterol, but that they don't know how to begin. "Patients want very specific directions," said Dr. Burke of the University of Pittsburgh School of Nursing.

Setting a proximal goal is a good way to

motivate a patient. For example, advise substituting fresh fruit for high-salt snacks.

After the goal has been set, have the patient record it and the process for achieving it in a diary. When the patient returns for the next appointment, be sure to be positive about any progress, Dr. Burke advised at the meeting.

The patient may not be the person who does the shopping or cooking in the family. Physicians should therefore get family members on board.

Whatever goals are set, practitioners dealing with patient nutrition should also take into account cultural factors and family issues. Ask patients what they are willing to do and then negotiate, she said. "There's no point asking a patient to [give up] something that he or she has no intention of giving up."

The next step is to give patients the skills they need to make changes. Patients need to learn how to reduce fat, salt, and caloric intake by reading food labels and measuring serving sizes.

Some hospitals and cardiac rehabilitation programs offer instructions on how to cook low-fat meals, eliminate salt, and begin a physical activity program, Dr. Burke said.

Social support is critical to helping patients make dietary changes: The patient may not be the person who does the shopping or cooking in the family. Physicians should therefore get family members on board and give them a chance to hear the dietary advice first hand so that everyone understands the goals. "It's very difficult to ask patients to make these changes in isolation," Dr. Burke said. ■

Urinary Potassium Sheds Light on Quality of One's Diet

BY MARY ELLEN SCHNEIDER
New York Bureau

RENO, NEV. — Twenty-four-hour urinary potassium excretion is an effective clinical marker for diet quality and can be used to identify patients with poor diets, Dr. Alexander G. Logan said at the annual meeting of the American College of Nutrition.

Physicians can use 24-hour urinary potassium excretion levels of less than 60 mmol/day in men and less than 41 mmol/day in women as a cutoff point in identifying patients with poor-quality diets.

"This is a simple test that can be done in the office," said Dr. Logan, of Mount Sinai Hospital in Toronto.

Assessing diet quality can be a difficult process, he said, and usually involves the use of 24-hour diet recall, a food diary, or a food frequency questionnaire. But measuring 24-hour urinary potassium excretion provides an objective marker that can be used in diet counseling, he said.

Dr. Logan and his colleagues enrolled 220 patients from a regional kidney stone center in Ontario. The patients, aged 18-50 years old, had idiopathic nephrolithiasis and were on unrestricted diets. Staff at the kidney center collected information on weight, height, and blood pressure. In addition, the staff collected 24-hour urine samples and administered a structured patient interview and a food frequency questionnaire. The

166-item food frequency questionnaire was used to derive the patient's diet quality score.

Dr. Logan and his colleagues found that diet quality scores increased as urinary potassium values increased. Patients who had the lowest levels of urinary potassium had an average dietary quality score of 34, compared with a score of 76 among individuals with the highest urinary potassium levels.

Individuals who had high potassium levels were also more likely to report eating more recommended foods. In addition, individuals who had a high-potassium diet reported consuming less red meat, less processed meat, less fast food, and fewer high-energy drinks, Dr. Logan said.

The researchers also examined how intermediate health outcome variables—including body mass index, blood pressure, and heart rate—were associated with urinary potassium levels. They found an inverse relationship between urinary potassium and BMI. Individuals with lower urinary potassium also had a higher BMI.

Findings related to blood pressure were mixed. Systolic blood pressure was not a factor, but there was a statistically significant drop in diastolic blood pressure among individuals with high urinary potassium. High urinary potassium was also associated with lower heart rate in the study participants. ■