Modest Weight Loss Benefits Type 2 Diabetic Patients

BY ROBERT FINN
San Francisco Bureau

San Francisco — A relatively modest amount of weight loss can normalize fasting plasma glucose and greatly improve insulin sensitivity in people with type 2 diabetes, according to a study reported by Dr. Gerald I. Shulman at the Third World Congress on Insulin Resistance Syndrome.

Eight obese patients with type 2 diabetes achieved these significant improvements after losing an average of just 8 kg (17.6 pounds), equivalent to about 8% of their body weight, said Dr. Shulman, assistant professor of medicine at Yale University, New Haven, Conn. Dr. Kitt Falk Petersen of the University of Southern Denmark and Dr. Sanja K. Kim of the University of Alberta also contributed to the study.

The study involved patients who had an average BMI of 30 kg/m2. Their fasting insulin averaged 174 pmol/L. Their fasting glucose averaged 8.8 mmol/L; an average of 78 kg and had an average BMI of 27.5. Their fasting glucose averaged 6.4 mmol/L, and their fasting insulin averaged 66 pmol/L.

In addition, the patients achieved a marked improvement in glucose response as measured by a fourfold increase in the glucose infusion rate required to maintain euglycemia during a hyperinsulinemic-euglycemic clamp. By measuring hepatic glucose metabolism with deuterium oxide infusion rate with insulin sensitivity, but had no effects on peripheral insulin sensitivity.

The study diet was a liquid diet formula with 50% carbohydrate, 41% protein, 3% fat, and 12 g of dietary fiber, which was supplemented with raw fruit and vegetables to about 1,200 kcal/day. The patients continued this diet until they achieved euglycemia, which took between 3 and 12 weeks. They were stabilized on an isocaloric diet for 4 weeks before the final metabolic measurements were taken.

Following the diet, the patients weighed an average of 78 kg and had an average BMI of 27.5. Their fasting glucose averaged 6.4 mmol/L, and their fasting insulin averaged 66 pmol/L. All these values represented statistically significant decreases from baseline.

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Rosiglitazone Reduces CRP And Carotid Atherosclerosis

BY MITCHEL L. ZOLER
Philadelphia Bureau

DALLAS — Treatment with rosiglitazone was linked with markedly reduced serum levels of C-reactive protein and regression of carotid atherosclerosis in a study with about 70 patients with type 2 diabetes. In contrast, treatment with metformin was unable to produce either of these effects.

These findings “point to potential superior efficacy of thiazolidinediones over metformin for cardiovascular outcomes, but direct studies are needed,” Dr. Allen J. Taylor said at the annual scientific sessions of the American Heart Association.

“The data are consistent with the biologically plausible hypothesis of a direct antithrombotic effect of rosiglitazone,” said Dr. Taylor, chief of cardiology services and professor of medicine at Walter Reed Army Medical Center in Washington.

The study, done at Walter Reed, had no commercial sponsorship.

The researchers enrolled patients with type 2 diabetes and a hemoglobin A1c level of more than 7% despite treatment with diet or a sulfonylurea drug.

Patients were randomized to treatment on an open-label basis to either 4 mg of rosiglitazone (Avandia) daily or 850 mg of metformin (Glucophage) twice daily. The randomization was stratified to assign patients with similar levels of statin use to both treatment groups.

The primary end point was the change in serum levels of C-reactive protein (CRP) after 24 weeks of treatment. In the rosiglitzone group, serum CRP fell by about half after the first 2 weeks of treatment, from an average of 6 mg/L at baseline to a mean of 3 mg/L. The CRP level continued to gradually drop during the study, and after 24 weeks, was at an average of 2 mg/L in 37 evaluable patients.

Every time CRP levels were measured, after 2, 4, 16, and 24 weeks of treatment, the reductions were significantly different, compared with baseline.

In contrast, metformin produced no significant drop in CRP at any of the measured times in 18 evaluable patients.

The secondary end point was a change in the ultrasonic measurement of carotid intimal medial thickness after 24 weeks of treatment, compared with baseline levels.

In the rosiglitzone group, the mean carotid intimal medial thickness decreased by an average of 0.069 mm in 35 evaluable patients, an indicator of reduced atherosclerotic progression.

An exploratory analysis indicated a modest statisticall significant difference between the rosiglitzone and metformin groups, which was statistically significant.

An exploratory analysis indicated a modest statisticall significant difference between the change in serum CRP and the change in carotid intimal medial thickness, Dr. Taylor said.

Neither drug had an effect on serum levels of low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, or triglycerides.

Surrogate Tests of Insulin Resistance Deemed More Practical

BY ROBERT FINN
San Francisco Bureau

San Francisco — Surrogate measures of insulin resistance, while not nearly as reliable, may be far more practical for routine clinical use than the hyperinsulinemic-euglycemic clamp and the insulin suppression test, which can take 3 hours or more.

At the Third World Congress on Insulin Resistance Syndrome, Dr. Sun H. Kim, of Stanford (Calif.) University, discussed available surrogate tests. Other speakers at the congress discussed two new instrumental measures likely to become available soon.

One problem with using any measure of insulin resistance is its continuous distribution in the general population. There is no absolute criterion by which to classify individuals as insulin resistant or sensitive. Dr. Kim follows the general practice of defining individuals who fall in the upper tertile of insulin resistance as insulin resistant or insulin sensitive. Dr. Kim makes use of fasting insulin and fasting glucose levels.

The two new instrumental measures, however, promise to become available soon.

The second instrumental measure is a 13C-glucose breath test called the Dittig. A fasting patient consumes nonradioactive 13C-glucose, after which 13CO2 in the patient’s expired breath is measured for 90 minutes by either an isotope ratio mass spectrometer, a large instrument that costs about $250,000. But Dr. Marc Hellerstein of the University of California, Berkeley, hopes to be able to employ a smaller, less expensive laser spectrometer that would have the additional advantage of a high throughput.

The second instrumental measure is a 1C-glucose breath test called the Dittig. A fasting patient consumes nonradioactive 1C-glucose, after which 1C02 in the patient’s expired breath is measured for 90 minutes by either an isotope ratio mass spectrometer or by nondispersive infrared spectroscopy to detect HCO3.

According to Dr. Richard Z. Lewanczuk of the University of Alberta, Edmonton, human studies have demonstrated that the breath test has a sensitivity of 78% and a specificity of 96%, compared with standard measures. The Food and Drug Administration has approved the breath test for use in clinical trials in the United States. Dr. Lewanczuk disclosed that he is a major stockholder and a consultant and adviser for KineMed, which hopes to market the 1C-glucose breath test. Dr. Kim stated that she has no potential conflicts of interest.