Oral Agents for Gestational Diabetes Show Promise

Acarbose or metformin could turn out to be helpful additions to the therapeutic armamentarium.

BY SHERRY BOSCHERT
San Francisco Bureau

SAN FRANCISCO — Two oral medications deserve further investigation as alternative therapies for gestational diabetes, results of separate small studies suggest.

Acarbose or metformin might be helpful additions to the therapeutic armamentarium if additional research supports these preliminary findings, investigators said in separate poster presentations at the annual meeting of the Society for Maternal-Fetal Medicine.

Neither drug is approved for the treatment of gestational diabetes. Both are Food and Drug Administration pregnancy category B. Injected insulin or oral glyburide are approved to treat gestational diabetes.

Having an oral option other than glyburide might allow patients to be managed on one or potentially two oral agents before resorting to injections of insulin, Dr. Jacquelyn Cortez said in an interview at one of the posters.

She and her associates conducted a prospective, double-blind trial that randomized 59 women who were diagnosed with gestational diabetes in their second or third trimester, prior to 34 weeks' gestation, to 50 mg acarbose t.i.d. or identical placebo pills taken with meals. All patients had failed diet therapy.

At regular follow-ups, if more than half of the patient's fasting glucose values were above 95 mg/dL, or more than half of her postprandial glucose values were above 135 mg/dL, the dosage was increased to 100 mg t.i.d. If this did not control blood glucose levels, the patient was considered to have failed single-agent therapy and was started on a second agent.

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Fewer patients in the acarbose group failed monotherapy and required a second agent, compared with the placebo group, but the difference did not quite reach statistical significance in this small study. Women in the acarbose group gained significantly less weight (19 pounds) than did women on placebo (27 pounds), said Dr. Cortez of the department of reproductive medicine at the University of California, San Diego.

Postprandial blood glucose levels were significantly lower on acarbose therapy (122 mg/dL), compared with placebo (130 mg/dL).

There were no differences between groups in perinatal outcomes, including gestational age at delivery, mode of delivery, or rate of macrosomia.

The failure rate with acarbose in this study and failure rates with glyburide in other studies both are high, but women on acarbose in the present study did not develop the hypoglycemia sometimes seen with glyburide, Dr. Cortez noted.

Acarbose is a glycosidase inhibitor that prevents intestinal breakdown of starches to glucose in the upper small bowel.

Metformin, an insulin sensitizer, was the subject of a separate review of data from two randomized trials in which 67 women with gestational diabetes took the drug. Of these patients, 59 met glycemic goals of fasting glucose values lower than 105 mg/dL and 2-hour postprandial glucose values lower than 120 mg/dL, reported Dr. Lisa E. Moore and her associates.

The eight women who did not meet glycemic goals started insulin therapy, said Dr. Moore of the University of New Mexico, Albuquerque.

Macrosomia occurred in four infants (6%), and all were delivered vaginally. The primary cesarean delivery rate (excluding elective repeat C-sections) was 15% (10 patients). There were no cases of fetal anomalies or maternal or fetal hypoglycemia. Eight neonates had hyperbilirubinemia, and two had 5-minute Apgar scores lower than 5.

The efficacy rate with metformin appeared to be similar to success rates with glyburide in other studies, Dr. Moore said. "[Metformin] is certainly better at controlling the fasting blood sugar than glyburide," she added.

Failure of metformin was not predicted by maternal body mass index or by the value of the 1-hour glucose challenge test.

Although metformin is not approved in the United States for this indication, there is a wealth of data from other countries on its use in gestational diabetes, she noted.

Neither Dr. Cortez nor Dr. Moore reported any financial relationships with the companies that make the medications studied. ■

Diabetic Foot Infection Classification System Found Valid in 2-Year Study

BY MARY ANN MOON
Contributing Writer

A system for classifying diabetic foot infection proved effective at predicting adverse clinical outcomes in a 2-year cohort study, reported Lawrence A. Lavery, D.P.M., of Scott & White Hospital, Round Rock, Tex., and his associates.

In 2004, the Infectious Diseases Society of America (IDSA) and the International Working Group on the Diabetic Foot (IWGDF) each published guidelines for managing diabetic foot infections. Both sets of guidelines included "essentially identical" systems for classifying the severity of infection. In contrast, previous guidelines "either did not specifically define infection or, if they did, only noted its presence or absence," the researchers said (Clin. Infect. Dis. 2007 Jan. 17 [Epub DOI:10.1086/511036]).

The new classification systems were applied to data that had already been collected on 1,666 subjects enrolled in a foot-care management program.

Both of the 2004 classification systems first categorize foot wounds as infected or not, based on the presence or absence of purulent secretions or local or systemic signs of inflammation or infection. They further categorize the infections as mild, moderate, or severe based on wound depth and size (especially the extent of cellulitis) and on the presence or absence of systemic manifestations of infection, such as fever, chills, leukocytosis, or metabolic aberrations.

The new classification systems were developed by "an international consensus of experts in various fields," but until now no study has validated their ability to predict outcomes. Dr. Lavery and his associates did so by applying the classification systems to data that had already been collected on 1,666 subjects enrolled in a foot-care management program and followed for a mean of 27 months.

A total of 247 patients (14.8%) developed a foot wound and 151 (9.1%) developed a foot infection. Of the foot infections, 27 were classified as severe, and 50 patients required an amputation of some type. "Considering that these patients were screened for foot disorders at enrollment in the study, were educated about proper foot care, and had ready access to a foot clinic, we observed a higher incidence of foot infection than expected," the investigators noted (Clin. Infect. Dis. 2007;44:562-5).

With increasing infection severity on the IDSA-IWGDF classification system, there were increasing risks of hospitalization, osteomyelitis, amputation, and other complications such as peripheral neuropathy and vascular disease.

"We believe the results of this study are the first to validate these new guidelines," Dr. Lavery and his associates said.

They added that a reliable infection classification system, "designed to be simple to apply and easy to remember," should help clinicians decide whether a patient should be hospitalized, whether to use parenteral or oral antibiotics, and how urgently surgery or other treatments should be performed. ■

Insulin Plus Rosiglitazone Appears Helpful in Type 2

Adding rosiglitazone therapy to an insulin regimen appeared to be safe and to improve glycemic control in patients with type 2 diabetes in a study funded by the drug's manufacturer.

Rosiglitazone is one of the thiazolidinediones, "the newer insulin sensitizers" that improve β-cell function and prolong β-cell survival.

That result, in turn, enhances insulin sensitivity and improves glucose utilization, according to Dr. Ranjna Garg and associates at the Blackburn (England) Royal Infirmary's diabetes unit.

The first thiazolidinedione used in type 2 diabetes was troglitazone, a drug that was withdrawn from the market because of idiosyncratic reactions and sometimes fatal hepatic damage. Rosiglitazone has a different biochemical and metabolic profile and a lower incidence of hepatotoxicity, they said.

Dr. Garg and associates assessed its safety and efficacy in a 1-year open-label study of 53 patients who had inadequate glycemic control with insulin alone. The study was funded by GlaxoSmithKline.

Daily rosiglitazone reduced mean hemoglobin A_{1c} by a statistically significant 1.53%, from an average of 9.82% to an average of 8.29%.

"Tight glycemic control with reduction in HbA_{1c} by 1% is associated with reduction in diabetes-related end points by 21%, including death," the investigators said (J. Diabetes Complications 2007;21:1-6).

The authors also noted, however, that the drug failed to reduce HbA_{1c} to target levels recommended by the American Diabetes Association.

Mean reduction in total insulin dose was 13.5%, which was not statistically significant. Twenty-eight patients were able to reduce their insulin dosage, and the remaining 25 were not.

Mean blood pressure improved significantly when rosiglitazone was added to insulin therapy.

There was no clinical hepatotoxicity during 12-month follow-up. Four patients discontinued the drug because of weight gain and another four because they perceived no benefit from therapy. Rosiglitazone was withdrawn in one additional patient because of fluid retention.

In addition to funding this study, GlaxoSmithKline has funded the diabetes unit at Blackburn Royal Infirmary and provided a travel grant to Dr. Garg. Dr. Garg's associate in this study, Dr. Geraint Rhys Jones, has been on the company's advisory board.

—Mary Ann Moon